Ann Ist Super Sanità 2020 | Vol. 56, No. 2: 157-167
DOI: 10.4415/ANN_20_02_05

Study on the health status of the population living in Marghera (Venice, Italy) through the use of a longitudinal surveillance system

Francesca Gessoni, Silvia Macciò, Claudio Barbiellini Amidei and Lorenzo Simonato

Dipartimento di Scienze Cardio-Toraco-Vascolari e Sanità Pubblica, Università degli Studi di Padova, Padua, Italy

Abstract

The aim of this study is to carry out an investigation to evaluate the industrial area of Porto Marghera (the only Site of National Interest – SNI – for clearance operations in the Veneto region) by means of data from the Venetian Epidemiological Surveillance System (SEIVE – Sistema Epidemiologico Integrato di Venezia). In particular, the aim is to assess the extent at which chronic exposure to industrial pollutants contributes to the genesis of non-communicable diseases such as tumors. We have employed healthcare administrative databases to analyze health conditions of the population residing in the area of Marghera, separately from the rest of the mainland. The results obtained highlight a series of critical problems concerning the population residing in Marghera. These issues, such as an excess in the overall cancer mortality rate, have been observed in both genders, as well as in the lung cancer incidence and mortality rate. In addition, we detected an increase in mortality for respiratory diseases only in the male population.

Key words

- contaminated site of national interest
- healthcare administrative databases
- longitudinal study
- Marghera, Italy

INTRODUCTION

The development of Marghera

Marghera, together with the neighborhoods of Catene and Malcontenta, represents one of the mainland municipalities of the city of Venice. Its structure consists of a residential neighborhood and an industrial waterfront area, known as Porto Marghera.

According to the popular tradition, the name "Marghera" came from an expression in the local dialect "Mar ghe jera", which can be translated as "There was sea/The sea was there" to recall the swampy territory that had hosted the port for many years.

The genesis of Marghera as well as its industrial area are relatively recent. At the beginning of 1900, the harbor of Venice was among the most important ones in Italy. However, it needed new spaces to grow as well as newer and modern infrastructures [1].

At that time, most areas of the Venetian mainland were being affected by the development of road and rail infrastructures, with large areas that had yet to be used. It was the engineer Giuseppe Volpi, Earl of Misurata, who identified this area as the most adequate for the establishment of the new port and to develop an industrial pole. In 1917 the project was assigned to Enrico Coen Cagli, and it was submitted to the Ministry of Public Works of that time. The project was approved in only 75 days. In 1918 the industrial center was born, also thanks to financial aids for reconstruction from the Veneto region [2].

At the same time, however, the historic center of Venice was facing overcrowding issues: most of the dwellers, in fact, were living in poor conditions in terms of health and housing.

For this reason, the engineer Pietro Emilio Emmer designed the residential area of Marghera following the criteria for a "Garden City".

The original project for the area included schools, offices, libraries, churches, leisure areas and more.

In the plan there were also supposed to be 80 meters wide tree-lined avenues, private citizens' houses, which could not be higher than three stories, all with a private garden [3-5].

Unfortunately, the project was abandoned due to the cuts on the funds. However, it is still possible to spot some of these traces in the oldest and most central part of the city of Marghera.

The geography of the area that now hosts Porto Marghera (Port of Marghera) can be divided into three

Address for correspondence: Francesca Gessoni, Dipartimento di Scienze Cardio-Toraco-Vascolari e Sanità Pubblica, Università degli Studi di Padova, Via Giustiniani 2, 35128 Padua, Italy. E-mail: francesca.gessoni@studenti.unipd.it

macro-areas that were developed at different times and hosted various types of industries:

- first industrial area: located in the Northern part of the city, where the industrial plants were initially established. It is the most critical area as it is the closest to Marghera's residential center. Hence, it was the first among the macro-areas that underwent clearance operations;
- commercial port and shipbuilding industries area;
- second industrial area: characterized by the presence of industrial plants associated to the chemical and petrochemical businesses.

The subdivision in macro-areas is particularly important because the lands in each area share a similar genesis. Some of the areas consisted of pre-existing land, whilst some others were reclaimed through the use of backfilling material. For instance, the second industrial area was built over lands built with the materials excavated from canals as well as wastes of the first industrial area.

A further project was proposed, to realize a third industrial area, which was abandoned as a result of the crisis in the 70's that involved all Porto Marghera.

Porto Marghera, therefore, was planned as an industrial area, located on the coast and faced an unprecedented development. By 1925 there were 33 operating companies with 3440 employees in the area.

In the 30's, metallurgical industries as well industries of non-ferrous materials were installed and developed in Porto Marghera. In addition to the former, other industries dedicated to the production of nitrogen fertilizers, food, contact lenses, and perfume. In this situation, also transport companies began operating and expanded across the area. Industries for energy production services also started developing. In 1935 Porto Marghera had the largest thermal power station in Italy.

During the Second World War, bombing of the area caused a sudden stop of the productive activities in Porto Marghera. With the end of the conflict, the facilities were re-built, and the industrial area started expanding again.

At the beginning of the 1950s, Porto Marghera was growing and employed about 2200-2500 people. In these years, the second industrial area underwent an enormous expansion, with the installation of petrochemical industries. In 1965, during the period of maximum productive activity, 3300 people were employed in Porto Marghera [6].

In the 70's the area suffered from an important crisis. Multiple causes contributed to this crisis: the rise in oil prices, the increased sensitivity to environmental issues and the global crisis of chemical industries. As a result, many plants and industries stopped.

Despite having been scaled down in its productivity, Porto Marghera still remains an important area for the economy of the whole Veneto region [7].

Porto Marghera – Site of National Interest

The industrial area of Porto Marghera is the only area in the region of Veneto that was inscribed in the sites of national interest (SNI) registry, for clearance operations. SNIs are vast contaminated areas that have been listed as dangerous for human and environmental health, according to specific Italian laws. These areas require clearance operations.

The extension of the area was defined by the 23/02/2000 Decree of the Ministry for the Environment (*Decreto del Ministro dell'Ambiente* – DMA) within the Venice-Porto Marghera SNI, which extends for about 5730 hectares. In addition to exclusively industrial areas, the SNI also includes areas that border with the lagoon. The administrative order underlines the presence in such area of chemical, petrochemical, metallurgical, electrometallurgical plants, refineries, as well as areas designated for energy production, docks and areas used as waste disposal [8-10].

The pollutants found in the SNI area of Porto Marghera have different origins and are not solely due to the industrial activity, but also to the bordering agricultural and farming activities. The Resites study, published in 2016, among the many observations, reports the analysis on the environmental contamination in the area of Marghera. In particular, the data collection following the soil survey has highlighted the presence of several groups of pollutants such as aliphatic carcinogens, chlorinated substances, hydrocarbons and dioxins. The highest concentration of these substances is found within the soil of the macro-areas that once were hosting refineries and petrochemical plants [11-17].

When focusing on the main air pollutants produced by the industries of Porto Marghera, we can list nitrogen oxides, sulphur dioxides, volatile organic compounds, chlorine and inorganic compounds of chlorine, vinyl chloride monomer, acrylonitrile and ammonia.

In the last decades, emissions of these substances have decreased. This is due to both a greater attention to environmental protection and a progressive decommissioning of many production plants.

The SENTIERI Project (National Epidemiological Study of Territories and Settlements Exposed to Pollution Risk) of the Italian National Institute of Health (*Istituto Superiore di Sanità*, *ISS*) carried out in collaboration with the Ministry of Health, aims at analyzing and monitoring the health conditions of populations that live close to major active and disused industrial areas, or close to contaminated areas that have been defined as SNIs.

Results of the findings of the SENTIERI Project were published in two reports in 2011 and 2014. Both publications contain a section on the SNI Porto Marghera [17, 18].

The study published in 2011 highlights an excess in the cancer incidence rate, both in men and women. Moreover, among the causes of death that are already known to be associated to an environmental exposure, from numerous studies, this work has underlined an excess in lung and pleura cancer mortality rate, in both genders. The same report also underlines a higher incidence of pleural mesothelioma in the male population residing in the city of Venice, which is most likely due to professional exposure to asbestos, as confirmed by the 2014 report. The limit of these two reports is the analysis of health effects on all residents of the city of Ven-

ice. Due to a high socioeconomic heterogeneity in the population that lives in the city of Venice, in a city-wide population-based study it is not possible to observe the impact on specific subjects at greater risk, such as industrial workers and residents in the area of Marghera. For this reason, previous works have analyzed the city of Venice, dividing it into smaller areas. These were historical divisions, especially in the insular part (the six *sestieri* or neighborhoods and the smaller islands of the lagoon) and in the mainland, the various neighborhoods, characterized by a more recent history and with a more homogeneous socioeconomic background, but with different environmental exposures.

MATERIALS AND METHODS

In order to carry out these analyses, data from the Venetian Epidemiological Surveillance System (*Sistema Epidemiologico Integrato di Venezia* – SEIVE) was employed. This system has been active in the area of Venice since the late 90s with the aim to monitor the state of health of the Venetian population and to assess its trends [19-30].

The building of this surveillance system can be divided in 4 different phases:

1. assessment phase: assessing the availability of both current and past population healthcare registers, which was the founding element of our system, as well as the availability of current sources such as death certificates, hospital discharge records comprising passive mobility, healthcare co-payment exemption and drug prescription records database;
2. testing phase: evaluating the completeness and the quality of the registers through standard logic controls;
3. record linkage phase: linking healthcare administrative databases by cross-referencing the data from the healthcare population register, by using a standard semi-deterministic approach. This allows to link all healthcare services provided or reimbursed by the National Health Service to the study population, in order to obtain a historical reconstruction of each patient's health profile;
4. analysis phase: analyzing the data collected, by applying disease-specific algorithms. This allowed us to identify and quantify the main diseases that affect the population and to calculate their incidence and prevalence.

The SEIVE (currently updated to 31/12/2014) examines the population that was assisted in the former Venetian Local Healthcare Unit (*Unità Locale Socio Sanitaria* – ULSS 12) and that was residing in one of the four municipalities that composed said unit from 2000 to 2014 (Venice, Marcon, Quarto d'Altino and Cavallino Treporti) [21] Furthermore, the former territories of the ULSS 12 were divided into two areas (insular and mainland) and then into 20 smaller territorial units (composed of the 3 smaller municipalities of Marcon, Quarto d'Altino and Cavallino Treporti, and 17 areas of the metropolitan city of Venice). The territories were divided in the following manner:

- the municipality of Cavallino Treporti is located in the insular area;
- the municipality of Marcon is located in the mainland area;
- the municipality of Quarto d'Altino is located in the mainland area;
- the municipality of Venice is separated into an insular part, which includes 11 units among which the *sestieri* (neighborhoods) and other islands of the lagoon and a mainland area, made of 6 neighborhoods.

This study is based on the data collected from the Municipality of Venice (mainland) and analyzes separately the areas of: Favaro-Campalto, Carpenedo-Bissuola, Mestre (city center), Cipressina-Zelarino-Trivignano, Chirignago-Gazzera, Marghera-Catene-Malcontenta. Based on their residence every subject of the cohort was assigned to one of the 20 possible territorial units in order to compare differences in the health conditions of the residents between these areas.

For these analyses, in addition to the aforementioned population registers, we have used the following healthcare administrative databases:

- death certificates;
- hospital discharge records database, drug prescription database;
- healthcare co-payment exemptions;
- cancer registry of the Veneto region.

Death certificates hold diagnoses on the cause of death, coded according to the International Classification of Diseases, ninth revision, Clinical Modification (ICD-9-CM). Hospital discharge records contain up to 6 diagnostic codes for each hospitalization, coded according to the ICD-9-CM and comprise of passive mobility. Drug prescription record databases hold data on all drugs reimbursed by the National Health Service, coded according to the anatomical therapeutic chemical (ATC) classification system that provides a univocal code to identify specific active ingredients. Healthcare co-payment exemptions contain disease-specific healthcare co-payment support, registered according to a national coding system. The cancer registry holds data on the date of incidence and the type of cancer (coded according to the ICD-9-CM) for all subjects affected by cancer in the region. Information held in these databases are commonly used by algorithms to identify subjects affected by specific diseases, in population-based studies [22]. All these archives have been updated to the year 2014, apart from the cancer registry of Veneto region which is updated only to 2010. All these databases were cross-referenced with the data from the population assisted and residing in the area of the former ULSS 12 from 2000 to 2014, by means of a procedure of record linkage. The latter is employed in order to determine whether two records belonging to different data sets refer to the same person. For this paper, we have employed a semi-deterministic record linkage procedure (stepwise). In each step, the exact correspondence between the records is assessed based on a sub-group of identifier fields. This procedure has been described in detail, in a previous paper [23].

Hence, in the SEIVE each subject of the cohort under examination is linked to the records of all health-related services funded by the National Health Service.

Mortality trends

Based on death certificates we have analyzed mortality rates in all areas of interest for all-cause mortality (all ICD-9-CM codes excluding all external causes of death = E*). Specific rates for the main causes of death were also estimated for malignant tumors (ICD-9-CM = 140-208) and diseases of the circulatory (ICD-9-CM = 390-459) and respiratory system (ICD-9-CM = 460-519), as well as for more specific causes: lung cancer (ICD-9-CM = 162), pleural mesothelioma (ICD-9-CM = 163) and ischemic heart disease (ICD-9-CM = 410-414). Incidence rate for colorectal cancer (ICD-9-CM = 153-154) and breast cancer (ICD-9-CM = 174-175) have also been estimated. General and disease-specific mortality analyses were based on death certificates. Incidence rates of malignant tumors were estimated by means of the data held in the cancer registry of the Veneto region.

Prevalence estimates

Prevalence estimates were calculated for some of the main health conditions, identified by applying disease-specific algorithms, as defined in the supplement of the journal *Epidemiologia & Prevenzione* [24]. By employing the algorithms offered by the National workgroup AIE/SISMEC (Italian Epidemiological Association/Italian Society for Medical Statistics and Clinical Epidemiology), we have estimated the prevalence of:

- asthma [25];
- diabetes [26];
- chronic obstructive pulmonary disease (COPD) [27].

The prevalence of each of these diseases was calculated on a yearly basis, from 2000 to 2014. The analyses of COPD only covered the period from 2006 to 2014, since information on the number of drug prescriptions was not present for the years 2000 to 2005.

Asthma case-identification algorithm

The prevalence of asthma was calculated on a population aged 0-34 years. Prevalent cases were identified by employing the following sources: hospital discharge records, death certificates, drug prescription database and healthcare co-payment exemptions. In particular, for each of the years under examination, we have selected patients deceased by asthma as first cause of death in death certificates (ICD-9-CM = 493*), and we have selected all hospital discharge records that displayed asthma as main or secondary diagnosis (ICD-9-CM = 493*). Healthcare co-payment exemptions for asthma (code = 007.493) were also selected, as well as prescriptions for anti-asthmatic medications according to specific conditions, such as the presence of "at least one prescription per year of interest" of any of the following drugs:

- adrenergic drugs – inhalers (ATC = R03A*);
- adrenergic drugs for systemic use (ATC = R03CC02, R03CC04, R03CK*);
- leukotriene receptor antagonists (ATC = R03DC01, R03DC03).

In order to be considered a prevalent case, the subject had to be recorded in at least one of the four health registers in the year of interest and for drug prescription record database, satisfy the algorithm's requirements.

Chronic obstructive pulmonary disease (COPD) case-identification algorithm

COPD prevalence was calculated exclusively on subjects aged over 35. The sources employed are the following: hospital discharge records, death certificates and drug prescription database. For each year under review, we have selected all hospitalized subjects (ICD-9-CM = 490*-492*, 494*, 496*) as well as those hospitalized at least once in the previous four years, who were still alive on January 1st of the year of interest. We have also selected cases with COPD as main cause of death. Drug prescriptions were also considered, taking account the following criteria:

- prescriptions of at least 5 packages of drugs for obstructive airway diseases (ATC = R03*) during the year of interest and with no more than 120 days distance between the prescriptions;
- prescriptions of 3 to 10 packages of drugs for obstructive airway diseases (ATC = R03*) during the year of interest with a distance between prescription dates of 2 to 3 months;
- prescriptions of a total of 3 to 4 packages of drugs for obstructive airway diseases (ATC = R03*) during the year of interest, with a distance between the prescription dates of 4 to 6 months.

Prevalent cases of COPD were defined as subjects that satisfied the algorithm's requirements in any registry used by the algorithm.

Diabetes case-identification algorithm

In order to identify diabetes cases, hospital discharge records, drug prescription database and healthcare co-payment exemptions were used. From the archives, we have selected all hospitalizations in the year under review as well as those dating back to the previous four years, with a main or secondary diagnosis of diabetes (ICD-9-CM = 250*). Among the prescriptions for anti-diabetic drugs during the year under review, we have selected those patients that had at least two prescriptions of drugs used in diabetes. This choice aimed at reducing false positive results and transcription errors. Lastly, from healthcare co-payment exemptions, we have selected subjects that had an exemption code for diabetes (code = 013.250) that was released during the year under review or during the previous three years. Prevalent cases were identified as subjects that had appeared in at least one of the archives used and that resulted to be alive and still residing in the area by January 1st of the analyzed year.

Data analyses

Data concerning residents of all areas belonging to Venice's mainland from the population health registry were linked to death certificates to estimate mortality rates and were linked to all other available healthcare administrative databases to estimate prevalence and incidence of specific diseases through case-identification algorithms.

Exposure was defined by the area of residence dur-

ing the study period. Subjects that changed residence during this period, from one area to the other, were excluded from the analyses. Residence changes within the same area did not lead to exclude the subject from the analyses. All results were standardized by age (reference population: Veneto region as of the census of 2011) and the respective 95% confidence intervals (95% CI) were calculated. Point estimates of specific areas, stratified by gender and for the entire population, were then compared to a reference value calculated as the average estimate of all areas, for that stratum. Separately we compared trend differences relative to each area included in the analyses and its 95% CI. Linear regression was performed on estimates concerning prevalence algorithms. All statistical analyses were conducted with SAS software (version 9.2, SAS Institute, Cary, NC, USA).

RESULTS

All-cause and cancer mortality rates

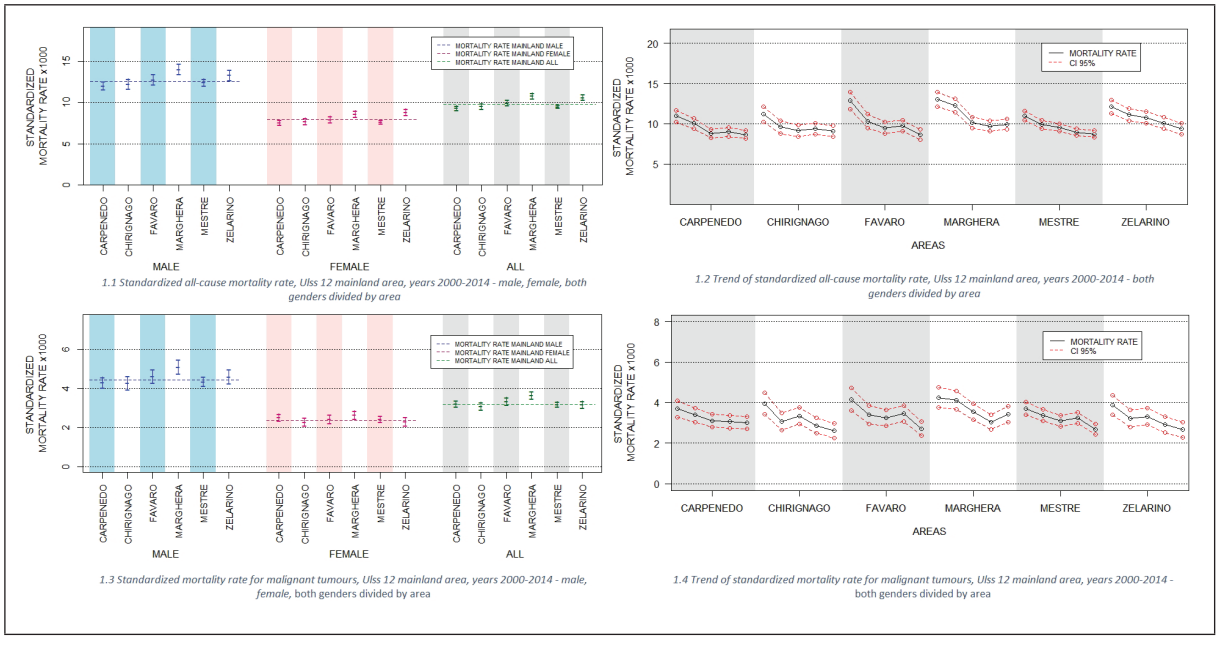
Standardized mortality rates for all causes of the population that resides in Marghera and that of the population residing in the other areas of the mainland of the city of Venice, compared to the average mortality in the mainland, stratified by gender and for men and women combined is shown in *Figure 1.1*. As shown in *Figure 1.1*, only the areas of Zelarino and Marghera present an excess in the mortality rate compared to the average mortality rate of the mainland, both in men and women. The mortality rate trend in the 15 years of follow-up is shown in *Figure 1.2*. The trend shows a decrease in the all-cause mortality rate for men and women, in all areas, throughout the entire period. The decrease is more marked in the areas where the mortality was higher at the beginning of the study period. Overall, there is a homogenization of mortality rates across all areas, that reach comparable values at the end of the study period.

Figure 1.3 shows the mortality rate for malignant tumors and a marked excess can be observed in the male population residing in Marghera, while among the female population, the excess is less pronounced. Moreover, Marghera is the only area that shows a mortality rate that differs significantly from the rest of the mainland. While analyzing the mortality trend for malignant tumors, once again, there is an overall downward trend, despite in each area the rate decreases at a different pace *(Figure 1.4)*.

Mortality and incidence rates of specific types of cancer

Figure 2.1 shows the mortality rate for lung cancer. We note a significant excess of lung cancer mortality in the male population of Marghera, compared to the other areas and compared to mainland area of the Venetian ULSS. The female population as well has an excess mortality compared to the average rate of the mainland, although it remains lower than the one observed in the male population. The trend in the mortality rate for lung cancer, in the male population is shown in *Figure 2.2*. Despite very heterogeneous rates at the beginning of the study period, there is an overall downward trend, also in the area of Marghera. Nevertheless, the rate at the end of the study period remains the highest compared to the other areas.

Figure 2.3 shows the mortality rates for pleural mesothelioma. We have only calculated the mortality rate for the entire study period because of a scarce number of



1.1 Standardized all-cause mortality rate, Ulss 12 mainland area, years 2000-2014 - male, female, both genders divided by area

1.2 Trend of standardized all-cause mortality rate, Ulss 12 mainland area, years 2000-2014 - both genders divided by area

1.3 Standardized mortality rate for malignant tumours, Ulss 12 mainland area, years 2000-2014 - male, female, both genders divided by area

1.4 Trend of standardized mortality rate for malignant tumours, Ulss 12 mainland area, years 2000-2014 - both genders divided by area

Figure 1
SEIVE analysis - Porto Marghera. 1.1 Standardized all-cause mortality rate, Ulss12 mainland area, years 2000-2014 - male, female, both genders divided by area. 1.2 Trend of standardized all-cause mortality rate, Ulss12 mainland area, years 2000-2014 -both genders divided by area. 1.3 Standardized malignant tumours mortality rate, Ulss12 mainland area, years 2000-2014, - male, female, both genders divided by area. 1.4 Trend of standardized malignant tumours mortality rate, Ulss12 mainland area, years 2000-2014 - both genders divided by area.

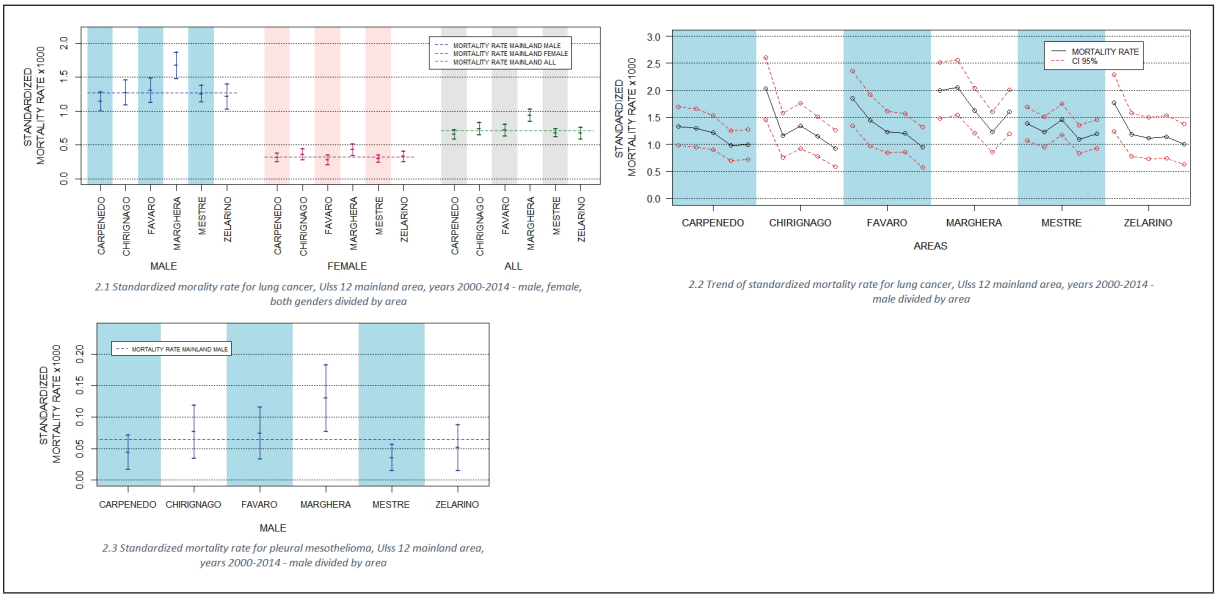


Figure 2
SEIVE analysis - Porto Marghera. 2.1 Standardized lung cancer mortality rate, Ulss12 mainland area, years 2000-2014 - male, female, both genders divided by area. 2.2 Trend of standardized lung cancer mortality rate, Ulss12 mainland area, years 2000-2014 - male divided by area. 2.3 Standardized pleural mesothelioma mortality rate, Ulss12 mainland area, years 2000-2014 - male divided by area.

cases affected by this disease. The figure highlights an excess in the mortality rate among the male population residing in Marghera, compared to the rest of the population living in mainland areas, despite the confidence intervals are quite large.

Figures 3.1 and 3.2 show the incidence for colorectal and anal cancer for the entire study period and the 2000-2010 trend. No differences in the incidence have been observed, among the various areas in the mainland.

Figure 3.3 and 3.4 represent the incidence of breast cancer (female population) for the entire study period and the 2000-2010 trend. Incidence rates are similar in the entire period and the trend is stable and homogenous across the areas.

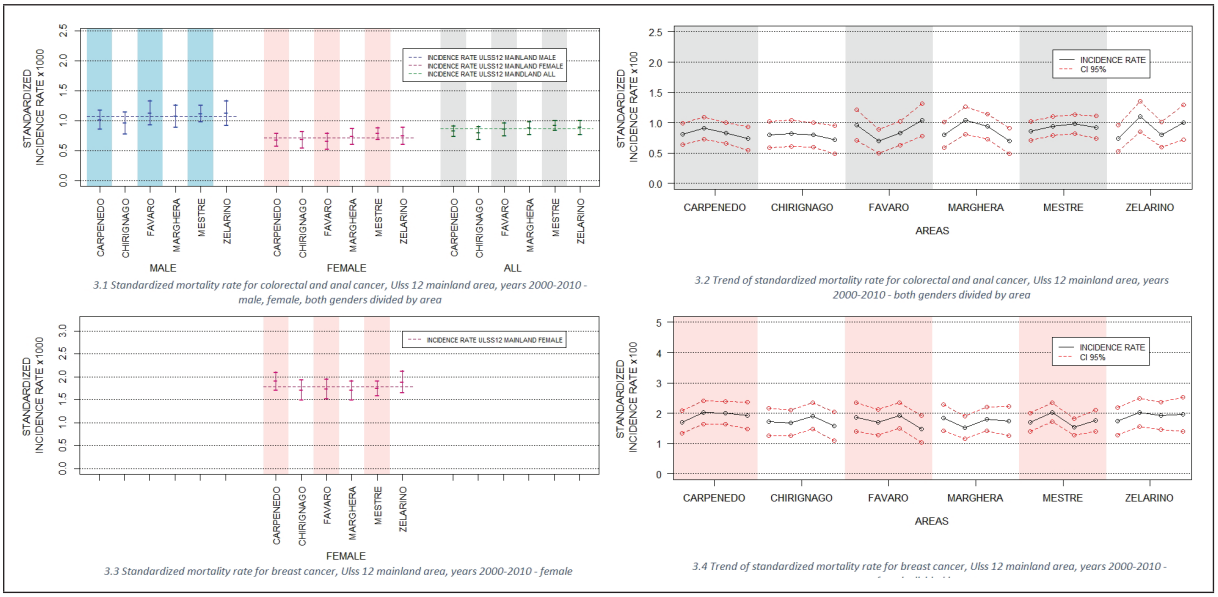


Figure 3
SEIVE analysis - Porto Marghera. 3.1 Standardized colorectal and anal cancer mortality rate, Ulss12 mainland area, years 2000-2010 - male, female, both genders divided by area. 3.2 Trend of standardized colorectal and anal cancer mortality rate, Ulss12 mainland area, years 2000-2010 - both genders divided by area. 3.3 Standardized breast cancer mortality rate, Ulss12 mainland area, years 2000-2010 - female divided by area. 3.4 Trend of standardized breast cancer mortality rate, Ulss12 mainland area, years 2000-2010 - female divided by area.

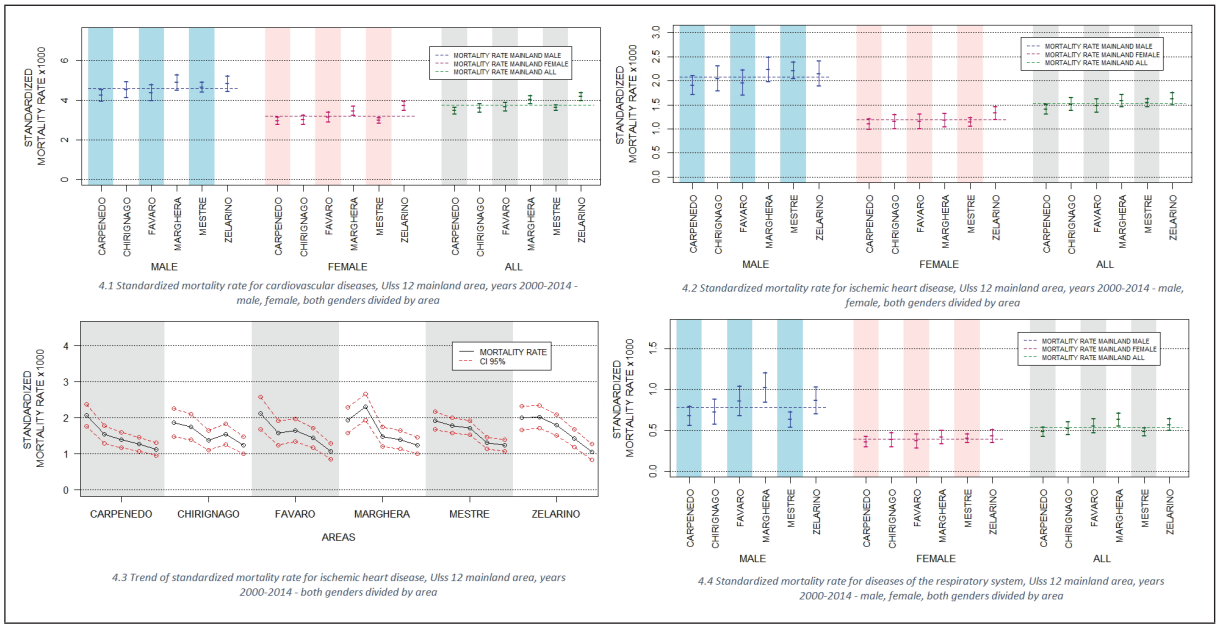


Figure 4
SEIVE analysis - Porto Marghera. 4.1 Standardized cardiovascular diseases mortality rate, Ulss12 mainland area, years 2000-2014 - male, female, both genders divided by area. 4.2 Standardized ischemic heart disease mortality rate, Ulss12 mainland area, years 2000-2014 - male, female, both genders divided by area. 4.3 Trend of standardized ischemic heart disease mortality rate, Ulss12 mainland area, years 2000-2014 - both genders divided by area. 4.4 Standardized diseases of the respiratory system mortality rate, Ulss12 mainland area, years 2000-2014 - male, female, both genders divided by area.

Mortality rate of the circulatory diseases and respiratory diseases

Figure 4.1 shows the mortality rate for diseases of the circulatory system [24]. The mortality rate among males in Marghera is not significantly different from the mortality rates observed in the rest of the mainland. On the other hand, the mortality among the female population in Marghera is slightly higher than that observed in the rest of the mainland, while the highest rate is present in Zelarino.

To further examine the diseases of the circulatory system, we have calculated mortality rates for ischemic heart disease *(Figures 4.2 and 4.3)*. No substantial differences can be observed between Marghera and the other areas in analysis, neither in the overall population, nor in the analyses stratified by gender.

Figure 4.4 shows the mortality rate for the diseases of the respiratory system [24]. There is a significant excess in the mortality rate for the male population living in Marghera. This excess is not present in the female population.

Prevalence of asthma, COPD and diabetes

We have also calculated the annual prevalence of the some common and highly impacting diseases, through the use of specific pathology algorithms.

Prevalence of asthma has slightly increased between 2000 and 2014 *(Figure 5.1)*. Residents in Marghera have similar prevalence trends compared to the other mainland areas.

Figure 5.2 shows the prevalence of COPD from 2006 to 2014. All areas have a similar downward trend and rates in the population of Marghera were comparable to those observed in the other areas.

Lastly, *Figure 5.3* shows the annual prevalence of diabetes between the years 2000 to 2014. There is a slight increasing trend in all the mainland of Venice. However, the prevalence of diabetes in Marghera is higher than that found in other areas.

DISCUSSION

An epidemiological surveillance system allows to identify individuals affected by specific diseases in a population to rapidly observe changes in health trends. This information is essential to evaluate issues concerning overall health conditions of citizens, as well as increases in specific conditions or in specific areas, which is especially important in neighborhoods at an increased environmental risk, such as Marghera. This possibility allows to plan interventions to promote improvements in the population's health conditions and to invest in prevention campaigns.

The SEIVE's structure allows to observe trends concerning the population living in the area of Marghera alone, separately from the rest of mainland. This is an important innovation, compared to previous studies published by the SENTIERI project, which were based on aggregated data on the entire population living in the municipality of Venice, with no possibility of greater spatial resolution. Areas belonging to the municipality of Venice exhibit a profound heterogeneity [29]. It is enough to think that the *sestieri*, in which the historic city center of Venice is divided, the islands and mainland all have different backgrounds, different urban developments and types of dwellers. If these differences are not taken into account, they might act as confounding variables in the analyses of the population and might not allow to identify relevant health conditions

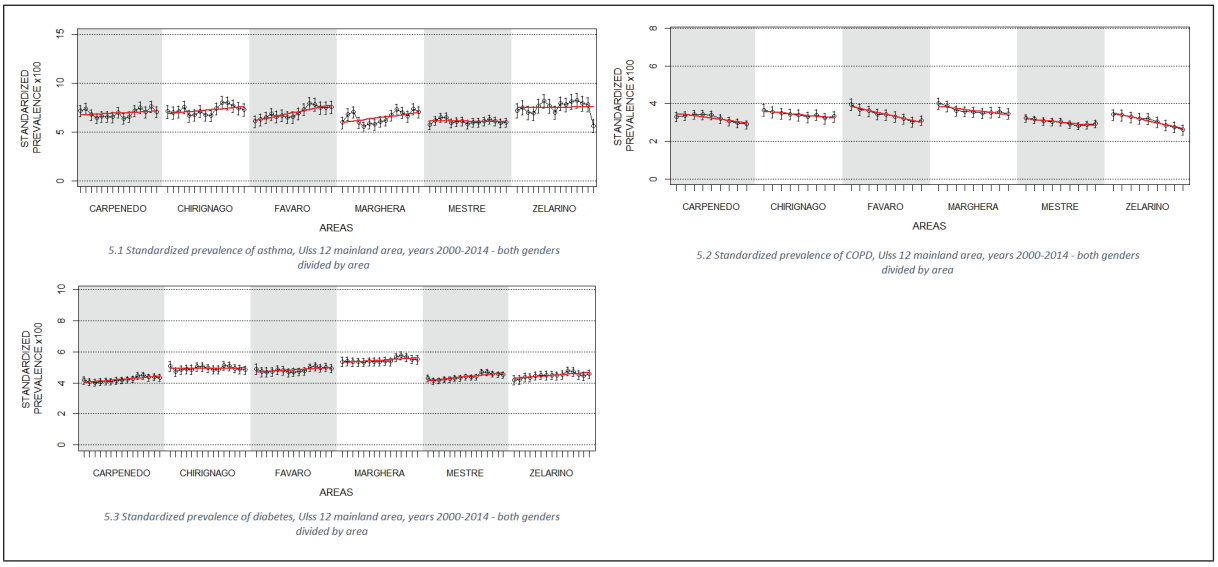


Figure 5
SEIVE analysis - Porto Marghera. 5.1 Standardized prevalence of asthma, Ulss12 mainland area, years 2000-2014 - both genders divided by area. 5.2 Standardized prevalence of COPD, Ulss12 mainland area, years 2000-2014 - both genders divided by area. 5.3 Standardized prevalence of diabetes, Ulss12 mainland area, years 2000-2014 - both genders divided by area.

that are present in specific subgroups of the population.

The trend that emerges from the study is a general improvement of overall health conditions of the population living in the Venetian mainland. Despite greater disparities in health conditions were present in the past, we have witnessed a gradual process of homogenization. Furthermore, the areas that presented worse health conditions at the beginning of the study period, underwent a more rapid improvement and have reached health parameters similar to the areas with a higher socioeconomic status [29].

The rate of all-cause mortality is decreasing in the entire mainland, but an excess was observed for men and women residing in Marghera, compared to the rest of the mainland.

A marked increase in cancer mortality rate is evident when comparing residents in Marghera to the other mainland areas. This excess mortality is especially high in the male population.

It is noticeable, that there seems to be a slightly higher cancer mortality rate, only among the residents of Marghera. We can also detect an excess in the mortality rate for lung cancer among all residents in Marghera. In this case, the higher mortality rate of lung cancer is mainly attributable to the male population. Nevertheless, in all mainland areas, the trend of lung cancer mortality rate is homogeneously decreasing. This trend can be observed also in Marghera, where, however, we an increase in lung cancer mortality rate is present in the final phase of the observation period. This increase is most likely responsible of the increase observed in the overall cancer mortality rate, for the area of Marghera. Although lung cancer has a multifactorial genesis, in which tobacco plays an important role, many epidemiological studies have identified elevated risks associated to occupational exposures, among employees that work in refineries and in the chemical industry [30, 31].

Pleural mesothelioma is a tumor that has a well-known association with asbestos exposure. The analysis that we have carried out has shown an increased mortality rate for pleural mesothelioma in the male population living in Marghera, compared to the population living in the other mainland areas. This observed increase is understandable as Marghera was a very important harbor of the region of Veneto and the exposure to asbestos among workers that commonly lived in that area, was very relevant, especially in relation to naval constructions [32]. The reduced number of cases did not allow us to carry out analyses on the female population or to establish trends in the male population [33, 34].

We have also assessed incidence rates of other common types of cancers: colorectal and anal cancer in both genders and breast cancer in women. These types of cancers do not have an etiology that is closely related to the exposure to industrial pollutants [35, 36]. Colorectal and anal cancer incidence rate in the total population resident in Marghera is in fact consistent with the incidence rate observed in all other areas of the mainland with a stable trend over time. A similar argument can be exemplified by the breast cancer incidence in the female population, where no substantial differences can be detected in the different areas, with stable trends.

In addition to the abovementioned health conditions, the study has also calculated cardiovascular mortality rates, which are one of the main causes of death in Italy and in other high-income countries. Punctual estimates of mortality rates from cardiovascular diseases among male residents in Marghera are slightly higher, but not significantly different from the mortality rates observed among the male population in the rest of the mainland, while female mortality rates for cardiovascular diseases in Marghera are significantly higher. Mortality rates for cardiovascular diseases in the female population living in Zelarino are also elevated. These higher rates are

potentially responsible for the increase in the general mortality rate of Zelarino, seen in *Figure 1.1*. The mortality rate for ischemic heart disease is similar across all mainland areas and has undergone a constant decrease and in the last study period with rates that reach comparable levels in all areas. Considering the relevance of ischemic heart disease in overall mortality, its decrease has strongly contributed to the overall decreasing trends that has been observed for all-cause mortality.

Mortality rates from respiratory diseases show an excess in the male population residing in Marghera, if compared to the rest of mainland. On the other hand, this excess risk is not present in the female population. This is likely due to occupational exposure of men living in Marghera who worked in the industrial area. Given this marked gender difference, environmental exposure seems to have played a marginal role in the genesis of this excess of respiratory mortality.

The study has employed algorithms that have been presented in the supplement of *Epidemiologia & Prevenzione* [23] to assess the prevalence of some of the most relevant chronic diseases: asthma, COPD and Diabetes. To estimate the prevalence of asthma (years 2000-2014), we have exclusively considered the population aged 0-34 years, as overlapping pharmaceutical treatments with COPD, would have led to a vast misclassification, especially for cases identified by means of drug prescriptions only [37]. A slightly increasing trend in the prevalence of asthma has been observed in all mainland areas. The prevalence of asthma in the population residing in Marghera has a similar trend to the one observed in the rest of the population of the mainland.

COPD prevalence (2006-2014) was calculated through the use of a COPD case-identification algorithm, that focused exclusively on the population aged 35 or more, always to avoid possible case misclassification with asthma. For the population of Marghera, we have not detected a higher prevalence of COPD compared to that of the other mainland areas.

Among chronic diseases, the prevalence of diabetes was also calculated through a disease-specific case-identification algorithm. It was possible to estimate the annual prevalence of diabetes from the year 2000 to 2014. As described by IDF Diabetes Atlas [38] for global trends of diabetes, our data also shows a slightly increasing prevalence of diabetes, which is common to all mainland areas of Venice. However, diabetes appears to be more prevalent in Marghera, than in the other areas, for the entire study period.

This epidemiological report shows the relevance of having an epidemiological surveillance system and the potential this tool has of analyzing in depth the heterogeneous realities that would otherwise risk to pass unnoticed. Furthermore, this study adds evidence to what has already been observed in literature, that there is a close connection between the exposure to pollutants, especially through occupational exposure as well as environmental exposure, and the development of chronic diseases and consequently worse health conditions, along with higher mortality rates.

CONCLUSION

These analyses stem from the SEIVE, which allows to monitor a population's health state. In particular, the novelty of this study is to focus on the resident population in a subdivision of the municipality of Venice, precisely the area of Marghera, that is the closest to the SNI of Porto Marghera. By doing so, it is possible to reduce the confounding effect that derives from different socioeconomic statuses and environmental exposures, that is inevitable when considering heterogeneous populations as a whole.

Despite the presence of an overall downward trend of mortality rates in all mainland areas, with decreasing differences among the areas, the present study has highlighted a number of critical issues concerning the population residing in Marghera. Nevertheless, it is important to notice the presence of higher cancer mortality rates and especially lung cancer mortality, in Marghera, compared to the other mainland areas. Higher mortality for diseases of the respiratory system as well as mortality for pleural mesothelioma, exclusively for the male population living in the area of Marghera. Both these diseases are closely linked to exposures to carcinogenic substances among which industrial pollutants that might likely affect the former employees of Porto Marghera's industrial area.

In particular, the latest observation period of mortality from malignant tumors and that of lung cancer among residents in the area of Marghera has increased. However, to have a more complete overview of the trends, future studies with a more extensive observation period are required.

This paper also confirms the need of a regular longitudinal monitoring system, to control a population's most relevant health parameters, especially for citizens that reside in proximity to an SNI. In fact, one of the most efficient ways to record epidemiological changes over time is through longitudinal observational studies.

This paper has also raised new concerns on the health state of residents in Marghera that can only be answered by a constant update of the Venetian epidemiological surveillance system.

Conflict of interest statement

Neither financial nor other relationships might lead to a conflict of interests.

Received on 31 May 2019.
Accepted on 20 April 2020.

REFERENCES

1. Chinello C. Le origini di Porto Marghera. In: Porto Marghera 1902-1926. Alle origini del "problema di Venezia". Venezia: Marsilio Editori; 2017.
2. Barizza S, Resini D. Le industrie di Porto Marghera. In Porto Marghera e il Novecento industriale a Venezia. Ponzano: Edizioni Grafiche Vianello srl/Vianello Libri; 2004.

3. Nappi AF. La fondazione di Marghera. In: Storia di Marghera, da periferia a città. Venezia: Cedit Edizioni; 1994.
4. Barizza S, Cogo C, Facca G. Il progetto di Porto Marghera. In: Marghera il quartiere urbano. Venezia: Alcione Editore, 2 ed.; 2002.
5. Gianni E, Peron I. Le origine di Porto Marghera. In Porto Marghera ATLAS. Trento: List Editore; 2019.
6. Barizza S. Marghera 1938-1955. Venezia: Alcione Editore; 2003.
7. Rubini C. La grande Venezia nel secolo breve, guida alla topografia di una metropoli incompiuta (1917-1993). Verona: Cierre Edizioni; 2016.
8. Italia. Legge 9 dicembre 1998, n 426. Nuovi interventi in campo ambientale. GU Serie Generale n. 11, 15 gennaio 1999.
9. Italia. Decreto del ministro dell'ambiente 23 febbraio 2002. Perimetrazione dei siti di interesse nazionale. GU Serie Generale n. 230, 1 ottobre 2002.
10. Italia. Decreto del ministero della salute 24 aprile 2013. Disposizioni volte a stabilire i criteri metodologici utili per la redazione del rapporto di valutazione del danno sanitario (VDS) in attuazione dell'articolo1-bis, comma2, del decreto-legge 3 dicembre 2012, n 207, convertito, con modificazione dalla legge 24 dicembre 2012, n. 231. GU Serie Generale n. 197, 23 agosto 2013.
11. Analisi della condizione ambientale, socio economica, logistica delle infrastrutture e dei vincoli legali del brownfield nell'area funzionale urbana (FUA). Venezia-interreg central europo-Resites; 2016.
12. Guerzoni S, Rossini P, Sarretta A, Raccanelli S, Ferrari G, Molinaroli E. POPs in the Lagoon of Venice: budgets and pathways. Chemosphere. 2007;67(9):1776-85.
13. Bernardello M, Secco T, Pellizzato F, Chinellato M, Sfriso A, Pavoni B. The changing state of contamination in the Lagoon of Venice. Part 2: Heavy metals. Chemosphere. 2006;64(8):1334-45.
14. Secco T, Pellizzato F, Sfriso A, Pavoni B. The changing state of contamination in the Lagoon of Venice. Part 1: organic pollutants. Chemosphere. 2005;58(3):279-90.
15. Frignani M, Bellucci LG, Favotto M, Albertazzi S. Pollution historical trends as recorded by sediments at selected sites of the Venice Lagoon. Environ Int. 2005;31(7):1011-22.
16. Mugnai C, Giuliani S, Bellucci LG, Carraro C, Favotto M, Frignani M. Polychlorinated biphenyls in two salt marsh sediments of the Venice Lagoon. Environ Monit Assess. 2011;181(1-4):243-54.
17. Pirastu R, Zona A, Ancona C, Bruno C, Fano V, Fazzo L, Iavarone I, Minichilli F, Mitis F. Risultati dell'analisi della mortalità nel Progetto SENTIERI. Epidemiol Prev. 2011;35(Suppl. 4):150-2.
18. Comba P, Ricci P, Iavarone I, Pirastu R, Buzzoni C, Fusco M, et al. Cancer incidence in Italian contaminated sites. Ann Ist Super Sanità 2014;50(2):186-91. Available from: www.iss.it/binary/publ/cont/ANN_14_02_13.pdf.
19. Simonato L, Canova C, Tessari R. La geografia delle malattie nel comune di Venezia. Padova: Cleup; 2009.
20. La Fisca S, Canova C, Inio A, Lorio M, Tessari R, Simonato L. 1° rapporto sulla salute dei veneziani 1999-2003.Padova: Relazione scientifica. 2005.
21. Macciò S, Barbiellini Amidei C, Palazzi B, Selle V, Simonato L. Aggiornamento del monitoraggio dello stato di salute della popolazione veneziana (ex ulss12) per mezzo di un sistema epidemiologico integrato. 51 congresso nazionale Siti: I primi 40 anni del servizio sanitario nazionale: il contributo dell'Igiene alla salute e all'equità. Proceedings: Riva del Garda 17-20 ottobre 2018. p. 75. Available from: www.aulss3. veneto.it/index.cfm?method=mys.apridoc&iddoc=14851
22. Canova C, Simonato L, Barbiellini Amidei C, Baldi I, Dalla Zuanna T, Gregori D, et al. A Systematic Review of Case-Identification Algorithms for 18 Conditions Based on Italian Healthcare Administrative Databases: A Study Protocol. Epidemiol Prev. 2019;43(4S2):8-16.
23. Fornari C, Madotto F, Demaria M, Romanelli A, Pepe P, Raciti M, et al. Procedure di record linkage in epidemiologia: uno studio multicentrico italiano. Epidemiol Prev. 2008;32(Suppl. 3):79-88.
24. Simonato L, Baldi I, Balzi D, Barchielli A, Battistella G, Canova C, et al. Obiettivi, strumenti e metodi per un utilizzo epidemiologico di archivi sanitari elettronici correnti in diverse aree italiane. Epidemiol Prev. 2008;32 (Suppl. 3):5-14.
25. Tessari R, Migliore E, Balzi D, Barchielli A, Canova C, Faustini A, et al. Stima della prevalenza dell'asma bronchiale basata su dati sanitari correnti mediante un algoritmo comune in differenti aree italiane. Epidemiol Prev. 2008;32(Suppl. 3):56-65.
26. Gnavi R, Karaghiosoff L, Balzi D, Barchielli A, Canova C, Demaria M, et al. Stima della prevalenza di diabete basata su dati sanitari correnti mediante un algoritmo comune in differenti aree italiane. Epidemiol Prev. 2008;32(Suppl. 3):15-21.
27. Faustini A, Cascini S, Arcà M, Balzi D, Barchielli A, Canova C, et al. Stima della prevalenza di broncopneumopatia cronico-ostruttiva basata su dati sanitari correnti, mediante l'uso di un algoritmo comune, in differenti aree italiane. Epidemiol Prev. 2008;32(Suppl. 3):46-5.
28. Classificazione delle malattie, dei traumatismi, degli interventi chirurgici e delle procedure diagnostiche e terapeutiche. Versione italiana della ICD9-CM "International Classification of Diseases – 9th revision – Clinical Modification". Roma: Ministero del lavoro, della salute e delle politiche sociali; 2007.
29. Simonato L, Canova C, Saracci R. Health inequalities and historically persistent socioeconomic differences in Venice. Int J Public Health. 2014;59(5):727-30.
30. Lo Presti E, Sperati A, Rapiti E, Di Domenicantonio R, Forastiere F, Perucci CA. Cause of death among workers of a refinery in Rome. Med Lav. 2001;327-37.
31. Bertazzi PA, Pesatori AC, Zocchetti C, Latocca R. Mortality study of cancer risk among oil refinery workers. Int Arch Occup Environ Health. 1989;61(4):261-70.
32. Marinaccio A, Binazzi A, Bonafede M, Branchi C, Bugani M, Corfiati M, Di Marzio D, Scarselli A, Iavicoli S, Verardo M, Mirabelli D, Gennaro V, Mensi C, Schallenberg G, Fedeli U, Negro C, Romanelli A, Chellini E, Grappasonni I, Masanotti G, Romeo E, Trafficante L, Angelillo IF, Cavone D, Cauzillo G, Tallarigo F, Tumino R, Melis M, Mazzoleni G, Carrozza F, gruppo di lavoro ReNaM. Il catalogo dell'uso di amianto nei comparti produttivi, macchinari e impianti. In: Il registro nazionale dei mesoteliomi. Roma: Sesto Rapport. Inail; 2018.
33. Roberti S, Merler E, Bressan V. L'incidenza del mesotelioma maligno in Regione Veneto nel periodo 1988-2002: analisi geografica, trend e confronto con la mortalita. Epidemiol Prev. 2007;31(6):309-16.
34. Comba P, Conti S, Manno V, Menegozzo S, Minelli G, Pasetto R, et al. Studio epidemiologico nazionale dei territori e degli insediamenti esposti a rischio da inquinamento: l'incidenza del mesotelioma. Binazzi A, Bruno C, Corfiati M, Fazzo L, Marinaccio A, Zona A (Eds). Epidemiol Prev. 2016;40(5):1-115.
35. García-Pérez J, Gómez-Barroso D, Tamayo-Uria I, Ramis R. Methodological approaches to the study of cancer risk in the vicinity of pollution sources: the experience of a

population-based case-control study of childhood cancer. Int J Health Geogr. 2019;18(1). Available from: https://ijhealthgeographics.biomedcentral.com/articles/10.1186/s12942-019-0176-x.
36. López-Abente G, García-Pérez J, Fernández-Navarro P, Boldo E, Ramis R. Colorectal cancer mortality and industrial pollution in Spain. BMC Public Health. 2012;12(1):589.
37. Di Domenicantonio R, Cappai G, Di Martino M, Agabiti N, Simonato L, Canova C, et al. A Systematic Review of Case-Identification Algorithms Based on Italian Healthcare Administrative Databases for Two Relevant Diseases of the Respiratory System: Asthma and Chronic Obstructive Pulmonary Disease. Epidemiol Prev. 2019;43(4S2):75-87.
38. Cho NH, Shaw JE, Karuranga S, Huang Y, da Rocha Fernandes JD, Ohlrogge AW, et al. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res Clin Pract. 2018;138:271-81.