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Hospitalisation costs of sinonasal cancer: Results from the Italian hospital discharge registry (2001–2018)

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ABSTRACT

Objective: This paper assesses hospital costs associated with sinonasal cancer (SNC) in Italy and evaluates related time trends.
Methods: All Italian hospitalizations treating patients with a diagnosis of SNC (N = 29,355) were extracted from the National Hospital Discharge Registry. Data refer to patients discharged from public and private hospitals between 2001 and 2018. Hospitalization cost, admission rate, length of stay and other hospitalization-level variables were used as the main outcome variables. Information on the relative disease intensity per hospitalization was used to specifically allocate total hospitalization costs to SNC medical resources.
Results: Over the 2001-2018 period, Italian hospitals have treated 1,631 admissions with SNC every year, on average. The mean annual hospitalization cost across all hospitals was 5,502,909 €, or 3,374 € per admission, and 60.0% of these costs were attributable to SNC only. Patient age at discharge (from 62 to 63 years), percentage of surgical procedures (from 29.3% to 46.8%) and of urgent cases (from 13.5% to 16.5%) increased over time. The percentage of costs attributable to SNC followed an inverted U-shaped pattern reaching the minimum level in 2006; conversely, mortality rose until 2007 then decreased steadily.
Conclusions: Good progress has been made in SNC treatments. Endoscopic techniques represent one of the most important advances in this field, reducing morbidity and hospital length of stay while keeping similar survival rates. Policies aimed at monitoring workers most exposed to SNC risk and at standardizing hospital treatments could help Public Health Institutions to plan optimal prevention policies.

Key Words: Sinonasal cancer, Sinonasal cancer burden, Hospital discharge data

1. INTRODUCTION

The nasal cavity is the space inside our nose, extending from the external nares to the pharynx. Paranasal sinuses are located close to the nasal cavity and come in four pairs of air-filled spaces: maxillary sinuses (located below the eyes), ethmoid sinuses (between the eyes), frontal sinuses (above the eyes) and sphenoid sinuses (behind the eyes).[1] Sinonasal cancer (SNC) is a rare tumor representing 1% of all malignancies, 3% of those of the upper aerodigestive tract and 4% of head and neck tumors.[2,3] The nasal cavity accounts for about 50% of all malignancies, whereas the maxillary or ethmoid sinus is where most of the remaining malignancies arise.[4,5] The most histological subtypes are of epithelial origin and includes squamous cell carcinomas (accounting for half of total SNC), adenocarcinomas (10%-20%), esthesioneuroblastoma (5%-10%), and adenoid cystic

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carcinoma (5%-10%).[6,7] SNC has a worldwide annual incident rate of 0.5-1/100,000.[8] Most affected patients have more than 50 years of age at diagnosis and are predominately males.[9,10] The overall incidence in the US was estimated at 0.8 cases per 100,000,[11] while in Europe at about 0.5 per 100,000.[12] In Italy (2010-2011) the male incident rate is almost 3 times the female one (0.86 vs. 0.31 per 100,000 inhabitants) and the most affected people are aged 75 years or older.[5] Despite the low incidence on the population overall, the risk of SNC strongly increases in specific occupational settings, above all in wood-related industries.[13] International Agency for Research on Cancer (IARC) classified wood dust as carcinogenic to humans and concluded that it causes cancer on the nasal cavities, paranasal sinuses, and nasopharynx.[14,15] About 3.6 million workers (2% of total employed population) were exposed to wood dust in Europe from 2000 to 2003, with the highest exposures in the construction sector and furniture mills.[16] In Italy, wood dust is the most frequent carcinogenic agent recorded in the national register containing Occupational Exposures to Carcinogens (Information System for Recording Occupational Exposures to Carcinogens), with 11,322 exposed workers in the period 1996-2006.[17] An elevated risk of SNC has been reported also for workers exposed to leather, solvents, chrome and formaldehyde and employed in specific industries such as footwear, leather and textile manufacturing, farming, construction, mining, drilling and metal industry (chromium and nickel compounds).[3] Despite industry exposures are well known, the treatment of these malignancies is challenging as they include a large variety of histological subtypes, can invade orbits or skull base and their symptoms appear only at a late stage. The multi-modality therapy including the surgical resection of the tumor (with endoscopic techniques as increasingly used option) seems to be associated with better outcomes.[18–20] The aim of this analysis was to estimate within-country hospital costs of SNC admissions, potentially serving as a guide for public health policies and hospitalization management in other countries as well. This paper is part of a wider project aimed at estimating the hospital costs due to main occupational respiratory diseases such as asbestosis, silicosis, mesothelioma[21–23] and SNC.

2. Materials and Methods

2.1 Study design

This is a retrospective population-based study of Italian hospitalizations treating SNC from the National Hospital Discharge Registry.

2.2 Settings

The Italian Public Health System is financed at regional level through diagnosis-related groups (DRG) coding.[24] A DRG is a classification system which standardizes payment to hospitals and covers all charges associated with an inpatient stay, including any services by an outside provider.[25] The Ministry of Health coordinates and controls the service and collects data from all Italian hospitals (with coverage close to 100%) in the National Hospital Discharge Registry, by coding patients diagnoses through the ninth version of the International Classification of Diseases (ICD-9-CM).[26] Every two years, central and local administrations establish National standard hospital charges (NSHCs) for interregional compensations by using DRGs.

2.3 Participants

This study analyzed all Italian hospital admissions with primary or contributing diagnosis of SNC (ICD-9-CM codes 160.0, 160.2-160.5, 160.8-160.9) of patients discharged from 2001 to 2018. Pregnancy-related hospitalizations were excluded from the analysis.

2.4 Outcome variables

Total and attributable costs of hospitalizations treating SNC were considered as the primary outcomes. Number and length of SNC hospital admission with their percentages with respect to all other types of admissions, the mean age of patients at discharge, hospital mortality, percentage of day hospital with other data details were considered as secondary outcomes.

2.5 Independent variables

Year of discharge was considered as independent variable for the trend analysis.

2.6 Data sources

Data was sourced from the National Discharge registry. The dataset contained gender, age and residence of patients, region of hospitals, up to six diagnoses and cares (primary and up to 5 secondary) ranked by employed resources and coded by ICD-9-CM, DRGs, type of DRGs (medical, surgical), type of activity (pregnancy-related, acute care, long term care, rehabilitation), type of hospitalization (planned, urgent), regimen of hospitalization (ordinary, daily), patient outcome at discharge (dead, alive) and hospital stay (days and number of accesses for ordinary and daily admissions respectively). Hospitalization data were linked with NSHCs through DRG codes to estimate hospitalization cost (in 2018 euros), that is deflated by means of annual consumer price indexes provided by the Italian National Institute of Statistics. In the analyzed period, there were three different versions of DRGs (10-th version for years 2001-2005, 19-th version for years 2006-2008 and 24-th for years 2009-2018) and seven related of NSHCs (for years 2001-2003, 2004-2005,

2006, 2007-2008, 2009, 2010-2011 and 2012- 2018). By considering the order of diagnoses in each record (ranked by consumed resources), hospitalization costs attributable to SNC were estimated as follows. For each record with n ($\leq$ 6) diagnoses, the fraction w_k (with $\sum_{k=1}^{n} w_k = 1$) of its total charge attributable to the k-th (k = 1,2,. . . ,n) diagnosis is assumed to be equal to

$$w_k = \frac{n+1-k}{\sum_{j=1}^{n} j}$$

These weights w_k decrease with k and are equal to 1 only if there is one diagnosis (n = 1). The cost of each hospitalization attributable to SNC was calculated by multiplying the estimated hospitalization cost with the weight w_k, where k is the diagnosis ranking of SNC in the corresponding data record.[21,23] The total length of hospital stay was estimated by considering accesses of day hospitals as whole days (a further breakdown was beyond the aim of the paper).

2.7 Statistical analysis

Linear, quadratic and cubic variables time-trends were evaluated by regression models (linear normal for continuous responses and the logistic one for binary outcomes), with year of discharge as the explanatory variable. To avoid collinearity problems (i.e., a strong reduction in estimates accuracy of the regression coefficients) among powers of the independent variable (year), only orthogonal (uncorrelated) polynomials of the variable "year" were included in the regression model (using the "poly" function in R). For linear trends, the coefficient of the linear normal model provided the estimated outcome variation for one-year increment, while the exponential function of the coefficient of the logistic model gave the estimated odds ratio (OR) of outcome for one-year increment. The year of max or min value was evaluated in quadratic trends while local max and min values were assessed in cubic trends. Statistical analyses were performed by the R Core Team (2013) and R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria and Knime Analytic Platform version 3.6.0.

3. RESULTS

3.1 Data description

In the period 2001-2018, SNC admissions were more frequent in the north-west regions (38.2%) and less frequent in the Islands (7.2%), and about 2 out of 3 referred to male patients. The tumor was located most frequently in nasal cavity (37.4%), then in maxillary (22.8%), ethmoidal (17.1%), unspecified (9.6%), other (6.6%), sphenoidal (2.6%) and frontal (0.9%) sinus. The remaining 3.0% of SNC were in multiple sites with maxillary and ethmoidal sinuses as the most frequent combination. About 12.6% of hospital admissions with SNC were also diagnosed with a secondary tumor (see Table 1). These subordinated cancers were located at lymph nodes of head, face, and neck (ICD-9-CM: 1960, 4.1%), bone and bone marrow (ICD-9-CM: 1985, 2.9%), lung (ICD-9-CM: 1970, 2.8%), brain and spinal cord (ICD-9-CM: 1983, 1.7%), liver (ICD-9-CM: 1977,1.3%), and other parts of nervous system (ICD-9-CM: 1984, 0.9%). Italian hospitals treated SNC in 29,355 admissions (0.015% of all hospitalizations), accounting for a total length of 236,808 days (0.019% of total hospitalization time) and with a total cost burden (expressed in 2018 euros) equal to 99,052,368 € (of which 58,982,358 attributable to SNC) (see Tables 2-3). Most hospitals treated only SNC (40%) or employed most medical resources for it (66%) (data not shown in tables for brevity). We estimated an average annual cost of 5,502,909 € (of which 3,276,798 attributable to SNC) and an overall hospitalization cost per admission of 3,374 € (of which 2,009 € attributable to SNC) (see Table 3). Most used diagnostic procedures were computerized axial tomography of bead (ICD-9-CM: 87.03, 3.2%), biopsy of nose (ICD-9-CM: 21.22, 3.0%), routine chest X-

Table 1. Descriptive statistics of hospitalizations with sinonasal cancer (Italy 2001-2018)

Variable	n	%
Gender		
Female	9,679	33.00
Male	19,676	67.00
Macro-region		
North-West	11,212	38.20
North-East	6,018	20.50
Center	5,790	19.70
South	4,217	14.40
Island	2,118	7.20
Site of SNC (ICD-9-CM code)		
Nasal Cavity (160.0)	10,959	37.3
Maxillary Sinus (160.2)	6,685	22.8
Ethmoidal Sinus (160.3)	5,021	17.1
Frontal Sinus (160.4)	266	0.9
Sfenoidal Sinus (160.5)	753	2.6
Other (160.8)	1,949	6.6
Unspecified (160.9)	2,827	9.6
Multiple	895	3.0
With additional diagnosis of Secondary* *tumor*		
Yes	3,701	12.6
No	25,654	87.4

Note. * ICD9-CM codes: 196-198

ray (ICD-9-CM: 87.44, 2.7%), closed endoscopic needle biopsy of nasal sinus (ICD-9-CM: 22.11, 1.5%), Magnetic resonance imaging of other and unspecified sites (ICD-9-CM: 88.97, 1.4%), computerized axial tomography of thorax (ICD-9-CM: 87.41, 1.4%) (data not shown in tables). Hospitalizations with surgical procedures (37%) were two times more expensive than others (5,130 € vs. 2,335 €). Most used surgical procedures were (see Table 4): ethmoidectomy (ICD-9-CM: 22.63) reported in 11% of hospitalizations with a mean cost of 4,701 €; local excision or destruction of intranasal lesion (ICD-9-CM: 21.31) reported in 6.2% of hospitalizations with a mean cost of 2,815 €; excision or destruction of nose, not otherwise specified (ICD-9-CM: 21.30) reported in 4.8% of hospitalizations with a mean cost of 3,076 €; excision of lesion of maxillary sinus with other approach (ICD-9-CM: 22.62) reported in 4.5% of hospitalizations with a mean cost of 4,504 €; sphenoidectomy (ICD-9-CM: 22.64) reported in 4.4% of hospitalizations with a mean cost of 6,183 €; intranasal antrotomy (ICD-9-CM: 22.2), reported in 3.7% of hospitalizations with a mean cost of 3,767 €; local excision or Destruction of other lesion of nose (ICD-9-CM: 21.32) reported in 3.6% of hospitalizations with a mean cost of 2,670 €. Most used medical treatments were: injection or infusion of cancer chemotherapeutic substance (ICD-9-CM: 99.25) reported in 17.3% of hospitalizations with a mean cost of 2,481 €; radiotherapy (ICD-9-CM: 92.2) reported in 4.5% of hospitalizations with a mean cost of 3,413 €.

Table 2. Number and length of all hospitalizations and of those with primary or contributing diagnosis of sinonasal cancer (Italy 2001-2018)

Year	All hospitalizations			SNC hospitalizations			% (× 1.000) [§] of SNC hospitalizations	
	n	Length* (days)	Length* (days) per admission	n	Length* (days)	Length* (days) per admission	n	Length* (days)
2001	12,582,758	81,571,226	6.5	1,870	17,563	9.4	14.9	21.5
2002	12,569,732	78,538,373	6.2	1,805	16,251	9.0	14.4	20.7
2003	12,430,367	76,681,945	6.2	1,842	15,339	8.3	14.8	20.0
2004	12,592,681	76,910,181	6.1	1,760	13,719	7.8	14.0	17.8
2005	12,573,449	76,997,605	6.1	1,785	13,871	7.8	14.2	18.0
2006	12,432,702	76,523,728	6.2	1,760	14,129	8.0	14.2	18.5
2007	11,915,577	74,873,170	6.3	1,740	14,569	8.4	14.6	19.5
2008	11,677,375	74,004,304	6.3	1,611	14,130	8.8	13.8	19.1
2009	11,238,809	72,073,231	6.4	1,753	14,228	8.1	15.6	19.7
2010	10,869,148	70,607,472	6.5	1,788	14,031	7.8	16.5	19.9
2011	10,347,388	68,159,173	6.6	1,667	13,802	8.3	16.1	20.2
2012	9,851,527	65,446,990	6.6	1,530	11,479	7.5	15.5	17.5
2013	9,450,543	63,101,264	6.7	1,355	9,583	7.1	14.3	15.2
2014	9,140,116	61,939,841	6.8	1,448	11,545	8.0	15.8	18.6
2015	8,930,979	61,366,673	6.9	1,500	10,917	7.3	16.8	17.8
2016	8,697,574	60,129,816	6.9	1,346	10,261	7.6	15.5	17.1
2017	8,522,456	58,896,885	6.9	1,446	10,669	7.4	17.0	18.1
2018	8,357,575	58,528,814	7	1,349	10,722	7.9	16.1	18.3
Overall	*10,787,820*	*69,797,261*	*6.5*	*1,631*	*13,156*	*8.1*	*15.1*	*18.8*
Trend L[#]	-	-	-	*-31.2*	*-378*	*-0.1*	*1.01*	*0.99*
Trend Q[&]	-	-	-	-	-	-	-	-
Trend C[†]	*2003(max) 2018(min)*	*2001(max) 2018(min)*	*2017(max) 2005(min)*	-	-	-	-	-

Note. * Length means number of days of hospital stay. Accesses in day hospitals are considered as whole days.

[#] Trend L means linear trend and represent annual variation (on average) for continuous variables (evaluated as coefficients of linear normal regression model) and one-year increment Odds ratio for percentages (evaluated as exponential function of logistic regression model).

[&] Trend Q means quadratic trend and is identified by the estimated coefficient of a linear regression with a quadratic term of year as independent variable.

[†] Trend C means cubic trend and is identified by the estimated coefficient of a linear regression with a cubic term of year as independent variable.

[§] We used % × 1.000 to highlight the time trend

Table 3. Estimates of hospitalization charges for sinonasal cancer (Italy 2001-2018)

Year	Hospitalization cost in 2018 €				% of hospitalization cost attributable to SNC
	Total	Per admission	Attributable to SNC	Per admission attributable to SNC	
2001	6,692,063	3,579	4,217,077	2,255	63.0
2002	6,530,992	3,618	3,892,136	2,156	59.6
2003	6,046,949	3,283	3,549,953	1,927	58.7
2004	5,797,339	3,294	3,372,518	1,916	58.2
2005	5,673,706	3,179	3,350,923	1,877	59.1
2006	5,828,061	3,311	3,368,944	1,914	57.8
2007	5,620,716	3,230	3,218,508	1,850	57.3
2008	5,805,749	3,604	3,313,962	2,057	57.1
2009	5,566,811	3,176	3,068,059	1,750	55.1
2010	5,839,131	3,266	3,513,743	1,965	60.2
2011	5,493,163	3,295	3,271,478	1,962	59.6
2012	4,961,542	3,243	3,084,671	2,016	62.2
2013	4,398,519	3,246	2,752,800	2,032	62.6
2014	4,993,158	3,448	3,115,539	2,152	62.4
2015	4,985,000	3,323	3,137,186	2,091	62.9
2016	4,689,301	3,484	2,864,943	2,128	61.1
2017	5,281,654	3,653	3,017,931	2,087	57.1
2018	4,848,514	3,594	2871987	2129	59.2
Overall	*5,502,909*	*3,374*	3,276,798	2,009	60.0
Trend L[*]	*-99,854*	-	*-55,992*	-	-
Trend Q[#]	-	*2009(min)*	-	-	-
Trend C[&]	-	-	-	*2016(max) 2007(min)*	*2014(max) 2006(min)*

Note. [*] Trend L means linear trend and represent annual variation (on average) for continuous variables (evaluated as coefficients of linear normal regression model) and one-year increment Odds ratio for percentages (evaluated as exponential function of logistic regression model).
[#] Trend Q means quadratic trend and is identified by the estimated coefficient of a linear regression with a quadratic term of year as independent variable.
[&] Trend C means cubic trend and is identified by the estimated coefficient of a linear regression with a cubic term of year as independent variable.

Table 4. Sinonasal cancer hospitalizations cost by type of DRG (surgical, medical) and most used procedures (Italy 2001-2018)

Procedure	ICD-9-CM	n	Cost x admission (2018 €)
Hospitalization treating sinonasal cancer with surgical DRG[*]	-	*10,931*	5,130
of which through:			
Ethmoidectomy	22.63	3,227	4,701
Local excision or destruction of intranasal lesion	21.31	1,829	2,815
Excision or destruction of nose, not otherwise specified	21.30	1,423	3,076
Excision of lesion of maxillary sinus with other approach	22.62	1,314	4,504
Sphenoidectomy	22.64	1,302	6,183
Intranasal antrotomy	22.2	1,093	3,767
Local excision or Destruction of other lesion of nose	21.32	1,066	2,670
Hospitalization treating sinonasal cancer with medical DRG[*]	-	*18,395*	2,335
of which through:			
Chemotherapy	99.25	5,090	2,481
Radiotherapy	92.2	1,318	3,413

Note. [*] DRG = diagnosis related group

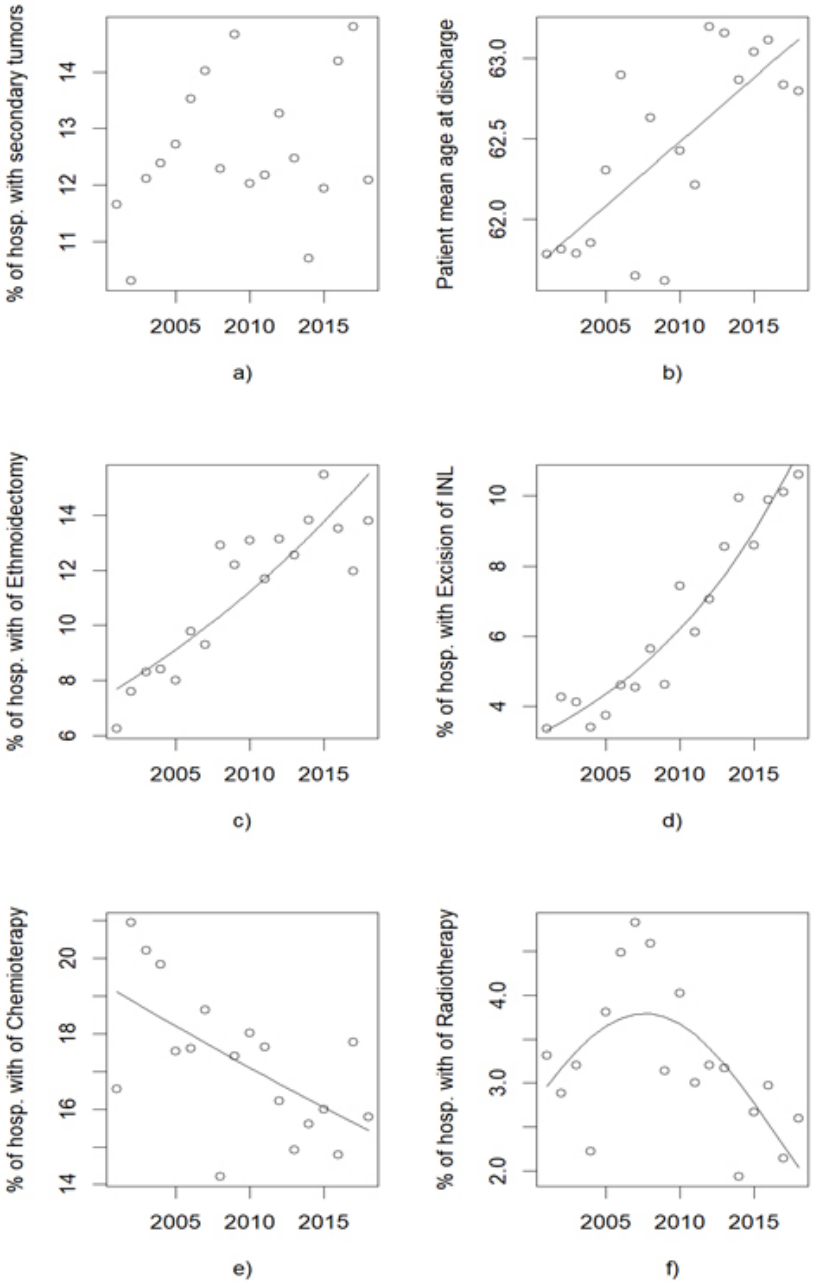

Figure 1. Italian hospitalizations (hosp.) tretaing sinonasal cancer (2001-2018): percentage of secondary tumors (a); patient mean age at discharge (b); percentage of ethmoidectomy (c); percentage of exicision of intranasal lesion (INL) (d), percentage of chemiotherapy (e); percentage radiotherapy (f).

3.2 Data trends

On average, hospitalizations reduced significantly over the last twenty years. In terms of frequency, there were 31 fewer admissions per year, while as per length of stay, there were 378 fewer days per year. The percentage of SNC hospitalizations shows a rising trend (OR = 1.01) while percentage of their length decreased over time (OR = 0.99) (see Table 2). Moreover, both total (99,854 €) and attributable (55,992 €) annual costs substantially decreased over time (see Table 1). Patients mean age at discharge grew significantly over time (by 1 month per year) (see Figure 1b) as well as the Odds ratios to be treated with surgery procedures (OR = 1.1) (see Table 5). Percentage of urgent hospitalizations, hospitalization costs per admission and percentage of males decreased until 2005, 2009 and 2012, respectively, then increased (see Table 3, Table 5). Percentage of day hospitals admissions and mortality followed an inverted U-shaped pattern reaching their highest value in 2007 (see Table 5). Percentages of

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hospitalizations with most used surgical treatments increased over time, showing a linear or quadratic trend (see Figure 1c-d). On the contrary, percentages of hospitalizations using chemotherapy and radiotherapy decreased by following respectively linear and quadratic patterns (see Figure 1e-f). The percentage of secondary tumors did not change significantly over time (see Figure 1a).

Table 5. Characteristics of hospital discharge data with primary or contributing diagnosis of sinonasal cancer (Italy 2001-2018)

Year	Males (%)	Age (mean)	Age (SD)	Mortality (%)	Day Hospital (%)	Surgery (%)	Urgent Hospitalizations (%)
2001	70.7	61.8	15.5	2.8	23.2	29.3	13.5
2002	67.9	61.8	16.6	2.3	21.4	28.1	13.5
2003	70.0	61.8	15.7	3.1	22.9	29.4	14.5
2004	65.1	61.9	16.7	2.8	26	30.7	13.9
2005	68.6	62.3	16.5	3.0	26.6	31.3	14.6
2006	68.6	62.9	16.5	2.9	27.6	34.9	13.0
2007	65.7	61.6	16.8	3.9	25.3	33.4	15.1
2008	65.0	62.6	16.3	3.6	27.7	37.9	14.6
2009	68.3	61.6	17.5	2.7	26.8	36.6	14.3
2010	67.8	62.4	16.9	2.9	26.7	38.3	13.6
2011	68.0	62.2	16.3	2.4	25.8	38.8	13.3
2012	62.9	63.2	15.9	2.4	23.5	40.3	15.2
2013	61.3	63.2	16.4	2.8	24.0	41.8	13.3
2014	65.4	62.9	16.9	2.3	21.3	45.2	14.9
2015	68.3	63.0	16.1	3.1	19.1	46.9	17.3
2016	66.6	63.1	17.2	2.2	16.6	47.3	*16.8*
2017	66.8	62.8	16.2	2.1	16.8	44.9	*17.7*
2018	66.8	62.8	16.5	2.0	15.3	46.8	16.5
Overall	*67.0*	*62.4*	*16.5*	*2.8*	*23.4*	*37.3*	*14.8*
Trend L[*]	-	*0.1*	-	-	-	*1.1*	-
Trend Q[#]	*2012(min)*	-	-	*2007(max)*	*2007(max)*	-	*2005(min)*
Trend C[&]	-	-	-	-	-	-	-

Note. [*] Trend L means linear trend and represent annual variation (on average) for continuous variables (evaluated as coefficients of linear normal regression model) and one-year increment Odds ratio for percentages (evaluated as exponential function of logistic regression model).

[#] Trend Q means quadratic trend and is identified by the estimated coefficient of a linear regression with a quadratic term of year as independent variable.

[&] Trend C means cubic trend and is identified by the estimated coefficient of a linear regression with a cubic term of year as independent variable.

4. DISCUSSION

During a typical workweek (40 hours), a worker airway (from nares to alveoli) touches up to 14,000 liters of air at the workplace. The cumulated inhalation of toxic substances (in form of dusts, fibers or fumes) may cause several respiratory diseases.[27] The exposure to this disease risk might in turn translate into substantial costs for regional hospitals, especially for those malignancies that are difficult to detect early. This paper is part of a wider project aimed at estimating hospitalizations costs and characteristics of important occupational respiratory diseases and presents novel evidence about SNC medical costs. Results on asbestosis, silicosis and mesothelioma costs can be found in other papers.[21–23]

This study has two limitations. First, the Italian Ministry of Health does not release an identifier patient code, so we could not evaluate the actual number of cases (however, this does not affect costs estimates). Second, the cost estimates are based on DRG and this does not allow the exact identification for the costs of medical procedure. However, we estimated the specific part of hospitalization cost attributable to SNC with a weightage formula and the hospitalization costs by type of DRG (medical or surgical). Consistently with previous findings,[4,5,9,10] our results confirm that more than half of records diagnosed SNC in the nasal cavity or maxillary sinus and that male patients were more frequent than female ones. This is not surprising, as nose and mouth

are the most exposed areas to cancer-causing dust and chemical agents which are mostly present in occupational settings with higher prevalence of males. In addition, consistently with territorial distribution of wood-related industries,[28] the northern regions hospitalized relatively more patients than other geographical parts of Italy (see Table 1). Considering that Italy is one of the leading exporter in the furniture sector all over the world, and it even maintains a high-ranked position in the European and North American markets for other wood-products exports,[29] the exposure to SNC risk is a more relevant issue for public health in these specific areas. From 2001 to 2018 Italy spent 99,052,368 € (5,502,909 € per year on average) to treat patients with SNC in 29,355 hospitalizations (1,631 per year on average). The 60% of those costs (58,982,358 €) referred to SNC treatments. Due to economic issues related to national public finance,[30] during the analyzed period Italian hospitalizations strongly decreased from 12,582,758 (for a length of 81,571,226 days) in 2001 to 8,357,575 (for a length of 58,528,814 days) in 2018. In line with the underlying context, the number of SNC hospitalizations decreased with a linear time-trend (of about - 31 admissions and 378 days per year), such as the total (of about -99,854 € per year) and attributable (of about -55,992 € per year) to SNC annual cost of hospitalizations. However, compared to all other diseases, the percentage of SNC hospitalizations shows a rising trend while percentage of their length decreased over time (see Table 2, columns 8 and 9). Since the percentage of recurrences does not increase significantly over time (see Figure 1a), the increased relative number of admissions could be presumably due to a higher number of early diagnoses or of people exposed at work. The fact that the patient mean age at discharge increased over time (see Figure 1b) is more suitable with the latter hypothesis. This issue should be investigated more in depth. Furthermore, the tendency to shorten hospital stay (see Table 2, 7-th column) could be due to an increased use of endoscopic endonasal approaches (EEA). Surgical procedures increased more than 1.5 times during the studied period (see Table 5, column 7), likely EEA led this trend (see Figure 1c-d) at expense to the medical treatments (see Figure 1e-f) and contributed to lower hospital stay per admission of 0.1 days each year on average (see Table 2, columns 7&9). Technological advances of last decades allowed a wider use of EEA, including treatments of SNC which started in USA from the 1990s.[31] Several studies have shown that while EEA reduces morbidity and hospital length of stay with respect to conventional external surgery, it results in similar survival rates.[32] The hospital mortality followed an inverted U-shaped curve where the point of max took place in 2007 (see Table 5). This squares with the first evidence-based publications of guidelines about SNC treatments.[33,34] The standardization and update of medical treatments through available data and the scientific consensus are important steps for reducing risk of treatments failure and for improving public health. Furthermore, the epidemiological surveillance system introduced in 2008 in Italy (article n. 244 of the legislative decree n. 81/2008) should have both increased the awareness of SNC risk among workers exposed to wood and leather dust and the importance to detect those tumors at early stage among occupational health professionals. However, data show 12.6% of records with secondary tumors (ICD-9-CM: 196-198) and (in line with other results[35]) the involvement of head, face, and neck lymphonod (ICD-9-CM: 1960) in 4.1% of records. Those type of results can be caused by surgical resection with positive margins and are predictors of worsened outcomes.[32] Today, SNC is often diagnosed at an advanced stage. The assessment of periodical endoscopic visits on exposed workers and the search of new techniques based on genomic information to predict this type of tumors could be some avenues for further research.

ETHICAL APPROVAL

European hospital data are regulated by Regulation 2016/679 of the European Parliament and they do not need approval by any ethical medical committee.

INFORMED CONSENT

European hospital data are regulated by Regulation 2016/679 of the European Parliament and they do not need informed consent.

CONFLICTS OF INTEREST DISCLOSURE

The authors declare no conflicts of interest.

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