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Hospitalisation costs of malignant mesothelioma: results from the Italian hospital discharge registry (2001–2018)

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ABSTRACT

Objectives This paper aims to establish hospitalisation costs of mesothelioma in Italy and to evaluate hospital-related trends associated with the 1992 asbestos ban.
Design This is a retrospective population-based study of Italian hospitalisations treating pleura, peritoneum and pericardium mesothelioma in the period 2001–2018.
Settings Public and private Italian hospitals reached by the Ministry of Health (coverage close to 100%).
Participants 157 221 admissions with primary or contributing diagnosis of pleural, peritoneal or hearth cancer discharged from 2001 to 2018.
Primary and secondary outcome measures: number, length and cost of hospitalisations with related percentages.
Results Each year, Italian hospitals treated a mesothelioma in 6025 admissions on average. Mean annual costs by site were €20 293 733, €3183 632 and €40 443 for pleura, peritoneum and pericardium, respectively. Pericardial mesothelioma showed the highest cost per admission (€6117), followed by peritoneal (€4549) and pleural cases (€3809). Percentage of hospitalisation costs attributable to mesothelioma was higher when it is located in pleura (53.4%) and pericardium (51.8%) with respect to peritoneum (41.2%). Overall annual hospitalisation cost, percentages of number and length of admissions showed an inverted U-shape, with maxima (of €25 850 276, 0.064% and 0.096%, respectively) reached in 2011–2013. Mean age at discharge and percentages of surgery and of urgent cases increased over time.
Conclusions The highest impact of mesothelioma on the National Health System was recorded 20 years after the asbestos ban (2011–2013). Hospitals should expect soon fewer but more severe patients needing more cares. To study the disease prevalence could help assistance planning of next decade.

Strengths and limitations of this study

- This is retrospective population-based study of Italian hospitalisations treating mesothelioma of pleura, peritoneum and pericardium in the period 2001–2018.
- The cost estimation of hospitalisations is based on all records collected by the Ministry of Health and takes into account the proportion of consumed resources by treated diagnosis.
- Time-trends of costs and of percentage of hospitalisation allow considerations about first effects of the 1992 asbestos ban.
- Hospitalisation diagnosis are coded according to the ICD-9 that does not contain specific codes for mesothelioma, adjustments with mortality data (coded by ICD-10) have been necessary.

INTRODUCTION

Malignant mesothelioma (MM) is an aggressive asbestos-related cancer, it develops mostly in the pleura (80%–85%) and peritoneum (15%–20%) and rarely in pericardium and tunica vaginalis testis (1%–2%). MM is characterised by a long period of latency and poor quality of life for patients.[1] Without treatments, it has a prognosis of up to 12 months for pleural (MM1), peritoneal (MM2) and pericardial (MM3) cases and of 23 moths for testis ones. There is no agreed consensus on standardised therapies,[2–6] however, research is ongoing and promising results seem not too far away.[7 8] Although WHO and the International Labour Organization began (decades ago) public awareness and prevention campaigns aimed at eliminating asbestos-related diseases[9] and the international Ban Asbestos Secretariat promote a world ban,[10] the WHO estimates that 125 million workers are exposed to asbestos worldwide.[9] Asbestos is banned in most developed countries, but the large use in constructions has left an environmental contamination causing occupational exposure among buildings maintainers and wreckers and among asbestos removers.[11 12] USA has not a federal ban but the use of asbestos has been reduced by the implementation of regulations and litigation.[13] Annual world production of asbestos has reached its peak (of about 4 500 000 metric tons) in the 1980s, then reduced to 2 000 000 metric tons (by restrictions in developed countries) up to 2000 and kept stable up to 2011. Canada (till 2011), USA and Italy (till 1980s) have been the strongest miners (>50 000 metric tons per year) among advanced nations. From 2012 to 2018, asbestos production decreased to 1150000 metric tons produced by Russia (710000 of metric tons), Kazakistan (202900 of metric tons), China (125000 of metric tons) and Brazil (110000 of metric tons).[14,15] China is the world's top chrysotile consumer and the third largest producer, over a million people may be occupationally exposed to asbestos.[16] It was estimated that in India up to 1000000 people are currently being occupationally exposed to asbestos.[17] Even if South Africa and Turkey banned asbestos (in 2008 and 2010, respectively), both have a serious environmental contamination, the former from past asbestos mining activity the latter from natural deposits.[18,19] Most affected states by MM pandemic in the period 2000–2010 have been the UK, the Netherlands, Malta, Belgium, Australia and New Zealand, but for some large Countries (Bangladesh, Brazil, Indonesia, Nigeria, Pakistan and Russia) data are not available or incomplete.[20] In this context, the UK, Netherlands, Germany, Italy, New Zealand, France, Spain, Australia and South Korea have established a national register of MM cases.[21] Italy banned asbestos from the 1992[14] and introduced low exposure limit for exposed workers (0.1 fibres/cm^3).[22] Since 2018, we started a research line aimed at investigating some of the most common occupational respiratory diseases (such as asbestosis, silicosis, MM and sinonasal tumour), by using data of the National Hospital Discharge Registry.[23,24] This paper aims to establish hospitalisation costs of MM in Italy and to evaluate their time trends in relation with the asbestos ban.

METHODS

Study design

This is a retrospective population-based study of Italian hospitalisations treating pleural, peritoneal and hearth cancer from the National Hospital Discharge Registry.

Settings

The financial burden of Italian Public Health System is borne by local institutions (regions).[25] The Ministry of Health coordinates and controls the provided service and archives 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).[26] National standard hospital charges (NSCs) for interregional compensations (when hospitals admissions refer to a resident of a different region) are defined in the permanent conference between central administration and regions by using diagnosis-related group (DRG) coding. If needed, updates are made every couple of years.

Participants

This study analysed all Italian hospital admissions with primary or contributing diagnosis of pleural (ICD-9 code 163), peritoneal (ICD-9 codes 158.8, 158.9; Kaposi sarcoma is not included) and hearth (ICD-9 code 164.1; tumour of great vessels is not included) cancer of patients discharged from 2001 to 2018. Selected data do not include pregnancy-related hospitalisations. The 0.4% of records with multiple tumours was considered for analysis of each malignancy.

Outcome variables

Hospitalisations costs and hospitalisation costs attributable to mesothelioma are primary outcomes. Number and length of MM hospital admission with their percentages were considered as secondary outcomes such as the mean age at discharge, hospital mortality, percentage of day hospital with other data details.

Independent variables

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

Data sources

Data were extracted from the national discharge data registry, managed by the Ministry of Health. Data contain gender, age and residence of patients, region of hospitals, up to six diagnoses and cares (primary and up to five secondary) ranked by consumed resources and coded by ICD-9, DRGs, type of DRGs (medical, surgical), type of activity (pregnancy-related, acute care, long term care, rehabilitation), type of hospitalisation (planned, urgent), regimen of hospitalisation (ordinary, daily), patient outcome at discharge (dead, alive) and hospital stay (days and number of accesses for ordinary and daily admissions, respectively). Hospitalisation cost have been estimated by the NSCs and expressed in 2018 euros by the annual consumer price indexes provided by the National Institute of Statistics. In the study period, there were three different versions of DRGs (10th version for years 2001–2005, 19th version for years 2006–2008 and 24th for years 2009–2018) and seven related NSCs (for years 2001–2003, 2004–2005, 2006, 2007–2008, 2009, 2010–2011 and 2012–2018). By taking into account diagnosis position in each admission, hospitalisation costs attributable to MM were also estimated. Given a record with $n\ (=1,2,\ldots,6)$ diagnoses, the fraction w_k (with $\sum_{k=1}^{n} w_k = 1$) of its charge attributable to the k-th (k=1,2,…, n) diagnosis is assumed equal to

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

These weights decrease with diagnosis ranking and are equal to 1 only if there is one diagnosis (n=1). The cost of each hospitalisation attributable to MM has been calculated by multiplying the estimated hospitalisation cost with the weight w_k (1), where k is the diagnosis ranking of MM in the corresponding data record. The total length of hospital stay was estimated by considering accesses of day hospitals as whole days (to split them was beyond the aim of the paper).

Data adjustment: tumours to mesothelioma weights

Since ICD-9 version does not include specific codes for MMs, each hospitalisation record has been weighted through an estimated fraction of MM among pleural, peritoneal and pericardial tumours. mesothelioma/tumour fractions by site, year, gender and age class (0–24, 25–34, 25–44, 45–54–55–64, 65–74, 75–84, 85+) have been estimated by using 2003–2016 Italian mortality data. Those data are coded through ICD-10 version containing specific codes for pleural (C45.0), peritoneal C(45.1) and pericardial (C45.2) MM. Remaining pleural, peritoneal e pericardial tumours have been extracted as codes C38.4 (pleural tumour other than MM), C48.1–2 (peritoneal tumour other than MM and Kaposi sarcoma) and C38.0 (cardiac and pericardial tumour other than MM and great vessels tumour), respectively. For years not covered by mortality data (2001–2002 and 2017–2018), we have considered estimates of the closest years (2003 and 2016, respectively).

Statistical analysis

Linear, quadratic and cubic variables time trends were evaluated by simple 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, we used orthogonal polynomials (poly function of *r*). For linear trends, the coefficient of the linear normal model has provided the estimated outcome variation for 1-year increment, the exponential function of the coefficient of the logistic model has provided the estimated OR of outcome for 1-year increment. For quadratic trends, the year of max or min value has been evaluated and for cubic trends years of local max and min value were assessed. 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 V.3.6.0 (Berthold *et al*, 2009).[27]

Linkage

Hospitalisations data have been linked with NSCs through DRG codes.

Patient and public involvement

There was no patient and public involvement in this study because it is based on hospital discharge data. European hospital data are regulated by Regulation 2016/679 of the European Parliament and they do not need informed consent.

RESULTS

Mortality data

In the period 2003–2016, the 82.8% of pleural tumours were a MM1. The percentage was higher for males than females (84,7% vs 78.3%), and for people aged 45–74 years (about 87%). There were zero deaths for MM1 under 25 years but five for other tumours (two of which were aged under 5 years). The 28.0% of peritoneal tumours (other than Kaposi sarcoma) were a MM2. The percentage was higher for males than females (43,2 vs 17.7%), and for people aged 25–74 years (about 36%). There were four deaths for MM2 under 25 years (one of which is recorded with age 5–9 years) and eight for other tumours (starting from 10 to 14 years). The 6.3% of hearth/pericardium tumours (other than great vessels cancer) were a MM3. The percentage was higher for males than females (7,8% vs 4.6%), and for people aged 45–54 years (about 20%). There were zero deaths for MM3 under 25 years and 5 for other tumours (one of which was an infant). Percentage of tumours other than MM by sites have been 55.9%, 39.0% and 5.1% for pleura, peritoneum and hearth/pericardium, respectively, corresponding percentages for mesothelioma have been 94.5%, 5.4% and 0.1%. The fractions of MMs by site, gender and age class can be found in online supplemental tables 1–3.

From tumour of pleura, peritoneum and hearth/pericardium to mesothelioma

In the period 2001–2018, Italian hospitals treated pleural or peritoneal or hearth/pericardium cancer in 157 221 admissions (0.08% of whole hospitalisations) of total length of 1 620 997 days (0.13% of whole hospitalisation time) and with a total cost burden (expressed in 2018 euros) equal to €633 064 845. Of these records about the 69% (108 449) treated a MM for a total length of 1 079 555 days (0.09% of whole hospitalisation time) and with a total cost (expressed in 2018 euros) equal to €422 616 004. There were 610 admissions (0.39%) treating tumours from multiple sites for a total time length of 6983 days (0.43%) and a total cost of €2 384 067. Among these records there were 179 admissions (0.11%) treating multiple MMs for a total time length of 2012 days (0.12%) and a total cost of €704 558. Percentage of hospitalisations by site have been 72.1%, 26.1% and 1.4% for pleura, peritoneum and hearth/pericardium tumours, respectively, the remaining 0.4% had multiple malignancies. Correspondent percentages for MM have been 87.8% for pleura, 11.4% for peritoneum and 0.1% for pericardium, multiple MM to pleura and peritoneum have been the 0.7%. Statistics of generic tumours by sites are presented in online supplemental tables 4–6 while in the following paragraphs we describe main results by site about MM related to the impact on the national health system (table 1), hospital characteristics (table 2) and costs (table 3) and most frequent hospital treatments (online supplemental table 7).

Hospitalisation with diagnosis of pleural mesothelioma

The 84% of pleural tumour treated by Italian hospitals were MM1s and the 73% of them refers to men. The number of records with primary or contributing diagnosis of MM1 was estimated as 95 912 (5 328 each year on average) for a total time length of 9 35 197 days (0.07% of total hospitalisations) and with an estimated overall cost of €365 287 197 (of which that attributable to MM1 was €195 077 128). Costs per hospitalisation with diagnosis of MM1 were €3809, of which those attributable to MM1

Table 1 Number and length of all hospitalisations and of those with primary or contributing diagnosis of mesothelioma

	Hospitalisations treating																	
	All			Pleural mesothelioma					Peritoneal mesothelioma					Pericardial mesothelioma				
Anno	n	Total LoS* (days)	LoS per Adm† (days)	n	Total LoS* (days)	LoS* Per Adm† (days)	Fraction of Adm† (x 10‡)	Fraction of LoS* (x 10‡)	n	Total LoS* (days)	LoS* Per Adm† (days)	Fraction of Adm† (x 10‡)	Fraction of LoS* (x 10‡)	n	Total LoS* (days)	LoS* Per Adm† (days)	Fraction of Adm† (x 10‡)	Fraction of LoS* (x 10‡)
2001	12582758	81571226	6.5	5493	55793	10.2	43.7	68.4	579	6658	11.5	4.6	8.2	0	0	0	0	0
2002	12569732	78538373	6.2	5693	55358	9.7	45.3	70.5	603	6693	11.1	4.8	8.5	0	0	0	0	0
2003	12430367	76681945	6.2	5417	52402	9.7	43.6	68.3	653	7379	11.3	5.3	9.6	0	0	0	0	0
2004	12592681	76910181	6.1	5783	54024	9.3	45.9	70.2	596	6854	11.5	4.7	8.9	32	286	8.9	0.3	0.4
2005	12573449	76997605	6.1	5767	55081	9.6	45.9	71.5	727	8215	11.3	5.8	10.7	23	216	9.4	0.2	0.3
2006	12432702	76523728	6.2	5818	55181	9.5	46.8	72.1	716	8234	11.5	5.8	10.8	0	0	0	0	0
2007	11915577	74873170	6.3	5810	54474	9.4	48.8	72.8	813	8862	10.9	6.8	11.8	0	0	0	0	0
2008	11677375	74004304	6.3	5792	54779	9.5	49.6	74	703	8225	11.7	6	11.1	0	0	0	0	0
2009	11238809	72073231	6.4	5873	56699	9.7	52.3	78.7	585	6903	11.8	5.2	9.6	27	462	17.1	0.2	0.6
2010	10869148	70607472	6.5	5649	55491	9.8	52	78.6	838	9469	11.3	7.7	13.4	2	44	21.8	0	0.1
2011	10347388	68159173	6.6	5766	55711	9.7	55.7	81.7	837	9626	11.5	8.1	14.1	18	155	8.6	0.2	0.2
2012	9851527	65446990	6.6	5375	53792	10	54.6	82.2	733	8723	11.9	7.4	13.3	0	0	0	0	0
2013	9450543	63101264	6.7	5014	50964	10.2	53.1	80.8	808	9534	11.8	8.5	15.1	15	211	14.1	0.2	0.3
2014	9140116	61939841	6.8	4980	49486	9.9	54.5	79.9	656	7938	12.1	7.2	12.8	0	0	0	0	0
2015	8930979	61366673	6.9	4527	45680	10.1	50.7	74.4	809	9546	11.8	9.1	15.6	2	20	9.8	0	0
2016	8697574	60129816	6.9	4620	46662	10.1	53.1	77.6	671	7381	11	7.7	12.3	0	0	0	0	0
2017	8522456	58896885	6.9	4271	41956	9.8	50.1	71.2	636	7250	11.4	7.5	12.3	0	0	0	0	0
2018	8357575	58528814	7	4264	41664	9.8	51	71.2	633	7533	11.9	7.6	12.9	0	0	0	0	0
Overall	10787820	69797261	6.5	5328	51955	9.8	49.4	74.4	700	8057	11.5	6.5	11.5	7	77	0.1	0.1	0.1
Trend L§	–	–	–	–	–	–	–	–	–		–	–	–	–	–	–	–	–
Trend Q¶	–	–	–	2006 (max)	2007 (max)	–	–	–	2010 (max)	2011 (max)	–	–	–	–	–	–	–	–
Trend C‡	2003 (max), 2018 (min)	2001 (max), 2018 (min)	2017 (max), 2005 (min)	–	–	2015 (max), 2006 (min)	2013 (max), 2001 (min)	2013 (max), 2002 (min)	–	–	–	2015 (max), 2001 (min)	2014(max), 2001 (min)	–	–	–	–	–

Italy 2001–2018.
*Accesses of day hospitals are considered as whole days.
†Adm: Hospital admission.
‡Trend C means cubic trend. Years of local max and min values are reported when the cubic trend was significant.
§Trend L means linear trend. It represents annual variation for continuous variables (evaluated as coefficients of linear normal regression model) and 1-year increment OR for percentages (evaluated as exponential function of logistic regression model). Values are reported if linear trend is significant.
¶Trend Q means quadratic trend. Years of max or min values are reported when the quadratic trend was significant.
LoS, length of stay.

Table 2 Characteristics of hospital discharge data with primary or contributing diagnosis of mesothelioma

	Hospitalisations treating																	
	Pleural mesothelioma						Peritoneal mesothelioma						Pericardial mesothelioma					
Anno	Males (%)	Age* (SD)	Mort (%)	DH (%)	Sur (%)	Urgent Adm(%)	Males (%)	Age* (SD)	Mort (%)	DH (%)	Sur (%)	Urgent Adm (%)	Males (%)	Age* (SD)	Mort (%)	DH (%)	Sur (%)	Urgent adm (%)
2001	69.8	66.3 (11.1)	9.0	28.4	17.0	31.1	50.8	61.9 (10.9)	7.9	21.4	29.0	28.0	0	0 (0)	0	0	0	0
2002	71.8	66.2 (10.7)	8.0	27.4	17.2	30.5	46.6	60.4 (12.7)	7.5	20.4	31.2	26.9	0	0 (0)	0	0	0	0
2003	71.0	66.4 (10.7)	8.7	30.0	17.5	28.6	49.6	60.6 (13)	8.6	20.2	30.8	28.2	0	0 (0)	0	0	0	0
2004	72.6	66.2 (10.8)	7.7	30.6	18.0	27.8	55.5	64.4 (9.7)	8.1	23.8	30.5	27.7	90.6	47.5 (12.9)	9.4	6.2	34.4	34.4
2005	72.0	67.1 (10.2)	8.6	29.9	18.9	30.4	60.7	65.7 (8.3)	9.2	24.8	29.4	28.5	0	50.7 (9.2)	4.3	4.3	17.4	47.8
2006	72.1	67.7 (9.9)	9.0	30.8	19.1	31.8	65.1	63.2 (10.5)	8.4	21.5	30.0	32.3	0	0 (0)	0	0	0	0
2007	73.1	68.1 (9.9)	8.5	30.6	20.1	32.8	59.5	61.7 (12.3)	7.5	22.4	28.9	30.1	0	0 (0)	0	0	0	0
2008	71.7	68.6 (9.8)	8.6	31.8	20.5	32.0	58.0	62.6 (12.1)	8.1	19.3	33.3	33.1	0	0 (0)	0	0	0	0
2009	72.2	69.1 (9.4)	8.8	31.2	21.2	33.4	66.0	65.5 (10.7)	10.8	22.9	32.1	35.7	100.0	58.1 (13.3)	11.1	11.1	18.5	51.9
2010	71.9	69.2 (9.5)	9.1	30.9	23.0	34.3	60.6	60.2 (17.1)	8.5	18.7	36.3	36.8	0	70.2 (15.1)	0	0	50	100
2011	72.9	69.3 (9.8)	8.6	32.3	23.6	34.5	60.8	62.9 (16.1)	9.4	18.3	34.6	34.9	55.6	56.6 (7.2)	11.1	11.1	22.2	44.4
2012	72.9	70.2 (9.8)	9.1	25.2	26.0	37.6	53.8	65.6 (13.3)	12.7	15.8	36.0	41.1	0	0 (0)	0	0	0	0
2013	75.1	70.6 (9.9)	8.4	23.1	29.3	41.2	51.7	66.1 (11.7)	10.5	17.2	38.1	40.0	40.0	57.9 (10.8)	0	13.3	26.7	46.7
2014	73.5	70.9 (9.8)	8.6	24.6	27.5	41.9	61.7	65.2 (12.8)	8.7	15.5	37.8	42.4	0	0 (0)	0	0	0	0
2015	74.0	71.4 (9.7)	8.7	23.3	29.4	41.4	58.3	65.8 (11.5)	8.4	15.6	40.0	43.8	100.0	71.7 (16.6)	0	0	50	100
2016	74.7	71.8 (9.7)	8.6	23.4	28.6	45.3	58.1	65 (14.3)	9.7	16.2	37.6	44.0	0	0 (0)	0	0	0	0
2017	73.5	71.9 (9.8)	8.7	17.7	32.7	46.4	60.2	67.7 (12.5)	10.7	13.5	36.2	48.6	0	0 (0)	0	0	0	0
2018	73.0	72.6 (10.0)	9.7	15.7	31.7	47.3	60.5	66.7 (13.4)	8.8	12.8	41.1	48.0	0	0 (0)	0	0	0	0
Overall	72.6	68.9 (10.1)	8.7	27.5	22.9	35.4	57.8	63.9 (12.6)	9.1	18.8	34.2	36.2	61.9	54.1 (12.9)	8.2	8.3	25.8	45.5
Trend L†	1.009 (1.007–1.012)	0.40 (0.38–0.42)	1.004 (0.999–1.008)	–	–	–	–	0.30 (0.15–0.46)	1.015 (1.003–1.028)	–	–	1.061 (1.053–1.068)	–	–	–	–	–	–
Trend Q‡	–	–	–	2007 (max)	–	–	–	–	–	2003 (max)	–	–	–	–	–	–	–	–
Trend C§	–	–	–	–	2018 (max), 2001 (min)	2018 (max), 2004 (min)	2018 (max), 2001 (min)	–	–	–	2017 (max), 2003 (min)	–	–	–	–	–	–	–

Italy 2001–2018.
*Age: Mean age at discharge.
†Trend L means linear trend. It represents annual variation for continuous variables (evaluated as coefficients of linear normal regression model) and 1-year increment OR for percentages (evaluated as exponential function of logistic regression model). All reported estimates are significant at level 0.05% but pleural mortality significant at level 0.1%.
‡Trend Q means quadratic trend. Years of max or min values are reported when the quadratic trend was significant at level 0.05%.
§Trend C means cubic trend. Years of local max and min values are reported when the cubic trend was significant at level 0.05%.
Adm, hospital admission; DH, day hospital; Mort, mortality; Sur, surgery.

Table 3 Estimates of hospitalisation charges for mesothelioma

Anno	Hospitalisation cost (€) with diagnosis of mesothelioma of			Hospitalisation cost (€) attributable to mesothelioma of			% of Hospitalisation cost attributable to mesothelioma of			Hospitalisation cost (€) per admission with diagnosis of mesothelioma of			Hospitalisation cost (€) per admission attributable to mesothelioma of		
	Pleura	Perit*	Peric†	Pleura	Perit*	Peric†	Pleura	Perit*	Peric†	Pleura	Perit*	Peric†	Pleura	Perit*	Peric†
2001	20223304	2532890	0	11094535	1136504	0	54.9	44.9	0	3681	4375	0	2020	1963	0
2002	21144886	2653368	0	11314360	1176537	0	53.5	44.3	0	3714	4400	0	1987	1951	0
2003	19328690	2907455	0	10515594	1214095	0	54.4	41.8	0	3568	4452	0	1941	1859	0
2004	20452140	2586514	191378	10965439	1091887	111080	53.6	42.2	58	3537	4340	5981	1896	1832	108
2005	20301536	2958048	115233	10596568	1254562	58561	52.2	42.4	50.8	3520	4069	5010	1838	1726	111
2006	20240936	3052340	0	10755613	1273450	0	53.1	41.7	0	3479	4263	0	1849	1779	0
2007	20011399	3233579	0	10773848	1361108	0	53.8	42.1	0	3445	3977	0	1855	1674	0
2008	19659283	3011275	0	10496263	1259097	0	53.4	41.8	0	3394	4283	0	1812	1791	0
2009	20659088	2467318	203290	10786755	1025048	83990	52.2	41.5	41.3	3518	4218	7529	1837	1752	115
2010	20257708	3750112	20785	10663559	1574573	12782	52.6	42	61.5	3586	4475	10393	1888	1879	3195
2011	20252590	3575820	83990	10380127	1466554	48689	51.3	41	58	3512	4272	4666	1800	1752	150
2012	22293654	3608652	0	11881410	1431419	0	53.3	39.7	0	4147	4923	0	2210	1953	0
2013	21589272	3939249	99179	11483805	1590340	55012	53.2	40.4	55.5	4306	4875	6612	2291	1968	244
2014	20741988	3339080	0	11273818	1302858	0	54.4	39	0	4165	5090	0	2264	1986	0
2015	19649497	4137475	14128	10693633	1635108	7226	54.4	39.5	51.1	4341	5114	7064	2362	2021	1806
2016	20140721	3223086	0	10742186	1322716	0	53.3	41	0	4359	4803	0	2325	1971	0
2017	19178015	3052951	0	10108962	1172638	0	52.7	38.4	0	4490	4800	0	2367	1844	0
2018	19162490	3276171	0	10550653	1310375	0	55.1	40	0	4494	5176	0	2474	2070	0
Overall	20293733	3183632	40443	10837618	1311048	20963	53.4	41.2	51.8	3809	4549	6117	2034	1874	3171
Trend L‡	–	56019 (21404–90635)	–	–	14924 (-19692–49539)	–	–	–	–	–	–	–	–	–	–
Trend Q§	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Trend C¶	–	–	–	–	–	–	2001 (max) 2009 (min)	2001 (max) 2018 (min)	–	2018 (max) 2005 (min)	2017 (max) 2005 (min)	–	2018 (max) 2006 (min)	2017 (max) 2006 (min)	–

Italy 2001–2018.
*Perit: Peritoneum.
†Peric: Pericardium.
‡Trend L means linear trend. It represents annual variation for continuous variables (evaluated as coefficients of linear normal regression model) and 1-year increment OR for percentages (evaluated as exponential function of logistic regression model). Total cost for peritoneum was significant at level 0.05% while the attributable one at 0.1%.
§Trend Q means quadratic trend. Years of max or min values are reported when the quadratic trend was significant at level 0.05%.
¶Trend C means cubic trend. Years of local max and min values are reported when the cubic trend was significant at level 0.05%.

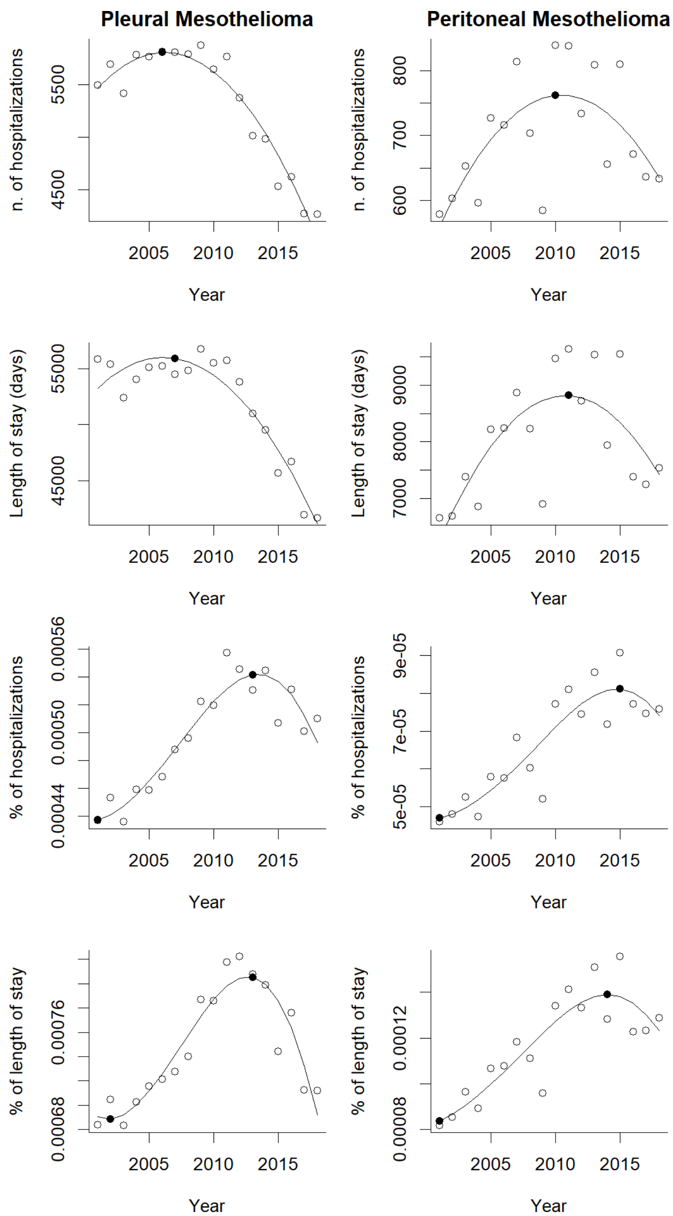

Figure 1 Number and length of hospitalisations of mesothelioma with corresponding percentages. Italy 2001–2018.

were €2034. Hospitalisations with surgical procedures (23%) were three times more expensive than others (€7831 vs €2616). The 1.1% of admissions treated patients with extrapleural pneumonectomy (ICD-9-CM procedure code: 32.5) and cost €11 009 on average, the 1.8% performed pleural decortication (ICD-9-CM procedure code: 34.51) and cost €9719. The 4.2% of records reported other excision of pleural (ICD-9-CM procedure code: 34.59) and cost €9559 on average, the 14.6% reported transpleural thoracoscopy (ICD-9-CM procedure code: 34.21) with a mean cost of €6964. Hospitals used chemotherapy (ICD-9-CM procedure code: 99.25) in 24.7% of admissions with a mean cost of €1665 and radiotherapy (ICD-9-CM procedure code: 92.2) in 0.8% of records with a mean cost of €3438. Estimated curves of number and of length of hospitalisations increased until 2006–2007, then decreased. Corresponding curves of percentages show the same behaviour but reached their peak in 2013 (figure 1). Annual total and attributable costs of MM1 hospitalisations are decreasing after 2012, while cost per admissions increased from €3681 in 2001 to €4494 in 2018. Mean age at discharge increased of 5 months per year, urgent cases (from 2004) and surgical procedures (from 2001) also increased.

Hospitalisation with diagnosis of peritoneal mesothelioma

The 30% of peritoneal tumours treated by Italian hospitals were MM2s, of these about the 60% refers to men. The number of records with one diagnosis of MM2 was estimated as 12 596 (700 each year on average) for a total time length of 145 023 days (0.01% of total hospitalisations) and with estimated overall costs of €57 305 383 (of which those attributable to MM2 were €23 598 869). Costs per hospitalisation with diagnosis of MM2 were €4549 on average, of which those attributable to MM2 were €1874. Hospitalisations with surgical procedures (34%) cost more than three times than others (€8241 vs €2638 per admission on average). Records with excision or destruction of peritoneal tissue (ICD-9-CM procedure code: 54.4) were the 11.1% of the total with a mean cost of €8172 on average, those with other partial resection of small intestine (ICD-9-CM code: 45.62) were the 2.8% and cost €10 816. Exploratory laparotomy (ICD-9-CM code: 54.11) was reported in 5.6% of records with a mean hospitalisation cost of €7965, laparoscopy (ICD-9-CM procedure code: 54.21) was reported in 6.3% of admissions which cost €6686 on average. Chemotherapy (ICD-9-CM procedure code: 99.25) was used in 22.9% of records which cost €2393 on average, radiotherapy (ICD-9-CM procedure code: 92.2) was used in 0.4% of records which cost €3440. As shown in figure 1, hospitalisations decreased in frequency (2010), length (from 2011) and in corresponding percentages from 2014 to 2015. Annual total and attributable costs increased of €56 000 and €15 000 per year on average, respectively. Mean age at discharge (+4 months per year) and ODDS of urgent cases (OR=1.06) and mortality (OR=1.02) linearly increased. Percentage of day hospital decreased from 2003.

Hospitalisation with diagnosis of pericardial mesothelioma

The 5% of heart tumours treated by Italian hospitals were MM3. The number of records with one diagnosis of MM3 was estimated as 119 (7 each year on average) for a total time length of 1394 days (0.0001% of total hospitalisations) and with an estimated overall costs of €727 983 (of which those attributable to MM3 were €377 340). Costs per hospitalisation were €6117, of which those attributable to MM3 were €3171. About 62% of hospitalisations refers to men, the mean age at discharge was 54 years, almost 50% of times patients were admitted as urgent cases and 26% received surgical treatments. Hospitalisations with surgical procedures (26%) were five times more expensive than others (€15 282 vs €2984 per admission on average). The 12.8% of records treated patients with excision or destruction of other lesion or tissue of heart, open approach (ICD-9-CM procedure code: 37.33) and cost €17 002 on average, the 4.4% performed pericardiocentesis (ICD-9-CM procedure code: 37.0) and cost €8152, the 2.9% reported pericardiotomy (ICD-9-CM procedure code: 37.12) and cost €12 128. The 21.8% of admissions reported chemotherapy (ICD-9-CM procedure code: 99.25) as treatment and cost €2341 on average, the 1.8% reported radiotherapy (ICD-9-CM procedure code: 92.2) and cost €3847.

DISCUSSION

In the last century, Italy was a strong asbestos miner and the amount of mineral production and consumption (yearly about 1.11 and 1.31 kg per resident, respectively, in the period 1920–1992) caused about 29 000 deaths by MM1 between 1970 and 2014.[28 29] Despite the national asbestos ban established in the 1992, the long latency of asbestos related diseases makes them still a significant issue. This study investigate Italian hospital discharge data with diagnosis of MM, in order to estimate hospitals costs and to provide a picture of the disease evolution recorded by the Italian Health System.

Mortality data have provided estimates about the portions by site of MM among tumours. As described in,[28] MM1 is the main pleural tumour (84%) and among the remaining ones (ICD-10=C38.4) there could be other MM1s because of misclassifications (diagnostic procedures are invasive and could not be tolerated by oldest people). MM2 accounts for less than one third of peritoneal tumours and MM3 is extremely rare (5% of hearth tumours).

As already highlighted for asbestosis[23 24] and consistently with Italian industrial history, hospitalisations concerning MM are strongly connected with specific industries with a very high prevalence of males and concentrated in the north-west of the country (data not shown in a table).

In 2001–2018, Italy spent €420 000 000 for hospitalising MM cases, annual charges were about €20 000 000 for patients with diagnosis of MM1, €3 000 000, for those with diagnosis of MM2 and about €40 000 for those with diagnosis of MM3. MM3 is the most expensive with a cost higher than €6100 per admission followed by MM2 (€4500 per admission) and MM1 (€3800 per admission). On average, MM accounted for half of the whole hospitalisation cost (in peritoneum cases percentage slowed down to 40%). Surgical procedures were used frequently (one out of four admissions treating MM1 and MM3 and one out of three treating MM2) and increased hospital charges from 3 (€8000 vs €2500 for MM1 and MM2) to five times (€15 000 vs €3000 for MM3). The increased use of surgery explains at least in part the increased cost per admission. Several studies investigated the social burden of mesothelioma, someone focused on years of life lost and years of potential life lost[30] others (like this) on the hospitalisation cost.[31–35] Even if direct comparisons are not possible because of different economies and financial management of hospitals between countries, we have found very similar ratios between mean hospital costs by surgical procedures with a recent American work[35] (table 2).

If the 1992 asbestos ban has been effective, we should observe decreasing time-trends in number and percentage of annual hospitals admissions from 20 to 25 years (the 5th percentile of MM latency[1]) later and older patients over time because the effects on disease incidence are quicker on younger ages (associated with shorter latency). First expectation is in line with time-trends in hospital admissions. While grand totals of 2001–2018 hospitalisations reached their maximum in 2003 (then strongly decreased year after year), hospitalisations (in number and length of stay) and their percentages with diagnosis of MM1 increased until 2006–2008 and 2013, respectively, before decreasing in the remaining years. Number and percentages of hospitalisations with diagnosis of MM2 reached their maximum later (2010–2011 and 2014–2015, respectively), with a very similar evolution. The second expectation is satisfied by the following time trends: the mean age at discharge increased of 0.4–0.5 months per year, the percentage of day hospital decreased from 2003 to 2007 and the urgent cases doubled for MM2; the costs per admission were increasing while the percentage of costs attributable to MM2 were decreasing. It would seem that hospitals treated over time older patients with more comorbidities (especially in MM2 cases) and needing more assistance.

This paper has several limitations. First, Italian hospitals record patients diagnoses thorough ICD-9-CM codes (that do not include specific codes for MMs), adjustments though mortality data (coded by ICD-10) for estimating the fractions by site of MM among tumours have been necessary. Second, data do not contain a patient identifier code so we could not assess the true number of cases nor analyse hospitalisations evolution of the same patient (however, this does not affect costs estimates nor general trends). Finally, time trend analysis for MM3 was not performed because of the very low disease rate.

In 2018 (ie, 27 years after the ban), we counted 4891 hospitalisations treating MM, for a total time length of 48 910 days and with a total cost of 22 413 853. In the future, hospitals will probably treat fewer but older patients, with a more severe course of disease. To study the prevalence of the disease may help National health system to manage the MM epidemic for the next decade, when the peak in mortality is expected.[28] Italian experience about exposures to asbestos fibres leaves a valuable awareness, Public Health Institutions of countries still producing or using asbestos should use these results to make pressure for establishing a national asbestos ban.

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