Journal of Community Medicine & Public Health
Petrarca C, et al. J Community Med Public Health 8: 450
www.doi.org/10.29011/2577-2228.100450
www.gavinpublishers.com

OPEN ACCESS

GAVIN PUBLISHERS

Research Article

Asbestos-Related and Non-Communicable Diseases in Formerly Exposed Workers: Relationship with Residential Asbestos, Smoke and Business Sector

Claudia Petrarca[1,2*], Davide Viola[1], Andrea Resta[2], Luca Di Giampaolo[2,3], Hiroo Wada[4]

[1]Department of Medicine and Aging Sciences, "G. d'Annunzio" University, Chieti-Pescara, Italy

[2]Specializing Post-graduation School of Occupational Medicine "G. d'Annunzio" University, Chieti-Pescara, Italy

[3]Department of Innovative Technologies in Medicine and Dentistry, "G. d'Annunzio" University, Chieti-Pescara, Italy

[4]Department of Public Health, Graduate School of Medicine, Juntendo University Tokyo Japan

[*]**Corresponding author:** Claudia Petrarca, Department of Medicine and Aging Sciences, "G. d'Annunzio" University, Chieti-Pescara, Italy

Hiro Wada ORCID: https://orcid.org/0000-0002-0752-3790

Claudia Petrarca ORCID: https://orcid.org/0000-0002-6910-0160, Scopus Author ID: 7004208483 SciProfiles: 1410649

Citation: Petrarca C, Viola D, Resta A, Di Giampaolo L, Wada H (2024) Asbestos-Related and Non-Communicable Diseases in Formerly Exposed Workers: Relationship with Residential Asbestos, Smoke and Business Sector. J Community Med Public Health 8: 450. DOI: https://doi.org/10.29011/2577-2228.100450

Received Date: 10 July, 2024; **Accepted Date:** 18 July, 2024; **Published Date:** 23 July, 2024

Abstract

Purpose: Asbestos-containing materials are found in industries as raw materials and in the living environment as dispersed waste. There is a need to assess the impact of non-dusty low-level compact asbestos on health in different job settings and whether other risk factors could synergize. To characterize the whole disease outline (deadly/non-deadly/disabling) of workers at risk of asbestos exposure. To discern the role of smoke and extra-work asbestos on the outcomes. To discern the role job type on the risk of ARD and diseases potentially associated.

Methods: A retrospective observational cohort study was performed. A broad research database was generated with anamnestic, job and diagnostic data of past asbestos workers (N=108). An epidemiology database was built up to evaluate comparatively the plausibility and novelty of our findings. RR were calculated for disease/category of disease in relation to residential asbestos, smoke and occupational groups/businesses to evaluate the predictivity of associations. **Results:** Pleural plaques, asbestosis, prostate cancer and lung nodules occurred at a significantly higher rate than generally observed. Respiratory/metabolic diseases were more frequent in our cohort than expected. ARD occurrence was not modified by exposure to residential asbestos or smoke. Manufacturing jobs were at higher risk of ARD and respiratory diseases. Production workers were at higher risk of metabolic syndrome. **Conclusions**: The processing manner of ACM is critical for the release of (few) inhalable fibres and the asbestos-related pathological consequences. Our findings are of concern for workers and residents of poorly managed settings engaged by industrial or natural erosion of ACM.

Keywords: ARD; Asbestos; Communicable; Diabetes; Environment; Lung; Nodules; Pleural; Prevention; Prostate; Respiratory; Cancer; Workers

Introduction

Even though asbestos as mining dusty crushed product has been banned by law from industrial processes in many Western countries since the nineties, the prevention and early detection of Asbestos-Related Diseases (ARD) in ex-exposed workers is still a pertinent goal of occupational medicine. Occasions of asbestos exposure still might occur for various jobs in workplaces worldwide, in the contemporary time [1]. ARD and its symptoms negatively affect the quality of life of workers and cause work discontinuation, work disability, and death. The diagnosis procedure is complex because of overlapping of signs/symptoms with other non-asbestos lung diseases. This is a restraint for the early detection, management, and right to compensation for occupational diseases. Former asbestos-exposed workers appear healthy during most of their lives and, thereof, are careless of their health condition unless suffering from physical dysfunction or symptoms. ARD mortality has been declining in countries where asbestos ban regulation was applied, such as in Italy and other European countries. Even in these protected working populations, there are identifiable groups at higher prevalence of ARD. For instance, individuals processing asbestos-containing materials are filed at risk of contracting ARD in a lifetime by the national worker's protection agencies, such as INAIL in Italy. More difficulty for medical and compensative aims is to distinguish between workplace exposure and/or exposure to naturally occurring asbestos (NOA). The ARD long latency makes unfeasible for the occupational health professionals to follow up with workers. Effect modifiers of asbestos toxicity such as sex, age [2], smoke status [3], workplace-, homeplace distance- presence of friable manufactures (ruined dwellings, canopies) [4], are more factors for risk assessment and public health preventive measures, too. Non-irrelevant levels of risk of work-related ARD have been shown for various contemporary workers' groups [5] (Table S1). Besides malignant mesothelioma, low-to-intermediate intensity of exposure, (i.e. <0.5 f/cc/0.1 ff/l, per year) has been associated to increased risk of lung cancer and (non-pleural) related death [6]. The risk of exposure to free asbestos cannot be excluded in the surrounding areas where are ACM (asbestos-containing materials), such as cement products [7]. Studies conducted on smokers have shown that asbestos is a multiplicative risk factor of lung cancer [8]. Epidemiological data showed that there is not a safe exposure limit and that the risk of ARD is proportional to the number of inhaled fibres. Hence, a higher relative risk of asbestos exposure is assumed for the workers, compared to the general population. Nowadays, (relatively) low amounts of breathable free fibres, not innocuous, could be released in the workplace from asbestos-containing materials (ACMs). For instance, detachment of free fibres can occur for tangential forces during the transformation processes, manoeuvres on friable materials, or moisture infiltration. Waste ACMs are given all over the national territory and still undisposed in the industry and in the living environment. Such current public harm needs to be secured by specialized workers. Asbestos is still found in industry plants in oven and pipes being potential exposure source for non-ACM workers, too [9]. It is of utmost importance to improve our knowledge of what impact non-dusty asbestos might have on health and whether other risk factors play a multiplicative/exacerbating role in the pathogenesis of ARD. Conversely, whether asbestos might influence the non-ARD pathologic outcome triggered by other chemical risk factors in the workplace. To elucidate the health status after 20 years (at admission and post-retirement) observation in the former workers of several firms of two automotive businesses, we conducted a health surveillance protocol to show ARD promptly in a cohort of former asbestos workers of the Abruzzi region of Italy. All the enrolled subjects lived in Abruzzi, a small rural region of central Italy where environmental exposure to Naturally Occurring Asbestos (NOA) is minimal [10]. We characterized this cohort thoroughly also to detect disabling/enabling conditions, known to affect productivity and potentially compensable. Furthermore, the data were analysed for the task, residential asbestos, and smoke to catch the predictivity of associated features.

Subjects and Methods

We performed a retrospective cohort analysis of the association between occupational exposure to asbestos and incident diseases, either pulmonary (ARD/respiratory) and extra-pulmonary (ARD or non-ARD). The study cohort consisted of ex-workers of the automotive sector of two different businesses, manufacturing and production. Description of the occupational groups and specific tasks and their numerosity of the Manufacturing and the Production sectors of employment are detailed in Table S2. Comparative analyses were performed between different pairs of complementing sub-cohorts of workers anthropometrically alike. Our population of ex-workers showed homogenous relevant characteristics of interest for this study (Table 1). Besides, the contribution of extra-occupational asbestos and smoke to disease risk were analyzed.

Clinical findings	**Etiopathogenesis**	**Worker** (this study)	**Reference population** (bibliographic sources)			**Statistics**		
	Role of asbestos	N. of cases / N. of workers (%)	N. of cases / N. of residents (%)	N. of residents	Reference	Incidence Ratio (IR)	95% CI	*P*
Pleural plaques	Yes	8 (7.4)	31 (1.9)	1570 Italian males (0 cases in Abruzzi)	[11]	3.7515	1.4899 to 8.343	0.0037
Asbestosis	Yes	3 (2.7)	19* (0.0019)	1,000,000* Centre regions	[12]	1462.0	277.09 to 4966.5	<0.0001
Colorectal carcinoma	Yes	3 (2.7)	45 (0.045)	100,000 Molise region§	[13]	61.728	12.271 to 192.29	<0.0001
Prostate cancer	Yes	3 (2.7)	86-159 (esteem) (0.08-0.15)	100,000 Italian	[14-15]	17.470	3.5649 to 51.989	0.0008
			1,114 (1.1)	295,624 Italian		7.3714	1.5179 to 21.598	0.0092
			4480 (1.7)	262,210 Abruzzi (males 45-75 y)		1.6258	0.3352 to 4.7544	0.3977
Larynx carcinoma	Yes	1 (0.9)	89 (0.089)	100,000 Italian	[14]	10.404	0.2605 to 59.476	0.0969
Malignant nodules (lung)	Yes	11 (10.1)	14 (14)	100 Occupationally exposed Italian workers	[16]	0.7275	0.2989 to 1.7250	0.4369
MGUS	Likely pre-malignant ARD	4 (3.6)	1334-2668 (3-6)	44,474 Italians (>50 y)	[17]	1.2348-2.4	0.3359 to 3.168	0.6333
MDS	Likely pre-malignant ARD	1 (0.9)	3–5 (0.003-0.005)	1,000 Lazio region (2002-2012)	[18]	3.0864	0.05879 to 38.439	0.3864
COPD	Plausible asbestosis-related	6 (5.5)	(4-50)	100 Elderly smokers	[19]	1.3889 0.1111	0.3294 to 6.6916 0.03893 to 0.2593	0.6303 < 0.0001
Thyroid nodules, hypothyroidism	Some evidence not conclusive	1 (0.9)	(0.02-0.04)	100 Italians	[20]	46.296	0.7847 to 889.31	0.0321

Benign prostate hyperplasia (BPH)	Never described as ARD	22 (20.4)	3380 (3.4)	100.000 Italians	[21]	6.2304	4.2848 to 9.0595	<0.0001
Metabolic syndrome	Never described as ARD	72 (66.7)	(21)	100 Italians	[22]	3.1746	1.9299 to 5.4360	< 0.0001
			(25)	100 Italians > 70 y		2.6667	1.6711 to 4.3879	< 0.0001
Hypertension	Never described as ARD	50 (46.3)	(10)	Italians		4.6296	2.3204 to 10.239	< 0.0001
Type 2 diabetes	Never described as ARD	18 (16.7)	400,000-750,000 (4.0-6.6)	11,000,000-12,000 Abruzzi/Tuscany region 69±15 y	[23]	2.6907	1.4883 to 3.9689	0.0006

*Hospitalizations for asbestosis in 15 years (2001-2015)
§ formerly part of Abruzzi region

Table 1: Health surveillance relevant clinical findings of the former asbestos Abruzzi workers are shown with the etiopathogenetic role of asbestos, the occurrence among several Italian national and regional reference populations, and the statistic results.

Study population

A representative sub-cohort of the retired past-asbestos exposed workers of Abruzzi, a low populous region in Central Italy, was enrolled in 2019. They were 64-65 years old and had worked for a period of 20 years without discontinuation, from 1971 till 1998, in automotive production and induced plants settled in the same region. A data set was gathered for each ex-worker through interviews, specific questionnaires, and risk-oriented clinical assessments. The subjects, all males, were considered eligible if seemingly healthy, not affected by chronic disease (except diabetes) nor recent acute seasonal disease, not employed in other jobs at risk of occupational exposure to asbestos. Questionnaires were compiled by the occupational physician during workers' interview to assess anthropometric values, occupational title, job duration, first year of employment, year of retirement, plant, plant location, home location, business sector, homeplace location, smoking habits, and extra-occupational sources of exposures to asbestos. Female workers were not included in this study. Our study population was evaluated against demographic groups of reference, which were selected for geographic proximity, wok exposure, age, sex, and year of survey from published data (Google, PubMed) (Table 1) (Figure 1).

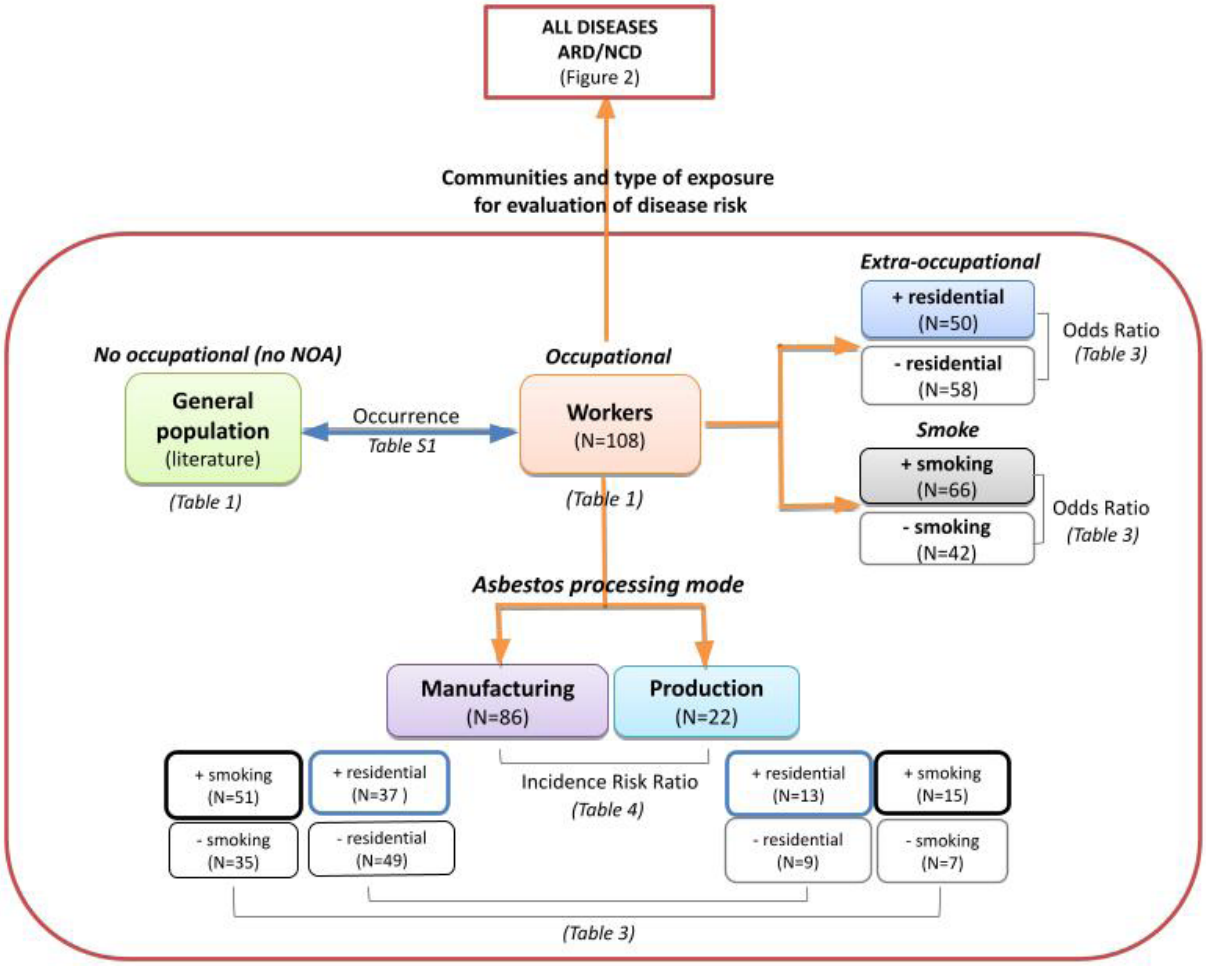

Figure 1: Study design.

Exposure attribution

All automotive employees in Abruzzi, including the one hundred-eight consecutive ex-workers who voluntarily joined the active health surveillance program of our O.U. of Occupational Medicine, had been previously classified at high Relative Risk of asbestos exposure for their business's groups and occupational titles by the regional workers' insurance institute INAIL and reviewed by us according to OSHA guidelines (OSHA, 2012). Two sub-cohorts of them were classified based on the smoking status as current/past smokers since at least 10 years (smoker), and never smokers (non-smokers). Other two categories were formed by one-sub-cohort declaring potential exposure to non-occupational asbestos sources, being resident in proximity of roof, chimney, garage, tank, and canopy (confirm), and the complementary sub-cohort denied (deny).

Pulmonary and extra-pulmonary disease outcomes

A data set was gathered for each ex-worker through interviews, questionnaires, and risk-oriented clinical assessments. The subjects were considered eligible if seemingly healthy, not affected by chronic disease nor acute seasonal disease within the month preceding the recruitment, not employed in other jobs at risk of occupational exposure to asbestos. Conclusive diagnosis and medical reports of diseases were made by specialized physicians based on the results of routine laboratory exams, lung function spirometry, echography, standard radiological examinations and/or HR-CT scans of the thorax performed on each recruited ex-worker. Diagnostic findings were blind checked by OM physicians of our group who categorized them as pulmonary disease or extra-

pulmonary disease. Dysplastic lesions without evidence of active ARD were considered pre-malignant ARD lesions. Digital images of all clinical items were stored in the OM online repository (https://www.myqnapcloud.com/home?lang=it). The occurrence of each disease in the whole cohort of ex-workers was evaluated for incidence rate and plausibility against the occurrence of each of the diseases among demographic groups of reference considered for geographic proximity/correspondence and year of our survey, found by extensive search of published data (Google, PubMed) (Table 1 and Figure 1). Categorical/numerical databases were built up from the row clinical data for further statistical analysis of matched occupational-clinical aggregated datasets.

Statistical analysis

Descriptive analysis was carried out using median and interquartile range (IQR) for quantitative variables or using frequencies and percentages to describe the qualitative variables. Normality distribution was tested by the Shapiro-Wilk test. To evaluate relationships between qualitative variables a Pearson chi square test e/o Fisher test was assessed. For quantitative variables, the Wilcoxon rank-sum (Mann-Whitney) test was used to find the differences between median values among the two different sub-cohorts of workers with three different exposure risk factors for the outcomes of interest, which are the exposure to residential asbestos, tabagism and processing modality of the asbestos-containing materials at workplace. Crude odds ratio (ORs) and corresponding 95% CI were calculated to quantify the risk associated with residential asbestos, or tabagism, or task/business features and clinical findings (disease, dysfunction) using the Wald test. Relative Risk (RR), and corresponding 95% CI, of occurrence of disease (ARD, or respiratory, or metabolic) between two sub-cohorts of workers (Manufacturing and Production) were calculated. Statistical significance was set at the $p<0.05$ level. All analyses were performed using 2024 MedCalc Software Ltd.

Results

Health surveillance findings

The ex-workers participating to the study (N=108) were free of mesothelioma and lung cancer at surveillance visit, in 2019. Compared to the (closest) age- and year-matched reference groups, pleural plaques (N=8) (IRR=3.7; 95% CI: 1.4899-8.343; p=0.0037), asbestosis (N=3) (IRR=1462.0; 95% CI: 277.09-4966.5; p<0.0001), colorectal carcinoma (N=3) (IRR= 61.7; 95% CI: 12.271-192.29; p<0.0001) and prostate cancer (IRR=17.470; 95% CI: 3.5649-51.989; p<0.0008 and IRR=7.3714; 95% CI: 1.5179-21.598; p=0.0092) occurred at significantly higher rates in our cohort (Table 1). Pulmonary nodules (N=11) incidence rate was slightly higher in our cohort (IRR=0.7275, 95% CI: 0.2989-1.7250) or seemingly much higher for larynx carcinoma (N=1) (IRR=10.404) and thyroid nodules (N=1) (IRR=46.2964 95% CI: 0.7847-889.31; p=0.031) (Table 1). Haematological disorders/malignancies such as MGUS (N=4), at an incidence rate slightly higher (IRR=1.2348-2.4; 95% CI: 0.3359 to 3.168), and MDS (N=1) (IRR=3.0864; 95% CI: 0.05879-38.439). Former asbestos workers were affected by one or more dysmetabolic signs including hypertension (N=50), hypercholesterolemia (N=25), hyperglycaemia (N=1), hypertriglyceridemia (N=2) hyperuricemia (N=10), glaucoma (N=4). Type-2 diabetes (N=18) and cardiovascular diseases as ischemic diseases (N=2), OSAS (N=2), venous thrombosis (N=1), all promoted by the above-mentioned conditions, were accordingly diagnosed, too. Overall, metabolic syndrome (N=72) was detected at significantly higher rate in our cohort (IRR=3.1746; 95% CI: 1.9299-5.4360; p<0.0001 vs. Italians; IR=2.6667; 95% CI: 1.6711-4.3879; p<0.0001, vs. over-70 patients). Hypertension (IRR=4.6296; 95% CI: 2.3204-10.239, p<0.0001). T2D incidence was significantly higher (IRR=2.6907; 95% CI: 1.4883-3.9689, p=0.0006, vs. Abruzzi/Tuscany residents). Gastric dysplasia (N=1) and multiple polyps of the colon (N=1), arthritis (N=1), thrombocytopenia (N=1) affected single workers at higher, but not significant, incidence rate (Table S1). Ex-workers were affected by various lung diseases (N=35) (Table S1). Of these, COPD (N=6) and asthma (N=4) rates approximated the national and regional incidence, respectively. Notably, COPD was significantly lower whether compared to elderly smokers (IRR=0.100, 95% CI: 0.03893-0.2593, p<0.0001). Even, dyspnoea after exertion (N=17) was statistically under-represented in our cohort, compared to other European populations (Table S1). Benign prostate hyperplasia (N=22) was seemingly more prevalent our workers than Italians (RR= 6.2304, CI 4.2848 to 9.0595, P<0.0001). The main results described in this paragraph are shown in Table 1, unless otherwise indicated. Anthropometric and job and health anamnestic data were not significantly different between the two sub-cohorts (Table S2).

Residential asbestos and smoking status

Residential asbestos: The whole original cohort of former asbestos workers included one sub-cohort of them living near non-occupational asbestos sources (N=50), and the other one not (N=58), accounting 96% and 89% of total disease cases, respectively (Table 2). Residential asbestos was not associated (OR<1) with higher occurrence of restrictive respiratory diseases, nor metabolic syndrome and T2D, nor BPH which were, conversely, all significantly associated (p<0.05) with occupational exposure alone (Table 2). Seemingly, although not significantly associated (OR>1; p>0.05), pulmonary nodules, asbestosis, colon carcinoma, and prostate cancer, and obstructive/inflammatory pulmonary conditions mostly gained in the cohort of workers exclusively exposed to occupational asbestos (Table 2). Residential asbestos resulted by a small margin and not significantly associated with

pleural plaques (OR<1; p>0.05) (Table 2). Smoke. One sub-cohort of the asbestos workers' whole cohort included (past/current) smokers (N=66), and non-smokers (N=42). No statistically significant differences resulted (p>0.05), for each pathology. Yet, non-smoking (asbestos-exposed) workers were those more often affected by pleural plaques (OR=1.6316; 95% CI: 0.3852-6.9109), pulmonary nodules (OR=1.3541; 95% CI: 0.3850-4.7430), prostate cancer (OR=3.2500; 95% CI: 0.2854-37.0125), and benign prostate hyperplasia (OR=1.7742; 95% CI: 0.6899-4.5628). Asbestosis occurred at a slightly higher rate among smokers of the asbestos cohort (OR=0.8125; 95% CI: 0.0713-9.2531), compared to the non-smokers. Larynx carcinoma, colorectal cancer, multiple colon polyps, and MDS were only diagnosed in (current) smokers, who were also more affected by T2D, glaucoma and other metabolic conditions, compared to the non-smokers. Smokers of our cohort were not affected by gastric dysplasia, thyroid nodules, and thrombocytopenia, and were less affected by asthma (Table 3).

	Occupational asbestos (N=58)	**Occupational asbestos and RESIDENTIAL asbestos (N=50)**	**OR>1**	**95% C.I.**	**P-**Statistically significant
Respiratory disease, restrictive (asthma, dyspnea) **(N=17)** n. (%)					
detected	17 (29.3)	2 (4.0)	9.9512	2.1692 to 45.6506	0.0031
undetected	41 (70.7)	48 (96.0)			
Cardiometabolic (N=72) n. (%)					
detected	52 (89.6)	20 (40.0)	13.0000	4.7018 to 35.9433	< 0.0001
undetected	6 (10.4)	30 (60.0)			
Type-2 Diabetes (N=18) n. (%)					
detected	16 (27.6)	2 (4.0)	9.1429	1.9853 to 42.1061	0.0045
undetected	42 (72.4)	48 (96.0)			
Benign prostate hypertrophy (N=22) n. (%)					
detected	21 (36.2)	1 (2.0)	27.8108	3.5765 to 216.2562	0.0015
undetected	37 (63.8)	49 (98.0)			
			>1		Not significant
Pulmonary nodules (N=11) n. (%)					
detected	7 (12.1)	4 (8.1)	1.5784	0.4338 to 5.7429	0.4885
undetected	51 (87.9)	46 (92.0)			
Asbestosis (N=3) n. (%)					
detected	2 (3.5)	1 (2.0)	1.7500	0.1539 to 19.8965	0.6518
undetected	56 (96.5)	49 (98.0)			
Respiratory disease, obstructive (COPD, silicosis, pneumoconiosis) **(N=6)** n. (%)					
detected	5 (8.6)	1 (20.0)	4.6226	0.5215 to 40.9722	0.1691
undetected	53 (91.4)	49 (98.0)			
Respiratory disease, inflammatory (N=7)					
detected	4 (6.9)	3 (6.0)	1.1605	0.2470 to 5.4523	0.8504

undetected	54 (93.1)	47 (94.0)			
Colorectal carcinoma (N=3) n. (%)					
detected	2 (3.5)	1 (2.0)	1.7500	0.1539 to 19.8965	0.6518
undetected	56 (96.5)	49 (98.0)			
Prostate cancer (N=3) n. (%)					
detected	3 (5.2)	0 (0.0)	6.3694	0.3211 to 126.3627	0.2245
undetected	55 (94.8)	50 (100.0)			
			< 1		Not significant
Pleural Plaques (N=8) n. (%)					
detected	4 (6.9)	4 (8.1)	0.8519	0.2017 to 3.5977	0.827
undetected	54 (93.1)	46 (92.0)			

Table 2: Distribution of diagnosed pathologies based on the presence or not of residential extra-occupational sources of asbestos.

	Occupational asbestos / NON-SMOKERS (N=42)	**Occupational asbestos / SMOKERS (N=66)**	**OR> 1**	**95% C.I.**	**P- No significant differences**
Pleural Plaques (N=8) n. (%)					
detected	4 (9.5)	4 (6.0)	1.6316	0.3852 to 6.9109	0.5063
undetected	38 (90.5)	62 (94.0)			
Pulmonary nodules (N=11) n. (%)					
detected	5 (11.9)	6 (9.1)	1.3514	0.3850 to 4.7430	0.6383
undetected	37 (88.1)	60 (90.9)			
Benign prostate hyperplasia BPH (N=22)					
detected	11 (26.2)	11 (16.7)	1.7742	0.6899 to 4.5628	0.2342
undetected	31 (73.8)	55 (83.3)			
Prostate cancer (N=3) n. (%)					
detected	2 (4.8)	1 (1.5)	3.2500	0.2854 to 37.0125	0.3423
undetected	40 (95.2)	65 (98.5)			
Asbestosis (N=3) n. (%) **< 1**					
detected	1 (2.4)	2 (3.0)	0.8125	0.0713 to 9.2531	0.8671
undetected	41 (97.6)	64 (97.0)			
Larynx cancer (N=1) n. (%)					
detected	0 (0.0)	1 (1.5)	0.5137	0.0204 to 12.9074	*0.6855*

undetected	42 ((100.0)	65 (98.5)			
Colorectal carcinoma (N=3) n. (%)					
detected	0 (0.0)	3 (4.5)	0.2134	0.0107 to 4.2385	0.3111
undetected	42 (100.0)	63 (95.4)			
Multiple polyps of the colon (N=1)					
detected	0 (0.0)	1 (1.5)	0.5137	0.0204 to 12.9074	0.6855
undetected	42 (100.0)	65 (98.5)			
Type-2 Diabetes (N=18) n. (%)					
detected	4 (9.5)	14 (21.2)	0.3910	0.1193 to 1.2818	0.1211
undetected	38 (90.5)	52 (78.8)			

Table 3: Distribution of the most diagnosed pathologies, based on the smoking status.

Diseases outcomes among Manufacturing and Production workers

Anthropometric characteristics, job history, allocation of the extra-occupational exposures/smoking status showed no significant differences among the two different sectors of employment (Table S1, Tables 2 and 3). However, smokers were mostly employed in the Production sector (OR=1.47; 95% CI: 0.25-1.83, p=0.448), and non-occupational asbestos was mainly declared by the Manufacturing workers (OR=1.80; 95% CI: 0.19-1.37; p=0.179) (Table 4). Diseases risk was unequally distributed. Manufacturing workers had a higher significant risk of overall ARD (RR=1.9; 95% CI:1.14262-3.1129; p=0.0126) and/or of pulmonary diseases (RR=2.6; 95% CI:1.4527-4.3393; p=0.0005) (Table 4), and Production workers had a significantly higher risk of developing metabolic syndrome (RR=1.3; 95% CI:1.0788-1.4975, p=0.0232) (Table 4), and displayed lung nodules without overt ARD.

Disease	Business		OR	95% CI	P	RR	95% CI	P
	Manufacturing (N=86)	Production (N=22)						
Respiratory, n. (%)								
Respiratory	32 (37)	3 (14)	3.75	0.99-14.15	0.035	2.6429	1.5263 to 4.5761	0.0005
Non-respiratory	54 (63)	19 (86)						
Asbestos-related, n (%)								
Asbestos-related	29 (34)	4 (18)	2.28	0.69-7.51	0.159	1.8889	1.1462 to 3.1129	0.0126
Non-asbestos-related	57 (66)	18 (82)						
Metabolic, n (%)								
Metabolic	53 (62)	17 (77)	0.47	0.15-1.42	0.172	0.8052	0.6678 to 0.9709	0.0232
Non-metabolic	33 (38)	5 (23)						
*Crude Odds Ratio; 95% interval confidence								

Table 4: Association between disabling/enabling conditions/diseases of three categories and business of employment of the workers (OR) and comparison of the risk of occurrence of these pathological conditions between the two automotive businesses using ACMs with different modalities of processing (RR).

Discussion

Principal finding of our study is that some past workers of the metalworking/construction industry, priory classified at high relative risk of exposure to asbestos - by the regional service of the National Institute against Accidents and professional diseases at Work (INAIL) - had been exposed to pathogenetic asbestos in the workplace. In fact, a variety of known asbestos-related diseases were diagnosed, and others could be related to it, according to recent published reports [24-32] (Figure 2). Pleural plaques, asbestosis and malignant pulmonary nodules, and prostate cancer were detected. Colorectal carcinoma and haematological (pre) malignant MGUS were also diagnosed. The attribution of these diseases to occupational exposure is supported by our finding that residential exposure was irrelevant to the disease outcome. Moreover, the workers lived in Abruzzi, a small region where the environment can be considered NOA-free [10]. Besides, our study shows that respiratory diseases compatible with (underlying) ARD [24,29,31] often affected the workers (Table 5). Unexpectedly, most of the workers were also affected by clinical traits of metabolic syndrome, more often than the community of the same geographic area (Table 5). In our study, cigarette smoke was not an influential factor for pleural plaques and asbestosis. Nevertheless, past workers with a diagnosis of larynx cancer, colorectal cancer, pulmonary nodules, polyps of the colon, and MDS (all potentially triggered and amplified by asbestos) were all smokers. As expected, smoking was associated with respiratory lung diseases, T2D and metabolic syndrome, displayed by our cohort of ex-asbestos workers at a higher incidence than control cohorts. The other relevant finding is that Manufacturing workers developed overall ARD and severe respiratory diseases at the highest rate, compared to the Production workers (Figure 2). Instead, Production workers, more often smokers, were affected by metabolic syndrome and no cases of pleural plaques and asbestosis were diagnosed. Briefly, this study shows that the manufacturing mode of processing of asbestos-containing materials posed the workers a higher risk of inhalation of released free asbestos and is crucially linked to the burden and arrangement of the pathological outline among the workers. Almost thirty years ago, many countries banned the use of massive dusty asbestos in workplaces. This commitment imposed the adoption of stringent hygienic working conditions, which contributed to the reduction of severe ARD cases in our region. Indeed, only two cases of ARD were reported among the Abruzzi workers (2022 protocol, INAIL open data) and, in our cohort, no mesothelioma nor overt lung cancer were diagnosed. In the time to come workers will experience an "emerging" risk of exposure to single free fibres detached from compact ACM. We believe that such exposure regarded our Manufacturing workers for most of their working period. Manufacturing workers were potentially exposed to released free asbestos for the type of jobs carried out that imply handling and modelling (through tangential forces) of materials having asbestos. Instead, the Production workers, dedicated to assembly and mounting and check of components, were at lower/null risk of dispersion of asbestos-inhalable fibrous particles. For our cohort of workers, this distinction of jobs corresponds to different relative risks and two different disease profiles showed by our study in the two businesses of employment. In Italy, it is predicted that occupational asbestos to lead to highly incident non-deadly chronic lung diseases and disability, rather than deadly ones [33], affecting workers' quality of life and health. This new scenario might be challenging for the national/regional medical care systems and the productivity of the companies dealing with ACM. Furthermore, asbestos is still considered a main oncologic risk factor for workers and citizens [34]. Rather, the occurrence of sporadic cases strongly suggests that genetic/epigenetic factors might drive the onset and progression of (multiple and scattered) ARD in these individuals [34-38]. Non-occupational asbestos exposure, expected to increase the risk of ARD, especially for children, women and the elderly [33], will arise from the close operation of object refinement, as for the manufacturing workers. Hence, the findings described here might be of inspiration to promote future research to clarify the non-carcinogenic role of occupational asbestos and inspire proper safety, health surveillance and regulative actions for both occupational and public health protection. In this study, we have shown that the mode of processing the asbestos-containing materials, rather than just permanency itself in the (working) environment, is crucial for the release of inhalable fibres and pathological consequences. This finding has important implications for the management of asbestos waste and the preservation of the natural living environment. The strength of this study consists of the possibility to study a cohort of past workers while alive and in good general health conditions, who were collaborative for interviews, visits and instrumental diagnostics for the characterization of familiar, job and anamnestic data for this study. Altogether, they formed a highly homogeneous cohort of past asbestos workers being males, the same age, with common lifestyles, residences, and absence of natural asbestos near homeplace, except for the features of interest for this study, that is job, smoke and residential asbestos. Furthermore, the study was conducted in 2019, when the maximal incidence of asbestos-related diseases worldwide was predicted [6, 13-15] to allow the highest enrolment of "healthy" past workers. The weakness of this study is the size of our cohort, which was not sufficiently large to detect the rare mesothelioma cases in Abruzzi and the possible overestimation of the differences with the reference population. Given the rarity and latency of these diseases, investigations of the complex network of crucial molecular factors involved in asbestos pathogenicity would need more subjects and prolonged periods [32]. Various ARD, indolent pre-cancerous and dysmetabolic

conditions were reported, also as multiple diseases. This suggests that common and/or overlapping pathogenetic pathways are triggered/worsened by asbestos, reflecting its complex and not fully understood toxicological profile figured out by diverse chemical-physical characteristics as iron content, fluoride content, zeta (ξ) potential of (Nano)fibres and their impingement/agglomeration [33-39]. Furthermore, our findings suggest that asbestos might act as an endocrine disruptor [40]. Rather, the occurrence of unique cases with lower rates compared to regional/national residents (gastric dysplasia, colon polyposis, thyroid nodules suggests that genetic/epigenetic predisposing factors might have driven the onset and progression in these individuals [41-44]. Workplace chemical risk factors other than asbestos might have been (co)responsible for the observed non-ARD outcomes [45-59] (Figure 2). Our findings might be of guidance for taking proper safety, health surveillance, and regulative actions. Implications for clinicians would be plant-specific and worker-tailored risk evaluation and management, focusing on smoke and metabolic syndrome at job placement, and workers at risk to take part in preventive visits and research, as the one reported here, to make latent cases appear prompt and to develop therapies. Implications for policymakers regard the potentially wider non-carcinogenic harm of asbestos highlighted by our study. Among unanswered issues are the non-carcinogenic role of occupational asbestos and other aero-dispersed substances in the workplace. Since the working settings might resemble those described by us, our cohort might stand for a "human model" of exposure to asbestos for further investigations. For instance, the identification of biological markers of exposure to asbestos and early disease would be auspicious. This study means asbestos toxicity might be more multifaced and prompt chronic diseases and lung and non-lung asbestos-related diseases, in occupational and environmental settings where asbestos-containing materials are forged and or disrupted [60].

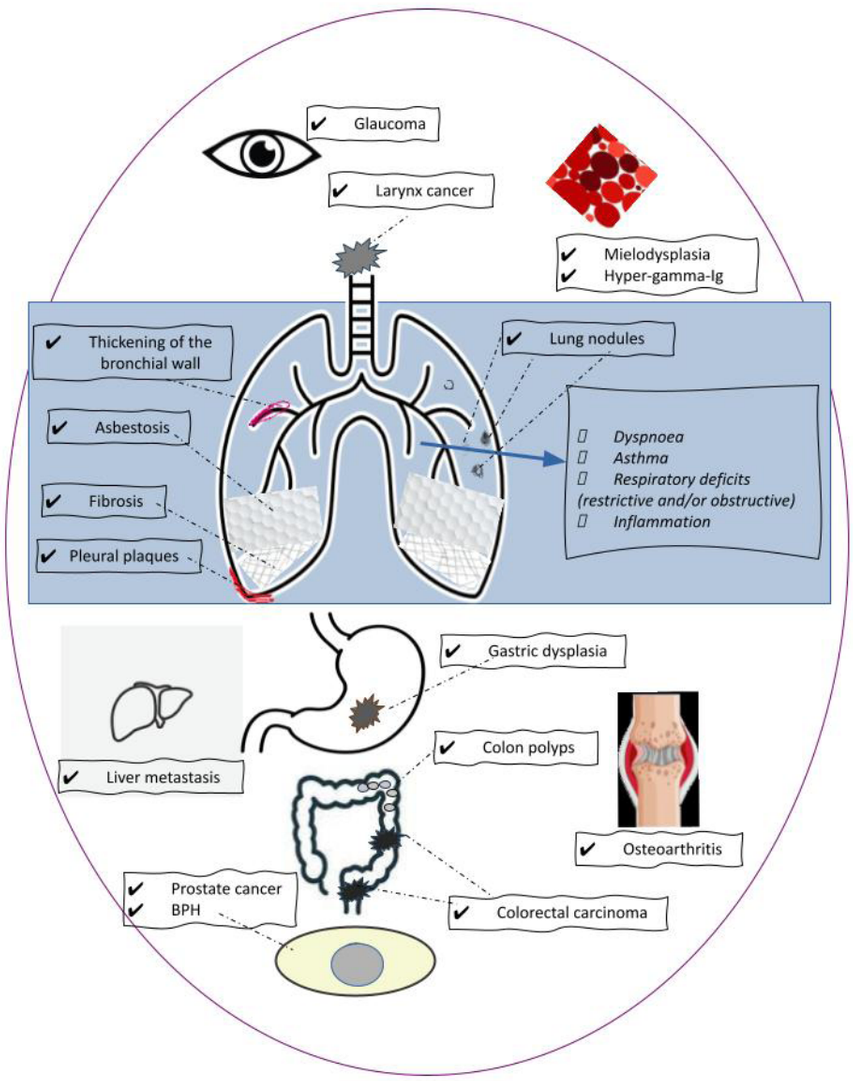

Figure 2: Infographic on the spectrum of Asbestos-Related Diseases (ARDs) and alterations which are reputed precursor of ARDs (pre-ARDs) and others cumulatively detected in the formerly asbestos-exposed workers by the proper diagnostic means.

Conclusions

On this subject, it is known that occupational asbestos exposure might occur in workplaces in the future. In Italy, 32 million tons of asbestos cement are present. ARD negatively affect the quality of life and causes work discontinuation, work disability, and death. Early diagnosis is limited for common symptoms with non-asbestos lung diseases, and the rapid onset and death. The causal relationship with occupational exposure is not always confirmed. This study adds evidence, for the first time, that asbestos human toxicity might be more extended than already assessed, including respiratory and metabolic diseases, and that concomitant occupational risk factors, smoke and genetic traits, can favour/amplify the onset of asbestos-related diseases, that are associated to the manufacturing of asbestos-containing materials jobs. The impact of our findings will lead to improving workability assessments to exclude multiplicative risk factors at first visit and early diagnosis, setting up registries of past exposures and organizing medical surveillance; and providing information on the hazards associated with asbestos-containing materials and products for the elimination of asbestos-related diseases.

Acknowledgments

All the participants are acknowledged with gratitude for their voluntary contribution to the study. The authors are grateful to all healthcare personnel who informed and took care of the ex-workers volunteer during the health surveillance visits.

Ethical Guidelines Compliance Statement

The study involving human participants were reviewed and approved by the reference ethical committee for the Chieti-Pescara provinces (Italy) on February 2nd, 2019 (Protocol No. 9/2019). All subjects were invited to read, understand, and voluntarily sign the informed consent to take part to the study to improving early diagnosis of ARD for workers and the general population was highlighted and lack of immediate benefits was clearly explained. All ethically relevant procedures were performed in agreement with European and Italian recommendations and guidelines (EU Rec/2006/4). Individual personal data were treated following the GDPR 2016.

Conflicts of Interest

The authors disclose any potential conflicts of interest that may influence the results or interpretations of the manuscript.

Funding

C.P. was funded by Italian Ministry of University and Research, MIUR (FAR 2021-2022). D.V. was funded by Department of Medicine and Science Aging, University of Chieti-Pescara, Italy, grants numbers CUP D55F21004250005 and CUP D53C22002740005. The APC was funded by Department of Medicine and Science Aging, University of Chieti-Pescara, Italy.

References

1. Furuya S, Chimed-Ochir O, Takahashi K, David A, Takala J (2018) Global Asbestos Disaster. Int J Environ Res Public Health 15: 1000.
2. Reid A, Berry G, de Klerk N, Hansen J, Heyworth J, et al. (2007) Age and sex differences in malignant mesothelioma after residential exposure to blue asbestos (crocidolite). Chest 131: 376-382.
3. Klebe S, Leigh J, Henderson DW, Nurminen M (2019) Asbestos, Smoking and Lung Cancer: An Update. Int J Environ Res Public Health 17: 258.
4. Zhang YL, Byeon HS, Hong WH, Cha GW, Lee YH, et al. (2021) Risk assessment of asbestos containing materials in a deteriorated dwelling area using four different methods. J Hazard Mater 410: 124645.
5. OSHA, Facts sheet Asbestos.
6. Ferrante D, Chellini E, Merler E, Pavone V, Silvestri S, et al. (2017) Italian pool of asbestos workers cohorts: mortality trends of asbestos-related neoplasms after long time since first exposure. Occup Environ Med 74(12):887-898.
7. Obminski A (2022) The natural reduction of threat in selected systems of old buildings containing asbestos. Sci Rep 12: 2580.
8. Brims FJH, Harris EJA, Murray C, Kumarasamy C, Ho A, et al. (2023) Lung cancer screening an asbestos exposed population: Existing lung cancer risk criteria are not sufficient. Respirology 28: 543-550.
9. Terracini B (2019) Contextualising the policy decision to ban asbestos. Lancet Planet Health 3: e331-e332.
10. Santucciu P, Guercio A, Malinconico S, Paglietti F, Della Staffa BC, et al. (2021) Amianto naturale e ambienti di lavoro. INAIL ISBN 978-88-7484-682-5.
11. Silva M, Sverzellati N, Colombi D, Milanese G, La Vecchia C, et al. (2017). Pleural plaques in lung cancer screening by low-dose computed tomography: prevalence, association with lung cancer and mortality. BMC Pulm Med. 25;17(1):155.
12. Ferrante, P., 2019. Asbestosis and silicosis hospitalizations in Italy (2001–2015): results from the National Hospital Discharge Registry. Eur J Public Health 29, 876–882.
13. Ministero della salute, 2019. L'incidenza dei tumori in Italia.
14. AIRTUM Working Group (2014) Italian Cancer Figures Report. Prevalence and cure of cancer in Italy. Epidemiol Prev 38, 1–144.
15. Bosetti C, Traini E, Alam T, Allen CA, Carreras G, et al. (2020). National **burden of cancer in Italy**, 1990–2017: a systematic analysis for the global burden of disease study 2017. Sci Rep 10, 22099.
16. Pastorino U, Silva M, Sestini S, Sabia F, Boeri M, et al. (2019) Prolonged lung cancer screening reduced 10-year mortality in the MILD trial: new confirmation of lung cancer screening efficacy. Ann Oncol 30: 1162-1169.
17. Vernocchi A, Longhi E, Lippi G, Gelsumini S (2016) Increased Monoclonal Components: Prevalence in an Italian Population of 44 474 Outpatients Detected by Capillary Electrophoresis. J Med Biochem 35: 50-54.

18. Mayer F, Faglioni L, Agabiti N, Fenu S, Buccisano F, et al. (2017) A Population-Based Study on Myelodysplastic Syndromes in the Lazio Region (Italy), Medical Miscoding and 11-Year Mortality Follow-Up: the Gruppo Romano-Laziale Mielodisplasie Experience of Retrospective Multicentric Registry. Mediterr J Hematol Infect Dis 9: e2017046.

19. Guerriero M, Caminati M, Viegi G, Senna G, Cesana G, et al. (2015) COPD prevalence in a north-eastern Italian general population. Respir Med 109: 1040-1047.

20. Pacini F, Basolo F, Bellantone R, Boni G, Cannizzaro MA, et al. (2018) Italian consensus on diagnosis and treatment of differentiated thyroid cancer: joint statements of six Italian societies. J Endocrinol Invest 41: 849-876.

21. Sayegh N, Gross K (2022) Benign prostatic hyperplasia: a global challenge of the ageing population. Lancet Healthy Longev 3: e725-e726.

22. Miccoli R, Bianchi C, Odoguardi L, Penno G, Caricato F, et al. (2005) Prevalence of the metabolic syndrome among Italian adults according to ATP III definition. Nutr Metab Cardiovasc Dis 15: 250-254.

23. Abbafati C, Nieddu L, Monasta L (2024) Measures of type 2 diabetes burden in Italy assessed using the AMD dataset over a twelve-year span across the Great Recession. Sci Rep 14: 4901.

24. Moitra S, Tabrizi AF, Machichi KI, Kamravaei S, Miandashti N, et al. (2020) Non-Malignant Respiratory Illnesses in Association with Occupational Exposure to Asbestos and Other Insulating Materials: Findings from the Alberta Insulator Cohort. Int J Environ Res Public Health 17: 7085.

25. Dutheil F, Zaragoza-Civale L, Pereira B, Mermillod M, Baker, JS, et al. (2020). Prostate Cancer and Asbestos: A Systematic Review and Meta-Analysis. Perm J 24.

26. Lauriola M, Bua L, Chiozzotto D, Manservisi F, Panetta A, et al, (2012). Urinary apparatus tumours and asbestos: the Ramazzini Institute case load. Archivio italiano di urologia, andrologia : organo ufficiale [di] Società italiana di ecografia urologica e nefrologica / Associazione ricerche in urologia 84, 189–96.

27. Vierikko T, Jarvenpaa R, Autti T, Oksa P, Huuskonen M, et al. (2006). Chest CT screening of asbestos-exposed workers: lung lesions and incidental findings. European Respiratory Journal 29, 78–84.

28. Würtz ET, Hansen J, Røe OD, Omland Ø (2020). Asbestos exposure and haematological malignancies: a Danish cohort study. Eur J Epidemiol 35, 949□960.

29. Yang X, Yan Y, Xue C, Du X, Ye Q (2018). Association between increased small airway obstruction and asbestos exposure in patients with asbestosis. Clin Respir J 12, 1676–1684.

30. Zeig-Owens R, Goldfarb DG, Luft BJ, Yang X, Murata K, et al. (2022). Myeloma precursor disease (MGUS) among rescue and recovery workers exposed to the World Trade Center disaster. Blood Cancer J 12, 120.

31. World Health Organization (2024) Chemical Safety and Health Impacts: Asbestos.

32. Bonner JC (2007) Lung fibrotic responses to particle exposure. Toxicol Pathol 35: 148-153.

33. Marinaccio A, Montanaro F, Mastrantonio M, Uccelli R, Altavista P, (2005). Predictions of mortality from pleural mesothelioma in Italy: a model based on asbestos consumption figures supports results from age-period-cohort models. International journal of cancer. Journal international du cancer 115, 142–7.

34. Liu G, Cheresh P, Kamp DW (2013) Molecular basis of asbestos-induced lung disease. Annu Rev Pathol 8: 161-187.

35. Miserocchi G, Sancini G, Mantegazza F, Chiappino G (2008) Translocation pathways for inhaled asbestos fibers. Environ Health 7: 4.

36. Ogino S, Nishihara R, VanderWeele TJ, Wang M, Nishi A, et al. (2016) Review Article: The Role of Molecular Pathological Epidemiology in the Study of Neoplastic and Non-neoplastic Diseases in the Era of Precision Medicine. Epidemiology 27: 602-611.

37. Cheng YY, Rath EM, Linton A, Yuen ML, Takahashi K, et al. (2020) The Current Understanding Of Asbestos-Induced Epigenetic Changes Associated With Lung Cancer. Lung Cancer (Auckl).

38. Petrarca C, Viola D, Mangifesta R, Di Gioacchino M, Di Giampaolo L (2022) Do microRNAs characterize exposure and asbestos-related diseases? Saf Health Work 13: S16.

39. Editorial (2019) Asbestos exposure: the dust cloud lingers. Lancet Oncol 20: 1035.

40. Hanley GD (2001) Toxicological profile for asbestos.

41. Asbestos (2006) National Academies Press, Washington, D.C.

42. Bloise A, Ricchiuti C, Punturo R, Pereira D (2020) Potentially toxic elements (PTEs) associated with asbestos chrysotile, tremolite and actinolite in the Calabria region (Italy). Chem Geol 558: 119896.

43. Vigliaturo R, Jamnik M, Dražic G, Podobnik M, Žnidaric MT, et al. (2022) Nanoscale transformations of amphiboles within human alveolar epithelial cells. Sci Rep 12: 1782.

44. Yao S, Iezzi G, Della Ventura G, Bellatreccia F, Petibois C, et al. (2017) Mineralogy and textures of riebeckitic asbestos (crocidolite): The role of single versus agglomerated fibres in toxicological experiments. J Hazard Mater 340: 472-485.

45. Mou Y, Liao W, Liang Y, Li Y, Zhao M, et al. (2023) Environmental pollutants induce NLRP3 inflammasome activation and pyroptosis: Roles and mechanisms in various diseases. Sci Total Environ 900: 165851.

46. Modica R, Benevento E, Colao A (2023) Endocrine-disrupting chemicals (EDCs) and cancer: new perspectives on an old relationship. J Endocrinol Invest 46: 667-677.

47. Hughes JM, Weill H (1991) Asbestosis as a precursor of asbestos related lung cancer: results of a prospective mortality study. Occup Environ Med 48: 229-233.

48. Roach HD, Davies GJ, Attanoos R, Crane M, Adams H, et al. (2002) Asbestos: when the dust settles an imaging review of asbestos-related disease. Radiographics 22: S167-S184.

49. Guidotti TL, Christiani D, Wagner G, Balmes J, Harber P, et al. (2004) Diagnosis and Initial Management of Nonmalignant Diseases Related to Asbestos. Am J Respir Crit Care Med 170: 691-715.

50. Takahashi K (2008) Asbestos-related diseases: time for technology sharing. Occup Med (Chic Ill) 58: 384-385.

51. Bunderson-Schelvan M, Pfau JC, Crouch R, Holian A (2011) Nonpulmonary outcomes of asbestos exposure. J Toxicol Environ Health B Crit Rev 14: 122-152.

52. Rajagopalan S, Brook RD (2012) Air Pollution and Type 2 Diabetes. Diabetes 61: 3037-3045.

53. Friedman-Jimenez G, Harrison D, Luo H (2015) Occupational asthma and work-exacerbated asthma. Semin Respir Crit Care Med 36: 388-407.

54. Fucic A, Galea K, Duca R, El Yamani M, Frery N, et al. (2018) Potential Health Risk of Endocrine Disruptors in Construction Sector and Plastics Industry: A New Paradigm in Occupational Health. Int J Environ Res Public Health 15: 1229.

55. Ghobrial IM, Detappe A, Anderson KC, Steensma DP (2018) The bone-marrow niche in MDS and MGUS: implications for AML and MM. Nat Rev Clin Oncol 15: 219-233.

56. Apostoli P, Boffetta P, Bovenzi M, Cocco PL, Consonni D, et al. (2019) Position Paper on Asbestos of the Italian Society of Occupational Medicine. Med Lav 110: 459-485.

57. Fazzo L, Binazzi A, Ferrante D, Minelli G, Consonni D, et al. (2021) Burden of Mortality from Asbestos-Related Diseases in Italy. Int J Environ Res Public Health 18: 10012.

58. Visonà SD, Capella S, Bodini S, Borrelli P, Villani S, et al. (2021) Evaluation of Deposition and Clearance of Asbestos (Detected by SEM-EDS) in Lungs of Deceased Subjects Environmentally and/or Occupationally Exposed in Broni (Pavia, Northern Italy). Front Public Health 9: 678040.

59. De Maria L, Pentimone F, Cavone D, Caputi A, Sponselli S, et al. (2024) Clinical investigation of former workers exposed to asbestos: the health surveillance experience of an Italian University Hospital. Front Public Health 12: 1411910.

60. Landrigan PJ, Lemen RA (2019) A Most Reckless Proposal — A Plan to Continue Asbestos Use in the United States. N Engl J Med 381: 598-600.