Volume 117 3/2026

Rivista fondata nel 1901 da Luigi Devoto Issn 0025 - 7818

La Medicina del Lavoro

Organo della Società Italiana di Medicina del Lavoro

Work, Environment & Health

Official Journal of the Italian Society of Occupational Medicine

www.lamedicinadellavoro.it

Poste Italiane s.p.a. - Sped. in A. P. - D.L. 353/2003 (conv. in L. 27/02/2004 n. 46) art. 1, comma 1, DCB Parma - Finito di stampare nel mese di Giugno 2026

Mattioli 1885

Volume 116

Issn 0025-7818

Rivista fondata nel 1901 da Luigi Devoto

elssn 2532-1080

La Medicina del Lavoro

Organo della Società Italiana di Medicina del Lavoro

Work, Environment & Health

Official Journal of the Italian Society of Occupational Medicine

Editorial office
La Medicina del Lavoro
Clinica del Lavoro «L. Devoto»
Via San Barnaba, 8 - 20122 Milano (Italy)
Tel. 02/50320125 - Fax 02/50320103
http://www.lamedicinadellavoro.it
redazione@lamedicinadellavoro.it

Publisher
Mattioli 1885 srl - Casa Editrice
Strada di Lodesana 649/sx, Loc. Vaio - 43036 Fidenza (PR)
Tel. 0524/530383 - Fax 0524/82537
e-mail: edit@mattioli1885.com
www.mattioli1885.com

Pubblicazione bimestrale - Direttore Responsabile: Antonio Mutti
Autorizzazione del Presidente del Tribunale di Milano 10/5/1948 Reg. al N. 47

La Medicina del Lavoro è indicizzata da / La Medicina del Lavoro is indexed in:
PubMed/Medline; Embase/Excerpta Medica; Abstracts on Hygiene; Industrial Hygiene Digest; Securité et Santé au Travail Bit-CIS; Sociedad Iberoamericana de Informaciòn Cientifica (SIIC); Science Citation Index Expanded (SciSearch®); Journal Citation Report/Science Edition; ISI Web of Science; Scopus (Elsevier); Bibliovigilance

La Medicina del Lavoro

Reviews, Commentaries, Perspectives

Med. Lav. 2026; 117 (3): 19093
DOI: 10.23749/mdl.2026.19903

Cadmium Exposure and Risk of Pancreatic Cancer: A Systematic Review and Meta-Analysis

Monireh Sadat Seyyedsalehi[1], Lorenzo Ciaccio[1], Rosa Francesca Marra[1], Paolo Boffetta[1,2,3*]

[1]Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy
[2]Stony Brook Cancer Center, Stony Brook University, Stony Brook, NY, USA
[3]Department of Family, Population and Preventive Medicine, Renaissance School of Medicine, Stony Brook University, Stony Brook, NY, USA

Keywords: Cadmium; Pancreatic Cancer; Occupational Factor; Environmental Exposure; Biomarkers; Urine

Abstract

Introduction: *Pancreatic cancer is a highly lethal malignancy with poor prognosis and limited treatment options. Environmental exposures, particularly to heavy metals such as cadmium, may contribute to its etiology. This systematic review and meta-analysis evaluated the association between cadmium exposure from different sources and pancreatic cancer incidence or mortality.* **Methods:** *Following PRISMA guidelines, we searched PubMed, EMBASE, and Scopus. Eighteen studies comprising 20 risk estimates were included. Random-effects meta-analyses were conducted overall and stratified by exposure source, gender, region, study design, and outcome. Dose-response relationships were assessed using meta-regression of cadmium exposure measures. Publication bias was evaluated using funnel plots and Egger's test.* **Results:** *Overall, cadmium exposure was associated with an increased risk of pancreatic cancer [relative risk (RR) = 1.69, 95% confidence interval (CI): 1.28-2.22]. Occupational exposure showed the most consistent association (RR = 1.38, 95% CI: 1.19-1.61), followed by urinary and blood/serum biomarkers. Risk was higher in men than in women, and in case-control than in cohort studies. Dose-response analysis did not reveal a linear trend. There was limited evidence of publication bias overall, though some asymmetry was observed for urinary cadmium studies (p = 0.045).* **Conclusion:** *Cadmium exposure was associated with pancreatic cancer risk, particularly in occupational and biomarker-based studies. While findings support a potential causal link, heterogeneity, residual confounding, and limited dose-response data necessitate cautious interpretation.*

1. Introduction

Pancreatic cancer is one of the most lethal forms of cancer; it ranks globally as the seventh most common cause of cancer-related death in both men and women. Incidence rates are four to five times higher in countries with a high Human Development Index (HDI), with the greatest burden observed in Europe, North America, and Australia/New Zealand [1, 2]. Despite advances in diagnostics and therapeutics, its prognosis remains poor, with a five-year survival rate lower than 10%, mainly because this type of cancer is frequently detected at an advanced stage [3].

The etiology of pancreatic cancer is multifactorial, involving genetic susceptibility and other risk factors. including tobacco smoking, smokeless tobacco use, excess body weight, high alcohol consumption,

Received 03.05.2026 – Accepted 12.06.2026
*Corresponding Author: Paolo Boffetta; E-mail: paolo.boffetta@unibo.it

and exposure to environmental pollutants [4]. Among environmental contributors, some research supports the role of environmental chemicals and heavy metals in the etiology of pancreatic cancer [5]. Heavy metal poisoning traditionally occurred in industrial settings and manifested with severe and overt clinical signs and symptoms; however, such cases are now uncommon. The development of more sensitive diagnostic techniques and biomarkers of toxicity has increased awareness of the health consequences of chronic environmental (non-industrial) exposure to heavy metals [6].

Cadmium (Cd) is a naturally occurring metal that is present in a variety of products and environmental settings [7]. It is a non-essential element with well-established toxicity in humans, with lung cancer being the only neoplasm causally associated with it [8]. Human exposure to cadmium occurs through various sources, including industrial processes and occupational settings such as battery manufacturing, metal plating, coating, pigment production, stabilizer use, and welding. Cadmium contamination of soil, air, and water is widespread due to its use in industrial products, contamination from phosphate fertilizers, and emissions from motor vehicle fuel combustion and tire wear [9, 10]. Additionally, cigarette smoking represents a significant source of exposure, while contaminated food - particularly leafy vegetables, cereals, and shellfish - is the primary source of cadmium intake in non-smokers [11, 12].

Cadmium can accumulate in the body over time, primarily in the liver and kidneys, but it may also affect the pancreas via systemic circulation and oxidative stress. Metal can interfere with cellular signaling pathways, induce chronic inflammation, promote DNA damage, and inhibit DNA repair mechanisms – all of which are hallmarks of cancer development [13, 14].

Understanding the potential link between cadmium exposure and pancreatic carcinogenesis is crucial for public health and may offer insights into preventive strategies and regulatory policies. We conducted a systematic review and meta-analysis of published cohort, nested case-control, and case-control studies to evaluate the association between cadmium exposure and pancreatic cancer risk.

2. Methods

This systematic review and meta-analysis were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Supplementary Tables S1a and S1b) [15]. The protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO), Registration number: CRD420251106774.

2.1. Study Design and Criteria

A comprehensive literature search was conducted in MEDLINE (PubMed), EMBASE (Ovid), and SCOPUS in July 2025, with no language restrictions. The study population included adults from all countries on the incidence or mortality of pancreatic cancer, as an outcome without restriction by publication year. For the search strategy, vocabulary terms and keywords related to cadmium exposure, cancer, and pancreatic neoplasms were combined (see Supplementary Table 2 for detailed search strategies used across the various databases). References of included articles and relevant reviews were handsearched to identify additional eligible studies.

We included observational studies (cohort, nested case-control, or case-control) that evaluated the association between cadmium exposure and pancreatic cancer risk. Eligible studies assessed cadmium exposure from environmental, occupational, or biological sources, including measurements in urine, blood, serum, plasma, or toenails, and reported effect estimates for pancreatic cancer incidence or mortality.

Studies were excluded if they: (i) Did not evaluate pancreatic cancer as an outcome, (ii) Did not assess cadmium exposure or failed to report cadmium specific effect estimates, (iii) Were based on occupational groups in which cadmium was not the primary exposure and cadmium-specific results could not be separated such as firefighters, uranium miners, textile workers, printing workers, chimney sweeps, shipyard or pipe trades workers, and ferromanganese plant workers, (iv) Consisted of abstracts, unpublished reports, theses, book chapters, non-peer-reviewed publications or study designs other than cohort and case control, (v) Duplicated

other reports or analyzed overlapping populations (in such cases only the most recent and comprehensive publications were included; see Supplementary Figure 1).

2.2. Study Selection, Data Extraction, and Quality Assessment

All records were uploaded into the online software, Rayyan, where duplicates were removed. Two reviewers independently screened titles and abstracts for potential relevance. The full texts of potentially eligible articles were independently assessed. Any disagreements at any stage of the review process were resolved by discussion. Two reviewers independently extracted the data using a standardized Excel form. Extracted information included study characteristics (authors, year of publication, country, study design), population details, sample size, source and method of cadmium exposure assessment, outcome definition (mortality, incidence), duration and level of exposure, and reported effect estimates [adjusted or unadjusted relative risks (RRs) or odds ratios (ORs) with 95% confidence intervals (CIs)] and adjustment list if available. Stratified results (e.g., by gender, age, exposure source, or exposure level) were recorded as separate entries.

The methodological quality of included studies was independently assessed by two reviewers using a modified Newcastle-Ottawa Scale (NOS) [16]. NOS evaluates study characteristics across three main domains: selection of participants, comparability of study groups, and ascertainment of either exposure or outcome. The maximum score was 9 for case-control studies and 10 for cohort studies, with higher scores indicating better quality. See Supplementary Table 3 for details of items for each study type, and the summarized results are presented in Supplementary Table 4.

2.3. Statistical Analysis

Random-effects meta-analyses were conducted to calculate pooled relative risks (RRs) and 95% confidence intervals (CIs), both overall and stratified by source of cadmium exposure (occupational, serum/blood, urine, and others), using the DerSimonian and Laird and the restricted maximum-likelihood (REML) methods [17]. Statistical heterogeneity was assessed using Cochran's Q test and quantified with the I^2 statistic [18]. Because pancreatic cancer is a rare outcome, ORs, HRs, SMRs, and SIRs were considered approximations of RR [19].

Subgroup analyses were performed by gender (male, female, both), study design (cohort, case-control), outcomes (incidence, mortality), region (North America, Europe, other countries), years of publication (<2011 vs. >2011, based on the median publication year of all included studies), adjusted to smoking (Yes, No), and quality score (<8.5 vs. >8.5, based on the median quality score of all included studies). Eventually, we assessed publication bias using contour-enhanced funnel plots and Egger's tests [20, 21].

Nine studies reported dose-response information, four of which assessed cadmium from sources not directly comparable to internal measures or without the necessary numbers for calculation. Therefore, five studies [26, 23, 30, 31, 35] reporting internal cadmium levels (urine, blood, serum, plasma, or toenails) were included in a random-effects meta-regression using REML estimation with Knapp-Hartung adjustment to explore the association between increasing cadmium exposure and pancreatic cancer risk [22]. All analyses were performed using Stata software version 18.5 (StataCorp LLC, College Station, TX, USA).

3. Results

The literature search identified 2,000 studies from PubMed, EMBASE, and Scopus. After removal of duplicates, followed by title and abstract screening and full-text review, 18 studies (twenty records) met the inclusion criteria and were included in the qualitative synthesis and meta-analysis (Supplementary Figure 1) [23-40]. They consisted of ten cohort studies [24, 27, 31-34, 36-39], six case-control studies [23, 25, 26, 28, 30, 40], and two nested case-control studies [29, 35]. Six studies were conducted in North America [24, 26, 28, 31, 35, 40], seven in Europe [23, 29, 30, 32, 34, 38, 39], and five in Asia [25, 27, 33, 36, 37]. Cadmium exposure was assessed using occupational records in six studies

[26, 32, 34, 38-40], biological markers in 11 studies [23-26, 28-31, 35-37], dietary intake in one study [27], and environmental indicators in two studies [26, 33]. Pancreatic cancer incidence was evaluated in 11 studies [23, 25-30, 34, 35, 38, 40], while seven studies [24, 31-33, 36, 37, 39] assessed mortality. Most studies reported adjusted risk estimates, controlling for age, gender, body mass index (n=6) [24, 27, 29, 31, 35, 37], tobacco smoking (n=13) [23-29, 31, 33, 35, 37, 38, 40], and other relevant covariates (Table 1).

Figure 1 shows the forest plot of the association between cadmium exposure and pancreatic cancer risk by exposure source using random-effects models. Overall, 20 risk estimates from 18 studies were included in the meta-analysis, indicating a statistically significant increase in the risk of pancreatic cancer associated with cadmium exposure (RR = 1.69, 95% CI: 1.28-2.22), with substantial heterogeneity (I^2 = 96.4%, p < 0.001). Occupational cadmium exposure was evaluated in 6 studies and was associated with an increased risk

Table 1. Selected characteristics of studies on cadmium exposure and pancreatic cancer.

Ref.	Country	Study design	Gender	Source of Cd	Outcome	Risks (CI95%)	If adjusted (list of variables)
Amaral, 2012 [23]	Spain	Hospital-based case-control study	Both	Toenails	I	OR:2.09(1.37_3.17)	Age, Gender, Region, Smoking status, Education, Diabetes, Mutual adjustment for relevant trace elements
Adams, 2012 [24]	USA	Prospective population-based cohort study (NHANES III)	Both	Urinary	M	HR:1.27(0.88_1.83)	Age, smoking history, BMI, education, race
			Male			HR:3.95(1.94_8.04)	
			Female			HR:0.84(0.55_1.29)	
Kriegel, 2006 [25]	Egypt	Hospital-based case-control study	Both	Serum	I	OR:1.12(1.04_1.23)	age, gender, province (Dakahlia), and smoking
Luckett, 2012 [26]	USA	Population-based case-control study	Both	Occupational	I	OR:1.69(0.14_20.39)	smoking, education, alcohol, family history, age, gender, region
				Urinary		OR:5.14(3.001_8.819)	
				Well water		OR:1.51(0.77_2.97)	
Sawada, 2012 [27]	Japan	Prospective population-based cohort	Both	Food intake	I	HR:1.26(0.95_1.66)	Age, area, BMI, smoking status, frequency of alcohol intake, leisure-time physical activity, intake of meat, soybean, vegetable, fruit, menopausal status, use of exogenous female hormones.
			Male			HR:1.36(0.87_1.98)	
			Female			HR:1.13(0.72_1.72)	
Carriga, 2007 [28]	USA	Case control study	Both	Pancreatic juice Cd (μg/L)	I	OR:1.18(0.56_2.5)	Age, gender, and smoking history
Duell, 2018 [29]	European countries	Nested case-control study within a prospective cohort (EPIC)	Both	Blood	I	OR:1.13(1.01_1.27)	Age, Gender, Study center, Smoking, Alcohol intake, BMI, Diabetes, Education, Other metals (Zn, Se)
Djordjevic, 2019 [30]	Serbia	Hospital-based case-control study	Both	Tissue	I	OR:13.31(10.75_16.5)	age and gender
			Male			OR:12.25(0.29_17.06)	
			Female			OR:14.11(0.44_18.64)	
Garca-Esquinas, 2014 [31]	USA	Prospective cohort study (Strong Heart Study)	Both	Urinary	M	HR:2.4(1.39_4.17)	Gender, age, smoking status, cigarette pack-years, BMI

Ref.	Country	Study design	Gender	Source of Cd	Outcome	Risks (CI95%)	If adjusted (list of variables)
Järup, 1998 [32]	Sweden	Retrospective occupational cohort study	Both	Occupational (Battery workers)	M	SMR:1.58(0.77_3.22)	Age, and gender
			Male			SMR:1.48(0.54_3.23)	
			Female			SMR:2.2(0.55_12.3)	
Nishijo, 2018 [33]	Japan	Population-based prospective cohort study	Both	The Cd-polluted areas (environmental exposure)	M	SMR:0.85(0.52_1.39)	Age, smoking status, and hypertension
			Male			SMR:1.15(0.6_2.4)	
			Female			SMR:0.67(0.4_1.3)	
Nyqvist, 2017[34]	Sweden	Population cohort study	Both	Occupational (Glassworks Sites)	I	SIR:1.32(1.1_1.58)	Age, and gender
			Male			SIR:1.4(1.07_1.79)	
			Female			SIR:1.24(0.93_1.62)	
Stolzenberg-Solomon, 2025 [35]	USA	Nested case-control study within a prospective cohort (PLCO Trial)	Both	Blood	I	OR:1.25(1.09_1.43)	Age, gender, race, and smoking, BMI, diabetes, alcohol use, education, physical activity, family history, and dietary factors
Sakurai,2021 [36]	Japan	population-based cohort study	Both	Urinary	M	HR:0.94(0.57-1.55)	Age
			Male			HR:0.86(0.39-1.90)	
			Female			HR:1(0.53-1.89)	
Sorahan,1995 [39]	England	Retrospective occupational cohort study	Male	Occupational (copper cadmium alloy workers)	M	SMR:2.18(0.59_5.58)	Age, year of starting work, factory, time since starting work.
Watanabe, 2020 [37]	Japan	Prospective cohort study	Both	Urinary	M	RR:1.13(1.03_1.24)	smoking, alcohol consumption, age, BMI, blood pressure, hypertension, living area
Weiderpass, 2003 [38]	Finland	Population-based cohort study with job-exposure matrix (JEM)	Female	Occupational	I	RR:1.35(0.97_1.86)	birth cohort, calendar period, and socioeconomic status; smoking (pancreatic cancer)
Zhang, 2005 [40]	USA	Population-based case-control study	Male	Occupational (Chemicals and allied products)	I	OR:3.5(1.3_9.2)	Age, Smoking status and duration, Physical activity, Red meat intake, Fruit intake, Family history of pancreatic cancer

BMI: body mass index, I: Incidence, M: Mortality,

of pancreatic cancer (RR = 1.38, 95% CI: 1.19-1.61), with no evidence of heterogeneity (I^2 = 0.0%, p = 0.477).

Exposure assessed using serum or blood biomarkers was examined in 3 studies, yielding a modest but statistically significant association (RR = 1.15, 95% CI: 1.08-1.22), with no heterogeneity (I^2 = 0.0%, p = 0.384). Urinary cadmium exposure was assessed in 5 studies and was associated with an increased risk of pancreatic cancer (RR = 1.69, 95% CI: 1.04-2.75); however, substantial heterogeneity was observed within this subgroup (I^2 = 89.1%, p < 0.001).

A statistically borderline difference between exposure-source subgroups was observed (p for heterogeneity between groups = 0.047).

Contour-enhanced funnel plots are shown in Supplementary Figure 2. Egger's test provided limited evidence of publication bias overall, although some asymmetry was observed for studies using urinary cadmium measurements (P = 0.045). No

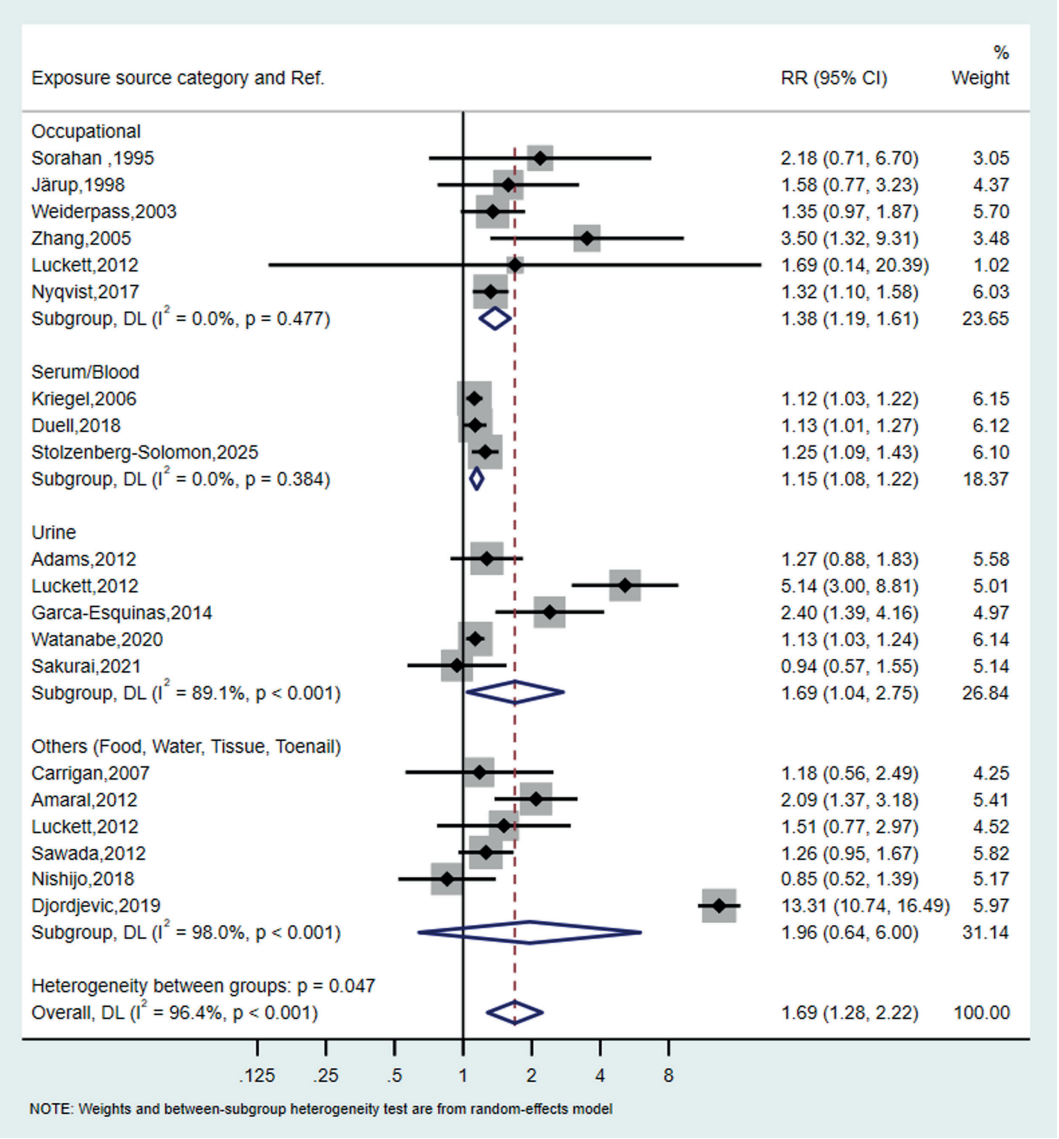


Figure 1. Forest plot (random-effects model) showing the association between cadmium exposure and pancreatic cancer by different exposure sources.

bias was detected for occupational, serum/blood, or other exposure sources.

Results of the stratified meta-analyses are presented in Table 2. By geographic region, a significant association was observed in North American studies (RR = 1.89, 95% CI: 1.28-2.81), and others (Japan and Egypt) (RR = 1.12, 95% CI: 1.06-1.19), whereas estimates from Europe were higher but imprecise (RR = 2.13, 95% CI: 0.95-4.75),with evidence of heterogeneity across regions (p_heterogeneity = 0.012). Stratification by gender showed an increased risk among men (RR = 1.71, 95% CI: 1.23-2.40) but not among women (RR = 1.13, 95% CI: 0.87-1.46); studies including both genders also showed an elevated risk (RR = 1.65, 95% CI: 1.22-2.22), with no heterogeneity between genders (p_heterogeneity = 0.073). Case-control studies reported higher risk estimates (RR = 2.20, 95% CI:

Table 2. Results of the meta-analysis of studies on overall association between cadmium exposure and pancreatic cancer stratified by Country, Year of publication, Quality score, Gender, Outcome, Study design, Smoking adjustment.

Characteristic	N Risk Estimates	RR, 95% CI	p Heterogeneity
Country			
North America (USA)	8	1.89 (1.28-2.81)	0.012
European Countries (Finland, England, Serbia, Spain, Sweden)	7	2.13 (0.95-4.75)	
Other Countries (Japan, Egypt)	5	1.12 (1.06-1.19)	
Year Of Publication			
<=2011	6	1.33 (1.05-1.70)	0.179
>2011	14	1.73 (1.29-2.33)	
Quality Score			
Low (< =8.5)	13	2.04 (1.39-3)	0.008
High (> 8.5)	7	1.19 (1.08-1.31)	
Gender			
Male	9	1.71 (1.23-2.40)	0.073
Female	8	1.13 (0.87-1.46)	
Both	17	1.65 (1.22-2.22)	
Outcome			
Incidence	13	1.92 (1.29-2.87)	0.060
Mortality	7	1.24 (0.99-1.55)	
Study Design			
Cohort	10	1.21 (1.07-1.37)	0.029
Case Control	10	2.20 (1.31-3.72)	
Smoking Adjustment			
No	5	2.26 (0.61-8.38)	0.445
Yes	15	1.36 (1.19-1.54)	

1.31-3.72) than cohort studies (RR = 1.21, 95% CI: 1.07-1.37), with evidence of heterogeneity (p_heterogeneity = 0.029). Studies published after 2011 showed stronger associations (RR = 1.73, 95% CI: 1.29-2.33) than those reported in earlier studies (RR = 1.33, 95% CI: 1.05-1.70). Associations were stronger for pancreatic cancer incidence (RR = 1.92, 95% CI: 1.29-2.87) than for mortality (RR = 1.24, 95% CI: 0.99-1.55), with no heterogeneity by either outcome or year-of-publication groups.

Further stratification by smoking adjustment indicated that studies that adjusted for smoking showed an RR = 1.36 (95% CI: 1.19-1.54), whereas studies that did not report a substantially higher RR = 2.26 (95% CI: 0.61-9.38) (p_heterogeneity = 0.445). Stratification by study quality revealed that studies with lower Newcastle-Ottawa Scale scores (<8.5) reported higher pooled estimates (RR = 2.04, 95% CI: 1.39-3.00) compared with high-quality studies (>8.5) (RR = 1.19, 95% CI: 1.08-1.31), with evidence of heterogeneity (p_heterogeneity = 0.008).

Table 3 summarizes the results of five studies [26, 23, 31, 35, 30] that evaluate pancreatic cancer risk across categories of cadmium exposure. A random-effects meta-regression including 14 estimates from five studies assessing internal cadmium measures was conducted to evaluate a linear dose-response

Table 3. Relative risk of pancreatic cancer by level of exposure to cadmium.

Ref.	Source of Cd	Dose Categories	Mid-Dose	Case	Control	Total	Estimates (CI 95%)
Luckett, 2012, USA [26]	Urine	<0.5 microgram/g creat.	0.25	10	71	81	OR: ref
		0.5<1 microgram/g creat.	0.75	16	33	49	OR:3.34(1.38-8.07)
		1<1.5 microgram/g creat.	1.25	13	18	31	OR:5.58 (2.03-15.34)
		>1.5 microgram/g creat.	1.75	24	19	43	OR:7.7(3.06-19.34)
Amaral, 2012, Spain [23]	Toenails	≤ 8.0 ng/g	5.35	17	100	117	OR: ref
		8.1-13.4 ng/g	10.75	11	99	110	OR:0.87 (0.37-2.03)
		13.5-29.1 ng/g	21.3	27	100	127	OR:2.04 (1-4.17)
		> 29.1 ng/g	36.9	59	99	158	OR:3.58 (1.86-6.88)
Garca-Esquinas, 2014, USA [31]	Urine	<0.70 microgram/g creat.	0.45	12	1257	1269	HR: ref
		0.71-1.22 microgram/g creat.	0.97	0	0	0	HR:0 (0-0)
		>1.23 microgram/g creat.	1.49	12	1245	1257	HR:2.47 (1.01-6.03)
Stolzenberg-Solomon, 2025, USA [35]	Blood	male= 0.27, female=0.31 µg/L	0.27	57	128	185	OR: ref
		male=0.34, female=0.38 µg/L	0.34	55	127	182	OR:1.06 (0.66-1.69)
		male=0.41, female=0.47 µg/L	0.83	49	127	176	OR:0.85 (0.52-1.38)
		male=0.52, female=0.59 µg/L	0.52	56	127	183	OR:1.04 (0.64-1.68)
		male=2.32, female= 3.13 µg/L	0.25	101	127	228	OR:1.81 (1.12-2.95)
Djordjevic, 2019, Serbia [30]	Tissue	<0.491 µg/g	0.46	6	10	16	OR: ref
		0.491-0.558 µg/g	0.52	1	4	5	OR:2.19 (0.67-7.1)
		0.558-0.966 µg/g	0.76	3	5	8	OR:3.2 (1.05-9.47)
		>0.966 µg/g	1.17	21	10	31	OR:3.99 (1.136-11.67)

Three studies (Nishijo et al., 2018, Japan; Sawada et al., 2012, Japan; and Weiderpass et al., 2003, Finlandreported dose-response relationships. However, they were not included in the dose-response analysis because they assessed different sources of exposure. Also, one study (Sakurai et al., 2021, Japan) was not included in the dose-response analysis because it did not report the necessary quantitative data required to perform the analysis.

relationship. The dose variable, expressed per 1 unit increase, was not statistically significant (RR = 1.28, 95% CI: 0.75-2.21; p = 0.334), indicating no evidence of a linear trend.

Substantial residual heterogeneity remained after adjustment (I^2 res = 72.2%), and the adjusted R^2 suggested that dose explained little of the between-study variability (Table 4).

4. Discussion

In this systematic review and meta-analysis of 18 observational studies, we found that cadmium exposure was associated with an increased risk of pancreatic cancer. Overall, individuals exposed to cadmium had a 69% higher risk of pancreatic cancer compared with those with no exposure. Elevated risks were consistently observed across different sources of exposure, with the strongest and most homogeneous associations seen in studies of occupational exposure, followed by studies using urine and then Blood/serum cadmium biomarkers. Stratified analyses revealed stronger associations in men than in women, and these associations were more pronounced in case-control studies compared with cohort studies. We observed evidence of publication bias in the studies related to urinary cadmium. Meta-regression analyses were based on limited data and did not reveal a clear linear dose-response relationship, and the substantial residual heterogeneity suggests that variations in exposure assessment and study characteristics may contribute to the observed differences.

Table 4. Random-effects meta-regression of dose on log odds ratio of cadmium exposure and risk of pancreatic cancer.

Variable	exp(β)	95% CI	p-value
Dose (per 1 unit)	1.28	0.75-2.21	0.334
Intercept	1.69	0.90-3.19	0.095

Model details: REML estimation; Knapp-Hartung modification; $\tau^2 = 0.353$; $I^2\_res = 72.2\%$; *adjusted* $R^2 = -4.7\%$; *n = 14 studies.*

Our findings are consistent with and extend previous evidence linking cadmium exposure to pancreatic cancer risk. Fanfani et al. (2024) provided a broad synthesis of cadmium-related cancer outcomes based on biological measures but did not conduct a pancreas-specific quantitative meta-analysis [41]. In contrast, our study focuses explicitly on pancreatic cancer, incorporates more recent studies, and provides pooled risk estimates with detailed stratification by exposure source and study characteristics. Our results align with the recent meta-analysis by Soleimani et al. (2025), which also reported a positive association between cadmium exposure and pancreatic cancer. Compared to that analysis, our study included additional recent evidence, distinguished between incidence and mortality outcomes, and explored heterogeneity by exposure circumstance, revealing stronger and more consistent associations in occupational and biomarker-based studies [42]. While Lee et al. (2025) reported evidence of a dose-response relationship, we did not observe a statistically significant linear trend, possibly due to differences in exposure harmonization, analytical approach, and the limited number of studies with comparable internal dose metrics[43]. Finally, our findings expand upon the earlier meta-analysis by Chen et al. (2015) by incorporating occupational exposures and more recent cohort and nested case-control studies, supporting the robustness of the association across diverse populations and exposure pathways [44].

Several biological mechanisms support the hypothesis of a causal link between cadmium exposure and the development of pancreatic cancer: (i) Cd is a strong inducer of oxidative stress, which leads to the production of reactive oxygen species. This can result in lipid peroxidation, protein oxidation, and oxidative damage to DNA [45-46]. (ii) Although Cd is not mutagenic, it disrupts multiple DNA repair pathways, including nucleotide excision repair and base excision repair. This interference enhances genomic instability and increases the risk of malignant transformation [47-48]. (iii) Additionally, Cd acts as an endocrine disruptor and tends to accumulate in the pancreas. Experimental studies have demonstrated that it causes toxicity to pancreatic β-cells, impairs insulin secretion, and disrupts glucose homeostasis. These mechanisms may link cadmium exposure to a higher risk of diabetes and pancreatic cancer [49]. (iv) Cd also promotes chronic inflammation by activating pro-inflammatory signaling pathways and altering immune responses, which creates a microenvironment conducive to tumor growth [50-51].

Considerable heterogeneity was observed across the available studies, with an overall I^2 of 96%, indicating substantial variability beyond chance. Stratified analyses by exposure source, study design, gender, and outcome type partially explained this heterogeneity. For instance, heterogeneity was reduced in studies examining occupational cadmium exposure and in blood/serum biomarker-based studies, suggesting that differences in exposure circumstances contributed to variability in effect estimates. The long biological half-life and bioaccumulation of cadmium may also contribute to between-study heterogeneity, as studies relying on occupational histories or biomarkers capture cumulative exposure more effectively than those based on short-term or indirect exposure assessments [52].

The association between cadmium exposure and outcomes was stronger in men than in women. This may be due to higher levels of occupational exposure among men, possible interactions with

smoking, or gender-specific biological susceptibility to cadmium-induced pancreatic toxicity [53]. Tobacco smoking is both an important source of cadmium exposure and an established risk factor for pancreatic cancer [54]. Smoking may therefore act as a confounder in studies examining cadmium and pancreatic cancer. Most studies included in our review adjusted for smoking, and associations remained significant, suggesting that cadmium exposure may contribute to pancreatic cancer independent of tobacco smoking. However, residual confounding cannot be entirely excluded, particularly in studies relying on self-reported smoking or biomarker-based exposure assessments.

In terms of study design, case-control studies generally reported higher effect estimates than cohort studies. This difference may be attributable to recall or selection biases commonly associated with retrospective designs. In contrast, cohort studies tended to yield more conservative and methodologically robust estimates; however, many did not fully adjust for potential confounders [55]. Geographic differences were also observed: studies conducted in North America typically reported stronger associations compared to those from Japan and Europe. This variation may be attributed to differences in cadmium exposure levels, dietary sources, occupational regulations, or genetic and lifestyle factors, as well as to the limited number of studies from other regions.

This study has several strengths. We conducted a thorough literature search across multiple databases (PubMed, EMBASE, and Scopus) following PRISMA guidelines. Our analysis focused specifically on pancreatic cancer and addressed the risk associated with multiple sources of cadmium exposure, including occupational exposure, biological markers, dietary intake, and environmental indicators. We also performed stratified and subgroup analyses based on exposure source, gender, study design, geographic region, and outcomes.

However, there are some limitations to note. Exposure misclassification is possible due to variability in cadmium assessment methods and reliance on single-biomarker measurements or occupational classifications. There was a limited number of studies from regions outside North America, and only a few studies were included in the dose-response analysis. Future research should focus on large, prospective studies using standardized cadmium biomarkers and gender-specific analyses to clarify exposure-risk relationships.

5. Conclusion

In conclusion, this study suggests a positive association between cadmium exposure and pancreatic cancer risk, particularly in occupational and biomarker-based studies. However, substantial heterogeneity, potential residual confounding, and limited dose response data needed cautious interpretation.

Supplementary Materials: The following are available online: Table S1a. PRISMA Checklist, Table S1b. PRISMA Abstract Checklist, Table S2. Detailed search strategy used on the different databases, Table S3. Modified version of the Newcastle-Ottawa Scale (NOS) for case-control and cohort studies adopted for quality assessment, Table S4: Quality Assessment of Included Studies Using the Newcastle-Ottawa Scale (NOS) mentioned in supplementary table 3, Figure S1. Flowchart describing the study selection process, Figure S2. Funnel plot results in the association between cadmium exposure and pancreatic cancer by different exposure sources.

Acknowledgments: We are thankful to Germana Giupponi for her assistance with the evaluation process.

Author Contributions: Conceptualization: M.S.S, P.B, Methodology: M.S.S, P.B, Data curation: M.S.S, L.C, R.F.M, Statistical analysis: M.S.S, P.B, Validation: M.S.S, L.C, R.F.M, Writing: M.S.S, L.C, R.F.M, Reviewing and editing: M.S.S, L.C, R.F.M, P.B, Supervision: P.B

Conflicts of Interest: None of the authors has any conflicts of interest to declare.

Data and Resource Availability: The datasets generated during and/or analyzed in the current study are available from the corresponding author upon reasonable request.

References

1. Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2024;74[3]:229-263. Doi: 10.3322 /caac.21834. Epub 2024 Apr 4. PMID: 38572751.

2. Arnold M, Abnet CC, Neale RE, et al. Global burden of 5 major types of gastrointestinal cancer. *Gastroenterology*. 2020;159:335-349.e15.
3. Walter FM, Mills K, Mendonça SC, et al. Symptoms and patient factors associated with diagnostic intervals for pancreatic cancer [SYMPTOM pancreatic study]: a prospective cohort study. *Lancet Gastroenterol Hepatol*. 2016;1[4]: 298-306. Doi: 10.1016/S2468-1253[16]30079-6.
4. Cai J, Chen H, Lu M, et al. Advances in the epidemiology of pancreatic cancer: Trends, risk factors, screening, and prognosis. *Cancer Lett.* 2021;520:1-11. Doi: 10.1016/j.canlet.2021.06.027. Epub 2021 Jun 30. PMID: 34216688.
5. Antwi SO, Eckert EC, Sabaque CV, et al. Exposure to environmental chemicals and heavy metals, and risk of pancreatic cancer. *Cancer Causes Control*. 2015;26[11]:1583-91. Doi: 10.1007/s10552-015-0652-y. Epub 2015 Aug 21. PMID: 26293241; PMCID: PMC4624268.
6. Johri N, Jacquillet G, Unwin R. Heavy metal poisoning: the effects of cadmium on the kidney. *Biometals*. 2010;23(5):783-92. Doi: 10.1007/s10534-010-9328-y. Epub 2010 Mar 31. PMID: 20354761.
7. Agency for Toxic Substances and Disease Registry [ATSDR]. Toxicological profile for cadmium. Atlanta [GA]: U.S. Department of Health and Human Services, Public Health Service; 2012.
8. International Agency for Research on Cancer. Cadmium and cadmium compounds. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Vol. 100C. Lyon, France: IARC; 2012.
9. Snoj Tratnik J, Kocman D, Horvat M, et al. Cadmium exposure in adults across Europe: Results from the HBM4EU Aligned Studies survey 2014-2020. *Int J Hyg Environ Health*. 2022;246:114050. Doi: 10.1016/j.ijheh.2022.114050. Epub 2022 Oct 17. PMID: 36265402.
10. Järup L, Berglund M, Elinder CG, Nordberg G, Vahter M. Health effects of cadmium exposure--a review of the literature and a risk estimate. *Scand J Work Environ Health*. 1998;24 Suppl 1:1-51. Erratum in: *Scand J Work Environ Health* 1998;24(3):240. PMID: 9569444.
11. European Food Safety Authority. Scientific opinion of the Panel on Contaminants in the Food Chain on a request from the European Commission on cadmium in food. *EFSA J*. 2009;980:1-139. Doi: 10.2903/j.efsa.2009.980.
12. World Health Organization. Cadmium in drinking water: background document for development of WHO Guidelines for Drinking water Quality. Geneva: World Health Organization; 2010. WHO/SDE/WSH/03.04/80. Available from: https://iris.who.int/handle/10665/75364
13. Thévenod F. Cadmium and cellular signaling cascades: to be or not to be? *Toxicol Appl Pharmacol.* 2009;238(3):221-39. Doi: 10.1016/j.taap.2009.01.013. Epub 2009 Jan 29. PMID: 19371614.
14. Filipič M. Mechanisms of cadmium induced genomic instability. *Mutat Res*. 2012;733(1-2):69-77. Doi: 10.1016/j.mrfmmm.2011.09.002. Epub 2011 Sep 17. PMID: 21945723.
15. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ*. 2021. 372, n. 71. https://doi.org/10.1136/bmj.n71
16. Wells G A, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale [NOS] for assessing the quality of non-randomised studies in meta-analyses. Ottawa Hospital Research Institute. 2011. Available from: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp
17. Viechtbauer W. Conducting meta-analyses in R with the metafor package. *J Stat Softw*, 2010;36[3]:1-48. Doi: https://doi.org/10.18637/jss.v036.i03
18. Higgins J P T, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327(7414):557-560. Doi: https://doi.org/10.1136/bmj.327.7414.557
19. Zhang J, Yu KF. What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. *JAMA*, 1998;280(19):1690-1691.
20. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ*, 1997;315(7109):629-634. Doi: https://doi.org/10.1136/bmj.315.7109.629
21. Peters JL, Sutton AJ, Jones DR, Abrams KR, Rushton L. Contour-enhanced meta-analysis funnel plots help distinguish publication bias from other causes of asymmetry. *J Clin Epidemiol*, 2008:61(10):991-996. Doi: https://doi.org/10.1016/j.jclinepi.2007.11.010
22. van Aert RCM, Jackson D. A new justification of the Hartung-Knapp method for random-effects meta-analysis based on weighted least squares regression. *Res Synth Methods*. 2019;10(4):515-527. Doi: 10.1002/jrsm.1356. Epub 2019 Aug 14. PMID: 31111673; PMCID: PMC6973024.
23. Amaral AFS, Porta M, Silverman DT, et al. Pancreatic cancer risk and levels of trace elements. *Gut*. 2012;61(11): 1583-1588. Doi: 10.1136/gutjnl-2011-300264.
24. Adams SV, Passarelli MN, Newcomb PA. Cadmium exposure and cancer mortality in the Third National Health and Nutrition Examination Survey cohort. *Occup Environ Med*. 2012;69(2):153-156. Doi: 10.1136/oemed-2011-100111. Epub 2011 Nov 7. PMID: 22068173; PMCID: PMC3289533.
25. Kriegel AM, Soliman AS, Zhang Q, et al. Serum cadmium levels in pancreatic cancer patients from the East Nile Delta region of Egypt. *Environ Health Perspect*. 2006;114(1):113-119. Doi: 10.1289/ehp.8035. PMID: 16393667; PMCID: PMC1332665.
26. Luckett BG, Su LJ, Rood JC, Fontham ETH. Cadmium exposure and pancreatic cancer in South Louisiana. *J Environ Public Health*. 2012;2012:180186. Doi: 10.1155/2012/180186.
27. Sawada N, Iwasaki M, Inoue M, et al. Long-term dietary cadmium intake and cancer incidence.

Epidemiology. 2012;23(3):368-376. Doi: 10.1097/EDE.0b013e31824d063c.
28. Carrigan PE, Hentz JG, Gordon G, et al. Distinctive heavy metal composition of pancreatic juice in patients with pancreatic carcinoma. *Cancer Epidemiol Biomarkers Prev.* 2007;16(12):2656-2663. Doi: 10.1158/1055-9965.EPI-07-0332.
29. Duell E, Lujan-Barroso L, Outzen M, et al. Prediagnostic erythrocyte cadmium, selenium, and zinc levels and pancreatic cancer risk in Europe. *Pancreatology*. 2018;18(4 Suppl).
30. Djordjevic VR, Wallace DR, Schweitzer A, et al. Environmental cadmium exposure and pancreatic cancer: Evidence from case-control, animal and in vitro studies. *Environ Int.* 2019;128:353-361. Doi: 10.1016/j.envint.2019.04.048.
31. García-Esquinas E, Pollan M, Tellez-Plaza M, et al. Cadmium exposure and cancer mortality in a prospective cohort: the Strong Heart Study. *Environ Health Perspect.* 2014;122(4):363-370. Doi: 10.1289/ehp.1306587. Epub 2014 Feb 14. PMID: 24531129; PMCID: PMC3984227.
32. Järup L, Bellander T, Hogstedt C, Spång G. Mortality and cancer incidence in Swedish battery workers exposed to cadmium and nickel. *Occup Environ Med.* 1998;55(11):755-759. Doi: 10.1136/oem.55.11.755. PMID: 9924452; PMCID: PMC1757526.
33. Nishijo M, Nakagawa H, Suwazono Y, et al. Cancer mortality in residents of the cadmium-polluted Jinzu River Basin in Toyama, Japan. *Toxics*. 2018 Apr 6;6(2):23. Doi: 10.3390/toxics6020023. PMID: 29642374; PMCID: PMC6027272.
34. Nyqvist F, Helmfrid I, Augustsson A, Wingren G. Increased cancer incidence in the local population around metal-contaminated glassworks sites. *J Occup Environ Med*. 2017;59(5). Doi: 10.1097/JOM.0000000000000984.
35. Stolzenberg-Solomon R, Jin D, Huang WY, Brockman J. Prediagnostic whole-blood cadmium and molybdenum associated with pancreatic cancer in an American cohort. *Am J Epidemiol.* 2025 7;194(5):1275-1284. Doi: 10.1093/aje/kwae165. PMID: 38965764; PMCID: PMC13070527.
36. Sakurai M, Suwazono Y, Nishijo M, et al. The relationship between the urinary cadmium concentration and cause-specific mortality in subjects without severe renal damage: a 35-year follow-up study in a cadmium-polluted area of Japan. *Int J Environ Res Public Health*. 2021;18(15):7747. Doi: 10.3390/ijerph18157747. PMID: 34360038; PMCID: PMC8345790.
37. Watanabe Y, Nogawa K, Nishijo M, et al. Relationship between cancer mortality and environmental cadmium exposure in the general Japanese population in cadmium non-polluted areas. *Int J Hyg Environ Health*. 2020;223(1):65-70. Doi: 10.1016/j.ijheh.2019.09.011.
38. Weiderpass E, Vainio H, Kauppinen T, Vasama-Neuvonen K, Partanen T, Pukkala E. Occupational exposures and gastrointestinal cancers among Finnish women. *J Occup Environ Med*. 2003;45(3):305-315. Doi: 10.1097/01.JOM.0000052963.43131.44.
39. Sorahan T, Lister A, Gilthorpe MS, Harrington JM. Mortality of copper cadmium alloy workers with special reference to lung cancer and non-malignant diseases of the respiratory system, 1946-92. *Occup Environ Med.* 1995;52(12):804-812. Doi: 10.1136/oem.52.12.804. PMID: 8563843; PMCID: PMC1128381.
40. Zhang Y, Cantor KP, Lynch CF, Zhu Y, Zheng T. Occupation and risk of pancreatic cancer: a population-based case-control study in Iowa. *J Occup Environ Med*. 2005;47(4):392-398.
41. Fanfani A, Papini S, Bortolotti E, et al. Cadmium in biological samples and site-specific cancer risk and mortality: A systematic review of original articles and meta-analyses. *Cancer Epidemiol.* 2024;92:102550. Doi: 10.1016/j.canep.2024.102550. Epub 2024 Mar 12. PMID: 38480109.
42. Soleimani Y, Nayebi M, Mahmoudi S, et al. Cadmium exposure and risk of pancreatic cancer: Systematic review and meta-analysis. *PLoS One.* 2025;20(4):e0319283. Doi: 10.1371/journal.pone.0319283. PMID: 40299947; PMCID: PMC12040173.
43. Lee FJ, Inchai H, Lin JT, Koh D, Lin RT. Dose-response relationship of cadmium and pancreatic cancer risk: a meta-analysis. *Occup Environ Med.* 2025;82(8):407-414. Doi: 10.1136/oemed-2025-110163. PMID: 40962531; PMCID: PMC12573421.
44. Chen C, Xun P, Nishijo M, Sekikawa A, He K. Cadmium exposure and risk of pancreatic cancer: a meta-analysis of prospective cohort studies and case-control studies among individuals without occupational exposure history. *Environ Sci Pollut Res Int.* 2015;22(22):17465-74. Doi: 10.1007/s11356-015-5464-9. Epub 2015 Oct 1. PMID: 26423282; PMCID: PMC4654666.
45. Stohs SJ, Bagchi D, Hassoun E, Bagchi M. Oxidative mechanisms in the toxicity of chromium and cadmium ions. *J Environ Pathol Toxicol Oncol*. 2000;19(3):201-13. PMID: 10983887.
46. Thévenod F, Lee WK. Cadmium and cellular signaling cascades: interactions between cell death and survival pathways. *Arch Toxicol.* 2013;87:1743-1786. Doi: https://doi.org/10.1007/s00204-013-1110-9
47. Hartwig A. Mechanisms in cadmium-induced carcinogenicity: recent insights. *Biometals*. 2010;23(5):951-60. Doi: 10.1007/s10534-010-9330-4. PMID: 20390439.
48. Joseph P. Mechanisms of cadmium carcinogenesis. *Toxicol Appl Pharmacol.* 2009;238(3):272-9. Doi: 10.1016/j.taap.2009.01.011. Epub 2009 Feb 6. PMID: 19371617.
49. Joshua R. Edwards, Walter C. Prozialeck, Cadmium, diabetes and chronic kidney disease, *Toxicol Appl Pharmacol*. 2009;238(3):289-293. Doi: https://doi.org/10.1016/j.taap.2009.03.007.
50. Kolawole TA, Palacios J, Husaini DC, Nwokocha CR. Inflammation and Oxidative Stress Biomarkers in Heavy Metal Toxicity: Bridging the Gap to

Personalized Clinical Interventions. *J Appl Toxicol*. 2025;45(12):2546-2579. Doi: 10.1002/jat.4874. Epub 2025 Aug 14. PMID: 40813054.
51. Liu J, Qu W, Kadiiska MB. Role of oxidative stress in cadmium toxicity and carcinogenesis. *Toxicol Appl Pharmacol.* 2009;238(3):209-14. Doi: 10.1016/j.taap.2009.01.029. Epub 2009 Feb 21. PMID: 19236887; PMCID: PMC4287357.
52. Davidova S, Milushev V, Satchanska G. The Mechanisms of Cadmium Toxicity in Living Organisms. *Toxics.* 2024;12(12):875. Doi: 10.3390/toxics12120875. PMID: 39771090; PMCID: PMC11679562.
53. Lu H, Delnicki M, Griffin G, Wise JL. Current Understanding of Sex Differences in Metal-Induced Diseases. *Curr Environ Health Rep*. 2025;12(1):18. Doi: 10.1007/s40572-025-00482-x. PMID: 40202678; PMCID: PMC12168244.
54. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Tobacco Smoke and Involuntary Smoking. Lyon [FR]: International Agency for Research on Cancer; 2004. [IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, No. 83.] Available from: https://www.ncbi.nlm.nih.gov/books/NBK316407/
55. Ahlbom A. Modern Epidemiology, 4th edition. TL Lash, TJ VanderWeele, S Haneuse, KJ Rothman. Wolters Kluwer, 2021. *Eur J Epidemiol.* 2021;36(8):767-768.Doi:10.1007/s10654-021-00778-w.Epub2021 Jul 3. PMID: 34216355; PMCID: PMC8416883.

Med. Lav. 2026; 117 (3): 19093 - DOI: 10.23749/mdl.2026.19903

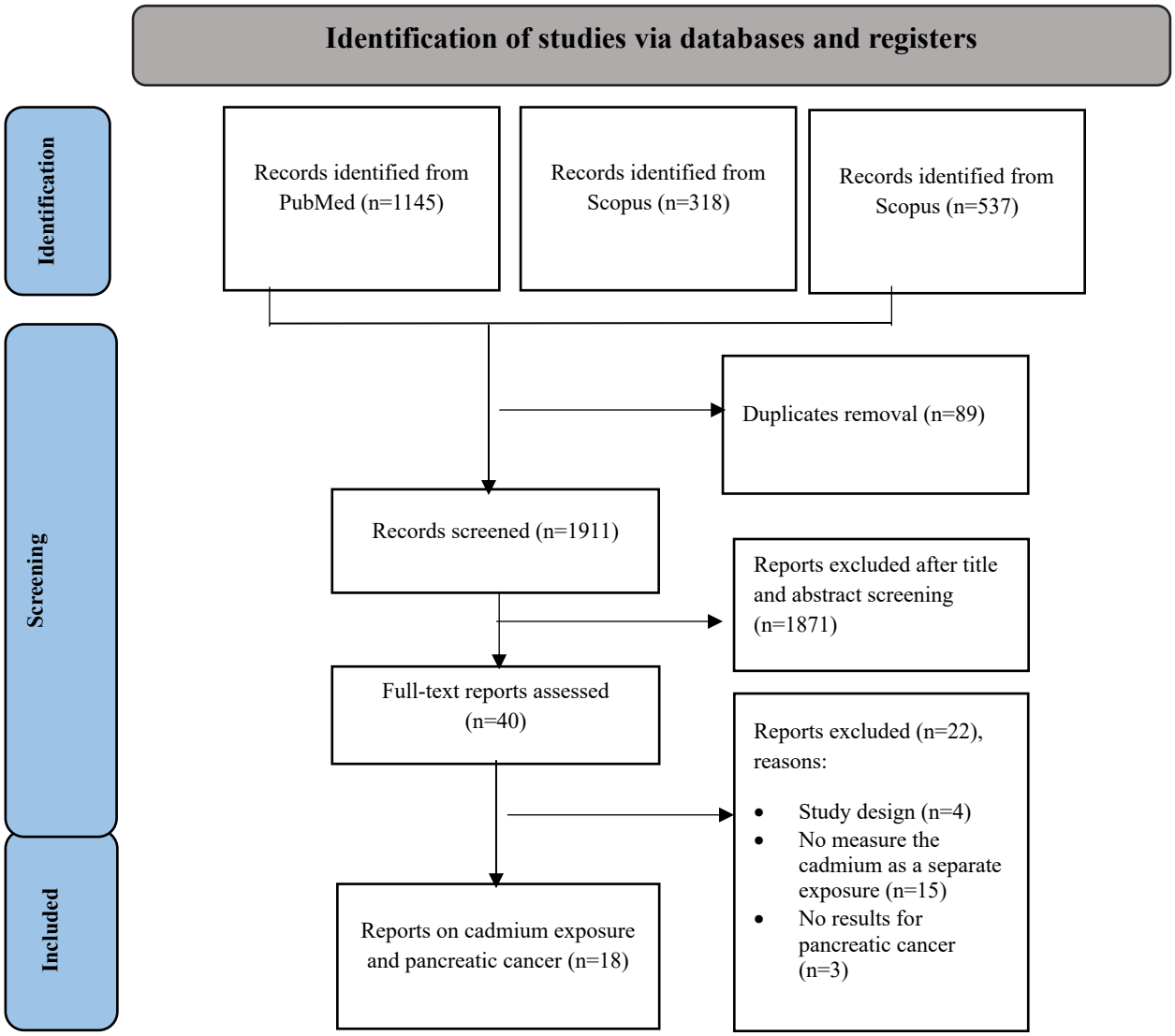
Cadmium Exposure and Risk of Pancreatic Cancer: A Systematic Review and Meta-Analysis

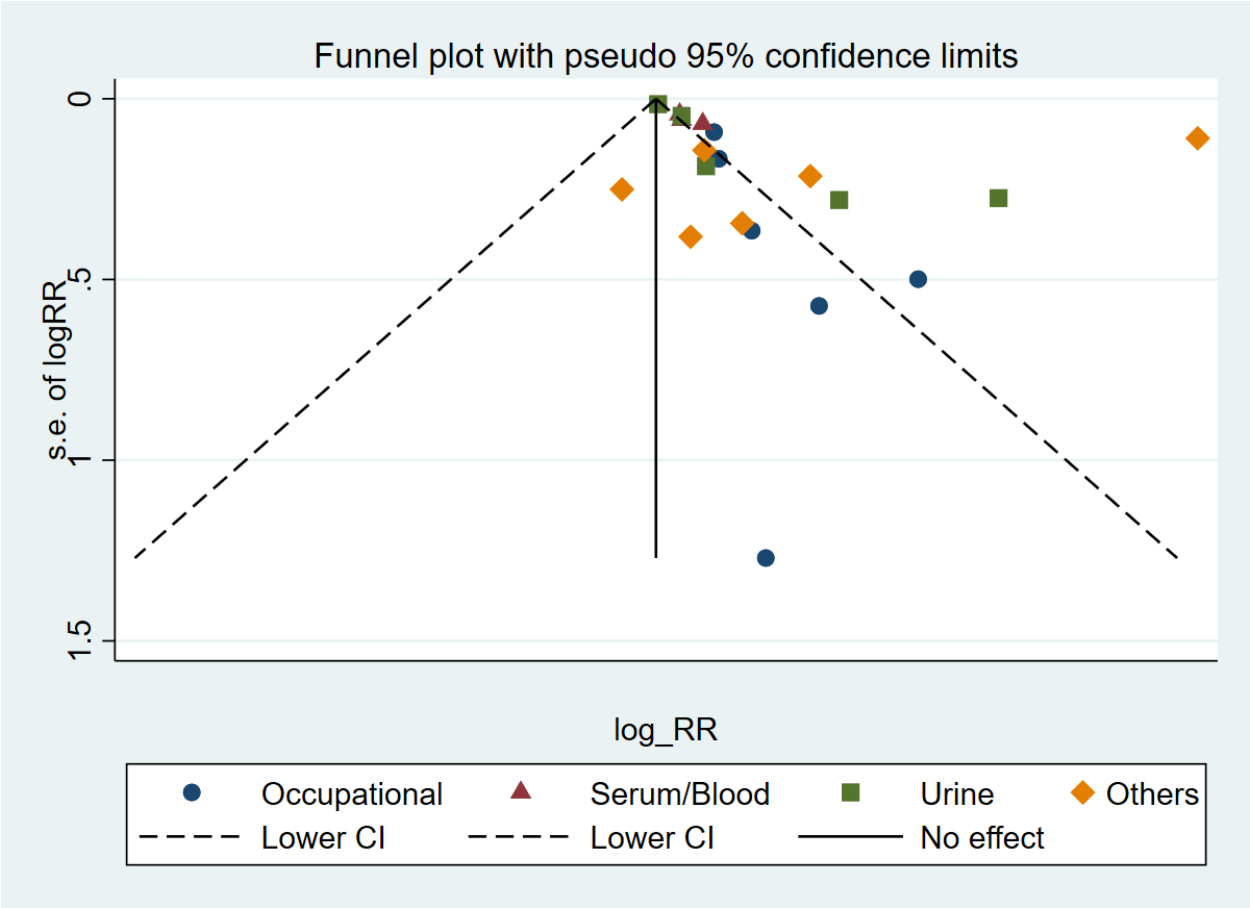
Monireh Sadat Seyyedsalehi, Lorenzo Ciaccio, Rosa Francesca Marra, Paolo Boffetta

SUPPLEMENTARY MATERIALS

Supplementary Table S1-a. PRISMA Checklist
Supplementary Table S1-b. PRISMA Abstract Checklist
Supplementary Table S2. Detailed search strategy used on the different databases.
Supplementary Table S3. Modified version of the Newcastle-Ottawa Scale (NOS) for case-control and cohort studies adopted for quality assessment.
Supplementary Table S4: Quality Assessment of Included Studies Using the Newcastle–Ottawa Scale (NOS) mentioned in supplementary table 4
Supplementary Figure 1. Flowchart describing the study selection process.
Supplementary Figure 2. Funnel plot results in the association between cadmium exposure and pancreatic cancer by different exposure sources.

Supplementary Figure 1. Flowchart describing the study selection process.





Supplementary Figure 2. Funnel plot results in the association between cadmium exposure and pancreatic cancer by different exposure sources. [Occupational [P = 0.087], Serum/blood [P = 0.371], Urine [P = 0.045], Others [P = 0.169]].

Supplementary Table S1. PRISMA Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	P1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	P2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	P3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	P3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	P4
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	P4
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	P4, Supplementary Table 1
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	P4
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	P4
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	P4
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	P4
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	P4
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	P5
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	P5
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	P5
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	P5
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	P5
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	P5
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	P5
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	P5
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of	P5

Section and Topic	Item #	Checklist item	Location where item is reported
		evidence for an outcome.	
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	P6, supplementary figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	supplementary figure 1
Study characteristics	17	Cite each included study and present its characteristics.	P6
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	P6
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimates and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	P6, Supplementary Table 3
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	P6, Supplementary Table 3
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	P6, Figures 1
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	P6, Figure 2
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	P6
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	P7
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	P7
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	P8
	23b	Discuss any limitations of the evidence included in the review.	P8
	23c	Discuss any limitations of the review processes used.	P8
	23d	Discuss implications of the results for practice, policy, and future research.	P8
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	P1, 4
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	NA
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	NA
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	P1
Competing interests	26	Declare any competing interests of review authors.	P1
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	P1

Supplementary Table S1-b. PRISMA Abstract Checklist

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	P2-line4
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Page3-line5
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	-
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	p3-line7
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Page3-line12
Synthesis of results	6	Specify the methods used to present and synthesise results.	page3-line10
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	page3-line9, line
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Page3-line 14 to 20

Supplementary Table S2. Detailed search strategy used on the different databases.

Database	Search string
PubMed	((Cadmium[MeSH Terms] OR cadmium[Text Word] OR cadmium exposure[Text Word] OR environmental cadmium[Text Word] OR cadmium toxicity[Text Word] OR Cd[Text Word]) AND ("Neoplasms"[MeSH Terms] OR cancer[Text Word] OR neoplasm[Text Word] OR malignant[Text Word] OR tumor[Text Word] OR tumour[Text Word] OR malignan[Text Word] OR carcinoma[Text Word])) AND ("pancreas"[MeSH Terms] OR pancreatic [Text Word] OR pancreas [Text Word]))
Scopus	(TITLE-ABS-KEY ("Cadmium")) AND (ALL("Neoplasms") OR ALL("cancer") OR ALL("neoplasm") OR ALL("malignant") OR ALL("tumor") OR ALL("tumour") OR ALL("malignan") OR ALL("carcinoma ")) AND (ALL ("pancreas") OR ALL ("pancreatic")) AND (LIMIT-TO (SRCTYPE,"j")) AND (LIMIT-TO (DOCTYPE,"ar")) AND (LIMIT-TO (LANGUAGE,"English")) AND (LIMIT-TO (EXACTKEYWORD,"Human") OR LIMIT-TO (EXACTKEYWORD,"Humans") OR LIMIT-TO (EXACTKEYWORD,"Male") OR LIMIT-TO (EXACTKEYWORD,"Female")) AND (EXCLUDE (SUBJAREA,"ARTS") OR EXCLUDE (SUBJAREA,"EART") OR EXCLUDE (SUBJAREA,"SOCI") OR EXCLUDE (SUBJAREA,"VETE") OR EXCLUDE (SUBJAREA,"MATE") OR EXCLUDE (SUBJAREA,"ENGI") OR EXCLUDE (SUBJAREA,"COMP") OR EXCLUDE (SUBJAREA,"CENG") OR EXCLUDE (SUBJAREA,"MULT") OR EXCLUDE (SUBJAREA,"BIOC") OR EXCLUDE (SUBJAREA,"PHAR") OR EXCLUDE (SUBJAREA,"NURS") OR EXCLUDE (SUBJAREA,"AGRI") OR EXCLUDE (SUBJAREA,"IMMU") OR EXCLUDE (SUBJAREA,"CHEM") OR EXCLUDE (SUBJAREA,"NEUR") OR EXCLUDE (SUBJAREA,"PSYC") OR EXCLUDE (SUBJAREA,"DENT") OR EXCLUDE (SUBJAREA,"PHYS"))
Embase	(Cadmium).tx. and (Neoplasms or cancer or neoplasm or malignant or tumor or tumour or malignan or carcinoma). tx. and (pancreas or pancreatic). tx. limit to original articles

	limit to (alternative & complementary medicine or clinical medicine or health professions or life & biomedical sciences or life sciences or medical humanities or nursing or patient education or pharmacology or public health or science or traditional Chinese medicine)

Supplementary Table S3: Newcastle - Ottawa quality assessment scale

CASE CONTROL STUDIES (maximum score: 9)

Selection

1) Is the case definition adequate?

a) yes, with independent validation **(1)**

b) yes, eg record linkage **(1)** or based on self-reports **(0.5)**

c) no description **(0)**

2) Representativeness of the cases

a) consecutive or obviously representative series of cases **(1)**

b) potential for selection biases or not stated **(0)**

3) Selection of Controls

a) community controls **(1)**

b) hospital controls **(0.5)**

c) no description **(0)**

4) Definition of Controls

a) no history of disease (endpoint) **(1)**

b) no description of source **(0)**

Comparability

1) Comparability of cases and controls on the basis of the design or analysis

a) study controls for age, gender, province **(0)**

b) study controls for age, gender, province +smoking **(1)**

c) study controls for age, gender, province +smoking + other additional factors **(2)**

Exposure

1) Ascertainment of exposure

a) secure record (eg surgical records) **(1)**

b) structured interview where blind to case/control status **(1)**

c) interview not blinded to case/control status **(0.5)**

d) written self-report or medical record only **(0.5)**

e) no description **(0)**

2) Same method of ascertainment for cases and controls

a) yes **(1)**

b) no **(0)**

3) Non-Response rate

a) one or both groups over 90% **(1)**

b) one or both groups between 60- 90% **(0.5)**

c) one or both groups under 60% **(0)**

d) no statemen **(0)**

COHORT STUDIES (maximum score: 10)

Selection

1) Representativeness of the exposed cohort

a) truly representative of the average _____ (describe) in the community **(2)**

b) somewhat representative of the average _____ in the community **(1)**

c) selected group of users eg nurses, volunteers **(0.5)**

d) no description of the derivation of the cohort **(0)**

2) Selection of the non-exposed cohort

a) drawn from the same community as the exposed cohort **(1)**

b) drawn from a different source **(0.5)**

c) no description of the derivation of the non-exposed cohort **(0)**

3) Ascertainment of exposure

a) secure record (eg surgical records) **(1)**

b) structured interview **(1)**

c) written self-report **(0.5)**

d) no description **(0)**

4) Demonstration that outcome of interest was not present at start of study

a) yes **(1)**

b) no **(0)**

Comparability

1) Comparability of cohorts on the basis of the design or analysis

a) study controls for age, gender, province **(0)**

b) study controls for age, gender, province +smoking **(1)**

c) study controls for age, gender, province +smoking + other additional factors **(2)**

Outcome

1) Assessment of outcome

a) independent blind assessment **(1)**

b) record linkage **(1)**

c) self-report **(0.5)**

d) no description **(0)**

2) Was follow-up long enough for outcomes to occur

a) yes (select an adequate follow up period for outcome of interest) **(1) (average 15 years)**

b) no **(0)**

3) Adequacy of follow up of cohorts

a) complete follow up - all subjects accounted for over 90% **(1)**

b) subjects lost to follow up unlikely to introduce bias - small number lost - > ___ % (select an adequate %) follow up, or description provided of those lost) between 60- 90% **(0.5)**

c) follow up rate < ___% (select an adequate %) and no description of those lost under 60% **(0)**

d) no statemen **(0)**

Supplementary Table S4: Quality Assessment of Included Studies Using the Newcastle–Ottawa Scale (NOS) mentioned in supplementary table 3										
Ref.	Study design	Selection				Comparability	Exposure			
		Item1	Item2	Item3	Item4	Item1	Item1	Item2	Item3	Total
Kriegel,2006	Case control	1	1	0.5	1	1	1	1	0	6.5/9
Luckett,2012	Case control	1	0.5	1	1	1	1	1	0	6.5/9
Sawada,2012	Cohort	2	1	1	1	2	1	1	1	10/10
Amaral,2012	Case control	1	0	0.5	0.5	2	1	1	0.5	6.5/9
Adams,2012	Cohort	2	1	1	1	2	1	1	1	10/10
Garca-Esquinas,2014	Cohort	2	1	1	1	2	1	1	1	10/10
Watanabe,2020	Cohort	2	1	1	1	2	1	1	1	10/10
Stolzenberg-Solomon,2025	Nested case control	1	1	1	1	2	1	1	1	9/9
Weiderpass,2003	Cohort	1	1	1	1	1	1	1	1	8/10
Djordjevic,2019	Case control	1	1	0.5	1	0	1	1	0	5.5/9
Zhang,2005	Case control	1	1	1	1	2	0.5	1	0.5	8/9
Duell,2018	Nested case control	1	1	1	1	2	1	1	1	9/9
Järup,1998	Cohort	2	0.5	1	1	1	1	1	1	8.5/10
Nishijo,2018	Cohort	2	1	1	1	1	1	1	1	9/10
Nyqvist,2017	Cohort	2	1	1	1	0	1	1	1	8/10
Sakurai,2021	Cohort	2	0	1	1	1	1	1	1	8/10
Sorahan ,1995	Cohort	1	1	1	1	0	1	1	1	7/10
Carrigan,2007	Case control	1	1	0.5	1	1	1	1	1	7.5/9

La Medicina del Lavoro

Original article

Med. Lav. 2026; 117 (3): 18795
DOI: 10.23749/mdl.2026.18795

Objective Assessment of Visual Workload in Video Display Terminal Workers Using a Non-Invasive Monitoring System

Edoardo Marelli[1,*], Davide Ruongo[1,*], Giacomo Beschi[2,3], Nicolò Valsecchi[2,3], Vito Romano[2,3], Francesco Semeraro[2,3], Simone Dalola[4], Emma Sala[1], Cesare Tomasi[1], Vittorio Ferrari[4], Marco Ferrari[4], Giuseppe De Palma[1,†]

[1]Unit of Occupational Health and Industrial Hygiene, Department of Medical and Surgical Specialties, Radiological Sciences, and Public Health, University of Brescia, Brescia, Italy
[2]Eye Unit, ASST Spedali Civili di Brescia, Brescia, Italy
[3]Eye Unit, Department of Medical and Surgical Specialties, Radiological Sciences, and Public Health, University of Brescia, Italy
[4]Department of Information Engineering, University of Brescia, Brescia, Italy

Keywords: VDT; Objective Assessment; Dry Eye; Workers; Ophthalmological Evaluation; Display; Ocular Surface; Occupational Health; Screen Fixation; Monitoring System

Abstract

Background: *The risk assessment for video display terminal (VDT) operators in occupational settings often relies on indirect estimates, such as self-reported screen time, which may not accurately reflect the true visual workload. The objective is to assess visual workload in VDT workers by measuring active screen fixation time with a non-invasive monitoring system and to explore its relationship with ocular surface alterations and fatigue-related indicators.* **Methods:** *An observational cross-sectional study was conducted on 38 administrative workers employed at a hospital booking center. Active VDT screen fixation, as well as shift duration and time spent in front of the VDT screen, were objectively measured using a patented video-based monitoring system. Ophthalmological evaluation included the Ocular Surface Disease Index (OSDI®), tear break-up time (BUT), and slit-lamp examination. Other investigated markers included blink rate, the Percentage of Eyelid Closure over the Pupil over Time (PERCLOS), and the Fatigue Assessment Scale (FAS).* **Results:** *Active screen fixation accounted for approximately 60% of the total recorded working time. Ophthalmological assessment identified alterations of the ocular surface in a substantial proportion of workers, with pathological BUT values observed in nearly half (47%) of the study population. No statistically significant associations were found between objectively measured fixation time and ocular or fatigue-related outcomes. PERCLOS80 and blink rate values remained within physiological ranges across the work shift.* **Conclusions:** *Objective measurement of screen fixation provides a more accurate characterization of visual workload among VDT workers than indirect exposure estimates and may support occupational health surveillance and risk assessment in VDT-exposed workers.*

Received 04.03.2026 – Accepted 04.06.2026
†Corresponding Author: Giuseppe De Palma; E-mail: giuseppe.depalma@unibs.it
* The first two authors contributed equally to this article

1. Introduction

In the contemporary digital era, video display terminals (VDTs) are widely used across occupational settings. Digitalization has profoundly transformed work organization, particularly in administrative and service sectors, where screen-based activities are a major component of daily tasks [1]. While digital technologies improve efficiency and productivity, they also introduce potential visual and systemic health risks that require systematic evaluations by occupational health professionals, including ergonomists, prevention technicians, and physicians [1, 2]. Italian occupational safety and health legislation [2] classifies workers as VDT-exposed and at risk when VDT use is at least 20 hours per week, including physiological recovery breaks. This threshold, absent in Council Directive 90/270/EEC, which limits itself to "daily work on display screen equipment for an hour or more at a time", represents a more operational national implementation of the EU minimum framework, incorporating requirements for workstation analysis (Annex XXXIV), breaks (15 minutes every 2 hours), biennial health surveillance, and specific training. Council Directive 90/270/EEC, the fifth individual directive under Framework Directive 89/391/EEC, emphasizes general ergonomic standards for equipment (adjustable display, separate keyboard), environment (noise <55 dB, adequate lighting), and human-machine interface (eye level 15° below screen horizon), and mandates risk assessments for visual, musculoskeletal, and psychosocial hazards, with "appropriate" breaks and free eye tests. This European legislation, from which the Italian approach derives, underscores the need to replace self-reported estimates with objective methods to accurately assess effective exposure, as proposed in the present study, because in real-world conditions, workers frequently alternate screen use with other activities, making self-reported exposure prone to misclassification.

Prolonged VDT use has been linked to visual and ocular disorders, including computer vision syndrome and dry eye disease, as well as musculoskeletal complaints and mental fatigue [3-12]. These outcomes are influenced by actual visual engagement with the screen [13], which is rarely quantified objectively in occupational settings.

Computer vision syndrome (CVS) is a possible health consequence characterized by a wide range of visual and ocular symptoms, frequently associated with prolonged computer use. CVS affects 75% to 90% of computer users, with an estimated global prevalence of approximately 60 million people [14-20]. Common symptoms (visual fatigue, blurred vision, dry eyes, red eyes, and headaches) are often linked to ocular surface discomfort and are commonly reported in patients with dry eye disease. During prolonged screen fixation, VDT operators tend to reduce their blink rate and exhibit a higher proportion of incomplete blinks. This leads to increased tear film evaporation, tear film instability, and consequent ocular surface symptoms. This process can be self-perpetuating and worsen over the years, severely affecting quality of life and, as suggested by some studies, correlating with mental disorders such as depression, depending on the severity of symptoms [21-28].

The Percentage of Eyelid Closure Over the Pupil Time (PERCLOS) is one of the most promising and widely validated markers of fatigue, drowsiness, and reduced alertness without interrupting ongoing activities [29-31]. Studies have demonstrated its effectiveness in detecting fatigue among vehicle drivers [32], nuclear power plant operators [33], and air traffic controllers [34]. In addition, PERCLOS has been integrated into real-time monitoring technologies, often combined with other physiological and behavioral parameters to improve detection sensitivity and accuracy [31]. However, PERCLOS can be influenced by moderate sleepiness, environmental factors, or individual variations, as highlighted by some recent research [29, 31]. Researchers suggest combining PERCLOS with other metrics, such as blink rate or eye movements, and conducting more in-depth studies in real-world settings [32-33].

In earlier research [13], we validated a novel system that objectively measures active VDT interaction. It does so by collecting electrical impulses produced by mouse and keyboard use, along with visual fixation on the screen detected via a camera. This system enables analysis of various job tasks and outlines unique interaction profiles for different users and VDTs. Building on this approach, the present study aimed to objectively assess visual workload in

VDT workers by measuring active screen fixation time with a non-invasive monitoring system and to explore potential relationships with ocular effects and fatigue markers.

2. Methods

2.1. Instruments

VDT Visual Monitoring System (VMS). VDT Visual Monitoring System (VMS) prototype was developed by the Department of Information Engineering in collaboration with the Unit of Occupational Medicine and Industrial Hygiene of the University of Brescia. The system has been previously described and validated [35]. Briefly, it consists of a webcam positioned on the PC monitor in front of the operator and a laptop running dedicated software that processes camera signals and generates a report of specific events, including true screen fixation and face detection without active interaction, along with their respective durations. Below is a scheme (Figure 1) representing the workstation equipped with the VDT VMS, which has been described elsewhere [35].

Compared with previous versions, the updated prototype can detect true eye–screen fixation by improving identification of the worker's pupils and their relative spatial positions. The system requires an initial calibration phase during which the individual pupil position is recorded while the worker fixates the screen. When pupil centers align with calibration coordinates, a screen fixation event is recorded and the corresponding time counter is updated. Deviations along the vertical or horizontal axis are recorded as face detection (worker at the workstation, in front of the screen) without fixation. Worker privacy is ensured because no facial images or screen content is stored.

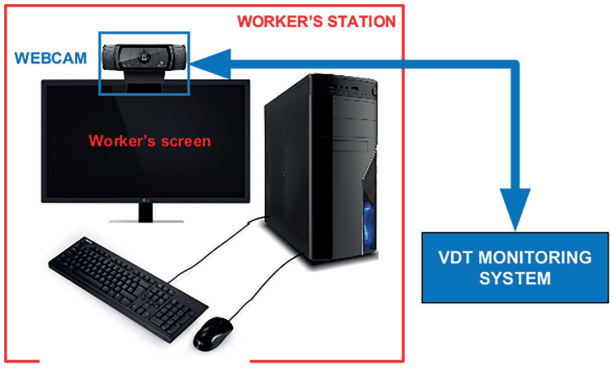


Figure 1. Setting of the monitoring system.

PupilCore® by Pupil Labs®. The Pupil Core® system (Pupil Labs®, Berlin, Germany) consists of a lightweight, glasses-like frame without corrective lenses, housing three cameras: one outward-facing camera and two inward-facing infrared cameras oriented toward the eyes. In this study, the outward-facing camera was occluded to ensure privacy. The manufacturer's software was used to collect raw data on eyelid opening and blinking behavior. Data analysis focused on blink rate and PERCLOS. Specifically, eyelid closure of at least 80% (PERCLOS80) was considered a marker of drowsiness [36]. Raw data were exported and processed using Microsoft Excel® (Office 365).

2.2. Study Design

This observational cross-sectional study included 38 administrative workers (6 males, 32 females; mean age 36.7 ± SD 11.2 years) employed at the booking center of the University Hospital ASST Spedali Civili of Brescia, Italy. Table 1 summarizes the main demographic and clinical characteristics of the study population. The sample consisted predominantly of female workers (84%). Relevant clinical conditions that may affect ocular surface status were recorded, including allergies (37%), thyroid disorders (16%), and hypertension (13%). Contact lens use was reported by 24% of participants.

The duration of service in the current job position was 5.7 ± 3.8 years, with a range of 0.5 to 10.5 years. Tasks included interacting with service users, computerized data entry, and printing reservation documents, with alternating periods of screen fixation and face-to-face interaction.

All the evaluations performed in the study were included in occupational risk assessment and health surveillance that are mandatory by law; therefore, approval by the local Ethics Committee was not required, consistent with the criteria established by the Italian Ministry of Health Decree of 30

Table 1. Demographic and clinical characteristics of the study population.

Parameters	Mean+SD (range)	No.	%
Gender, M/F		6/32	16/84
Age	36.7+11.2 (20-60)		
Work Seniority	6, 4 (1-11)		
BUT Values, Right; Left	8.7+2.5 (0.5-10); 8.1+2.9 (0.5-10)		
BUT Bilateral, Altered/Normal		18/20	47/53
Contact Lenses Use		9	24
Thyroid Disorders		6	16
Hypertension		5	13
Autoimmune Diseases		2	5
Allergies		14	37
Use of Antihistamines		7	18
Use of Antidepressants		2	5
Glaucoma		1	3
Eye Surgery		1	2.6

January 2023 for observational studies conducted in the context of occupational health monitoring. The study was conducted in accordance with the WMA Declaration of Helsinki and the General Data Protection Regulation (GDPR, Regulation EU 679/2016).

Participants followed a standardized protocol: (a) administration of the Fatigue Assessment Scale (FAS) [37-38]; (b) reading a standardized text (introductory chapter of *The Leopard* by Giuseppe Tomasi di Lampedusa) on a laptop for approximately 10 minutes while wearing the Pupil Core® device; (c) performance of routine work activities at a workstation equipped with the VDT VMS for the entire work shift, including breaks; (d) removal of the VDT VMS at the end of the shift; and (e) repetition of the reading task.

For interpreting the FAS questionnaire, the following criteria were used: scores below 22: absence of fatigue; scores between 22 and 34: mild to moderate fatigue; scores above 34: severe fatigue [37].

The shifts varied in length, depending on the internal organization, that guarantees the service from 6 a.m. to 9 p.m., with shifts lasting from 4 to 8 hours, including breaks.

All participants underwent comprehensive ophthalmological evaluation including medical history, Ocular Surface Disease Index (OSDI®) questionnaire, tear Non-Invasive Break-up Time (NI-BUT) measurement evaluated with HD Analyzer aberrometer (Visiometrics S.L., Terrassa, Spain), and slit-lamp examination. OSDI® scores were classified as normal (0–12), mild (13–22), moderate (23–32), or severe (33–100) dry eye disease. BUT values below 10 seconds were considered altered.

2.3. Statistical Analysis

VDT VMS data were processed using dedicated software and stored in a Microsoft Excel® database. Pupil Core® recordings were analyzed to extract blink rate and PERCLOS80 values. PERCLOS80 has been calculated in Microsoft Excel® from single-frame data processed by the PupilCore® software, which provided precise eyelid aperture percentages based on infrared camera captures.

Ophthalmological and occupational data were merged into a single dataset. Data were analyzed using IBM SPSS® Statistics (version 30.01; IBM SPSS Inc., Chicago, Illinois) and Stata® (version 19.1; Stata Corporation, College Station, Texas). Normality was assessed with the Kolmogorov-Smirnov test. Continuous variables were summarized as mean ± standard deviation or as median (range), depending on their distribution. Group comparisons were performed using parametric or non-parametric tests, based on the assessment of normality. Correlation analyses were conducted using Pearson's or Spearman's coefficients, as appropriate. When the assumptions for parametric analysis were met, Pearson's correlation was complemented by univariable linear regression models to further characterize the magnitude and direction of the association between exposure and outcome variables.

3. Results

Table 2 resumes the descriptive statistics of the times recorded by the VDT VMS in workers stratified by gender. Males showed significantly higher exposure indices than females (p values ranging from p=0.0368 to p=0.0023).

Such job-related gender differences were not associated with any significant differences in the investigated markers of ocular effects, drowsiness, or fatigue.

Based on OSDI® questionnaire scores, 21 workers (55%) reported no symptoms consistent with dry eye disease. Mild dry eye disease (DED) was identified in 7 workers (18%), moderate DED in 3 workers (8%), and severe DED in 7 workers (18%). Tear break-up time (BUT) assessment showed normal values in 20 workers (53%), whereas altered BUT values (<10 sec. in at least one eye) were observed in 18 workers (47%).

The OSDI® questionnaire scores were significantly correlated with screen fixation time (Spearman's rho = 0.34, p = 0.0349) but not with shift duration or workers' time at the workstation.

Figure 2 illustrates the significant positive relationship between shift duration and employees' time at the workstation (Linear regression analysis: Y = 0.562X; $R^2 = 0.92$, $p < 0.001$).

Figure 3 illustrates the significant relationship between employees' time at the workstation and the duration of active VDT screen fixation (Linear regression analysis: Y = 0.342X; $R^2 = 0.86$, $p < 0.001$).

Figure 4 shows the relationship between the time workers spent in front of the VDT screen and active screen fixation, with an even stronger correlation observed (Linear regression analysis: Y=0.611X; $R^2=0.94$, $p < 0.001$).

The blink rate at the end of the shift showed an increase of about 34% (mean of 17 ± 12.3 blinks/min), as compared to the values recorded at the beginning of the work shift (mean of 13.1 ± 8.3 blinks/min), approaching statistical significance (p = 0.051). PERCLOS80 values did not show significant variations throughout the shift (mean values of 10.7 ± 16.3% *vs* 10.8 ± 15.0% before and at the end of the shift, respectively), indicating mild drowsiness without significant variation over the shift. Such results were in agreement with the FAS questionnaire, whose results indicated absence of fatigue in most of the workers (n=23, 60%), mild to moderate fatigue in 14 workers (37%), and severe fatigue in 1 worker (3%) only.

In correlation analysis, the PERCLOS80 values before and at the end of the shift showed significant relationships with the blink values at the corresponding times (Spearman's rho of 0.67 and 0.72 before and after the shift, respectively, p <0.001).

In the analysis of workers grouped by comorbidities, subjects with thyroid dysfunction did not show significant differences in eye blinking, PERCLOS80

Table 2. Distribution of measures recorded by the VDT VMS in workers stratified by gender.

		Percentiles			
Parameters	**Min.**	**25**	**50**	**75**	**Max.**
Males, N = 6					
Shift Duration, sec.	22911	26366.50	29486***	31491	31708
Face Detection Time, sec.	12448	14422.75	14817**	18964.25	23000
Screen Fixation Time, sec.	2387	9245	11201*	12350	16743
Females, N = 32					
Shift Duration, sec.	11899	13617.50	18681	24483	31516
Face Detection Time, sec.	2620	7726.50	10482.50	15001	19032
Screen Fixation Time, sec.	1589	4325.25	6306.50	8179.50	15882

**p=0.0368; **p=0.0208; ***p=0.0023*

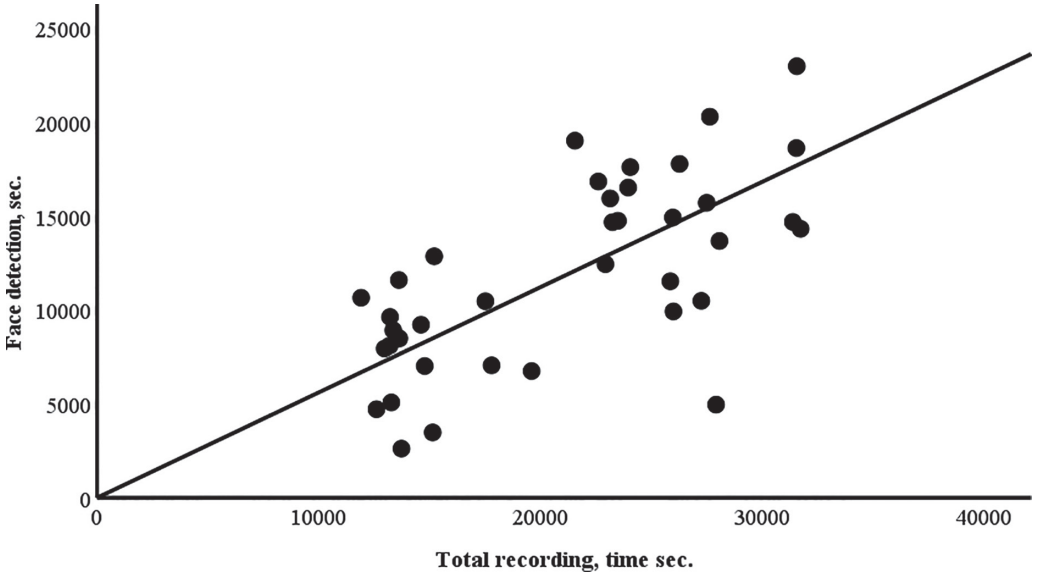


Figure 2. Relationship between shift duration and the time employees spend in front of the VDT screen, as recorded by the VDT Visual Monitoring System.

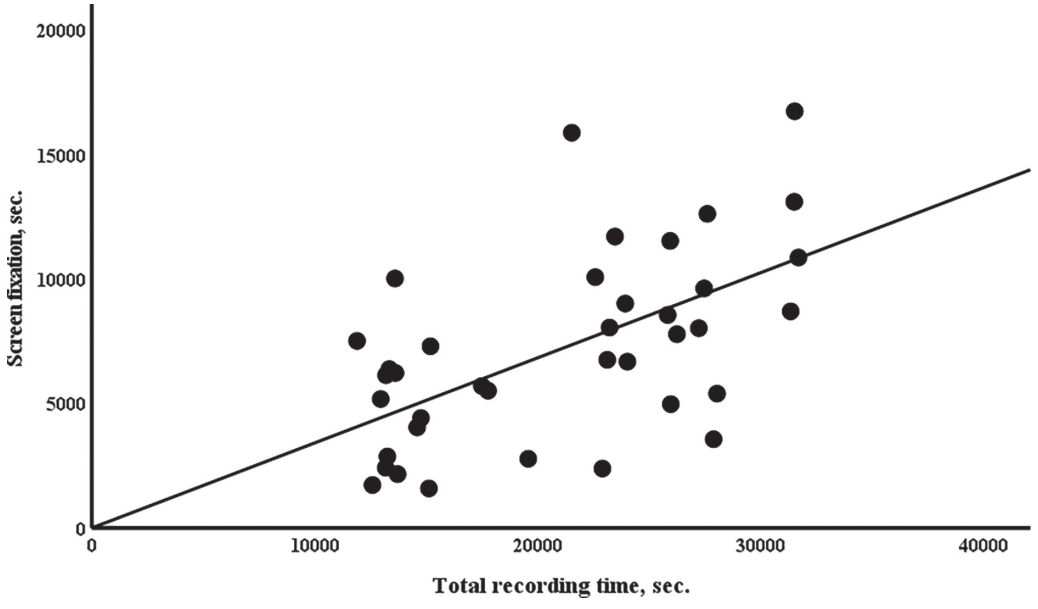


Figure 3. Relationship between shift duration and screen fixation time, as recorded by the VDT Visual Monitoring System.

or FAS results. On the other hand, hypertensive subjects showed significantly (p=0.01) higher end-of-shift values of blinks/min (median values of 23.9 *vs.* 15.1), PERCLOS80 (median values of 19.6 *vs.* 3.9) and FAS questionnaire score, limited to physical fatigue (median values of 14 vs. 11).

4. DISCUSSION

The present study explored the feasibility of objectively assessing visual workload among video display terminal (VDT) workers by measuring true screen fixation time with a novel, non-invasive monitoring

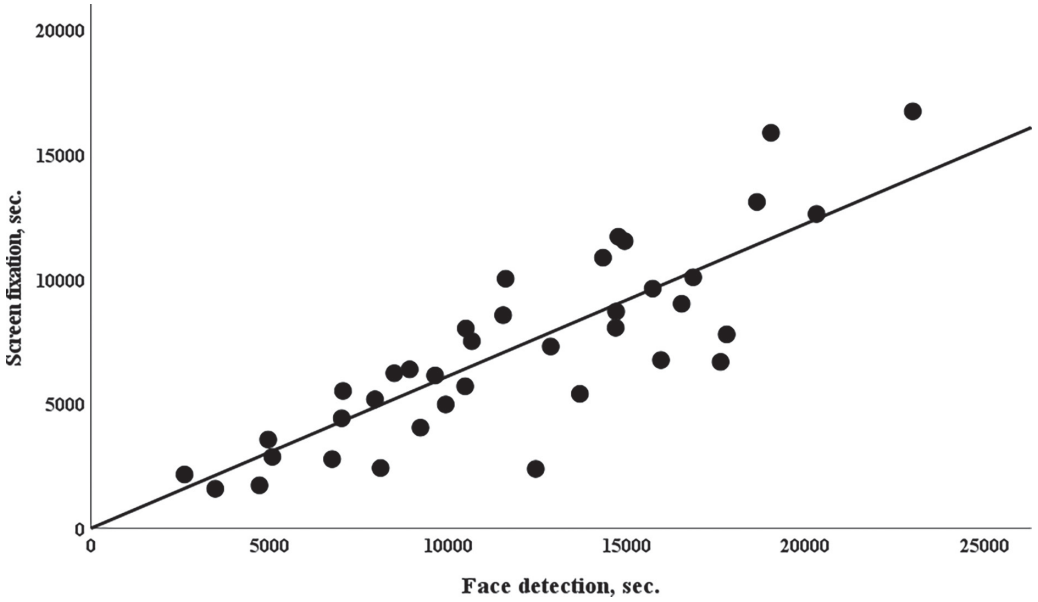


Figure 4. Relationship between face detection time and screen fixation time, as recorded by the VDT Visual Monitoring System.

system. By integrating objective exposure metrics with ophthalmological evaluation and fatigue-related indicators, this study provides an interdisciplinary contribution to occupational health research.

The primary finding of this study is the confirmation of the VDT Visual Monitoring System (VMS) as a reliable and well-tolerated tool for quantifying active screen fixation during routine administrative work. The job characteristics of our worker sample, a mix of VDT work and front-office tasks, make it challenging to evaluate the system's ability to discriminate between simply staying in front of the VDT screen and actual screen fixation. The results demonstrate that these metrics differed significantly, with total recording times (i.e., the whole work shift, about 8 h and 19 min, on average) higher than the time spent simply at the workstation in front of the screen (about 4 h and 11 min, on average), which in turn was higher than the time of active screen fixation (about 3 h and 11 min, on average). These differences are particularly relevant in real-world occupational settings, where VDT use is often discontinuous and difficult to quantify accurately through self-reported estimates. In terms of worker ocular and mental strain, the true VDT screen fixation time is the most relevant parameter to consider. According to Italian law, the investigated worker group would be classified as at risk considering both the shift duration and the time spent at the VDT workstation. However, our results indicate that the true dangerous fixation time is lower than 4 hours, which is the cut-off for VDT risk. The instrument's accuracy in discriminating between mere presence at the VDT workstation and actual visual engagement with the display through fixation is demonstrated by the lower regression coefficient of screen fixation time vs. face detection when both are considered vs. total recording time, and by the highest R^2 obtained in the relationship between screen fixation and face detection times. These results confirm our previously obtained ones [35].

From an ophthalmological perspective, a substantial proportion of workers exhibited signs of ocular surface alteration. Approximately half of the study population had pathological tear break-up time values, and OSDI® scores indicated varying degrees of dry eye disease. These findings are consistent with previous reports documenting an increased prevalence of dry eye symptoms among VDT-exposed workers [39].

Interestingly, a significant correlation was found between the OSDI® scores and the extent of screen VDT fixation, but not with shift duration or the time the employee was in front of the VDT screen while performing other tasks at the workstation. This confirms the specificity of the fixation time collected by the VDT VSM. Although no statistically significant associations were identified between fixation time and BUT, this could be attributable to the limited sample size and the cross-sectional nature of the study. The lack of a significant association between objectively measured screen fixation time and BUT needs further consideration. While acute VDT exposure during a single shift reduces blink rates and leads to incomplete blinks, resulting in evaporative stress and transient tear film instability, the observed ocular surface alterations may primarily reflect chronic/cumulative effects of prolonged VDT use. Chronic exposure has been linked to persistent meibomian gland dysfunction (MGD) and compositional changes in the tear film lipid layer, promoting ongoing instability independent of daily fixation duration. Indeed, previous studies among VDT workers report discrepancies between OSDI (subjective symptoms) and objective signs such as BUT, attributable to a multifactorial etiology, including individual susceptibility, environmental factors (e.g., low humidity), and comorbidities. OSDI scores, which correlated with fixation time (Spearman's ρ=0.34, p=0.05), may capture symptomatic burden from both acute visual strain and chronic tear film alterations, whereas single measure BUT primarily reflects instantaneous stability. Longitudinal studies with repeated ophthalmological assessments could elucidate whether acute workloads exacerbate pre-existing chronic tear-film derangements, thereby informing targeted interventions in occupational settings.

Fatigue assessment using the Pupil Core® system did not reveal significant differences in PERCLOS80 values between the start and end of the work shift. Blink rate remained within physiological ranges and showed only a modest, significant increase over the shift. These findings suggest that the administrative tasks performed by the study population may not have been sufficiently demanding to induce measurable visual or cognitive fatigue within a single work shift. Alternatively, PERCLOS80 may be less sensitive to low-to-moderate levels of visual strain in office-based occupations.

The results of the FAS questionnaire further support this interpretation, with most participants reporting no or only mild fatigue. The concordance between subjective questionnaire data and objective PERCLOS80 measurements strengthens the internal consistency of the findings, although both approaches may lack sensitivity in detecting subtle or early fatigue-related effects.

A key strength of this study is the integration of occupational medicine, ophthalmology, and digital monitoring technologies. The objective quantification of visual exposure marks a significant advance over traditional assessment methods that rely on indirect estimates. The non-invasive nature of the VMS prototype and its minimal interference with routine work activities further enhance its potential applicability in occupational risk assessment and preventive strategies.

Several limitations must be acknowledged. The variability in shift duration and timing may have introduced heterogeneity in exposure conditions. In addition, the public-facing nature of the work tasks inherently involves unpredictable interruptions, which may affect both fixation patterns and fatigue measures. While this variability reflects real-world working conditions, it complicates exposure standardization. The relatively small sample size limits statistical power and precludes definitive conclusions regarding exposure–response relationships.

From a practical standpoint, the VDT Visual Monitoring System (VMS) offers actionable implications for occupational physicians under Italian Legislative Decree 81/2008. Integration of VMS data into the risk assessment document (DVR) enables precise quantification of active screen fixation, surpassing self-reported estimates and supporting tailored health surveillance protocols. Physicians could leverage real-time VMS reports to identify workers exceeding fixation thresholds (e.g., >60% shift time), prioritizing biennial ophthalmological exams (art. 176) and ergonomic interventions, such as mandatory 15-min breaks every 2 hours or workstation adjustments. In fitness-for-work judgments, VMS profiles may inform suitability restrictions,

correlating fixation duration with OSDI scores to detect early visual strain. Future deployment in multi-shift settings, combined with wearable metrics (e.g., blink rate), would enhance DVR updates, preventive training, and compliance verification, ultimately reducing VDT-related morbidity in administrative cohorts.

Future research should aim to include larger study populations and repeated measurements across multiple workdays to improve exposure characterization and statistical robustness. The application of the VDT VMS in different occupational settings and its integration with ergonomic and musculoskeletal assessments may further elucidate the relationship between visual workload and work-related health outcomes.

5. Conclusion

The VDT VMS proved to be an effective tool for objectively quantifying true eye (and mental) engagement among VDT-exposed employees. Although ophthalmological assessments revealed a notable prevalence of ocular surface alterations, no clear exposure–response relationship was identified, likely due to the study's small sample size. Nonetheless, the proposed approach offers a promising framework for more accurate, evidence-based assessment of VDT-related visual workload in occupational contexts to support health protection.

Institutional Review Board Statement: Consistent with the criteria established by the Italian Ministry of Health Decree of 30 January 2023 for observational studies conducted in the context of occupational health monitoring, formal approval by an Ethics Committee was not required. All participants provided written informed consent prior to enrollment. The study was conducted in accordance with the WMA Declaration of Helsinki and the General Data Protection Regulation (GDPR, Regulation EU 679/2016).

Declaration of Interest: The authors declare no conflict of interest.

Author Contribution Statement: Conceptualization, G.D.P, E.M, D.R. V.R. and F.S.; Methodology, E.S., G.D.P. and V.R..; Software, S.D. and M.F.; Validation, E.S., V.F., V.R. and G.D.P.; Formal analysis, G.D.P.; Investigation, E.M., D.R., G.B. and N.V.; Resources, V.F. and G.D.P.; Data curation, S.D. and C.T.; Writing—original draft, E.M., D.R. and G.D.P:; Writing—review & editing, G.D.P, E.M. and D.R..; Supervision, E.S., V.F., V.R. and G.D.P.; Project administration, G.D.P. All authors have read and agreed to the published version of the manuscript.

References

1. Decision (EU) 2022/2481 of the European Parliament and of the Council of 14 December 2022 Establishing the Digital Decade Policy Programme 2030. OJ L 323, 19 December 2022, pp. 4–26. Available online: https://eur-lex.europa.eu/eli/dec/2022/2481/oj
2. Italian Legislative Decree No. 81, 9 April 2008. Italy. Available online at: https://www.gazzettaufficiale.it/atto/serie_generale/caricaDettaglioAtto/originario?atto.dataPubblicazioneGazzetta=2008-04-30&atto.codiceRedazionale=008G0104&elenco30giorni=false
3. Andersen MF, Svendsen PA, Nielsen K, Brinkmann S, Rugulies R, Madsen IEH. Influence at work is a key factor for mental health - but what do contemporary employees in knowledge and relational work mean by "influence at work"?. *Int J Qual Stud Health Well-being*. 2022;17(1):2054513. Doi: 10.1080/17482631.2022.2054513
4. Tsou MT. Influence of Prolonged Visual Display Terminal Use on Physical and Mental Conditions among Health Care Workers at Tertiary Hospitals, Taiwan. *Int J Environ Res Public Health*. 2022;19(7):3770. Doi: 10.3390/ijerph19073770
5. Skelly DL. Assessment of computer workstations for compliance with ergonomic guidelines: A field study. *Work*. 2021;69(3):1019-1026. Doi: 10.3233/WOR-213532
6. Sánchez-Brau M, Domenech-Amigot B, Brocal-Fernández F, Quesada-Rico JA, Seguí-Crespo M. Prevalence of Computer Vision Syndrome and Its Relationship with Ergonomic and Individual Factors in Presbyopic VDT Workers Using Progressive Addition Lenses. *Int J Environ Res Public Health*. 2020;17(3):1003. Doi: 10.3390/ijerph17031003
7. Morelli S, Grigioni M, Ferrarin M, et al. A monitoring tool of workers' activity at Video Display Terminals for investigating VDT-related risk of musculoskeletal disorders. *Comput Methods Programs Biomed*. 2012;107(2):294-307. Doi: 10.1016/j.cmpb.2011.10.011
8. Murata K, Araki S, Yokoyama K, Yamashita K, Okumatsu T, Sakou S. Accumulation of VDT work-related visual fatigue assessed by visual evoked potential, near point distance and critical flicker fusion. *Ind Health*. 1996;34(2):61-69. Doi: 10.2486/indhealth.34.61
9. Waersted M, Hanvold TN, Veiersted KB. Computer work and musculoskeletal disorders of the neck and upper extremity: a systematic review. *BMC Musculoskelet Disord*. 2010;11:79. Doi: 10.1186/1471-2474-11-79

10. Hoe VC, Urquhart DM, Kelsall HL, Zamri EN, Sim MR. Ergonomic interventions for preventing work-related musculoskeletal disorders of the upper limb and neck among office workers. *Cochrane Database Syst Rev*. 2018;10(10):CD008570. Doi: 10.1002/14651858.CD008570.pub3
11. Gerr F, Monteilh CP, Marcus M. Keyboard use and musculoskeletal outcomes among computer users. *J OccupRehabil*. 2006;16(3):265-277. Doi: 10.1007/s10926-006-9037-0
12. Shin S, Yang EH, Lee HC, Moon SH, Ryoo JH. The relationship between visual display terminal usage at work and symptoms related to computer vision syndrome. *Ann Occup Environ Med*. 2023;35:e1. Doi: 10.35371/aoem.2023.35.e1
13. De Palma G, Sala E, Rubino S, et al. Objective Evaluation of Active Interactions between the Operator and Display Screen Equipment Using an Innovative Acquisition System. *Bioengineering (Basel)*. 2023;10(6):686. Doi: 10.3390/bioengineering10060686
14. Singh S, McGuinness MB, Anderson AJ, Downie LE. Interventions for the Management of Computer Vision Syndrome: A Systematic Review and Meta-analysis. *Ophthalmology*. 2022;129(10):1192-1215. Doi: 10.1016/j.ophtha.2022.05.009
15. Artime Ríos EM, Sánchez Lasheras F, Suarez Sánchez A, Iglesias-Rodríguez FJ, Seguí Crespo MDM. Prediction of Computer Vision Syndrome in Health Personnel by Means of Genetic Algorithms and Binary Regression Trees. *Sensors (Basel)*. 2019;19(12):2800. Doi: 10.3390/s19122800
16. Parihar JK, Jain VK, Chaturvedi P, Kaushik J, Jain G, Parihar AK. Computer and visual display terminals (VDT) vision syndrome (CVDTS). *Med J Armed Forces India*. 2016;72(3):270-276. Doi: 10.1016/j.mjafi.2016.03.
17. Ccami-Bernal F, Soriano-Moreno DR, Romero-Robles MA, et al. Prevalence of computer vision syndrome: A systematic review and meta-analysis. *J Optom*. 2024;17(1):100482. Doi: 10.1016/j.optom.2023.100482
18. Artime-Ríos E, Suárez-Sánchez A, Sánchez-Lasheras F, Seguí-Crespo M. Computer vision syndrome in healthcare workers using video display terminals: an exploration of the risk factors. *J Adv Nurs*. 2022;78(7):2095-2110. Doi: 10.1111/jan.15140
19. Mataftsi A, Seliniotaki AK, Moutzouri S, et al. Digital eye strain in young screen users: A systematic review. *Prev Med*. 2023;170:107493. Doi: 10.1016/j.ypmed.2023.107493
20. Lissak G. Adverse physiological and psychological effects of screen time on children and adolescents: Literature review and case study. *Environ Res*. 2018;164:149-157. Doi: 10.1016/j.envres.2018.01.015
21. Tsai CY, Jiesisibieke ZL, Tung TH. Association between dry eye disease and depression: An umbrella review. *Front Public Health*. 2022;10:910608. Doi: 10.3389/fpubh.2022.910608
22. Sheppard J, Shen Lee B, Periman LM. Dry eye disease: identification and therapeutic strategies for primary care clinicians and clinical specialists. *Ann Med*. 2023;55(1):241-252. Doi: 10.1080/07853890.2022.2157477
23. Huang R, Su C, Fang L, Lu J, Chen J, Ding Y. Dry eye syndrome: comprehensive etiologies and recent clinical trials. *Int Ophthalmol*. 2022;42(10):3253-3272. Doi: 10.1007/s10792-022-02320-7
24. Mohamed HB, Abd El-Hamid BN, Fathalla D, Fouad EA. Current trends in pharmaceutical treatment of dry eye disease: A review. *Eur J Pharm Sci*. 2022;175:106206. Doi: 10.1016/j.ejps.2022.106206
25. Narang P, Donthineni PR, D'Souza S, Basu S. Evaporative dry eye disease due to meibomian gland dysfunction: Preferred practice pattern guidelines for diagnosis and treatment. *Indian J Ophthalmol*. 2023;71(4):1348-1356. Doi: 10.4103/IJO.IJO_2841_22
26. Rolando M, Merayo-Lloves J. Management Strategies for Evaporative Dry Eye Disease and Future Perspective. *Curr Eye Res*. 2022;47(6):813-823. Doi: 10.1080/02713683.2022.2039205
27. Kamøy B, Magno M, Nøland ST, et al. Video display terminal use and dry eye: preventive measures and future perspectives. *Acta Ophthalmol*. 2022;100:723-739. Doi: doi.org/10.1111/aos.15105
28. Stapleton F, Velez FG, Lau C, Wolffsohn JS. Dry eye disease in the young: A narrative review. *Ocul Surf*. 2024;31:11-20. Doi: 10.1016/j.jtos.2023.12.001
29. Nie B, Huang X, Chen Y, Li A, Zhang R, Huang J. Experimental study on visual detection for fatigue of fixed-position staff. *Appl Ergon*. 2017;65:1-11. Doi: 10.1016/j.apergo.2017.05.010
30. Hu X, Lodewijks G. Detecting fatigue in car drivers and aircraft pilots by using non-invasive measures: The value of differentiation of sleepiness and mental fatigue. *J Safety Res*. 2020;72:173-187. Doi: 10.1016/j.jsr.2019.12.015
31. Abe T. PERCLOS-based technologies for detecting drowsiness: current evidence and future directions. *Sleep Adv*. 2023;4(1):zpad006. Doi: 10.1093/sleepadvances/zpad006
32. Kovalenko S, Mamonov A, Kuznetsov V, et al. OperatorEYEVP: Operator Dataset for Fatigue Detection Based on Eye Movements, Heart Rate Data, and Video Information. *Sensors (Basel)*. 2023;23(13):6197. Doi: 10.3390/s23136197
33. Dai L, Li Y, Zhang M. Detection of Operator Fatigue in the Main Control Room of a Nuclear Power Plant Based on Eye Blink Rate, PERCLOS and Mouse Velocity. Applied Sciences. 2023;13(4):2718. Doi: https://doi.org/10.3390/app13042718
34. Hu Y, Liu Z, Hou A, et al. On Fatigue Detection for Air Traffic Controllers Based on Fuzzy Fusion of Multiple Features. *Comput Math Methods Med*. 2022;2022:4911005. Doi: 10.1155/2022/4911005

35. Marelli E, Ruongo D, Dalola S, et al. Objective Assessment of Active Display Screen Fixation Among Office Workers Using an Innovative Nonwearable Acquisition System: A Pilot Study. *Applied Sciences*. 2024; 14(23):11307. Doi: https://doi.org/10.3390/app142311307
36. Dinges DF, Grace R. PERCLOS: A Valid Psychophysiological Measure of Alertness as Assessed bY Psychomotor Vigilance. Washington, DC: Federal Highway Administration; 1998. Publiction No. FHWA - MC - 98 - 006
37. Michielsen HJ, De Vries J, Van Heck GL. Psychometric qualities of a brief self-rated fatigue measure: The Fatigue Assessment Scale. *J Psychosom Res*. 2003;54(4):345-352. Doi: 10.1016/s0022-3999(02)00392-6
38. De Vries J, Michielsen H, Van Heck GL, Drent M. Measuring fatigue in sarcoidosis: the Fatigue Assessment Scale (FAS). *Br J Health Psychol*. 2004;9(Pt 3): 279-291. Doi: 10.1348/1359107041557048
39. Fjaervoll K, Fjaervoll H, Magno M, et al. Review on the possible pathophysiological mechanisms underlying visual display terminal-associated dry eye disease. *Acta Ophthalmol*. 2022;100(8):861-877. Doi: 10.1111/aos.15150

La Medicina del Lavoro

Original article

Med. Lav. 2026, 117, (3): 17620
DOI: 10.23749/mdl.2026.17620

Validation of the Italian Version of the Perception of Aggression Scale (POAS): A Cross-Sectional Study

David Shaholli[1], Beatrice Bottini[1], Stefan Muhulica[1], Giorgia Mantione[1], Adolfo Bei[2], Shizuka Kibi[1], Giuseppe La Torre[1,*]

[1]Sapienza University of Rome, Department of Public Health and Infectious Diseases, Rome, Italy
[2]University of Cassino and Southern Lazio, Cassino, Italy

Keywords: Aggression; Healthcare Professionals; POAS; Psychometric Validation; Workplace Violence

Abstract

Background: *Aggression in healthcare settings is a persistent occupational hazard that affects staff well-being, the quality of patient care, and organizational dynamics. Understanding healthcare professionals' perceptions of aggression is crucial for designing effective interventions and improving workplace safety. This study aimed to validate the Italian version of the short-form Perception of Aggression Scale (POAS) and to examine how demographic and professional variables influence staff attitudes toward aggression in clinical settings.* **Methods:** *The POAS was administered to a heterogeneous sample of 475 healthcare professionals across multiple hospital departments and educational settings. Psychometric properties, including internal consistency and test-retest reliability, were evaluated. Bivariate and multivariate analyses assessed associations between perceptions of aggression and sociodemographic variables.* **Results:** *The Italian POAS demonstrated strong psychometric performance, with high internal consistency ($\alpha = 0.82$ for dysfunctional; $\alpha = 0.76$ for functional aggression) and temporal stability. While dysfunctional interpretations of aggression were prevalent across the sample, functional perceptions, viewing aggression as contextually meaningful or communicative, were more common among male participants and physicians. Multivariate analysis revealed a strong inverse relationship between functional and dysfunctional perceptions, suggesting a polarized interpretive schema.* **Conclusions:** *The validated Italian POAS is a reliable tool for assessing healthcare workers' attitudes toward aggression. Its integration into clinical training, audits, and risk management systems could facilitate early identification of negative attitudes and support the development of targeted de-escalation strategies. Future research should investigate longitudinal shifts in perception and the tool's adaptability across diverse healthcare settings.*

1. Introduction

Patients' aggressive behaviors within hospital settings represent a critical concern, both clinically and organizationally. These behaviors, ranging from verbal threats and non-verbal intimidation to physical assaults, are particularly prevalent in high-stress departments such as psychiatric units and emergency care settings [1, 2]. Aggression not only compromises the physical and psychological well-being of healthcare workers but also undermines the therapeutic alliance, potentially impairing care quality and patient outcomes [3, 4]. The assessment of aggression in clinical contexts is essential for developing appropriate management strategies. Several studies have investigated the environmental and organizational variables contributing to violent incidents, including staffing ratios, ward architecture,

Received 02.08.2025 – Accepted 27.04.2026
*Corresponding Author: Giuseppe La Torre; E-mail: giuseppe.latorre@uniroma1.it

staff training and experience, and workload intensity [5, 6]. In psychiatric and emergency departments in particular, healthcare professionals report increased exposure to aggression due to the complexity and acuity of patient conditions [1, 7].

Importantly, research has also highlighted the role of healthcare workers' perceptions and attitudes in shaping their responses to aggression. Studies by Whittington and Higgins [4] and Trenoweth [7] emphasized that individual attitudes, shaped by prior experience, training, and team culture, play a pivotal role in shaping risk perception and intervention style. In a seminal study, Finnema et al. [2] examined how psychiatric nurses construed aggression and identified a range of functional and dysfunctional beliefs that appeared to influence staff-patient dynamics. These insights led to the development of the Perception of Aggression Scale (POAS), originally composed of 60 items and later refined to a more practical 12-item format [3]. The POAS has since been used in various settings to evaluate healthcare workers' cognitive framing of aggression and to inform training, supervision, and policy decisions [1]. However, Italy still lacks a validated version of this scale. The absence of such an instrument significantly hampers research on aggression in Italian-speaking populations and limits the implementation of effective prevention programs.

Given the growing number of reports of violence against healthcare professionals in Italy and the increasing recognition of workplace aggression as a public health issue [8, 9], developing a culturally and linguistically validated version of the POAS is imperative. This study aims to address that gap by validating the short version of the POAS in Italian through forward and backward translation, expert panel review, and psychometric analysis.

In the Italian healthcare system, aggression toward healthcare workers is increasingly recognized not only as an occupational safety issue but also as a cultural and organizational challenge. National surveillance data and ministerial recommendations indicate that aggressive incidents are often underreported and inconsistently normalized across clinical settings, and that healthcare workers differ in how they cognitively frame and tolerate such behaviors. Understanding how aggression is perceived, whether as an unacceptable violation or as a contextualized expression of patient distress, is therefore particularly relevant in the Italian context, where preventive strategies are still unevenly implemented.

The present study aims to (a) cross-culturally adapt and validate the Italian version of the short form of the Perception of Aggression Scale (POAS) and (b) examine associations between POAS subscale scores and sociodemographic and professional variables in a heterogeneous sample of healthcare workers and students.

2. Methods

2.1. POAS Instrument

The short-form Perception of Aggression Scale (POAS) comprises 12 items grouped into two conceptually distinct subscales: Dysfunctional Perception (aggression as unjustified, harmful, and unacceptable) and Functional Perception (aggression as communicative or contextually meaningful). Items are rated on a 5-point Likert scale (1 = strongly disagree to 5 = strongly agree). Subscale scores were computed as the mean of items within each subscale, with higher scores indicating greater endorsement of the corresponding conceptualization. No established clinical cutoffs are available for the POAS short form; therefore, scores were treated as continuous variables. Example items include: 'Aggression is a sign of failure' (Dysfunctional) and 'Aggression can be a form of communication' (Functional).

2.2. Translation and Cross-Cultural Adaptation

The Italian version was developed using a standardized forward–backward translation process adapted from the guidelines proposed by Beaton et al. Two independent bilingual translators performed forward translations, which were reconciled into a single Italian version. A native English speaker, blinded to the original questionnaire, conducted the backward translation. An expert panel of clinicians and occupational health researchers reviewed semantic, idiomatic, experiential, and conceptual equivalence. Cognitive pretesting was conducted

with a convenience sample of 20 participants (students and staff) to assess clarity and cultural relevance; minor wording adjustments were made based on feedback.

2.3. Sample and Recruitment

Participants were recruited from October 2022 to May 2025 from a large public hospital network in Rome, Italy, including Medical, Surgical, Emergency/ICU, Ambulatory care, and Didactic structures. The Didactic structures subgroup comprised undergraduate healthcare students in clinical placements within the hospital network. All healthcare workers and students aged ≥18 years assigned to the selected units were invited via internal communications and in-person announcements. Participation was voluntary and anonymous. Exclusion criteria included refusal to participate or incomplete responses to core POAS items. Written informed consent was obtained at the start of the questionnaire. The sample size (n = 475) exceeded common psychometric recommendations for 12-item instruments (e.g., ≥10–20 participants per item) and was consistent with prior validation studies.

2.4. Ethical Considerations

According to institutional policy, the study was considered exempt from formal Institutional Review Board review because it consisted of an anonymized, non-interventional survey with no identifiable personal data. Written informed consent was obtained from all participants prior to participation.

2.5. Statistical Analysis

All statistical analyses were conducted in SPSS (version 27). Descriptive statistics (means, standard deviations, and frequencies) were computed for demographic and professional variables. Internal consistency of the two POAS subscales ('Aggression as dysfunctional and undesirable' and 'Aggression as functional and understandable') was assessed using Cronbach's alpha.

Bivariate analyses were conducted to assess associations between POAS scores and categorical variables (e.g., gender, education, marital status, job role) using independent-samples t-tests and one-way ANOVA, and Pearson's correlation was used for continuous variables such as age.

To further investigate predictors of perceived aggression, we conducted multivariate linear regression analyses for both POAS subscales (dysfunctional and functional). For each outcome, we tested two models: a full model including all independent variables (age, gender, marital status, education, job category, and the opposing subscale score), and a stepwise model in which variables were retained based on statistical significance to optimize explanatory power. We evaluated the goodness of fit for each model using the coefficient of determination (R^2), which indicates the proportion of variance explained by the predictors.

3. Results

The final sample comprised 475 participants recruited from various departments of a large public hospital network in Italy. Participants were distributed across five main areas: Medical (n = 65), Surgical (n = 42), Emergency/Intensive Care Units (n = 60), Didactic Structures (n = 282), and Ambulatory Care (n = 26). This heterogeneous composition was intended to enhance the generalizability of the findings and to reflect diverse professional experiences with patient aggression (Table 1).

Participants completed the POAS questionnaire twice, over two sessions held 24 hours apart. Cases with missing values on outcome variables were excluded pairwise from relevant analyses. missing data were below 5% for all variables. The inclusion of multiple sessions allowed the researchers to evaluate the temporal stability of the instrument.

Cronbach's alpha coefficients indicated strong internal consistency for both the Dysfunctional Perception subscale ($\alpha = 0.82$) and the Functional Perception subscale ($\alpha = 0.76$). No significant differences were observed between the two administrations, supporting short-term test-retest reliability.

Descriptive trends suggested that women tended to perceive aggression as more dysfunctional, while men more frequently interpreted it as functional. Similarly, participants with higher educational

Table 1. Characteristics of the Sample.

Variable	n (%) or mean (SD)
Gender	
Female	331 (69.7)
Male	144 (30.3)
Age (years)	33.24 (13.46)
Sons	
Yes	103 (21.7)
No	372 (78.3)
Marital Status	
Single	339 (71.4)
Married or Cohabiting	117 (24.6)
Separated or Divorced	18 (3.8)
Widowed	1 (0.2)
Educational Level	
University Degree	178 (37.5)
Middle School	3 (0.6)
High School	294 (61.9)
Job	
Physicians	36 (7.6)
Nurses	163 (34.3)
Other Healthcare Professionals	34 (7.2)
Students	242 (50.9)
Type of Ward/Department	
Medical	65
Surgical	42
Emergency/ICU	60
Didactic Structure	282
Outpatient Care	26

attainment and those working as physicians appeared more inclined to endorse functional perceptions of aggression. However, these trends were not consistently supported by inferential statistics and should be interpreted cautiously. A detailed overview of the univariate and bivariate results is presented in Table 2.

Results show that gender was significantly associated with the perception of functional aggression ($p = 0.026$), with males reporting higher mean scores ($M = 1.54$; $SD = 0.88$) compared to females ($M = 1.38$; $SD = 0.63$). This suggests that men may be more inclined to attribute a functional or constructive value to aggressive behaviors. In contrast, no significant differences were found in dysfunctional aggression by gender ($p = 0.940$), indicating similar perceptions of negativity across sexes. Age, on the other hand, did not show significant correlations with either dysfunctional ($r = –0.081$; $p = 0.079$) or functional aggression ($r = 0.010$; $p = 0.834$). While the negative correlation with dysfunctional aggression was marginally non-significant, it reflects a trend in line with the multivariate analysis, suggesting a possible age-related attenuation in perceiving aggression as harmful.

There were no statistically significant differences in either dimension of aggression based on whether participants had children. Mean scores were very close across both groups, and p values remained well above the threshold of significance (dysfunctional $p = 0.584$; functional $p = 0.268$).

Perceptions of both dysfunctional and functional aggression did not differ significantly across marital status groups ($p = 0.907$ and $p = 0.497$, respectively). Although widowed participants reported higher levels of functional aggression ($M = 2.50$), this result should be interpreted with caution due to the very small subgroup size (likely $n = 1$).

No significant differences emerged across educational levels for either aggression type (dysfunctional $p = 0.290$; functional $p = 0.714$). However, individuals with a university degree reported slightly lower dysfunctional aggression ($M = 4.69$; $SD = 0.41$) and slightly higher functional aggression ($M = 1.45$; $SD = 0.69$) than other educational groups, suggesting a trend warranting further investigation. Job category, instead, did not yield significant differences in perceptions of aggression (dysfunctional $p = 0.317$; functional $p = 0.142$). Nonetheless, physicians had the highest mean functional aggression score ($M = 1.64$; $SD = 0.99$), consistent with the results observed in the multivariate model. Other healthcare professionals had the lowest perception of functional aggression ($M = 1.26$; $SD = 0.39$), suggesting a narrower attribution of constructive value to aggressive behavior [7, 8, 9].

Multivariate regression results are summarized in Table 3. In the full model, being a physician was positively and significantly associated with higher

Table 2. Univariate and Bivariate Analysis.

Variable	Dysfunctional Relation Mean (SD) or *r*	Functional Relation Mean (SD) or *r*
Gender		
Female	4.72 (0.41)	1.38 (0.63)
Male	4.72 (0.40)	1.54 (0.88)
p	0.94	0.026
Age	-0.081	0.010
P	0.079	0.834
Sons		
Yes	4.70 (0.40)	1.50 (0.79)
No	4.72 (0.41)	1.41 (0.69)
p	0.584	0.268
Marital Status		
Single	4.73 (0.41)	1.44 (0.74)
Married or Cohabiting	4.71 (0.37)	1.43 (0.64)
Separated or Divorced	4.58 (0.67)	1.37 (0.66)
Widowed	4.83	2.50
p		0.497
Educational Level		
University Degree	4.69 (0.41)	1.45 (0.69)
Middle School	5.00 (0.00)	1.11 (0.19)
High School	4.73 (0.41)	1.43 (0.74)
p	0.290	0.714
Job		
Physicians	4.75 (0.42)	1.64 (0.99)
Nurses	4.67 (0.42)	1.46 (0.64)
Other Healthcare Professionals	4.76 (0.29)	1.26 (0.39)
Students	4.74 (0.42)	1.41 (0.75)
p	0.317	0.142

levels of perceived dysfunctional aggression (β = 0.082; p = 0.041), suggesting that physicians tend to attribute more negative and disruptive meanings to aggression compared to nurses (reference group). However, this association lost significance in the stepwise model (β = 0.121; p = 0.083), although the direction of the effect remained consistent. Age was negatively associated with dysfunctional aggression; although the association was only marginally significant in the stepwise model (β = –0.003; p = 0.052), it suggests that older individuals tend to perceive aggression as less dysfunctional, possibly reflecting increased professional experience or improved emotion regulation over time. The most robust predictor was functional aggression, which showed a significant and negative association with dysfunctional aggression (β = –0.178; p < 0.001). This finding supports the notion that a greater ability to recognize constructive or communicative aspects of aggression is linked to a reduced tendency to interpret it as inherently harmful or inappropriate. All multivariate regression models included job category (physicians, nurses, other healthcare professionals, and students) as an independent variable to account for potential confounding due to professional role and experience. Given that students

Table 3. Multivariate Analysis.

	Dysfunctional		Functional	
Variables	**Full model** β (*p*)	**Stepwise** β (*p*)	**Full model** β (*p*)	**Stepwise** β (*p*)
Age	-0.004 (0.060)	**-0.003 (0.052)**	-0.002 (0.621)	
Female gender	-0.004 (0.917)		**-0.170 (0.016)**	**-0.159 (0.019)**
Married	0.039 (0.456)		0.010 (0.914)	
University Degree	-0.071 (0.280)		-0.156 (0.169)	
Nurse (Ref)	----------		----------	
Physicians	**0.082 (0.041)**	**0.121 (0.083)**	0.240 (0.073)	**0.248 (0.040)**
Other Healthcare Professionals	-0.177 (0.283)		-0.190 (0.155)	
Students	-0.004 (0.584)		-0.199 (0.187)	
Functional Aggression	-0.177 (<0.001)	**-0.178 (<0.001)**	----------	
Dysfunctional Aggression	----------		**-0.537 (<0.001)**	**-0.541 (<0.001)**
	R^2 = 0.111	**R^2 = 0.105**	**R^2 = 0.119**	**R^2 = 0.112**

represented a substantial proportion of the sample, results should be interpreted as reflecting a mixed population of practicing healthcare workers and trainees rather than experienced professionals alone.

Regarding functional aggression, gender emerged as a significant predictor: women (compared to men, the reference group) were more likely to attribute functional meaning to aggressive behaviors (β = –0.170; p = 0.016 in the full model; β = –0.159; p = 0.019 in the stepwise model). This may reflect gender-related differences in emotional framing or social cognition. Again, being a physician was a significant positive predictor of functional aggression (β = 0.248; p = 0.040 in the stepwise model), indicating that physicians, while perceiving higher levels of dysfunctional aggression, are also more likely to acknowledge its functional aspects—perhaps due to the complex and high-pressure nature of their clinical environments. Finally, dysfunctional aggression was negatively and significantly associated with the perception of functional aggression (β = –0.541; p < 0.001), confirming a strong inverse relationship between the two constructs. This supports the theoretical assumption that cognitive appraisals of aggression are multidimensional, influenced by whether the behavior is framed as harmful or potentially constructive.

4. Discussion

Aggression in healthcare settings is widely recognized as a critical occupational hazard with significant implications for workers' physical safety, psychological well-being, and organizational functioning [10, 11]. Although traditionally viewed as purely disruptive or pathological, contemporary trauma-informed and relational care models suggest that aggression may, in certain clinical contexts, be a communicative act reflecting distress, unmet needs, or acute psychological dysregulation [2, 3]. Within this framework, healthcare workers' cognitive appraisals of aggression play a pivotal role in shaping both individual responses and institutional management strategies [12].

Repeated exposure to patient violence may lead to emotional desensitization, heightened moral distress, and ultimately burnout, a constellation of symptoms including emotional exhaustion, depersonalization, and reduced professional efficacy [13, 14]. These psychological sequelae may shape how aggressive behaviors are interpreted, whether as threats requiring containment or as signals warranting empathetic understanding [15, 16]. In the present study, the Dysfunctional Perception subscale of the Italian POAS yielded consistently high scores

(M = 4.72, SD = 0.41), indicating that aggression is widely perceived as undesirable, harmful, and unjustifiable among healthcare professionals. Notably, no sociodemographic or professional variables, including age, gender, educational level, marital status, parenthood, or job category, were significantly associated with dysfunctional perception. This finding suggests that viewing aggression as inherently negative may reflect a pervasive, culturally reinforced belief within Italian healthcare settings, rather than an attitude shaped solely by individual characteristics.

Conversely, Functional Perception scores were markedly lower (M = 1.45, SD = 0.73), indicating limited endorsement of aggression as meaningful, communicative, or contextually understandable. However, important differences emerged. Male participants reported significantly higher functional perception scores than females, consistent with previous findings in psychiatric and emergency care contexts, where male staff tend to frame aggression more often within procedural or clinical models rather than affective ones [7, 17]. When stratified by professional role, physicians had the highest functional perception scores, followed by nurses, students, and other healthcare professionals. Although these differences did not always reach statistical significance, the observed gradient suggests a role-related cognitive framing influenced by clinical responsibility, training, and repeated exposure to aggressive incidents [4, 14].

Multivariate regression analyses further clarified these relationships. Functional perception emerged as the strongest negative predictor of dysfunctional perception, supporting the hypothesis that recognizing aggression as situationally driven or communicative may buffer against interpreting it as purely threatening or illegitimate. This bidirectional, inverse relationship confirms the multidimensional nature of aggression appraisal and aligns with theoretical models that emphasize cognitive framing as a key determinant of behavioral response [12]. Age showed a marginal inverse association with dysfunctional perception, suggesting that professional experience or emotional regulation may slightly attenuate negative appraisals over time, although this effect did not reach conventional statistical significance.

From an occupational medicine perspective, these findings have direct practical implications. The availability of a validated Italian version of the POAS provides occupational physicians with a structured, reliable tool for assessing healthcare workers' cognitive and emotional framing of patient aggression. Integrating the POAS into occupational health surveillance programs may facilitate early identification of professionals who predominantly endorse dysfunctional perceptions of aggression and who may therefore be at higher risk for stress-related outcomes, reduced coping capacity, or burnout. Furthermore, repeated POAS administration before and after preventive interventions could support the evaluation of organizational strategies to mitigate the psychological impact of workplace violence.

Importantly, perceptions of aggression are shaped not solely by individual characteristics but also by broader organizational and contextual dynamics [1]. While exposure to repeated aggressive incidents has been linked to emotional exhaustion, depersonalization, and burnout [13, 14], educational and organizational interventions have been shown to improve staff attitudes, perceived self-efficacy, and preparedness in managing aggressive situations [2]. In this context, the POAS may function not only as an assessment instrument but also as a monitoring tool within risk management frameworks, complementing incident reporting systems and supporting targeted training initiatives.

Several limitations should be acknowledged. A major limitation concerns the composition of the sample, in which healthcare students represented more than half of the participants. Although students were included because they are exposed to patient aggression during clinical training, their perceptions may differ substantially from those of experienced professionals due to limited clinical responsibility, shorter exposure, and different coping strategies. Consequently, the findings should not be generalized exclusively to practicing healthcare workers. Future validation studies should prioritize stratified sampling by professional role and clinical unit, particularly in high-risk settings such as emergency departments, psychiatric units, and intensive care.

A further limitation concerns the 24-hour interval used for test–retest assessment. While appropriate

for evaluating short-term reproducibility, this design does not permit conclusions about long-term temporal stability or sensitivity to training-related changes. Longitudinal studies with extended retest intervals are needed to determine whether attitudes toward aggression evolve over time or in response to organizational interventions. Future research should also examine the role of mediating variables, such as burnout, empathy, and perceived organizational support, to better understand the mechanisms linking exposure to aggression and cognitive appraisal.

5. Conclusion

The present study confirms the psychometric validity and reliability of the Italian short version of the Perception of Aggression Scale (POAS). The translated instrument demonstrated strong internal consistency and test-retest stability, supporting its applicability across a heterogeneous population of healthcare professionals and trainees. The absence of significant changes over time suggests that healthcare workers' attitudes toward aggression are relatively stable, underscoring the need for proactive educational and organizational strategies.

These results underscore the importance of assessing healthcare workers' attitudes toward aggression as part of comprehensive workplace violence prevention strategies. Integrating the POAS into occupational health practice may support early detection of maladaptive cognitive frames, guide targeted training initiatives, and contribute to safer, more supportive care environments. By providing a culturally validated instrument, this study offers a valuable resource for occupational physicians, healthcare organizations, and researchers seeking to better understand and manage aggression-related risks.

Further longitudinal and multicenter studies are recommended to assess predictive validity, long-term attitude shifts, and the scale's cultural adaptability in varied healthcare settings.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki. According to institutional policy, the study was considered exempt from formal Institutional Review Board approval, as it involved an anonymous, non-interventional survey.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Acknowledgments: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. The authors thank all participants for their valuable contribution to the study.

Declaration of Interest: The authors declare no conflict of interest.

Author Contribution Statement: D.S., S.M., B.B., A.B. and G.L.T contributed to the design and implementation of the research, G.M., S.K., A.B., G.L.T and D.S. contributed to the analysis of the results, and D.S., G.M. and G.L.T. contributed to the writing of the manuscript.

References

1. Palmstierna T, Barredal E. Evaluation of the Perception of Aggression Scale (POAS) in Swedish nurses. *Nord J Psychiatry*. 2006;60(6):447-451. Doi: 10.1080/08039480601021803
2. Finnema EJ, Dassen T, Halfens R. Aggression in psychiatry: a qualitative study focusing on the characterization and perception of patient aggression by nurses working on psychiatric wards. *J Adv Nurs*. 1994;19(6):1088-1095. Doi: 10.1111/j.1365-2648.1994.tb01192.x
3. Jansen G, Dassen T, Moorer P. The perception of aggression. *Scand J Caring Sci*. 1997;11(1):51-55. Doi: 10.1111/j.1471-6712.1997.tb00430.x
4. Whittington R, Higgins L. More than zero tolerance? Burnout and tolerance for patient aggression amongst mental health nurses in China and the UK. *Acta Psychiatr Scand*. 2001;106:37-40.
5. Duxbury J, Pulsford D, Hadi M, Sykes S. Staff and patient views on the impact of aggression management training: a longitudinal study. *J Psychiatr Ment Health Nurs*. 2013;20(5):437-446.
6. Nijman H, Rector G. Crowding and aggression on inpatient psychiatric wards. *Psychiatr Serv*. 1999;50:830-831.
7. Trenoweth S. Perceiving risk in dangerous situations: Risks of violence among mental health inpatients. *J Adv Nurs.* 2003;42:278-287.
8. Firenze A, Santangelo OE, Gianfredi V, et al. Violence on doctors. An observational study in Northern Italy. *Med Lav.* 2020;111(1):46-53.
9. D.Lgs. 502/1992 "Riordino della disciplina in materia sanitaria, a norma dell'articolo 1 della legge 23 ottobre

1992, n. 421" (pubblicato il 30 dicembre 1992), integrato dal D.Lgs. 229/1999. Disponibile al sito https://www.normattiva.it/uri-res/N2Ls?urn:nir:stato:decreto.legislativo:1992-12-30;502!vig=
10. Abderhalden C, Needham I, Friedli TK, Poelmans J, Dassen T. Perception of aggression among psychiatric nurses in Switzerland. *Acta Psychiatr Scand*. 2002;106(Suppl 412):1107.
11. Whittington R, Richter D. From the individual to the interpersonal: Environment and interaction in the escalation of violence in mental health settings. In Richter D, Whittington R, eds. Violence in Mental Health Settings: Causes, Consequences, Management. New York: Springer; 2006. p. 47-68.
12. Edward KL, Ousey K, Warelow P, Lui S. Nursing and aggression in the workplace: a systematic review. *Br J Nurs*. 2014;23(12):653-4, 656-9.
13. Maslach C, Schaufeli WB, Leiter MP. Job burnout. *Annu Rev Psychol*. 2001;52:397-422.
14. Bowers L, Nijman H, Simpson A, Jones J. The relationship between leadership, teamworking, structure, burnout and attitude to patients on acute psychiatric wards. *Soc Psychiatry Psychiatr Epidemiol.* 2011;46(2):143-148.
15. Alaerts K, Nackaerts E, Meyns P, Swinnen SP, Wenderoth N. Action and emotion recognition from point light displays: an investigation of gender differences. *PLoS One.* 2011;6:e2098.
16. Blanch-Hartigan D. An effective training to increase accurate recognition of patient emotion cues. *Patient Educ Couns.* 2012;89:274-280.
17. Price O, Baker J, Bee P, Lovell K. The influence of de-escalation training and environmental physical changes on inpatient aggression: a systematic review. *Aggress Behav*. 2018;44(1):4-23.

La Medicina del Lavoro

Original article

Med. Lav. 2026; 117 (3): 18027
DOI: 10.23749/mdl.2026.18027

Multiple Fatal Accidents at Work in Italy: How They Occur and Causal Factors for Identifying Specific Prevention Measures

Giuseppe Campo, Armando Guglielmi, Vanessa Manni*

Department of Medicine, Epidemiology, Occupational & Environmental Hygiene, Italian National Institute for Insurance against Accidents at Work (INAIL), Italy

Keywords: Multiple Fatal Accidents; Mode of Occurrence; Organizational Factors; Surveillance

Abstract

Background: *Workplace accidents represent a significant health problem for workers. In 2022, the EU recorded over 3,000 workplace deaths and nearly 3 million non-fatal accidents. The aim of this paper is to provide an in-depth analysis of multiple fatal accidents in Italy in recent years, analyzing their occurrence patterns and causal factors to increase useful information for risk management.* **Methods:** *The statistics come from the INAIL Database and the Infor.MO National Surveillance System, which collects detailed information on accident dynamics and uses a multifactorial model to analyze the causes of injuries. In this system, the in-depth analysis of multiple fatal accidents was conducted on a cluster of 181 events that occurred between 2008 and 2022.* **Results:** *Data sources show that road accidents are a significant cause of multiple injuries. Other recurring accidents include collapses, fires, explosions, and asphyxiation in confined spaces. The construction and manufacturing sectors are the most affected. The main causes, highlighted particularly in the Infor.MO system, include poor worker training, inadequate workplace organization, and a lack of safety devices.* **Conclusions:** *To reduce workplace accidents, especially those with dramatic consequences such as multiple accidents, the importance of a stronger organizational safety culture is reiterated, in which training enables workers to understand risk analysis and gain greater awareness of hazards.*

1. Introduction

Workplace accidents continue to represent a significant issue for the health conditions of working populations [1, 2]. According to Eurostat, which bases European statistics on work-related accidents on the ESAW classification system [3], in 2022 in the EU there were over 3 thousand work-related deaths and almost 3 million non-fatal accidents, with a ratio of approximately 905 non-fatal accidents for every fatal accident.

For Italy, more recent data are provided by the National Institute for Insurance against Accidents at Work (INAIL) through reports and public online databases. In 2023, 550 fatal accidents were recognized at work [4]. INAIL data report each year the share of multiple fatal accidents, which occurred both at work and *in itinere*, i.e. on the way to and from work. The balance of recent years shows that in the decade 2015-2024, 160 multiple fatal accidents occurred, for a total of 429 victims with an average of almost 3 deaths per event. Furthermore, over the ten-year period, fatalities associated with multiple-casualty events constituted more than 3% of all occupational deaths [5].

Received 07.10.2025 – Accepted 08.05.2026
Corresponding Author: Vanessa Manni; E-mail: v.manni@inail.it

Nine out of ten workers who sustain fatal injuries die in an accident in which they are the only fatality. For the remaining 10% of worker deaths, the fatal accident resulted in the death of more than one worker. These accidents are of particular interest to safety professionals and risk researchers because preventing each of these accidents results in the saving of more lives [6].

Multiple fatal accidents are often associated with activities and processes that by their very nature are high risk and can put several workers at risk at the same time. Examples of this include establishments that use hazardous substances, for which there are regulations on aspects related to the prevention of major accident risks [7, 8], and the operational procedures carried out in confined-space working environments [9].

The most common types or situations associated with multiple fatal workplace accidents were road traffic accidents, coal mine explosions, and accidents involving maritime transport (3,978 fatalities) [10]. In relation to the construction sector, a case study of the sector in England highlighted that the situation is such that a catastrophic event can represent a plausible scenario, with the potential for multiple casualties and serious consequences [11].

Despite their significance, the prevalence of accidents resulting in multiple work-related fatalities is not well documented. Multi-fatal accidents occur mainly in few circumstances. The main situations involve transportation accidents, fires and explosions, and violence [12].

The aim of this paper is to present an analysis of multiple fatal accidents that have occurred in Italy in recent years, examining their occurrence patterns and causal factors in order to increase the information useful for risk management.

2. Methods

The data illustrated refer first of all to the statistics published by INAIL in its Annual Reports and in its periodic publication "Dati Inail". For these sources, multiple fatal accidents are defined as tragic events where two or more workers lose their lives at the same time [13].

Based on this information, the most striking events that have occurred from January 2007 to December 2024 have been identified and the ways in which they occurred have been highlighted.

Within the INAIL database, statistical data originates primarily from local offices. These collect administrative data on accident reports, which are then validated and entered into the Institute's central archive. From this data, statistics are compiled on reported, defined (for which the investigation into the report has been concluded with a positive or negative recognition), and compensated (accidents positively recognized and for which the worker is entitled to compensation).

In order to highlight the causal factors that determined the modalities of multiple accidents, we used the archive of the national surveillance system for fatal and serious accidents Infor.MO [14]. This information source provides detailed data on the dynamics of accident events, allowing for the expansion and integration of available data on reports and compensation of the INAIL insurance databases.

For the analysis of multiple fatal accidents, a cluster of 181 events was considered within the Infor.MO system, with multiple workers injured simultaneously and at least one death recorded, occurring between the beginning of 2008 and the end of 2022 (the latest year with available data). These events were selected using a specific "collective event" variable present within the information system's record trace.

The Infor.MO system records information from accident investigations conducted by the Italian Workplace Prevention Services of Local Health and Safety Departments (LHSDs) on the most serious incidents. A multifactorial model, developed and validated by INAIL and the Italian Regions, is used to enter the data into the archive to identify the causes of the accident [15].

The system has gradually consolidated, moving from an original experimental phase (2002-2004) to a phase in which it was permanently adopted by the project promoters, who confirmed its organizational structure, objectives, and methodologies. It is listed in the Ministry of Health's National Prevention Plan (2020-2025) as one of the active surveillance systems useful for planning prevention, promotion, assistance, and monitoring interventions [16].

The multifactorial model is one of the causal tree models [17, 18, 19, 20] and allows for a structured evaluation of the event dynamics, starting from the elements that describe the injury event:

- The accident, or the unexpected event that 'supplies' dangerous and uncontrolled energy in the workplace (e.g., overturning of a work vehicle, explosion of materials being processed, etc.);
- Contact, determined between the injured body part and the environmental element involved (e.g., the leg trapped under an overturned tractor);
- Biological damage, defined by the nature and location of the injury (e.g., fracture of the tibia and fibula).

Furthermore, the model allows us to identify all the possible factors that contributed to the accident, classifying them as determinants or modulators and describing them in detail. The determinant is the factor that increases the probability of an accident occurring (for example, working on a roof without adequate protection increases the probability of a worker falling from a height). The modulator is the factor that, while not affecting the probability, contributes to increasing the severity of the injury (for example, failure to wear a safety helmet leads to greater consequences in the event of objects falling on the worker).

The factors identified as determinants or modulators can be divided into one of the following six categories:

- Activity developed by an injured person, inappropriate actions, movements, etc., carried out by an injured worker during the event;
- Activity developed by a third subject Incorrect actions developed by other workers or people (different from the injured one) during the event;
- Equipment, machine, plant, working tool Equipment of any type (or part of it) that presented criticalities in the dynamics of the event;
- Materials Issues on the processed materials that influenced the dynamics of the event
- Working environment conditions Critical aspects related to workplace conditions;
- Working environment conditions: critical aspects related to workplace conditions;
- Personal Protective Equipment and clothing issues that influenced the injury occurrence.

For each category, safety issues are identified, i.e., the critical issues that characterize the determinant and modulator within the accident dynamics. For example, with regard to Activities, the lack of training; and with regard to Equipment, the absence of machine protection systems.

3. Results

Among the multiple accidents, the most sensational cases, also from a media perspective, are reported below:

- 2007: 7 workers killed in fire at a Turin steelworks;
- 2008: 6 workers died while cleaning a sewage treatment plant tank in the province of Catania;
- 2009: 3 workers asphyxiated by toxic gases in Sardinia;
- 2013: 7 victims in fire at a textile factory in Prato;
- 2015: Two accidents in fireworks factories killed 4 workers in the Campania region and 10 workers near Bari;
- 2017: A landslide killed 29 people, including 11 hotel employees in a mountain resort; 6 deaths (including 5 crew members) in crash of an emergency helicopter;
- 2018: Over 30 deaths have resulted from two road accidents: the collapse of a major bridge in Genoa; a head-on collision between a truck and a farm workers' van In the Italian region of Puglia;
- 2022: 19 multiple deaths, 46 deaths total, 44 of which were due to road accidents;
- 2023: 5 workers hit by a train while performing railway track maintenance in Brandizzo, near Turin;
- 2024: 5 workers killed during sewer maintenance in Italian region of Sicily.

From this preliminary examination of the most significant events, several recurring patterns of multiple-fatality incidents can be identified, particularly those associated with fires and explosions, transport-related accidents, confined-space environments, and environmental catastrophes.

In more recent years, based on the available Inail data, a first observation regarding multiple accident data is that trends over time are strongly influenced by road accidents, often during commuting, which are covered by INAIL under workers' insurance regulations. For example, the peak of 82 fatalities observed in 2018 (Table 1), compared to an average of 35-40 multiple deaths annually, is due to two serious road accidents that year, which alone resulted in over 30 worker deaths.

Focusing on the most common causes of multiple fatal accidents, in INAIL data we observe:

- Accidents involving means of transport both at work and while commuting;
- Crushing injuries;
- Falls from heights;
- Fires, explosions;
- Suffocation, asphyxiation (often in confined spaces).

Further characteristics of multiple fatal accidents derive from the analysis of the cluster of events extracted from the Infor.MO surveillance system.

Of the 181 cases extracted from the Infor.MO archive for the years 2008-2022 (Table 2), two-thirds occurred in the Construction and Manufacturing sectors (Istat, Ateco[1] classification of economic activities). Focusing only on events that resulted in fatality, the percentage of cases for these two sectors drops to approximately 50%. Two other sectors where the incidence of multiple fatal accidents is significantly higher than that of fatal cases are Water Supply and Waste Management, and Electricity Distribution.

In the Infor.MO system, in the sectors with the highest incidence of multiple accidents, the most common types of accidents are collapses, landslides, explosions, and contact with gas in confined spaces. With the exception of road accidents, which are almost never directly investigated by the Local Health and Safety Departments (LHSDs) and therefore not recorded in Infor.MO, the same patterns of occurrence previously highlighted in the INAIL database are confirmed.

The causal factors of fatal accidents can be explored further using the Infor.MO database (Table 3). Comparing the cluster of multiple accidents with other accidents, a greater weight is observed for risk factors related to workplace layout, the activities of third parties in teamwork, the management of personal protective equipment, and the materials handled in production processes.

Going into greater detail about the safety issues that characterize multiple accidents compared to other accidents, the most common factors are, in decreasing order, a lack of worker training, information, and instruction, which is recurrent in the "teamwork" factor (14.4% for multiple accidents vs. 10.7% for other accidents). This is followed by inadequate signage, lack of ventilation, and unexpected presence of electricity or gas (12.3% vs. 5.6%), which characterize the "work environment" factor. The storage of gaseous and liquid materials and their characteristics constitute a more recurring safety issue among multiple fatal accidents (8.7% vs. 3.2%). The problem of a lack of training, information, and instruction also recurs in the use and management of PPE (2.4% vs. 0.8%). Finally, regarding work equipment, problems with multiple accidents are often related to poor maintenance (15.2% vs. 8.8%).

Table 1. Extract of the most recent multiple fatal accidents in Italy by INAIL databases in the period 2018-2024.

Year	N
2024	39
2023	36
2022	46
2021	40
2020	27
2019	44
2018	82

[1]Italian version of the European NACE classification, used to classify businesses by their economic activity for official statistics, fiscal, and administrative purposes.

Table 2. Distribution of multiple accidents by sector of activity.

Ateco Business Sector	% Multiple Accidents	% Other Injuries
Constructions	38.4	32.2
Manufacturing Activities	25.4	18.4
Agriculture, Forestry and Fishing	10.2	30.9
Transport and Warehousing	7.9	7.8
Water Supply; Sewerage, Waste Management and Remediation Activities	4.4	2.1
Supply of Electricity, Gas, Steam and Air Conditioning	3.5	0.8
Wholesale and Retail Trade; Repair of Motor Vehicles and Motorcycles	3.5	3.3
Other sectors	6.7	4.5

Table 3. Distribution of causal factors of multiple accidents by category.

Risk Factor Categories	% Multiple Accidents	% Other Injuries
Activity Developed by an Injured Person	25.5	47.4
Working Environment Conditions	21.6	13.9
Activity Developed by a Third Subject During the Event	17.6	8.8
Equipment, Machine, Plant, Working Tool	17.0	19.6
Personal Protective Equipment (PPE) and Clothing	10.7	7.5
Materials	7.6	2.8
Total	100.0	100.0

Workplaces characterized by confined spaces are recurrent for multiple accidents, both in INAIL data on reports and in data extracted from the Infor.MO system. The latter shows that the location where multiple fatal accidents occur in two-thirds of cases is represented by tanks, reservoirs, basins, and wells.

The main risk factors are once again improperly executed teamwork procedures, especially in emergency situations where workers die not because they were directly involved in the operational procedures but instinctively assisting the first injured person, and the environmental factor, due to the presence of gases and vapors not assessed prior to access and the lack of suitable worker recovery systems. Both the procedures and the rescue intervention, in multiple accidents, appear to have occurred without the use of adequate protective equipment (e.g., self-contained breathing apparatus, environmental monitoring).

4. Discussion

Analysis of data provided by INAIL (National Institute for Insurance against Accidents and Workers' Compensation) and the national surveillance system Infor.MO highlights several critical areas of occupational risk. A significant share of workplace accidents and multiple fatalities involve the use of transportation, both during work activities and during commuting, underscoring the importance of road-related risks in the overall burden of fatal workplace accidents.

Surveillance data reveals that multiple accidents frequently occur in operational settings characterized by moving equipment, inadequate safety measures, or insufficient organizational controls. Falls from heights are another significant risk factor, often associated with the absence or improper use of protective equipment and deficiencies in workplace safety management.

Although the studies available in the literature are not directly comparable due to differences in data extraction methods and the nature of the information collected, the evidence is consistent in focusing on the critical areas identified in this review.

One study [9] examined operational procedures implemented in confined work environments, contributory factors that have been frequently identified following enclosed space accident investigations are non-compliance with procedures, inappropriate equipment, poor supervision, complacency and over familiarity leading to short cuts being taken, detection and monitoring equipment not used or not working properly and improper action in an emergency.

The literature indicates that the most common circumstances associated with multiple fatal workplace accidents include road traffic accidents, coal mine explosions, and accidents involving shipping, which together resulted in 3,978 fatalities [10].

In the construction sector, a case study conducted in England highlighted that the occurrence of a catastrophic event represents a plausible scenario, given the nature of the work processes and the potential for multiple fatalities and serious consequences [11].

Despite their relevance, the prevalence of multiple fatal workplace accidents remains insufficiently documented, with such events typically occurring under a limited set of conditions, most often involving transport accidents, fires and explosions, and acts of violence [12].

The safety issues most frequently identified in the Infor.MO system for multiple fatal accidents draw attention to organizational factors, particularly the need for adequate training for workers and for the organization of work areas, not to mention appropriate training for complex work activities and the correct use of protective equipment.

These aspects were also highlighted in the recent report produced by the Parliamentary Commission of Inquiry into working conditions in Italy, exploitation and the protection of health and safety in public and private workplaces [21] established in 2023. The report, approved in September 2024, concerned the work carried out by the Commission in relation to the railway accident which occurred in Brandizzo in the province of Turin in 2023, where 5 workers died during maintenance of the railway tracks.

Among the points highlighted by the Commission, as fundamental recommendations to ensure adequate health and safety conditions for workers, the following passages from the report are reported:

- Periodic assessment of personnel skills to detect any deviations through actual observation of worker behavior (supervision by company supervisors);
- Training activities aimed at enabling workers to conduct their own risk assessments to become aware of the inherent dangers of their activities;
- Verification of processes in the field through structured audits and effective management of identified non-conformities to monitor risks, including organizational and interference-related risks;
- Contracts/subcontracting: Improvement of contract awarding processes that give adequate importance to worker health and safety by amending the rules governing procurement;
- Promotion of participation and whistleblowing processes, such as reporting near misses and OSH issues.

Regarding the last point, it should be noted that the accident resulted, in addition to the multiple fatal injuries of five workers, in two near misses. Indeed, the worksite consisted of seven people, all exposed, albeit in different ways, to the risk of being hit by the passing train due to the railway line not being interrupted.

From a prevention perspective, it is essential to increase knowledge not only about the occurrence and causes of accidents, but also about near misses that occur in the workplace without causing harm to workers. Near misses effectively represent sentinel events that must be addressed during the risk assessment review phase before workers suffer the consequences. A key element in detecting and monitoring such events is the communication process between all parties in the company supply chain.

Worker characteristics, particularly age, can interact with the type of contract and the organizational fragmentation typical of contract work, influencing

the level of occupational health and safety protection. All these factors constitute a complex system that must be taken into account when analyzing accident dynamics [22].

The report, as stated by the Commission, represents a starting point for an in-depth examination of multiple fatal accidents that can lead to "comprehensive legislative proposals to be submitted to Parliament, which embody the essence of best practices in workplace safety".

Therefore, the Commission's recommendations become particularly significant when compared with the data obtained from the current study, which highlights critical shortcomings related to the risk assessment process, such as insufficient company controls and inadequate worker information and training.

These findings underscore the need to strengthen worker safety, including through the role of health surveillance and occupational physicians, ensuring the constant updating of preventive practices.

In contexts characterized by a lack of awareness of social responsibility and work ethics, some measures, such as continuous monitoring of risk conditions in the workplace, require constant attention to the surveillance of risk factors, particularly those of an organizational nature.

5. Conclusions

The analysis of workplace accidents with multiple fatalities highlights organizational risk factors and those related to operational interference, which are more significant than those that cause single fatalities.

The most common safety deficiencies observed in workplace accidents with multiple fatalities include inadequate information and training systems for workers, poor workplace organization, and the absence or inadequacy of safety devices.

As noted by the Parliamentary Commission of Inquiry into Working Conditions in Italy, internal company processes play a fundamental role in controlling risk factors, starting with the identification of near misses that often lead to serious or fatal injuries, including multiple injuries. Continuous data collection on workplace risk conditions is essential for proper occupational health and safety management.

Ultimately, reducing workplace accidents requires strengthening the organizational safety culture and a more participatory relationship between workers and the company, starting with the involvement and constant dialogue between all legally required stakeholders of the company's prevention system.

Identifying workplace prevention measures is also facilitated by greater cooperation between the relevant institutional bodies and social partners. Specifically, this involves implementing a nationwide monitoring system for in-depth causal analysis of accidents and near misses, timely and coordinated emergency response management, and verifying the effectiveness of preventive measures.

Declaration of Interest: There is no conflict of interest for the authors of the manuscript.

Author Contribution Statement: All authors contributed to the content and interpretation of the submitted article.

References

1. ILO. "A call for safer and healthier working environments" 2023. Doi: https://doi.org/10.54394/HQBQ8592.
2. Ariani F, Baldasseroni A, Rondinone B, et al. Burden of occupational injuries occurred in Italy, 1900-2017. *Eur J Public Health*. 2020;30(5):ckaa165.1116. Doi: https://doi.org/10.1093/eurpub/ckaa165.1116
3. Come valutare gli effetti degli interventi di prevenzione degli infortuni sul lavoro? Osservazioni sugli indicatori INAIL-ISPESL-Regioni [How to assess the effects of interventions for preventing work injuries? Observations on INAIL-ISPESL-Regioni indicators] Italian. *Epidemiologia e Prevenzione*. 2008;32(3): 168-75.
4. Relazione annuale INAIL 2024. [INAIL Annual Report 2024.] Italian. Available at: https://www.inail.it/portale/it/inail-comunica/news/notizia.2025.07.news-presentazione-relazione-annuale-inail-24.html#:~:text=Scarica%20file%3A,Dimensione%202.36%20MB.
5. Andamento degli infortuni sul lavoro e delle malattie professionali [Trends in accidents at work and occupational diseases]. [Italian]. Dati INAIL January 2025. Available at: https://www.inail.it/portale/it/inail-comunica/pubblicazioni/dati-inail/dati-inail-dettaglio.2025.01.dati-inail-anno-2025.html.
6. Drudi D, Zak M. Work-related multiple-fatality incidents. *Mon Labor Rev*. Oct 2004, pp. 20-37.

7. [Directive 2012/18/EU – Seveso III – on the control of major-accident hazards involving dangerous substances [Italian].
8. [Legislative Decree no. 105 of 26 June 2015 implementing Directive 2012/18/EU – Seveso III]. [Italian].
9. Kulkarni Ajit C. Deaths due to hydrogen sulphide on a jack up rig at Bombay High: an avoidable accident. 2023. *Int Marit Health*. 2023;74(3):171-174.
10. Tao Z, Ming-Xiao W, Miao-Rong X, Ming-Qiu J.A. Analysis of traumatic occupational fatalities in China. *J Ind Med*. 2011;54(7):560-4. Doi: 10.1002/ajim.20958. Epub 2011 Apr 22.PMID: 21520213.
11. Carpenter J. Release of data following a serious incident in the UK construction industry. 2015;168(3): 140-147.
12. Pierce B. How rare are large, multiple-fatality work-related incidents? *Accid Anal Prev*. 2016;96:88-100. Doi: 10.1016/j.aap.2016.07.014. Epub 2016 Aug 6.PMID: 27505100.
13. Andamento degli infortuni sul lavoro e delle malattie professionali. Trends in accidents at work and occupational diseases]. [Italian] Dati INAIL January 2024. Available at: https://www.inail.it/portale/it/inail-comunica/pubblicazioni/dati-inail/dati-inail-dettaglio.2024.03.dati-inail-anno-2024.html.
14. INAIL. Infor.Mo sistema di sorveglianza nazionale degli infortuni mortali e gravi sul lavoro (National surveillance system for fatal and serious accidents at work). [Italian] Available at: https://www.inail.it/portale/ricerca-e-tecnologia/it/ambiti-di-ricerca/area-salute-sullavoro/sistemi-di-sorveglianza--gestione-integrata-del-rischio-e-modell/infor-MO.html.
15. De Merich D, Gnoni MG, Guglielmi A, et al. Designing national systems to support the analysis and prevention of occupational fatal injuries: Evidence from Italy. *Saf Sci*. 2022;147:105615. Doi: 10.1016/j.ssci.2021.105615
16. Piano Nazionale di Prevenzione 2020-2025. Italy, Ministry of health, National Prevention Plan 2020-2025. [Italian] https://www.salute.gov.it/new/it/tema/piano-nazionale-della-prevenzione/piano-nazionale-della-prevenzione-2020-2025/
17. Kjellen, Urban, Larsson, Tore J. Investigating accidents and reducing risks – A dynamic approach. *J Occup Accid*. 1981;3(2):129-140. Doi: https://doi.org/10.1016/0376-6349(81)90005-5
18. Laflamme, Lucie, 1990. A better understanding of occupational accident genesis to improve safety in the workplace. *J Occup Accid*. 12(1-3):155-165. Doi: https://doi. org/10.1016/0376-6349(90)90094-C.
19. Laflamme L. Mod'eles et methodes d'analyse de l'accident du travail: del'organisation du travail aux strategies de prevention. Italian version edited by Pianosi G, ARPAT, 2000, Firenze.
20. Campo G, Guglielmi A, Marconi M, Pianosi G. The reconstruction of the causes and dynamics of work-related injuries using the model "We learn by our mistakes" [Italian]. *Prevenzione Oggi*. 2006;2:(1-2):27-38.
21. Parliamentary Commission of Inquiry into Working Conditions in Italy, Exploitation, and Health and Safety in Public and Private Workplaces. 10th September 2024. Pages 71-73. Available at: https://documenti.camera.it/leg19/resoconti/commissioni/bollettini/html/2024/09/10/82/comunic.htm#.
22. Nilsen M, Kongsvik T, Almklov PG. Splintered structures and workers without a workplace: How should safety science address the fragmentation of organizations? *Safety Science*. 2021;142:105382. Doi: 10.1016/j.ssci.2021.105382.

La Medicina del Lavoro

Original article

Med. Lav. 2026; 117 (3): 18244
DOI: 10.23749/mdl.2026.18244

Clinical Characteristics and Interstitial Findings on High-Resolution Computed Tomography in Patients with Coal Workers' Pneumoconiosis

Merve Acun Pinar[1]*, Gülden Sari[2], Adem Koyuncu[3], Rabia Ezber[3], Hakan Ertürk[4] and Cebrail Şimşek[3]

[1]Department of Occupational Diseases, Gazi Yaşargil Training and Research Hospital, Diyarbakır, Türkiye
[2]Department of Occupational Diseases, Yıldırım Beyazıt University Yenimahalle Training and Research Hospital, Ankara, Türkiye
[3]Department of Occupational Diseases, Ankara Atatürk Sanatorium Training and Research Hospital, Ankara, Türkiye
[4]Department of Radiology, Ankara Atatürk Sanatorium Training and Research Hospital, Ankara, Türkiye

Keywords: Coal Workers' Pneumoconiosis; Interstitial Lung Disease; High-Resolution Computed Tomography

Abstract

Background: *Coal workers' pneumoconiosis (CWP) is a parenchymal lung disease resulting from the prolonged inhalation of coal dust. Coal dust exposure may also lead to a spectrum of airway and parenchymal disorders. This study aimed to investigate the clinical characteristics, radiological and functional findings of CWP, as well as the presence of interstitial changes and associated risk factors.* **Methods:** *Patients with CWP who were admitted to the occupational diseases clinic of a tertiary hospital between 2017 and 2023 were included. Demographic, radiological, and pulmonary functional data were analyzed. High-resolution computed tomography (HRCT) scans were reviewed for interstitial lung abnormalities (ILA) and interstitial lung disease (ILD). Factors associated with ILD were assessed using logistic regression analysis. Statistical significance was defined as $p<0.05$.* **Results:** *One hundred male patients with CWP (mean age, 61.7 ± 11.7 years) were evaluated. Large opacities were present in 37% of cases. Pulmonary function testing revealed restrictive impairment in 35% and obstructive impairment in 38% of patients. Compared with those working lignite mines, bituminous coal miners exhibited a significantly higher prevalence of large opacities and lower lung function values. ILAs were identified in 63% of patients, and ILD in 42%. ILD prevalence was significantly higher among those with exposure durations exceeding 10 years, working in bituminous coal mines, and with predominant small opacities larger than 3 mm.* **Conclusions:** *Coal dust exposure is a risk factor not only for CWP but also for impaired lung function, ILA, and ILD. Comprehensive surveillance of coal workers is essential for early detection and timely management of these conditions.*

1. Introduction

Coal workers' pneumoconiosis (CWP) is a chronic parenchymal lung disease caused by prolonged inhalation of coal dust [1]. The prevalence and severity of CWP depend on coal type, dust concentration, exposure duration, and the composition of carbon, silica, and other minerals [2]. Based on coal rank, sub-bituminous coal and lignite are classified as "soft coal," whereas bituminous coal and anthracite are considered "hard coal." Differences in mining methods also affect the particle surface area, free

Received 17.11.2025 – Accepted 07.05.2026
*Corresponding Author: Merve Acun Pinar; E-mail: mrvacn@hotmail.com

radical potential, and silica content of the inhaled dust. The characteristic lesion of CWP is the coal macule, composed of dust-laden macrophages surrounding respiratory bronchioles, often associated with focal emphysema. Fibrotic nodules and progressive massive fibrosis (PMF) may also develop, reflecting more advanced disease [3, 4]. Because miners are typically exposed to mixed dusts containing coal, kaolin, mica, and silica, most patients also present with mixed-dust fibrosis and silicotic nodules. Together with CWP, silicosis, mixed-dust pneumoconiosis, coal dust-related diffuse fibrosis (DDF), emphysema, and chronic bronchitis, these entities constitute the clinical spectrum of coal mine dust lung disease (CMDLD) [5].

Diffuse interstitial pulmonary fibrosis may also be present in coal miners. Autopsy studies have demonstrated DDF in 15-20% of miners [6]. DDF is characterized by bridging fibrosis related to macular, nodular, or PMF lesions of CWP or silicosis, typically exhibiting pigmented interstitial septal thickening [5, 6]. Moreover, coal dust exposure has been associated with chronic interstitial pneumonias, desquamative interstitial pneumonia (DIP), and combined pulmonary fibrosis and emphysema (CPFE) [7-9]. Despite these observations, data regarding the prevalence and determinants of interstitial abnormalities on high-resolution computed tomography (HRCT) in CWP remain limited.

This study aimed to evaluate the clinical and radiological characteristics of patients with CWP in a tertiary occupational diseases clinic, to analyze pulmonary function findings, and to investigate interstitial abnormalities on HRCT and their associated risk factors.

2. Methods

2.1. Study Population

This retrospective, cross-sectional study was approved by the Ethics Committee of Ankara Atatürk Sanatorium Training and Research Hospital (Dated 12 July 2023 and numbered 2012-KAEK-15/2749). Patients diagnosed with CWP in the occupational diseases outpatient and inpatient clinics between January 2017 and January 2023 were screened. Those with available HRCT scans in the hospital information system were included. Patients with suspected interstitial lung diseases (ILDs) due to other causes (e.g., DIP, RB-ILD, hypersensitivity pneumonitis) were evaluated using laboratory and pathological findings; those with alternative ILD diagnoses were excluded. Demographic data, smoking status, occupational history, pulmonary function test (PFT) results, chest radiographs, and HRCT scans were obtained from patient files and hospital records.

2.2. Chest Radiography Assessment

Chest radiographs were evaluated according to the International Labour Organization (ILO) classification system for pneumoconiosis [10]. Small opacities <1 cm were classified as irregular (s, t, u) or rounded (p, q, r) based on shape, and graded into categories 1, 2, or 3 according to profusion. Large opacities ≥1 cm were considered PMF and classified as A, B, or C. Patients with PMF were categorized as having complicated pneumoconiosis, whereas those without PMF were categorized as having simple pneumoconiosis. Radiographs were independently assessed by three certified ILO readers (all pulmonologist and occupational medicine specialists). In cases of disagreement, consensus was reached through joint review.

2.3. Pulmonary Function Testing

Pulmonary function testing was performed by experienced technicians in accordance with the American Thoracic Society / European Respiratory Society (ATS/ERS) standards. Spirometry results were expressed as percentages of predicted values. An FEV1/FVC ratio <0.7 was defined as obstructive impairment [11], while an FEV1/FVC ratio ≥0.7 with FVC <80% predicted was defined as restrictive impairment [12]. Patients with both obstruction and reduced FVC were classified as having mixed impairment.

2.4. HRCT Imaging and Evaluation

Thin-section CT images with a slice thickness of 1 mm, obtained using a 128-slice multidetector

Philips Ingenuity CT scanner, were evaluated with a bone reconstruction algorithm in the lung window settings (window width: 1500, window level: –600) by a radiologist with 30 years of experience in thoracic radiology. HRCT patterns were interpreted using standardized descriptors for occupational and environmental lung diseases, consistent with the International Classification of HRCT for Occupational and Environmental Respiratory Diseases [13].

2.5. Assessment of Interstitial Abnormalities

In addition to CWP-specific findings, interstitial lung abnormalities (ILA) and ILD were assessed according to the 2025 ATS Clinical Statement (14). Bilateral, nondependent ground-glass opacities, reticular abnormalities, architectural distortion, traction bronchiectasis, and/or honeycombing involving >5% of a lung zone were considered ILA. Consistent with the ATS definition of ILD in individuals with ILA, a diagnosis of ILD required the presence of at least one additional criterion beyond HRCT abnormalities. These criteria included: respiratory symptoms attributable to ILD (dyspnea and/or cough); objective physiological impairment on pulmonary function testing, defined as reduced FVC and/or DLCO (<80% of predicted); radiological progression on serial chest CT; or pathological evidence of fibrotic ILD. Nodular and macular CWP-related lesions were not classified as ILA/ILD.

2.6. Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA). Categorical variables were presented as counts and percentages, whereas continuous variables were expressed as medians with interquartile ranges (IQR). The chi-square or Fisher's exact tests were used for comparisons of categorical variables, and the Mann–Whitney U or Kruskal–Wallis tests were used for continuous variables, as appropriate. Univariate logistic regression analyses were conducted to assess the associations between independent variables and ILD. Variables with a p-value <0.20 in the univariate analysis were considered potential candidates and subsequently included in the multivariate logistic regression model. Before multivariate analysis, correlations among independent variables were examined using a correlation matrix. To avoid multicollinearity and ensure model stability, variables with a pairwise correlation coefficient (r) greater than 0.6 were considered highly correlated. In such cases, the variable deemed less clinically relevant or statistically significant was excluded from the final model. The results of logistic regression analyses were expressed as odds ratios (ORs) with 95% confidence intervals (CIs). A p-value <0.05 was considered statistically significant.

3. Results

Between January 2017 and January 2023, 130 patients were diagnosed with CWP, of whom 100 with available HRCT scans were included in the analyses. All patients were male, with a mean age of 61.7 ± 11.7 years. Sixty-seven had worked in bituminous coal mines and 33 in lignite coal mines. Comorbidities other than pneumoconiosis were present in 67 patients. COPD was the most common comorbidity (n=46), followed by hypertension (n=11) and malignancy (n=10). Of those with malignancy, five had lung cancer. Other descriptive findings are summarized in Table 1.

The presence of PMF was about three times more common in bituminous miners than in lignite miners (p=0.025; OR=3.012; 95% CI: 1.149–7.893). Mean exposure duration was 20.5 ± 6.6 years in patients with complicated pneumoconiosis and 19.4 ± 6.5 years in those with simple pneumoconiosis. Among PMF patients, 3 (8.1%) had ≤10 years of exposure, 10 (27%) had 11–20 years, and 24 (64.9%) had >20 years. Exposure duration was significantly linked to PMF development (p=0.031; OR=1.077; 95% CI: 1.007–1.152). Age and smoking were not significantly associated.

Pulmonary tests showed obstruction in 38 (38%) patients and restriction in 35 (35%). Of those with obstruction, 12 (31.6%) had pure obstruction, and 26 (68.4%) had mixed impairment. No significant difference in obstruction or restriction prevalence between smokers and non-smokers (p=0.394 and

Table 1. Descriptive Findings.

		n	%
Age (mean ± SD)		61.66±11.66	
Smoking (Pack-Years) (mean ± SD)		26.72±17.76	
Smoking Status	Non-Smoker	23	23
	Current or Former Smoker	77	77
Exposure Duration (Years) (mean ± SD)		20.50±6.63	
Coal Type	Bituminous	67	67
	Lignite	33	33
Predominant Small Opacity	p	20	20
	q	39	39
	r	16	16
	s	12	12
	t	13	13
	u	0	0
Predominant Opacity Shape	Irregular	25	25
	Rounded	75	75
Small Opacity Profusion	Category 1	31	31
	Category 2	60	60
	Category 3	9	9
Large Opacities	Absent	63	63
	Present	37	37
Size of Large Opacities	A	22	59
	B	12	32
	C	3	8.1
FEV_1 (mean ± SD)		72.47±20.13	
FVC (mean ± SD)		75.11±20.01	
FEV_1/FVC (mean ± SD)		73.80±12.42	
Comorbidity	Absent	33	33
	Present	67	67
Respiratory Symptoms	Absent	39	39
	Present	61	61

FEV_1: Forced Expiratory Volume in 1 second, FVC: Forced Vital Capacity.

p=0.980). Obstruction was more common in complicated pneumoconiosis (p=0.035), but restriction prevalence was similar (p=0.680). The distribution of respiratory abnormalities is shown in Figure 1.

When factors associated with pulmonary function were analyzed, FEV_1, FVC, and FEV_1/FVC values were significantly lower in bituminous coal miners compared with lignite miners (Table 2). No significant differences in pulmonary function parameters were observed between patients with and without a history of smoking (Table 2). Pulmonary function parameters and other related factors are presented in Table 2.

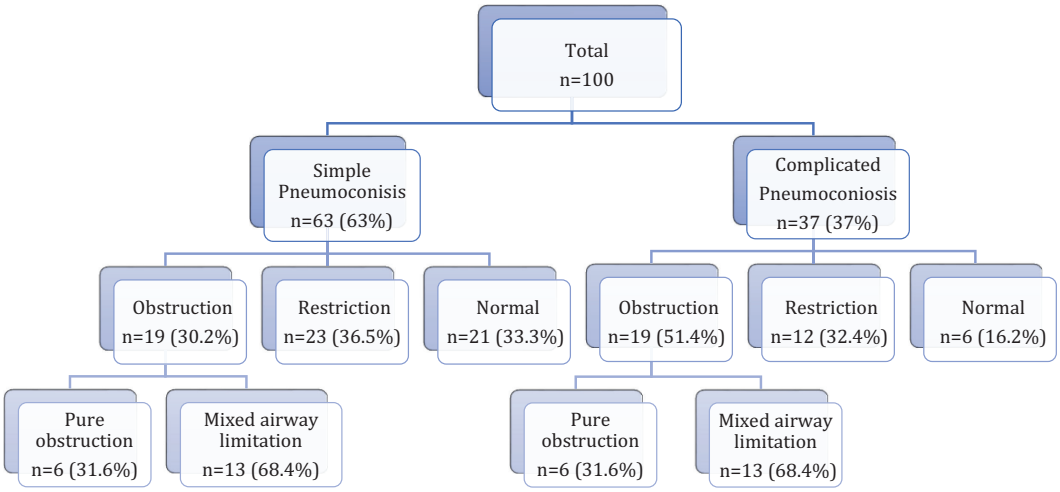


Figure 1. Distribution of respiratory dysfunction in simple and complicated pneumoconiosis.

When HRCT findings of patients diagnosed with CWP were evaluated, the most common findings were nodules, lymph node enlargement, and interlobular septal thickening. All HRCT findings observed in the cases are presented in Table 3.

Among patients with nodules, 66 had a peribronchovascular distribution, 8 had a centrilobular distribution, and 24 had a nonspecific distribution. Among patients with emphysema, 37 had paraseptal, 7 had bullous, 10 had centrilobular, and 3 had panacinar emphysema. The prevalence of emphysema was 47.8% in never-smokers and 59.7% in smokers; however, the difference between the groups was not statistically significant (p=0.311).

ILA were identified in 63 (63%) cases. Of these, 42 patients (66.7%) also exhibited features consistent with ILD. Patients with ILD were significantly older than those without ILD (p=0.034), whereas there was no statistically significant difference in exposure duration between the two groups (p=0.341). Figure 2 shows HRCT images of a patient with ILD.

Univariate logistic regression analyses revealed that the risk of ILD was approximately 3.2-fold higher in workers employed in bituminous coal mines, 5.2-fold higher in those with more than 10 years of exposure, and 4.8-fold higher in those with small opacities >3 mm in diameter (Table 4). Factors associated with ILD and the results of the univariate logistic regression analysis are presented in Table 4. In the multivariate logistic regression analysis including exposure duration, coal type, and small opacity size, only the presence of small opacities >3 mm remained independently associated with ILD. Patients with predominant small opacities >3 mm had a 4.66-fold increased risk of ILD (p=0.026; OR=4.661; 95%CI: 1.202–18.078).

The presence of ILA or ILD was significantly associated with a higher prevalence of respiratory symptoms (ILA: p=0.001; OR=6.943; 95%CI: 2.099–22.964; ILD: p=0.001; OR=34.286; 95%CI: 4.276–274.930). While no significant differences in pulmonary function parameters were observed between patients with and without ILA, those with ILD had significantly lower FEV_1 and FVC values (both p<0.001).

4. Discussion

Coal dust exposure, due to its complex composition, is a major cause of respiratory disease. All respiratory disorders potentially associated with coal dust are collectively termed Coal Mine Dust Lung Disease (CMDLD) [5]. In CWP, a principal

Table 2. Factors associated with pulmonary function parameters.

		FEV_1 Median (IQR)	p*	FVC Median (IQR)	p*	FEV_1/FVC Median (IQR)	p*
Coal Type	Bituminous	73 (55-83)	0.020	73 (63-86)	0.049	74 (61-79)	0.043
	Lignite	82 (68-94)		81 (72-93)		79 (70-85)	
Smoking Status	Never-smoker	77 (62-87)	0.734	78 (57-86)	0.756	77 (69-87)	0.231
	Current/ ex smoker	73 (59-87)		74 (64-90)		74 (67-80)	
Size of Small Opacity	<1.5 mm	79.5 (69.5-93.5)	0.001	79.5 (72.5-87.5)	0.024	79 (71.5-84.5)	0.027
	1.5-3 mm	75 (58-87.5)		77.5 (62.5-92)		74 (67-81)	
	>3 mm	58 (43.5-69.5)		64 (56.5-71.5)		69 (59-76)	
Predominant Small Opacities	Irregular	73 (55-83)	0.360	74 (61-80)	0.093	78 (64-84)	0.561
	Rounded	75 (60-88)		78 (65-90)		74 (67-81)	
Small Opacity Profusion	Category 1	80 (64-91)	0.391	77 (66-90)	0.842	79 (70-87)	0.008
	Category 2	75 (58.5-86.5)		74.5 (62-87.5)		74.5 (69-80)	
	Category 3	72 (58-72)		75 (67-100)		64 (60-69)	
Large Opacities	Absent	78 (66-94)	0.001	78 (67-94)	0.064	78 (70-84)	0.016
	Present	66 (53-79)		70 (59-84)		70 (60-77)	
Size of Large Opacities	A	71.5 (58-80)	0.019	76.5 (63-87)	0.026	73.5 (64-80)	0.429
	B	59 (51.5-73.5)		69 (60.5-79.5)		70.5 (59-76)	
	C	36 (28-40)		44 (31-50)		61 (60-69)	
Pulmonary Disease	Absent	83.5 (73-93)	<0.001	80.5 (74-93)	0.001	80 (74-86)	<0.001
	Present	62.5 (47-75)		66.5 (54-84)		68.5 (59-76)	
Respiratory Symptoms	Absent	87 (80-94)	<0.001	86 (74-97)	0.002	80 (74-84)	0.050
	Present	71 (55-79)		72 (57-84)		73 (64-79)	

*FEV_1: Forced Expiratory Volume in 1 second, FVC: Forced Vital Capacity *Mann-Whitney U test.*

Table 3. HRCT findings in patients with coal workers' pneumoconiosis.

HRCT findings	n (%)	HRCT Findings	n (%)
Nodule	98 (98)	Consolidation	64 (64)
Lymph Node Enlargement	98 (98)	Emphysema	57 (57)
Interlobar Septal Thickening	98 (98)	Distortion	49 (49)
Pleural Retraction	96 (96)	Mosaic Attenuation	40 (40)
Pleural Thickening	95 (95)	Mass Lesion	37 (37)
Reticulation	87 (87)	Lymph Node Calcification	35 (35)
Atelectasis	77 (77)	Cyst	20 (20)
Ground-Glass Opacities	73 (73)	Subpleural Lines	11 (11)
Interlobular Septal Thickening	72 (72)	Air Bronchogram	8 (8)
Bronchiectasis	69 (69)	Honeycombing	3 (3)

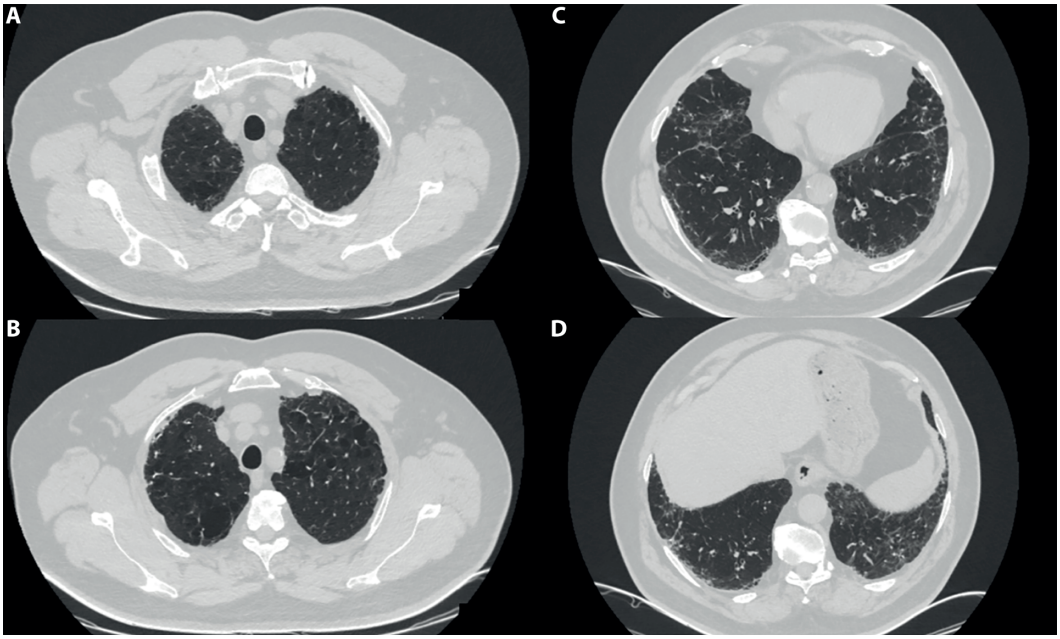


Figure 2. HRCT in a 70-year-old male who worked in a bituminous coal mine for 20 years and had a 20 pack-year smoking history (ex-smoker), showing predominant upper-lobe emphysematous changes and peripheral/subpleural reticular and reticulonodular interstitial opacities in the lower lobes, with interlobular septal and peribronchial thickening, mild bronchiectasis, focal honeycombing, and associated ground-glass opacities and millimetric nodules.

Table 4. Factors associated with interstitial lung disease (ILD) in patients with coal workers' pneumoconiosis: univariate logistic regression analysis.

		ILD			
		Absent n=58	Present n=42		
		n (%)	n (%)	P	OR (95%CI)
Age (mean ± SD)		59.2±13.0	65.1±8.5	**0.014**	**1.049 (1.010-1.090)**
Coal Type	**Lignite**	25 (43.1)	8 (19.0)	**0.014**	1 (Ref)
	Bituminous	33 (56.9)	34 (81.0)		**3.220 (1.271-8.153)**
Exposure Duration	**<10 years**	12 (20.7)	2(4.8)	**0.037**	1 (Ref)
	≥10 years	46 (79.3)	40 (95.2)		**5.217 (1.101-24.724)**
Smoking	**Never-smoker**	17 (29.3)	6 (14.3)	0.084	1 (Ref)
	Current/former Smoker	41 (70.7)	36 (85.7)		2.488 (0.886-6.988)
Size of Small Opacity	**<1,5 mm**	22 (37.9)	10 (23.8)	-	1 (Ref)
	1,5-3 mm	31 (53.4)	21 (50)	0.401	1.490 (0.588-3.779)
	>3 mm	5 (8.6)	11 (26.2)	**0.017**	**4.840 (1.326-17.666)**
Predominant Small Opacities	**Rounded**	46 (79.3)	29 (69.0)	0.245	1 (Ref)
	Irregular	12 (20.7)	13 (31.0)		1.718 (0.690-4.277)

Table 4 (*Continued*)

		ILD			
		Absent n=58	Present n=42		
		n (%)	n (%)	P	OR (95%CI)
Small Opacity Profusion	**Category 1**	19 (32.8)	12 (28.6)	-	1 (Ref)
	Category 2	35 (60.3)	25 (59.5)	0.786	1.131 (0.466-2.744)
	Category 3	4 (6.9)	5 (11.9)	0.372	1.979 (0.441-8.873)
PMF	**Absent**	41 (70.7)	22 (52.4)	0.063	1 (Ref)
	Present	17 (29.3)	20 (47.6)		2.193 (0.958-5.020)

OR: Odds Ratio; CI: Confidence Interval; ILD: Interstitial lung disease; PMF: progressive massive fibrosis.

component of CMDLD, assessing coal type, coexisting pulmonary disease, and HRCT findings is key to clarifying its clinical, functional, and radiological features. In the present study, patients working in bituminous coal mines had more severe radiological and functional impairment than those in lignite mines. HRCT showed that most patients had concomitant ILA and ILD. ILD was significantly associated with age, exposure duration, coal type, and small opacity size. Pulmonary function impairment occurred independently of smoking status and appeared with obstructive, restrictive, or mixed patterns.

CWP is an occupational lung disease in which radiological findings are usually dominated by small nodular opacities resembling silicosis. However, several studies have reported that coal dust exposure may also be associated with bilateral reticular abnormalities and, occasionally, honeycombing, a pattern defined as DDF and frequently seen in these patients [6]. Although DDF is a well-established pathological entity, its radiological features can overlap with those of other interstitial lung diseases. Bilateral reticular abnormalities, honeycombing, and traction bronchiectasis may be present and can mimic the usual interstitial pneumonia (UIP) pattern and idiopathic pulmonary fibrosis (IPF) [5]. Prior work has also shown that other interstitial lung diseases, including DIP, chronic interstitial pneumonia, and CPFA, may be associated with coal dust exposure [7-9]. Earlier series reported diffuse pulmonary fibrosis in 10-40% of coal miners [15-18], generally confirmed histopathologically and including all miners with coal dust exposure.

In the current study, radiological assessment revealed ILA in 63% and ILD in 42% of cases, rates higher than those previously reported. This likely reflects the inclusion of only patients already diagnosed with CWP, who by definition have had sufficiently intense and prolonged exposure to develop pneumoconiosis and, consequently, pulmonary fibrosis at higher-than-expected frequencies. The observation that ILD was approximately 5.2-fold more frequent in patients with ≥10 years of exposure supports this hypothesis. However, the retrospective design, lack of key physiological parameters (such as DLCO), and absence of histopathological data may have contributed to overestimation of ILD.

Recent studies have demonstrated a strong association between cumulative coal dust exposure and radiological ILD patterns [19], and an association between radiological ILD and mortality [19]. Another study of 45 coal miners with interstitial fibrosis showed that mean survival was significantly longer than in patients with non-occupational interstitial fibrosis [20]. Overall, interstitial fibrosis is not rare among coal miners and may follow a distinct clinical course compared with non-occupational forms. Thus, recognizing ILA and ILD in this population is critical: failure to obtain a detailed occupational history can lead to misdiagnosis and inappropriate management. Comprehensive occupational exposure assessment in patients with ILA or ILD may prevent unnecessary interventions and facilitate timely exposure cessation, potentially reducing disease progression.

In this study, 73% of patients had pulmonary function test abnormalities, classified as obstructive,

restrictive, or mixed patterns. Obstruction or restriction was not significantly related to smoking status, but obstruction was significantly more frequent among patients with PMF. Cumulative dust exposure leads to reductions in FEV_1, FVC, and the FEV_1/FVC ratio and to emphysema, even in never-smokers. Consequently, differences in pulmonary function between smokers and non-smokers tend to diminish or disappear. In PMF, pulmonary function impairment is more pronounced, as exposure is usually longer and more intense. Paracicatricial emphysema in PMF further accentuates obstructive changes. Previous studies have consistently shown a dose-response relationship between respirable coal dust exposure and pulmonary function parameters [4, 21, 22]. In a study of 7,139 coal miners, cumulative coal dust exposure was inversely correlated with FEV_1, FVC, and FEV_1/FVC [23]. Similarly, in former miners, abnormal spirometric findings were found in 56.6% of workers, regardless of pneumoconiosis status, and both the frequency and severity of abnormalities increased with disease category [24].

Multiple studies indicate that coal dust exposure is an independent risk factor for obstructive lung disease, chronic bronchitis, and emphysema [23, 25-27]. In an autopsy study of 722 individuals, the emphysema severity index was sixfold higher in never-smoking coal miners than in never-smokers without mining exposure [28]. Smoking and coal dust exposure had similar effects in predicting emphysema severity, and emphysema was reported in one-third of never-smoking coal miners [19]. In the current study, emphysema was radiologically detected in 57% of all cases and in 47.8% of never-smokers. The absence of a significant difference in emphysema prevalence between smokers and non-smokers further supports coal dust exposure as an independent risk factor for emphysema.

Coal types differ markedly in rank, moisture content, mineral composition, and physicochemical properties [2, 29]. Owing to its higher carbon content, bituminous coal is considered more cytotoxic and pathogenic than lignite [30]. In the study by Reisner and Robock, workers exposed to dust of similar mass concentrations showed greater cytotoxicity and higher pneumoconiosis prevalence in mines extracting higher-rank coal [31]. Other studies similarly reported that exposure to higher-rank coal is associated with increased CWP incidence [32, 33]. In a 37-year follow-up study by Graber et al., the exposure-response relationship between cumulative coal dust exposure and pneumoconiosis-related mortality varied by region, with the strongest associations where coal rank was highest [34].

Consistent with this, in the present study PMF was approximately threefold more frequent among CWP cases working in bituminous than in lignite mines, and FEV_1, FVC, and FEV_1/FVC values were significantly lower, independent of smoking status. ILD was also about 3.2-fold more common in bituminous coal miners. These differences in functional impairment and disease severity cannot be attributed solely to geological factors: exposure intensity, particle characteristics, production methods, and concomitant crystalline silica exposure are also important. Bituminous coal is predominantly extracted through underground mining, where gallery excavation and blasting generate large quantities of fine particulate matter and effective dilution is difficult. This results in prolonged exposure to high concentrations of respirable dust. In contrast, lignite is often produced in open-pit mines, where natural ventilation and lower mechanical fragmentation energy generally yield lower alveolar dust concentrations [35]. Thus, cumulative dust exposure tends to be higher in bituminous mines.

Workers exposed to higher-rank coal dust, especially in underground mines, should therefore be regarded as at increased risk not only for the development and severity of pneumoconiosis but also for pneumoconiosis-related morbidity and mortality. Occupational health and safety strategies and health surveillance programs should prioritize these high-risk groups.

4.1. Strengths of the Study

This study was conducted at one of the leading national reference centers for pneumoconiosis, allowing evaluation of patients from multiple regions and different coal mine types. Interstitial findings

were assessed according to the 2025 ATS guideline, ensuring a current and objective evaluation.

4.2. Limitations of the Study

This retrospective cross-sectional study included only CWP cases referred to a single tertiary center. Individuals without CWP who might have exhibited interstitial changes or pulmonary function impairment were not included, potentially introducing selection bias. The retrospective and single-center design limits generalizability and precludes causal conclusions. Several estimates had wide confidence intervals due to limited sample size and few events in some subgroups; thus, the precision of some effect estimates is limited and the findings should be interpreted cautiously.

HRCT images were assessed by a single radiologist, an important limitation, particularly for subtle interstitial abnormalities, and a source of possible diagnostic uncertainty and classification bias. The lack of key physiological parameters (such as DLCO) and histopathological data, again related to the retrospective design, may have led to overestimation of ILD prevalence. Dust concentration measurements were not available, so pneumoconiosis severity and pulmonary function impairment could not be directly linked to exposure levels. Because occupational histories were self-reported, recall bias cannot be excluded.

Despite using a composite clinicoradiological and physiological framework aligned with ATS recommendations, some overlap between ILA and early or mild ILD cannot be excluded. This is an inherent challenge of observational retrospective studies and highlights the need for longitudinal follow-up and multidimensional assessment.

5. Conclusion

In this study of patients with CWP, abnormalities in pulmonary function were detected in 73% of cases, PMF in 37%, and ILD unrelated to other causes in 42%. The development of PMF and ILD was associated with exposure duration and coal type, with workers in bituminous coal mines at substantially higher risk of PMF, ILD, and pulmonary function decline. To better protect workers and prevent harmful exposure, large-scale prospective studies exploring the relationship between coal rank and disease severity are needed.

Given the high prevalence of ILA and ILD in CWP, obtaining a detailed occupational history in all patients presenting with interstitial lung disease is essential. Such comprehensive assessment, together with timely exposure cessation when indicated, may help reduce the morbidity and mortality associated with these conditions.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ankara Atatürk Sanatorium Training and Research Hospital Clinical Research Ethics Committee (2012-KAEK-15/2749 and approved on 12 July 2023)

Declaration of Interest: The authors declare no conflict of interest.

Author Contribution Statement: M.A.P. and G.S. contributed to the conceptualization and design of the study; M.A.P., G.S., A.K., R.E., H.E., and C.Ş. conducted the investigation; M.A.P. performed the formal analysis; M.A.P., G.S., A.K., R.E., and H.E. contributed to data curation; M.A.P. drafted the original manuscript, and G.S., A.K., R.E., H.E., and C.Ş. revised and edited the manuscript, and C.Ş. supervised the study. All authors have read and approved the final version of the manuscript.

References

1. Balmes J. R. Occupational Lung Disease. In: Eds Ladou J, Harrison R. J, eds. CURRENT Diagnosis & Treatment: Occupational & Environmental Medicine, 6e. McGraw Hill; 2021:293-315.
2. Berkowitz, Norbert. An introduction to coal technology. Academic Press, New York, 1979.
3. Akira M, Suganuma N. Imaging diagnosis of pneumoconiosis with predominant nodular pattern: HRCT and pathologic findings. *Clinical Imaging* 2023;97: 28-33.
4. Cohen RA, Petsonk EL, Rose C, et al. Lung pathology in U.S. coal workers with rapidly progressive pneumoconiosis implicates silica and silicates. *Am J Respir Crit Care Med*. 2016;193:673-80.
5. Petsonk EL, Rose C, Cohen R. Coal mine dust lung disease: new lessons from an old exposure. *Am J Respir Crit Care Med.* 2013;187:1178-1185.

6. McConnochie K, Green PHY, Vallyathan V, et al. Interstitial fibrosis in coal workers – experience in Wales and West Virginia. *Ann Occup Hyg.* 1988;32:553-560.
7. Brichet A, Tonnel AB, Brambilla E, et al. Chronic interstitial pneumonia with honeycombing in coal workers. Sarcoidosis Vasc *Diffuse Lung Dis.* 2002;19(3):211-219.
8. Heppleston AG. The pathological recognition and pathogenesis of emphysema and fibrocystic disease of the lung with special reference to coal workers. *Ann NY Acad Sci*. 1972;200:347-369.
9. Jelic TM, Estalilla OC, Sawyer-Kaplan PR, et al. Coal Mine Dust Desquamative Chronic Interstitial Pneumonia: A Precursor of Dust-Related Diffuse Fibrosis and of Emphysema. *Int J Occup Environ Med.* 2017;8(3):153-165.
10. International Labour Office. Guidelines for the Use of the ILO International Classification of Radiographs of Pneumoconiosis, Revised edn. Occupational Safety and Health Series, Vol. 22. International Labour Organization– Geneva: ILO, 2022.
11. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the prevention, diagnosis and management of COPD: 2025 report [Internet]. 2024 Available online: https://goldcopd.org/wp-content/uploads/2024/12/Pocket-Guide-2025-v1.2-FINAL-covered-13Dec2024_WMV.pdf (Last Accessed on 22 Jul 2025).
12. Pellegrino R, Viegi G, Brusasco V, et al. Interpretative strategies for lung function tests. *Eur Respir J.* 2005;26(5):948-968.
13. Kusaka Y, Hering KG, Parker JE. International Classification of HCRT for Occupational and Environmental Respiratory Diseases.Tokyo: Springer Vering, 2005.
14. Podolanczuk AJ, Hunninghake GM, Wilson KC, et al. Approach to the Evaluation and Management of Interstitial Lung Abnormalities: An Official American Thoracic Society Clinical Statement. *Am J Respir Crit Care Med.* 2025;211(7):1132-1155.
15. Cockcroft A, Lyons JP, Andersson N, Saunders MJ. Prevalence and relation to underground exposure of radiological irregular opacities in South Wales coal workers with pneumoconiosis. *Br J Ind Med*. 1983;40(2):169-172.
16. Trapnell DH. Septal lines in pneumoconiosis. *Br J Radiol*. 1964;37:805-810.
17. Laney AS, Petsonk EL. Small pneumoconiotic opacities on U.S. coal worker surveillance chest radiographs are not predominantly in the upper lung zones. *Am J Ind Med*. 2012;55(9):793-798.
18. Cox CW, Rose CS, Lynch DA. State of the art: Imaging of occupational lung disease. *Radiology*. 2014;270:681.
19. Sangani RG, Ghio AJ, Deepak V, et al. Impact of coal mine dust exposure and cigarette smoking on lung disease in Appalachian coalminers. *Respir Res.* 2025;26(1):184.
20. McConnochie K, Green FHY, Vallyathan V, et al. Interstitial fibrosis in coal workers: experience in Wales and West Virginia. *Ann Occup Hyg.* 1988;32:553-560.
21. Centers for Disease Control and Prevention. Current intelligence bulletin 64: coal mine dust exposures and associated health outcomes - a review of information published since 1995. DHHS (NIOSH) Publication No. 2011-172; 2011 April. Available online: http://www.cdc.gov/niosh/docs/2011-172/ (Last Accessed on 11 Aug 2025).
22. Seixas NS, Robins TG, Attfield MD, Moulton LH. Exposure-response relationships for coal mine dust and obstructive lung disease following enactment of the Federal Coal Mine Health and Safety Act of 1969. *Am J Ind Med.* 1992;21:715-734.
23. Attfield MD, Hodous TK. Pulmonary function of U.S. coal miners related to dust exposure estimates. *Am Rev Respir Dis.* 1992;145(3):605-609.
24. Go LHT, Almberg KS, Rose CS, et al. Prevalence and severity of abnormal lung function among US former coal miners with and without radiographic coal workers' pneumoconiosis. *Occup Environ Med.* 2022;79(8):527-532.
25. Nemery B, Veriter C, Brasseur L, Frans A. Impairment of ventilatory function and pulmonary gas exchange in nonsmoking coalminers. *Lancet*. 1987;2:1427-1430.
26. Marine WM, Gurr D, Jacobsen M. Clinically important respiratory effects of dust exposure and smoking in British coal miners. *Am Rev Respir Dis.* 1988;137:106-112.
27. Carta P, Aru G, Barbieri MT, et al. Dust exposure, respiratory symptoms, and longitudinal decline of lung function in young coal miners. *Occup Environ Med.* 1996;53:312-319.
28. Kuempel ED, Wheeler MW, Smith RJ, et al. Contributions of dust exposure and cigarette smoking to emphysema severity in coal miners in the United States. *Am J Respir Crit Care Med*. 2009;180(3):257-264.
29. Sarı G. Coal Workers' Pneumoconiosis: A Comparative Analysis of Lignite and Hard Coal Mine Workers. *ESTUDAM Public Health Journal.* 2022;7(3):497-505.
30. Dalal NS, Newman J, Pack D, et al. Hydroxyl radical generation by coal mine dust: possible implication to coal workers' pneumoconiosis (CWP). *Free Radic Biol Med.* 1995;18(1):11-20.
31. Reisner MT, Robock K. Results of epidemiologicalm mineralogical and cytotoxicological studies on the pathogenicity of coal-mine custs. I In: Walton, W.H. (Ed.), Inhaled Particles IV, Part 2. Pergamon Press, Oxford 1975:703-716.
32. Dalal NS, Jafari B, Petersen M, Green FHY, Vallyathan V. Presence of stable coal radicals in autopsied coal miners' lungs and its possible correlation to coal workers' pneumoconiosis. *Arch Environ Health.* 1991;46(6):366-372.

33. Page SJ. Relationships between electrostatic charging characteristics, moisture content, and airborne dust generation for subbituminous and bituminous coals. *Aerosol Sci Technol*. 2000;32(4):249-267.
34. Graber JM, Stayner LT, Cohen RA, et al. Respiratory disease mortality among US coal miners; results after 37 years of follow-up. *Occup Environ Med*. 2014; 71(1):30-39.
35. Hartman HL, Mutmansky JM. Introductory Mining Engineering; Wiley: Hoboken, NJ, USA, 2002.

La Medicina del Lavoro

Original article

Med. Lav. 2026; 117 (3): 18246
DOI: 10.23749/mdl.2026.18246

Effects of Breathing Exercises Applied to Intensive Care Nurses on Fatigue and Perceived Stress: A Randomized Controlled Trial

Yasemin Sazak[1,*], Meltem Kalayci[2], Nermin Olgun[3]

[1]Kahramanmaras Istiklal University, Faculty of Health Sciences, Department of Nursing, Kahramanmaras, Türkiye
[2]Kahramanmaras Provincial Health Directorate, Necip Fazil City Hospital, Intensive Care Clinic, Kahramanmaras, Türkiye
[3]Hasan Kalyoncu University, Faculty of Health Sciences, Department of Nursing, Gaziantep, Türkiye

Keywords: Fatigue; Perceived Stress; Breathing Exercise; Intensive Care; Nurse

Abstract

Background: *Fatigue and stress are common challenges for intensive care nurses. Reducing stress and fatigue among nurses is important for improving nurse and patient safety. Breathing exercises are a nonpharmacological approach that effectively reduces fatigue and stress. This study aimed to evaluate the effects of breathing exercises on fatigue and stress among intensive care nurses.* **Methods:** *The research was conducted as a randomized controlled trial between October and December 2024. The study included 66 nurses, 33 in the control group and 33 in the intervention group. Nurses in the intervention group performed breathing exercises lasting approximately 20 minutes for 30 days. No intervention was performed in the control group. Data were collected using the Piper Fatigue Scale and Perceived Stress Scale at the beginning of the study, on the 15th day, and on the 30th day.* **Results:** *A statistically significant difference was identified in the group effect, time effect, and group-time interaction for the mean scores on the Piper Fatigue Scale and the Perceived Stress Scale ($p<0.01$). The fatigue and stress scores of nurses in the intervention group decreased on the 15th and 30th days.* **Conclusions:** *This study shows that breathing exercises positively affect fatigue and stress among intensive care nurses. The breathing exercise protocol can be applied to intensive care nurses, and these exercises can be taught to nurses through in-service training.*

1. Introduction

Intensive care units (ICUs) are specialized units where patients with organ dysfunction or at risk of developing organ dysfunction are hospitalized, where complex technologies are used, and where patients are continuously monitored and followed up [1]. A multidisciplinary team approach is required to monitor and follow up patients in ICUs. Nurses, an indispensable part of this team, have essential roles and responsibilities [1, 2], such as diagnosing patients, providing advanced, high-quality care, continuously monitoring vital functions, administering treatments, and establishing therapeutic relationships with patients and their relatives [3].

ICU nurses may experience fatigue due to an intense workload, shift work, insomnia, environmental factors, prolonged standing, and physically demanding tasks (such as patient transfers and positioning) [4, 5]. Fatigue has adverse effects on cognition, psychology, and biology. Individuals may experience irritability, difficulty concentrating, reduced physical

Received 19.12.2025 – Accepted 11.05.2026
Corresponding Author: Yasemin Sazak; E-mail: yaseminsazak44@gmail.com

capacity, communication difficulties, and decreased perception and reaction time due to fatigue, a health problem [6]. Fatigue adversely impacts nurses' well-being, patient safety, and care. It creates serious problems for patient and employee safety, including an increased likelihood of errors and an increased risk of injury [7].

Fatigue and its adverse effects constitute a major source of stress for nurses. The literature reports a positive relationship between stress and fatigue [8]. Because of the nature of intensive care, ICU nurses follow critically ill patients and witness longer hospitalizations and higher mortality rates more frequently than nurses in other units. Numerous factors, such as sudden deterioration of patient condition, rapid decision-making, an intense workload, and the use of complex technological equipment, are also sources of stress for nurses [2]. Increased fatigue and stress lead to adverse effects such as joint and muscle pain, insomnia, anxiety, depression, burnout, and communication problems among nurses [8-12].

Non-pharmacological interventions have recently gained importance for reducing stress and fatigue among nurses. Many alternative medical treatments, such as massage, progressive relaxation exercises, acupressure, and music therapy, have been reported to reduce stress and fatigue in nurses [2, 13-15]. Breathing exercises are also among the non-pharmacological methods that effectively reduce fatigue and stress [16, 17]. Deep, controlled breathing exercises activate the parasympathetic nervous system, thereby lowering stress hormone levels, such as cortisol [18]. Breathing exercises are easy to apply, cost-free, and effective methods that promote relaxation of the mind and body [19]. In this respect, three-step breathing and 4-7-8 breathing techniques are among those that effectively reduce fatigue and stress [17, 20]. The three-step breathing exercise is also known as full yogic breathing (Dirgha). The aim of this breathing technique is to take deep breaths. The steps of deep breathing are performed to the abdomen, chest, and collarbone, respectively [21, 22]. In the 4-7-8 breathing technique, an individual inhales through the nose by counting to 4, holds breath by counting to 7, and exhales through the mouth by counting to 8. It is an easy-to-apply and simple breathing technique that quite effectively reduces stress, fatigue, and restlessness [17].

No study in the literature has examined the effects of breathing exercises on fatigue and stress among ICU nurses. Research indicates that breathing exercises are most often used in conjunction with other nonpharmacological interventions, suggesting that they reduce stress and fatigue among ICU nurses [13, 15]. The literature reports that the breathing techniques used in this study have been applied to adults and patients [16, 20-21, 23]; however, no studies have investigated their application to nurses or the working population. ICU nurses experience high levels of stress and fatigue, which have significant effects on both patients and nurses. In light of this information, the current study was conducted to assess the effects of breathing exercises on fatigue and stress among ICU nurses.

The research hypotheses propose that implementing breathing exercises for nurses will lead to measurable improvements in well-being: specifically, it is expected that nurses who participate in the breathing-exercise protocol will report lower levels of fatigue compared with those in the control group, and, concurrently, will exhibit reduced perceived stress relative to their untreated colleagues.

2. Methods

2.1. Design

The current research was conducted as a randomized controlled experimental trial in the intensive care units of a state hospital in the Mediterranean region of Türkiye between October and December 2024. The CONSORT checklist [24] was followed when reporting the study. The study was registered on Clinicaltrials.gov (NCT06642376).

2.2. Inclusion and Exclusion Criteria

The study included nurses with at least 6 months of experience in intensive care units who volunteered to participate in the research and did not use complementary therapies, such as breathing exercises, acupuncture, massage therapy, relaxation techniques, and yoga, that could affect perceived stress

and fatigue during the study. Nurses who had a condition that prevented nasal breathing and the use of breathing exercises, were receiving psychotherapy, had a mean PFS total score of 3 or lower, were pregnant, or had physical or mental health problems that impaired communication were not included in the study. Figure 1 displays the CONSORT flow chart for the nurses included in the study.

2.3. Setting and Sample

The hospital where the research was conducted has 6 ICUs (internal medicine, neurology, coronary, anesthesia and reanimation, surgery, and cardiovascular surgery) that provide care and treatment to adult patients. One hundred and fifty nurses work in the intensive care units. Similar studies have shown that the effect size of breathing exercises across different groups is large [16, 25]. The program G*Power 3.1.9.7 was used to calculate the sample size. With an effect size of 0.80, the sample size was 26 per group, with 80% power and a 5% margin of error. No sample selection was performed in our study, and we attempted to reach the entire population. The research was completed with 66 nurses who met the inclusion criteria (control group: 33; intervention group: 33) (Figure 1).

2.4. Randomization and Blinding

A simple randomization method was used to ensure an equal and random distribution of nurses between the two groups. Nurses who met the inclusion criteria were listed in numerical order and numbered from 1 to 66. The numbers to be selected before randomization were determined by a lottery method to form the intervention group. Subsequently, 33 numbers were selected from the 66 using the website https://www.randomizer.org/. The remaining 33 nurses formed the control group. An independent statistician analyzed the research data, and the groups were anonymized by referring to them only by numbers.

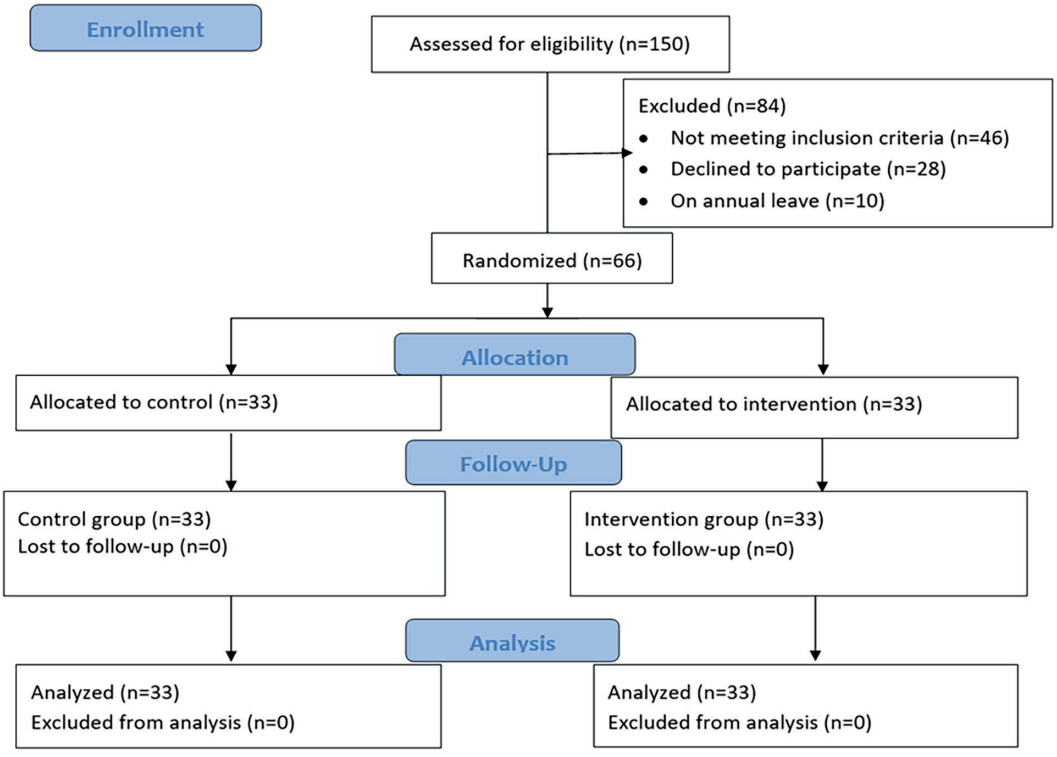


Figure 1. CONSORT flow diagram of the study.

2.5. Data Vollection Tools

2.5.1 Nurse Demographic Information Form

It is a questionnaire consisting of 16 questions (age, sex, education level, marital status, unit of employment, and duration) prepared by the researchers based on the literature [2, 10, 26].

2.5.2 Piper Fatigue Scale

The scale, developed in 1987 by Piper et al., assesses subjective fatigue using the "integrated fatigue model" [27]. Can et al. conducted a validity and reliability study of this scale in Türkiye in 2004. The scale comprises 22 items, each rated on a 0-10-point Visual Analog Scale. It also includes five items that allow expression of thoughts about fatigue not included in the scoring. The scale consists of four subscales: behavior, affect, sensory, and cognitive/psychological. The behavior subscale assesses the impact of fatigue on daily life and its severity. The affect subscale evaluates the emotional meaning attributed to fatigue. The sensory subscale assesses the mental, physical, and emotional symptoms of fatigue. The cognitive/psychological subscale evaluates the extent to which fatigue affects cognitive functions and mental state. The total score and the subscale scores range from 0 to 10. A high score on the scale indicates increased fatigue [27, 28]. On the scale, a score of 0 indicates "no fatigue", a score of 1-3 indicates "mild fatigue", a score of 4-6 indicates "moderate fatigue", and a score of 7-10 indicates "severe fatigue". The scale is used in studies assessing fatigue among ICU healthcare professionals [29, 30]. In the validity and reliability study for the scale, Cronbac's alpha reliability coefficient was found to be between 0.92 and 0.96 for the subscales and 0.97 for the overall scale [28]. In the present study, the scale's Cronbach's alpha reliability coefficient was lowest (0.86) for the pre-test, mid-test, and post-test.

2.5.3 Perceived Stress Scale

Cohen et al. developed the scale in question in 1983 [31]. Eskin et al. performed their validity and reliability study in Türkiye. The scale comprises 14 items. Additionally, there are 10-item and 4-item short versions of the scale, along with a 14-item version. The current study employed the 14-item version. The possible score on the scale ranges from 14 to 56. A high score indicates that perceived stress increases. Cronbach's alpha reliability coefficient was 0.84 in the scale's validity and reliability study [32]. The scale is used to assess perceived stress among ICU nurses [15, 26]. In this study, Cronbach's alpha reliability coefficient was 0.86 for the pre-test, 0.85 for the mid-test, and 0.94 for the post-test.

2.6. Breathing Exercises Applied

The first researcher holds an internationally valid and university-approved certificate in breathing techniques. The three-step and 4-7-8 breathing techniques were applied to nurses in our study. Expert opinions were obtained from a breathing techniques trainer of trainers and a faculty member with a certificate in breathing techniques regarding the applicability of the breathing exercise protocol. The application protocol for the breathing techniques was finalized in line with the expert opinions received. The application steps of the breathing techniques are presented in the breathing techniques application protocol (Supplemental Material S1).

2.7. Intervention and Data Collection

Nurses in the intervention and control groups were informed about the study's purpose and implementation. Written and verbal consent was obtained from the nurses who confirmed their willingness to participate in the study. Pre-test data for the intervention and control groups were collected in person from nurses using data collection forms (Nurse Demographic Information Form, PFS, and PSS). It took 10-15 minutes to complete the data collection forms. On the 15th day of the intervention, face-to-face interviews were conducted with nurses, and mid-test forms were completed using the PFS and PSS. Post-test data were collected by conducting face-to-face interviews with nurses on the 30th day of the study.

The primary researcher showed nurses in the intervention group how to perform the breathing exercises face-to-face at the beginning of the study. Nurses were taught the correct techniques by practicing breathing exercises through demonstrations. Then, to implement the breathing exercises technique, a WhatsApp group was created for nurses in the intervention group and the researchers. A video recording of the researcher's breathing techniques was sent to this group. Since the video duration is limited via WhatsApp, this video includes the correct implementation techniques of the breathing exercises. The researcher created an audio recording of the breathing exercises (20 minutes), including a full session. This audio recording was shared in the group. Breathing exercises were performed once a day for 30 days. Breathing exercises were performed face-to-face with nurses three days a week. Days for face-to-face application were arranged according to nurses' shift days. On other days, feedback was received from nurses who used WhatsApp to apply the breathing exercises and ensure they exercised regularly. Nurses in the intervention group were told not to share the breathing exercises to avoid affecting nurses in the control group.

Nurses in the control group were placed on a waiting list and received no intervention during the research process. After the study was completed and the final data were collected, the breathing exercise protocol was taught to the control group through in-person demonstrations. Video and audio recordings demonstrating the breathing exercises were shared with the control group.

2.8. Data Analysis

IBM SPSS 27 was used to analyze the data. Individuals' descriptive characteristics were presented as numbers, percentages, means, and standard deviations. To compare the study groups with categorical variables, Fisher's exact test was used in 2x2 and rxc tables [33]. The Shapiro-Wilk test and Q-Q plots were used to assess whether the data were normally distributed. The data were found to be normally distributed. The two-way mixed-design ANOVA evaluated the effects of time, group, and their interaction on the repeated measurements. Before the two-way mixed design ANOVA test, the homogeneity of variances was assessed using Levene's test, and it was found that the assumption of homogeneity of variances was met (p values range from 0.149 to 0.951). The homogeneity of the covariance matrices was examined using Box's M test, and it was found that the assumption was met (p values range from 0.167 to 0.851). The sphericity assumption for the repeated-measures factor was tested using Mauchly's test, and it was met (p values range from 0.081 to 0.343). The Bonferroni test was used to determine in which group and at which time the group-time interaction differed. Partial eta squared (η^2) was used to assess the effect size [34].

2.9. Ethical Considerations

Approval was obtained from the university's non-interventional research ethics committee (decision number 2024/11-02, dated July 22, 2024) and from the institution where the research would be conducted. Nurses were informed about the study, and their written and verbal consent was obtained. The current study was conducted in accordance with the principles of the Declaration of Helsinki and publication ethics. No adverse events related to the research were observed.

3. Results

There were no differences between the control and intervention groups, which were initially homogeneous. Furthermore, 45.5% of nurses in the control group and 51.5% of those in the intervention group reported experiencing fatigue for a year or more (Table 1).

A statistically significant difference was observed between the group effect, time effect, and group-time interaction on the PFS mean scores and the PSS total mean scores ($p < 0.001$; Table 2).

The comparison test found no statistically significant differences between the groups in the PFS total score ($p = 0.671$), PFS subscales behavioral fatigue ($p = 0.197$), affective fatigue ($p = 0.760$), sensory fatigue ($p = 0.235$), and cognitive fatigue ($p = 0.155$) mean scores before the intervention. On the 15th and 30th days, the PFS total score ($p < 0.001$ for both) and subscale behavioral fatigue ($p = 0.022$

Table 1. Comparison of nurses' descriptive characteristics (N=66).

	Control Group (n=33)	Intervention Group (n=33)		
Variables	**Mean ± SD**	**Mean ± SD**	**t**	**p**
Age Years (min.-max.)	32.15 ± 4.84 (25.00-48.00)	31.76 ± 5.32 (24.00-47.00)	0.315	0.754
Years as a Nurse-years (min.-max.)	9.67 ± 3.92 (1.00-19.00)	9.18 ± 4.89 (1.00-20.00)	0.445	0.658
Years in the ICU-years (min.-max.)	4.76 ± 3.08 (1.00-12.00)	4.55 ± 3.43 (1.00-14.00)	0.399	0.792
Variables	**n (%)**	**n (%)**	**p**	
Gender				
Female	21 (63.6)	19 (57.6)	0.801	
Male	12 (36.4)	14 (42.4)		
Marital status				
Married	20 (60.6)	19 (57.6)	1.000	
Single	13 (39.4)	14 (42.4)		
Education Level				
High School	2 (6.1)	1 (3.0)	0.750	
Bachelor's Degree	28 (84.8)	30 (90.9)		
Postgraduate	3 (9.1)	2 (6.1)		
ICU Worked In				
Internal Medicine	13 (39.4)	14 (42.4)	0.767	
Anesthesiology and Reanimation	10 (30.3)	7 (21.2)		
Neurosurgery	4 (12.1)	2 (6.1)		
Coronary	2 (6.1)	5 (15.2)		
Cardiovascular Surgery	2 (6.1)	2 (6.1)		
Surgical	2 (6.1)	3 (9.1)		
Work Shift				
Day Shift	3 (9.1)	6 (18.2)	0.596	
Night Shift	22 (66.7)	20 (60.6)		
Rotating Day and Night Shifts	8 (24.2)	7 (21.2)		
Presence of a Chronic Disease				
Yes	1 (3.0)	2 (6.1)	1.000	
No	32 (97.0)	31 (93.9)		
Smoking Status				
Current Smoker	11 (33.3)	9 (27.3)	0.917	
Quit Smoking	2 (6.1)	2 (6.1)		
Never Smoked	20 (60.6)	22 (66.7)		
Alcohol Consumption				
Drinking Alcohol	5 (15.2)	3 (9.1)	0.479	
Quit	0 (0.0)	2 (6.1)		
Never Drunk Alcohol	28 (84.8)	28 (84.8)		
Duration of Fatigue				
0-6 Months	17 (51.5)	13 (39.4)	0.422	
7-12 Months	1 (3.0)	3 (9.1)		
1 Year Over	15 (45.5)	17 (51.5)		

Table 2. Comparison of the change in mean scores on the Piper Fatigue Scale and Perceived Stress Scale between the intervention and control groups.

Scales and Measurements	Control Group (n=33) Mean ± SD	Intervention Group (n=33) Mean ± SD	Between-Group Mean Difference (95% CI)		Group	Time	Group*Time Interaction
Piper Fatigue Scale							
Behavioral Fatigue							
Baseline	5.36 ± 1.81$^{A, a}$	5.89 ± 1.51$^{A, a}$	-0.54 (-1.36, 0.28)	F	9.374	21.951	29.198
15th day	5.41 ± 1.71$^{A, a}$	4.45 ± 1.61$^{B, b}$	0.96 (0.14, 1.77)	p	**0.003**	**<0.001**	**<0.001**
30th day	5.57 ± 1.83$^{A, a}$	2.90 ± 1.63$^{B, c}$	2.67 (1.82, 3.52)	η^2	0.128	0.255	0.313
Affective Fatigue							
Baseline	6.58 ± 1.74$^{A, a}$	6.42 ± 1.63$^{A, a}$	0.16 (-0.67, 0.99)	F	32.534	34.150	45.633
15th day	6.42 ± 1.70$^{A, a}$	4.43 ± 1.97$^{B, b}$	1.99 (1.08, 2.89)	p	**<0.001**	**<0.001**	**<0.001**
30th day	6.86 ± 1.65$^{A, a}$	2.84 ± 1.76$^{B, c}$	4.02 (3.18, 4.86)	η^2	0.337	0.348	0.416
SensoryFatigue							
Baseline	6.47 ± 1.79$^{A, a}$	5.93 ± 1.82$^{A, a}$	0.53 (-0.36, 1.42)	F	28.515	18.538	28.417
15th day	6.27 ± 1.68$^{A, a}$	4.69 ± 1.57$^{B, b}$	1.58 (0.78, 2.37)	p	**<0.001**	**<0.001**	**<0.001**
30th day	6.74 ± 1.55$^{A, a}$	3.34 ± 1.54$^{B, c}$	3.40 (2.64, 4.16)	η^2	0.308	0.225	0.307
Cognitive Fatigue							
Baseline	5.25 ± 1.71$^{A, a}$	5.84 ± 1.60$^{A, a}$	-0.59 (-1.40, 0.23)	F	13.465	16.282	24.156
15th day	4.90 ± 1.80$^{A, a}$	4.22 ± 1.45$^{A, b}$	0.69 (-0.12, 1.49)	p	**0.005**	**<0.001**	**<0.001**
30th day	5.60 ± 2.00$^{A, a}$	2.99 ± 1.40$^{B, c}$	2.61 (1.75, 3.46)	η^2	0.115	0.203	0.274
Total Fatigue Score							
Baseline	5.86 ± 1.44$^{A, a}$	6.01 ± 1.39$^{A, a}$	-0.15 (-0.84, 0.55)	F	20.904	38.549	54.930
15th day	5.70 ± 1.52$^{A, a}$	4.44 ± 1.42$^{B, b}$	1.26 (0.54, 1.98)	p	**<0.001**	**<0.001**	**<0.001**
30th day	6.14 ± 1.52$^{A, a}$	3.01 ± 1.43$^{B, c}$	3.13 (2.40, 3.85)	η^2	0.246	0.376	0.462
Perceived Stress Scale							
Total Score							
Baseline	28.76±6.42$^{A, a}$	29.30±7.68$^{A, a}$	-0.55 (-4.02, 2.93)	F	15.376	8.601	9.420
15th day	28.88±6.08$^{A, a}$	26.06±5.51$^{A, a}$	2.82 (-0.04, 5.67)	p	**<0.001**	**<0.001**	**<0.001**
30th day	29.00±9.23$^{A, a}$	19.09±7.29$^{B, b}$	9.91 (5.82, 13.40)	η^2	0.194	0.118	0.128

F= Two-way mixed design ANOVA, SD: Standard Deviation, values of p<0.05 are shown in bold.
η^2= Partial eta squared (small effect=0.01, medium effect=0.06, large effect=0.14)
A, B: Different capital letters in the same row indicate the difference between the intervention and control groups.
a, b, c: Different lowercase letters in the same column indicate the difference between measurement times.

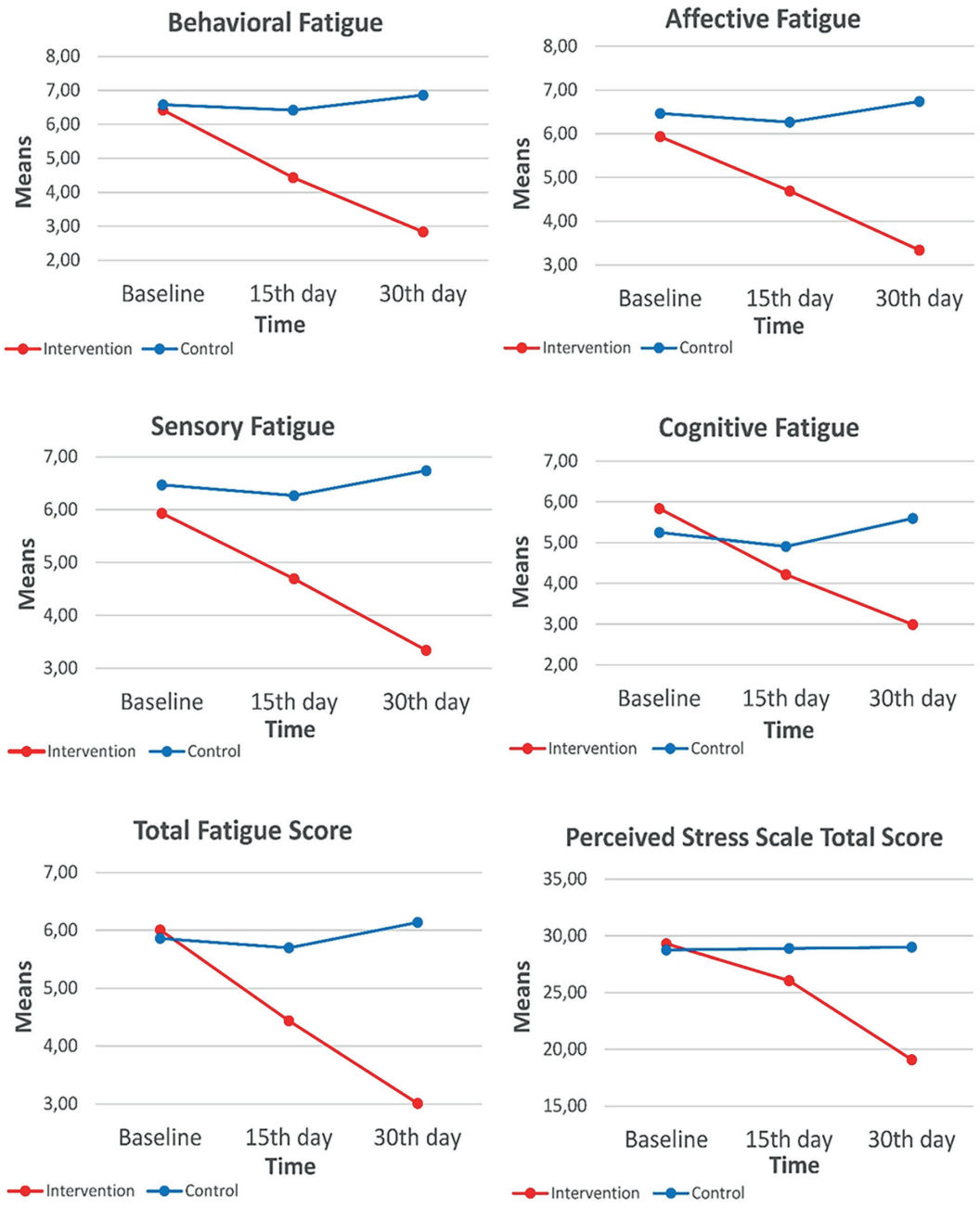


Figure 2. Changes in mean fatigue and stress scores of the intervention and control groups over time.

for 15th day, $p < 0.001$ for 30th day), affective fatigue ($p < 0.001$ for both), and sensory fatigue ($p < 0.001$ for both) mean scores were lower in the intervention group (Table 2) (Figure 2). Additionally, there was no statistically significant difference between the PFS total score ($p = 1.000$ for baseline-15th day, $p = 0.755$ for baseline-30th day, $p = 0.086$ for 15th-30th days) and subscale behavioral fatigue ($p = 1.000$ for baseline-15th day, baseline-30th day, 15th-30th days), affective fatigue ($p = 1.000$ for baseline-15th, baseline-30th day, $p = 0.240$ for 15th-30th days), sensory fatigue ($p = 1.000$ for baseline-15th day, baseline-30th day, $p = 0.098$ for 15th-30th days), cognitive fatigue ($p = 0.817$ for baseline-15th day,

$p = 0.965$ for baseline-30th day, $p = 0.106$ for 15^{th}-30^{th} days) mean scores in the control group over time. In the intervention group, a statistically significant difference was observed between the PFS total score and the subscale mean scores measured at three time points ($p < 0.001$; Table 2) (Figure 2).

The PSS total mean scores were similar between the groups before the intervention. The PSS mean scores were lower in the intervention group than in the control group on the 30^{th} day ($p < 0.001$, Table 2) (Figure 2). Moreover, the PSS mean scores did not change statistically significantly in the control group over time ($p = 1.000$). In the intervention group, the PSS mean score on the 30^{th} day was significantly lower than the pre-intervention and 15^{th}-day mean scores ($p = 0.001$, Table 2) (Figure 2).

The intervention had a large effect size on the PSS total mean score and subscale mean scores ($\eta 2 > 0.14$). However, it had a medium effect size on the PSS mean score ($\eta 2 = 0.128$, Table 2).

4. Discussion

This study was designed as a single-blind, randomized, controlled trial to investigate the effects of breathing exercises for ICU nurses on their fatigue and stress. Although the effects of breathing exercises on stress and fatigue have been assessed in different groups, no study on ICU nurses has been found. In the literature, breathing exercises are most often included in interventions such as progressive relaxation and yoga [13, 15]. In this regard, our research is the first to evaluate the effects of breathing exercises alone on fatigue and stress among ICU nurses. The current study revealed that breathing exercises positively affected fatigue and stress among ICU nurses. According to the research findings, applying breathing exercises for 30 days reduced fatigue and stress levels among nurses in the intervention group, confirming the hypotheses of our study.

Due to the nature of intensive care, ICU nurses experience greater fatigue and stress than nurses in other units. Fatigue and stress can also deteriorate an individual's quality of life and pose significant risks to the safety and health of patients and nurses [7]. Breathing exercises are effective non-pharmacological methods for reducing fatigue [17]. This study found that nurses in both groups initially experienced moderate fatigue, as measured by the PFS. Following the breathing exercises administered to the intervention group, nurses' overall fatigue decreased to mild levels. However, the fatigue levels of nurses in the control group, which received no intervention, remained moderate. Additionally, the breathing exercise intervention had a large effect on fatigue. Hence, we could not make a direct comparison with the current research results. In the literature, breathing exercises are included in progressive relaxation, music therapy, and mindfulness-based non-pharmacological interventions for nurses. It was determined that the interventions applied in these studies reduced fatigue and, similar to our research findings, had medium-to-large effect sizes [13, 15, 35]. However, breathing exercises applied to patients effectively reduce fatigue [36, 37]. In light of these findings, studies in the literature support our research results. Controlled breathing helps balance the autonomic nervous system by suppressing excessive sympathetic activity and increasing parasympathetic activity [38]. Inhibition of the sympathetic nervous system reduces energy consumption, whereas increased activation of the parasympathetic nervous system reduces it. This reduces fatigue effectively [39]. In this regard, the present study is significant for evaluating the effectiveness of breathing exercises in reducing fatigue among ICU nurses. It appears that the research protocol effectively reduces fatigue among nurses.

ICUs are specialized units where patients are continuously monitored and receive complex treatments; thus, ICUs can create a stressful work environment for nurses [2]. Breathing exercises are effective non-pharmacological interventions for reducing stress [20]. Given that the PSS score used in this study ranges from 14 to 56, nurses had moderate stress levels before the intervention. While stress levels did not change significantly in the control group after the intervention, they remained low in the intervention group. Additionally, the study found that the intervention had a moderate effect size on perceived stress levels. According to a systematic review evaluating the effects of breathing exercises in adults, these exercises reduce stress and anxiety [40]. Another meta-analysis also reported that breathing

exercises had a moderate effect size in reducing stress [41]. A study assessing the effects of breathing exercises on young women found a significant decrease in blood cortisol levels at the end of the exercises [18]. Likewise, healthy adults performed diaphragm breathing exercises for 20 sessions over 8 weeks. Participants' salivary cortisol levels decreased over time [20]. Another study revealed that anxiety decreased in the group where the 4-7-8 breathing exercise was applied to patients after bariatric surgery [16]. Studies that included breathing exercises as part of non-pharmacological interventions among ICU nurses found that these interventions reduced nurses' stress [15, 42]. Breathing exercises activate the parasympathetic nervous system, thereby lowering stress hormone levels, such as cortisol, in the body [18]. Proper breathing techniques, along with their effects on the autonomic and cerebral systems, promote increased cortical and subcortical activity [38]. Breathing exercises have also been reported to increase blood serotonin levels, increase alpha waves, and decrease theta waves on an electroencephalogram [43]. These findings demonstrate the effects of breathing exercises on stress reduction in individuals [38, 44].

4.1. Limitations

The study was conducted at a single center, and the sample size was limited by the small population, which restricts the generalizability of our results. Furthermore, fatigue and stress assessments were based on nurses' subjective reports. Environmental or individual factors that might confound the results could not be assessed. Confounding factors such as nurses' workload, number of shifts, or exposure to stressful situations during work were not evaluated. Nurses who received interventions or therapies that could affect stress and fatigue at the beginning of the study were excluded. However, the inability to systematically assess this situation throughout the study constitutes one of its limitations. Participants could not be blinded due to the nature of the research. This may introduce a risk of bias in the results due to nurses' self-reports. The absence of any intervention in the control group and the fact that the control group remained in constant contact with the intervention group may have influenced the independent outcomes of the breathing exercises. Our study aimed to reach the entire population, and all volunteer nurses who met the inclusion criteria were included. Therefore, stratified sampling could not be used for selecting the ICU sample. Additionally, the fact that breathing exercises were implemented for 30 days limits the ability to evaluate their effects in the future.

No study in the literature has evaluated the effects of breathing exercises on fatigue and stress among ICU nurses. Repeating our intervention with ICU nurses using a larger sample size is important for verifying and generalizing our results. Furthermore, it is recommended that future research monitor the effects of breathing exercises on fatigue and stress over a longer term. Additionally, it is recommended that our application protocol be used for intensive care nurses.

5. Conclusion

ICU nurses in the present study reported high levels of fatigue and stress. Intensive care nurses may experience fatigue and stress due to factors such as monitoring high-risk patients and using advanced technology. This study found that the breathing exercise protocol reduced fatigue and stress among ICU nurses. Therefore, breathing exercises can be applied to nurses through in-service training in hospitals. It can be ensured that nurses receive training certificates for breathing exercise applications. It is thought that this will be beneficial overall for nurses and the patients they care for.

Institutional Review Board Statement: Prior to the study, ethical approval was obtained from the Non-Interventional Research Ethics Committee at Kahramanmaras Istiklal University (Ethics approval code: 2024/11-02). Participation in the study was voluntary. Accordingly, nurses were informed about the study, and verbal and written informed consent was obtained from nurses who agreed to participate. Institutional permission was received from the institution where the research was conducted. Before starting the study, it was registered on ClinicalTrials.gov (NCT06642376; Registration Date: October 12, 2024; https://clinicaltrials.gov/). Our study was conducted in line with the principles of the Declaration of Helsinki and publication ethics.

Informed Consent Statement: Informed consent, both verbal and written, was obtained from all participating nurses.

Acknowledgments: The authors would like to thank all the intensive care nurses who participated in the study.

Declaration of Interest: The authors declare no conflict of interest.

Data Availability: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contribution Statement: Y.S.: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Methodology, Investigation, Formal analysis, Conceptualization. M.K.: Writing – review & editing, Writing – original draft, Visualization, Validation, Investigation, Conceptualization. N.O.: Writing – review & editing, Validation, Supervision, Resources, Conceptualization.

References

1. Marshall JC, Bosco L, Adhikari NK, et al. What is an intensive care unit? A report of the task force of the World Federation of Societies of Intensive and Critical Care Medicine. *J Crit Care*. 2017;37:270-276. Doi: https://doi.org/10.1016/j.jcrc.2016.07.015
2. Gök Metin Z. Yoğun bakım hemşirelerinde stresin azaltılmasına yönelik nonfarmakolojik yaklaşımlar: Sistematik bir derleme. *Yoğun Bakım Hemşireliği Dergisi*. 2019;23(2):87-101.
3. Şen Atasayar B. Examination of 'The Good Nurse' Movie In The Context Of Intensive Care Nursing. *Yoğun Bakım Hemşireliği Dergisi*. 2024;28(1):1-7. Doi: 10.62111/ybhd.1408978
4. Steege LM, Drake DA, Olivas M, Mazza G. Evaluation of physically and mentally fatiguing tasks and sources of fatigue as reported by registered nurses. *J Nurs Manag*. 2015;23(2):179-189.Doi:https://doi.org/10.1111/jonm.12112
5. Chen S, Wu H, Sun M, et al. Effects of shift work schedules, compensatory sleep, and work–family conflict on fatigue of shift-working nurses in Chinese intensive care units. *Nursing in critical care*. 2023;28(6):948-956. Doi: https://doi.org/10.1111/nicc.12909
6. Graves K, Simmons D. Reexamining fatigue: Implications for nursing practice. *Crit Care Nurs Q*. 2009; 32(2):112-115. Doi: 10.1097/01.CNQ.0000348198.16788.df
7. Querstret D, O'Brien K, Skene DJ, Maben J. Improving fatigue risk management in healthcare: A scoping review of sleep-related/ fatigue-management interventions for nurses and midwives (reprint). *Int J Nurs Stud*. 2020;112:103745. Doi: https://doi.org/10.1016/j.ijnurstu.2020.103745
8. Sun T, Huang XH, Zhang SE, et al. Fatigue as a cause of professional dissatisfaction among chinese nurses in intensive care unit during COVID-19 pandemic. *Risk Manag Healthc Policy*. 2023;16:817-831. Doi: 10.2147/RMHP.s391336
9. Younan L, Clinton M, Fares S, et al. The relationship between work-related musculoskeletal disorders, chronic occupational fatigue, and work organization: A multi-hospital cross-sectional study. *J Adv Nurs*. 2019;75(8):1667-1677. Doi: 10.1111/jan.13952
10. Çelik S, Taşdemir N, Kurt A, et al. Fatigue in intensive care nurses and related factors. *Int J Occup Environ Med*. 2017;8(4):199-206. Doi: 10.15171/ijoem.2017.1137
11. Scott LD, Arslanian-Engoren C, Engoren MC. Association of sleep and fatigue with decision regret among critical care nurses. *Am J Crit Care*. 2014;23(1):13-23. Doi: 10.4037/ajcc2014191
12. Abdul Rahman H, Abdul-Mumin K, Naing L. Psychosocial work stressors, work fatigue, and musculoskeletal disorders: Comparison between emergency and critical care nurses in Brunei public hospitals. *Asian Nurs Res*. 2017;11(1):13-18. Doi: 10.1016/j.anr.2017.01.003
13. Aşkar SE, Ovayolu O, Ovayolu N. The effect of progressive relaxation exercise on fatigue level of intensive care nurses: A randomised controlled trial. *Aust Crit Care*. 2024;37(5):767-774. Doi: 10.1016/j.aucc.2024.01.011
14. Cho Y, Joo JM, Kim S, Sok S. Effects of meridian acupressure on stress, fatigue, anxiety, and self-efficacy of shiftwork nurses in South Korea. *Int J Environ Res Public Health*. 2021;18(8). Doi: 10.3390/ijerph18084199
15. Ozgundondu B, Gok Metin Z. Effects of progressive muscle relaxation combined with music on stress, fatigue, and coping styles among intensive care nurses. *Intensive Crit Care Nurs*. 2019;54:54-63. Doi: 10.1016/j.iccn.2019.07.007
16. Aktaş GK, İlgin VE. The effect of deep breathing exercise and 4-7-8 breathing techniques applied to patients after bariatric surgery on anxiety and quality of life. *Obes Surg*. 2023;33(3):920-929. Doi: 10.1007/s11695-022-06405-1
17. McNair D. Flipping on the creative switch using the 4, 7, 8 breathing technique. *The Creativity Workbook for Coaches and Creatives*. Routledge; 2020:4-6.
18. Örün D, Karaca S, Arıkan Ş. The effect of breathing exercise on stress hormones. *Cyprus J Med Sc*. 2021;6(1): 22-27. Doi: 10.4274/cjms.2021.2020.2390
19. Bernardi L, Gabutti A, Porta C, Spicuzza L. Slow breathing reduces chemoreflex response to hypoxia and hypercapnia, and increases baroreflex sensitivity. *J Hypertens*. 2001;19(12):2221-9. Doi: 10.1097/00004872-200112000-00016
20. Ma X, Yue Z-Q, Gong Z-Q, et al. The Effect of diaphragmatic breathing on attention, negative affect and stress in healthy adults. Original Research. *Front Psychol*. 2017;8:874. Doi:10.3389/fpsyg.2017.00874
21. Klinsophon T, Thaveeratitham P, Janwantanakul P. The effect of three-part breathing exercise on smoking cessation: A 6-month cluster-randomized clinical trial. *J Bodyw Mov Ther*. 2022;32:156-162. Doi: 10.1016/j.jbmt.2022.04.015

22. Kupershmidt S, Barnable T. Definition of a yoga breathing (Pranayama) protocol that improves lung function. *Holist Nurs Pract*. 2019;33(4):197-203. Doi: 10.1097/hnp.0000000000000331
23. Konya I, Watanabe K, Shishido I, et al. Post-work recovery from fatigue and sleep episodes among nurses who are engaged in 16-hour night shifts: A prospective observational study. *Healthcare (Basel, Switzerland)*. 2022;10(6):1089. Doi: 10.3390/healthcare10061089
24. Hopewell S, Chan A-W, Collins GS, et al. CONSORT 2025 statement: updated guideline for reporting randomised trials. *BMJ*. 2025;389:e081123. Doi: 10.1136/bmj-2024-081123
25. Gauthier F, Güneş Ü. The effect of music therapy and breathing exercise on anxiety and pain in patients undergoing coronary angiography: A randomized controlled study. *Nurs Crit Care*. 2024;29(6):1325-1333. Doi: 10.1111/nicc.13145
26. Parlak AG, Akkuş Y, Araz Ö. The effect of foot reflexology on stress, fatigue, and low back pain in intensive care unit nurses: A randomized controlled trial. *Pain Manag Nurs*. 2024;25(5):494-500. Doi: 10.1016/j.pmn.2024.05.013
27. Piper BF, Dibble SL, Dodd MJ, et al. The revised Piper Fatigue Scale: psychometric evaluation in women with breast cancer. *Oncol Nurs Forum*. 1998;25(4):677-84.
28. Can G, Durna Z, Aydiner A. Assessment of fatigue in and care needs of Turkish women with breast cancer. *Cancer nursing*. 2004;27(2):153-61. Doi: 10.1097/00002820-200403000-00009
29. Aslankoç R, Yalçın A, Tunca Ü, et al. The relationshıp between the fatigue and sleep quality of the workers in the intensive care unit. *Uyku Bülteni*. 2020;1(2):32-37.
30. Demir OB, Yilmaz FT. The effect of posture regulation training on musculoskeletal disorders, fatigue level and job performance in intensive care nurses. *BMC nursing*. 2024;23(1):778. Doi: 10.1186/s12912-024-02387-w
31. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. *J Health Soc Behav*. 1983;24(4):385-96.
32. Eskin M, Harlak H, Demirkıran F, Dereboy Ç. Algılanan stres ölçeğinin Türkçeye uyarlanması: güvenirlik ve geçerlik analizi. *New/Yeni Symposium Journal*. 2013;51(3):132-140.
33. Mehta CR, Patel NR. A hybrid algorithm for Fisher's exact test in unordered rxc contingency tables. *Commun Stat Theory Methods*. 1986;15(2):387-403.
34. Cohen J. The analysis of variance and covariance. *Statistical power analysis for the behavioural sciences*. 1988;2nd ed. Doi: https://doi.org/10.4324/9780203771587
35. Duarte J, Pinto-Gouveia J. Effectiveness of a mindfulness-based intervention on oncology nurses' burnout and compassion fatigue symptoms: A non-randomized study. *Int J Nurs Stud*. 2016;64:98-107. Doi: https://doi.org/10.1016/j.ijnurstu.2016.10.002
36. Neşe A, Samancıoğlu Bağlama S. The effect of progressive muscle relaxation and deep breathing exercises on dyspnea and fatigue symptoms of COPD patients: A randomized controlled study. *Holist Nurs Pract*. 2022;36(4):E18-e26. Doi: 10.1097/hnp.0000000000000531
37. Serçe S, Ovayolu Ö, Bayram N, et al. The effect of breathing exercise on daytime sleepiness and fatigue among patients with obstructive sleep apnea syndrome. *J Breath Res*. 2022;16(4). Doi: 10.1088/1752-7163/ac894d
38. Zaccaro A, Piarulli A, Laurino M, et al. How breath-control can change your life: A systematic review on psycho-physiological correlates of slow breathing. Systematic Review. *Front Hum Neurosci*. 2018;12:353.
39. Gerbarg PL, Dickson F, Conte VA, Brown RP. Breath-centered virtual mind-body medicine reduces COVID-related stress in women healthcare workers of the Regional Integrated Support for Education in Northern Ireland: a single group study. Original Research. *Front Psychiatry*. 2023:14:1199819.
40. Morgan SP, Lengacher CA, Seo Y. A Systematic review of breathing exercise interventions: An integrative complementary approach for anxiety and stress in adult populations. *J Holist Nurs*. 2024:08980101241273860. Doi: 10.1177/08980101241273860
41. Fincham GW, Strauss C, Montero-Marin J, Cavanagh K. Effect of breathwork on stress and mental health: A meta-analysis of randomised-controlled trials. *Scientific reports*. 2023;13(1):432. Doi: 10.1038/s41598-022-27247-y
42. Bernstein AM, Kobs A, Bar J, et al. Yoga for stress management among intensive care unit staff: A pilot study. *Altern Complement Ther*. 2015;21(3):111-115. Doi: 10.1089/act.2015.28999.amb
43. Yu X, Fumoto M, Nakatani Y, et al. Activation of the anterior prefrontal cortex and serotonergic system is associated with improvements in mood and EEG changes induced by Zen meditation practice in novices. *Int J Psychophysiol*. 2011;80(2):103-11. Doi: 10.1016/j.ijpsycho.2011.02.004
44. Yu F, Somerville D, King A. Exploring the impact of 12-hour shifts on nurse fatigue in intensive care units. *Applied nursing research: ANR*. 2019;50:151191. Doi: 10.1016/j.apnr.2019.151191

APPENDIX

Supplemental Material S1. Breathing exercise application protocol

Preparation stage before applying the breathing exercise

The setting (quiet, calm, etc.) where the application will be performed should be prepared.

Individuals should have a meal at least 2-4 hours before the application.

The bladder and intestines should be empty before the application.

Individuals should wear comfortable clothing during the application.

According to an individual's preference, they should be ensured they feel comfortable, sit on the chair/sofa with their knees and hips at the same level, or take a semi-lying position with the spine straight.

Since the nose is used during breathing exercises, the tongue should be touched to the point where the teeth and palate meet without applying pressure (in some cultures, it is called the "fire point" to increase energy).

Individuals are asked to close their eyes and obey the commands.

Application Stage	Duration	Applications
1. **Focusing on breathing**	2-3 min	Relax, close your eyes, and place your hands on your knees, palms down. Breathe in and out through your nose. As you breathe in and out, try to feel your breath. Relax and do not try to control your breathing. Just try to feel your breath and how it spreads through your body. Do not try to control your breathing. Just try to feel your breath and your body.
2. **Three-part breathing technique (full yogic breathing)**		
Stage 1: abdominal breathing	5 min	Place your right hand on your abdomen to feel your breath. Continue breathing in and out through your nose. Imagine a colorful balloon in your abdomen; inflate it while breathing deeply through your nose, and deflate it while breathing. Notice that your abdominal swelling is reduced. Feel the movement of your hand on your abdomen.
	30 s	Breathe normally.
Stage 2: chest breathing+abdominal breathing	5 min	Place your left hand on your chest while your right hand is on your abdomen. Keep breathing through your nose. As you breathe, feel the air first expand into your belly and then fill your chest. Feel the movement in your hands. Slowly exhale, feeling the air that has been in your chest first and now in your abdomen emptying.
	30 seconds	Breathe normally.
Stage 3: shoulder breathing+chest breathing+abdominal breathing	5 min	Place your left hand on your right collarbone while your right hand is on your abdomen. Keep breathing through your nose. As you breathe, feel the air first inflate your abdomen and then fill your chest and rise to your collarbone. Feel the air filling up your shoulders. Monitor the movements of both your hands.

(*Continued*)

Application Stage	Duration	Applications
	30 s	Breathe normally.
4-7-8 Breath	4 times	With your mouth closed and your tongue tip at the point of fire, breathe in through your nose for a count of 4. Hold your breath for a count of 7. Exhale the breath you are holding by making a wind sound with your mouth for a count of 8. Then breathe in again through your nose, counting to 4 for the second time.
	30 s	Breathe normally.
3. Focusing on breathing	2-3 min	Use only your nose to breathe. Observe your breathing and try to feel the distribution of your breath throughout your body. Relax, listen to your inner voice, and try to feel the air you breathe in and out. Do not think about how to breathe better. Release these feelings. Do not try to control your breathing. Just try to feel your breath and your body.
		Slowly open and close your eyes several times. Then, slowly open your eyes.

La Medicina del Lavoro

Original article

Med. Lav. 2026; 117 (3): 18637
DOI: 10.23749/mdl.2026.18637

Work Ability and Associated Factors Among Nurses in a Teaching Hospital: A Cross-Sectional Study

Paola Ferri[1], Angela Contri[1]*, Loretta Casolari[2], Alberto Modenese[1], Sergio Rovesti[1], Elena Righi[1], Lucia Rampino[3], Domenico Cannizzaro[4], Annalisa Bargellini[1]

[1]Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy
[2]Health Surveillance and Workers Health Promotion Service, University Hospital of Modena, Modena, Italy
[3]University Hospital of Modena, Modena, Italy
[4]Clinical and Experimental Medicine PhD Program, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy

Keywords: Work Ability; Work Ability Index; Nurses; Work Environment; Work-Life Balance; Job Satisfaction; Shift Work; Occupational Health; Musculoskeletal Disorders; Healthcare Workforce Retention

Abstract

Background: *Preserving nurses' work ability (WA) is essential for healthcare sustainability, especially given the current global workforce crisis and an ageing population. This study aims to assess the prevalence of inadequate WA among hospital nurses and to identify the personal, domestic, and organisational predictors that influence it, focusing on modifiable factors to inform targeted retention strategies.* **Methods:** *A cross-sectional study was conducted at an Italian university hospital (August–October 2022). Data from 182 nurses were collected during mandatory health surveillance visits using the Work Ability Index (WAI), alongside assessments of socio-demographic, occupational, and extra-work responsibilities (caregiving/education). Multivariable binary logistic regression was performed to identify independent predictors of WA, adjusting for confounders such as BMI and lifestyle factors.* **Results:** *Inadequate WA was reported by 44.5% of participants (mean age 45.8±11.1 years). A significant health burden was observed, with 41.8% suffering from musculoskeletal disorders. The regression model ($\chi^2_{(9)}$=31.026; p<0.001) revealed that the likelihood of adequate WA decreased significantly with advancing age (OR=0.93 per year; p<0.001) and high extra-work burdens (OR=0.97 per hour; p=0.041). Conversely, satisfaction with working conditions emerged as the primary modifiable protective factor, significantly increasing the likelihood of adequate WA (OR=2.41; p=0.010). No significant associations were found for sex, BMI, or smoking status.* **Conclusions:** *Nearly half of the nursing workforce exhibits vulnerable work ability. Findings suggest a detrimental 'double duty' effect where domestic responsibilities and age intersect. Organisational interventions should prioritise work-life balance and improved work climates to mitigate the impact of demographic shifts and preserve workforce sustainability.*

1. Introduction

Nurses are the largest group of healthcare professionals worldwide. They play a pivotal role in improving health, providing essential care, and advancing primary healthcare. They also deliver care in emergency settings, shape health policies, and safeguard the sustainability of health systems globally [1, 2].

Estimates suggest that by the year 2030, there will be a workforce shortage of 4.5 million nurses

Received 02.02.2026 – Accepted 11.05.2026
*Corresponding Author: Angela Contri; E-mail: angela.contri@unimore.it

worldwide [2] and of nearly 2.5 million nurses across 23 Organization for Economic Co-operation and Development (OECD) countries [3, 4]. Italy is one of the OECD countries with the fewest nurses per 1,000 inhabitants, at 6.4, compared with an average of 9.5 in Europe as a whole. It also ranks last in nursing graduates per 100,000 inhabitants: only 17 compared with the European average of 48 [4]. A recent analysis has revealed a significant deficit of at least 65,000 nurses within the Italian healthcare system. Furthermore, the Court of Auditors has estimated that over the next decade, approximately 100,000 nurses will exit the profession due to reaching retirement age [5]. Recent years have seen a further decline in the popularity of the profession, as evidenced by the consistent decrease in applications for admission to nursing degree courses (approximately 10%) [5]. This scenario appears even more critical in light of the increasing demand for nursing care and assistance, driven by the progressive ageing of the population and the growing prevalence of chronic diseases.

An imbalance between the number of registered nurses available and healthcare demand may negatively affect care quality, with potential consequences including higher adverse event rates and increased patient mortality risk [6].

Excessive workload among nurses is associated with reduced job satisfaction, increased rates of burnout, a higher incidence of occupational diseases and workplace injuries, early retirement and attrition from the profession [7-11].

The combination of the aforementioned factors, in conjunction with the ageing nursing workforce, engenders elevated physical and mental demands for nurses who continue to practice. This underscores the need for nurses to maintain peak physical and mental health, which translates into optimal work ability (WA) [1, 12]. WA refers to an individual's ability, or their perceived ability, to meet the demands of their job. It is influenced not only by personal resources, including physical, mental, and social functioning, but also by the specific requirements of the work itself [13]. As a result, an individual's WA may vary across their working lifespan and in relation to their specific occupation and professional context.

In the 1980s, the Finnish Institute of Occupational Health developed the concept of WA and the Work Ability Index (WAI) to measure: "How good is the worker at present, in the near future, and how able is he or she to do his or her work with respect to work demands, health, and mental resources?" [14, 15]. Its goal is to promote a healthy quality of working life, and its key domains encompass workers' needs, the work environment, organizational factors, and workers' health and functional capacity [16]. The WAI demonstrates reliable predictive validity for extended sick leave, occupational incapacity, poor quality of life, early retirement intentions, and even mortality [14, 17]. Similarly, high levels of WA are associated with safer workplaces, improved performance, and enhanced quality of life and workers' well-being [16]. The WAI is therefore a preventive self-assessment tool for nurses to evaluate their ability to meet work demands based on their health status and physical, mental, and social resources. Some studies suggest that nurses' WA may be influenced by both intrinsic work characteristics (night shifts, job satisfaction, etc.) and extra-work factors (family roles, work-life balance, commuting distance, hobbies, etc.) [18, 19].

While WA has been extensively studied in various professions, little research has been conducted on nurses' WA. A recent systematic review highlighted significant risks of compromised WA in nursing staff [20]. Nevertheless, the included studies were all conducted before the pandemic, none investigated the Italian nursing context, and, crucially, most failed to provide separate prevalence data for registered nurses versus nursing assistants [20]. Grouping registered nurses and nursing assistive personnel together is methodologically inappropriate, as the latter are typically assigned more physically demanding and repetitive tasks, often with lower autonomy and fewer opportunities for professional satisfaction, factors known to negatively influence WA [21]. This highlights the need for additional research with disaggregated data by professional category.

In light of the current nursing shortage, prolonged working lives, and the simultaneous high demand for nursing services, understanding the WA of Italian nurses seems to be particularly crucial, and

identifying factors influencing WA could prove highly valuable. Given the gaps presented above, this study aimed to investigate the prevalence of WA and to determine which personal and work-related factors are associated with it, exploring their relationships and the strength of their associations with WAI scores.

2. Methods

2.1. Design and Sample

A cross-sectional study was conducted at a university hospital in Northern Italy using a convenience sample of nurses to assess WA levels and their association with socio-demographic, family, and work characteristics. The only inclusion criterion was employment at the university hospital, either on a fixed-term or permanent contract. To estimate the sample size, G*Power was used for a medium effect size at an alpha level of 0.05 and 80% power, yielding 143 nurses, to which 30 were added to account for attrition. A total of 182 nurses were recruited in the present study, all of whom completed the survey instrument.

2.2. Data Collection Procedure

All nurses attending regular health surveillance visits, as required by Italian law, between 1 August 2022 and 24 October 2022 were invited to participate in the study. A researcher provided each of them an information form about the study, detailing the study's design, objectives, and methods. The researcher assured them that their involvement was entirely voluntary, and that respondents' anonymity and the confidentiality of their information would be strictly preserved. The consent form also emphasised that participants had the right to withdraw from the study at any time. Nurses who provided their written informed consent were then given the questionnaire in an enclosed envelope. The questionnaire was completed on site and prior to the visit, in a private room without the researcher's presence. Participants were then instructed to place the completed questionnaire in a box, ensuring complete anonymity.

2.3. Instrument

The instrument consisted of the following three sections:

2.3.1. Socio-Demographic, Family, and Personal Characteristics

The first part of the questionnaire covered the following topics: age, sex, educational qualifications, family composition, presence of dependent adults, the extent of caregiving responsibilities outside the workplace, assistance and educational activities, balancing work schedules with personal and family commitments, and the time taken to get to work. Information was also requested on smoking habits, weight, and height.

2.3.2. Job Characteristics and Satisfaction

The last section of the questionnaire covered the following topics: type of employment contract; length of service; operating unit; type of work shift; and satisfaction with current working conditions. The clinical setting operates on a standardized institutional shift schedule. The nursing staff follows a 12-hour rotation system consisting of daytime shifts (07:00–19:00) and nighttime shifts (19:00–07:00). This organizational model allows for a compressed workweek, typically involving three shifts per week to reach the standard 36-hour weekly requirement. In compliance with national health regulations and safety protocols, a mandatory minimum of 11 consecutive hours of rest is guaranteed between shifts to ensure adequate psychophysical recovery.

2.3.3. Work Ability Index

The WAI is the most commonly used tool for evaluating work capacity [2-6], which, as mentioned above, is a self-assessment questionnaire designed to measure the WA of healthcare workers, developed by Tuomi et al. [15].

The index is determined on the basis of the answers to a series of questions which take into consideration the demands of work, the worker's health, and resources. It consists of 60 items distributed

in seven dimensions, that assess: (a) current WA compared with lifetime best (1 item), (b) WA in relation to the demands of the job (2 weighted items), (c) number of current diseases diagnosed by a physician (out of a list of 51 diseases), (d) estimated work impairment due to disease (1 item), sick leave during the past 12 months (1 item), (e) own prognosis of WA 2 years from now (1 item), and (f) mental resources (3 items). Scores on each dimension are summed, with a range of 7 to 49, allowing workers to be classified into four categories: poor (7 – 27); moderate (28 – 36); good (37 – 43); and excellent (44 – 49). However, since then, numerous studies have dichotomized the WAI total score by aggregating the 4 dimensions into only two categories [20]:

- *inadequate WA* when the score is between 7 and 36 (combination of the poor and moderate categories);
- *adequate WA* with a score between 37 and 49 (combination of the good and excellent categories).

The reliability of the questionnaire in the present study (Cronbach's alpha) was 0.81, while in other studies it ranged from 0.65 to 0.80 [22, 23].

2.4. Data Analysis

Descriptive statistics were used to summarise participants' socio-demographic and occupational characteristics, with continuous variables expressed as means and standard deviations and categorical variables as frequencies and percentages.

The WAI was initially categorised into four levels (poor, moderate, good, excellent) and subsequently dichotomised into a dummy variable, coded as 'adequate' when the WA score ranged from 37 to 49 and 'inadequate' when it ranged from 7 to 36, in accordance with previous studies [20]. Comparisons between groups were conducted using χ^2 tests for categorical variables and Student's t-test for continuous variables. To assess the internal consistency between the occupational indicators (job satisfaction and work-life balance) and the WAI dimensions, a bivariate correlation analysis was performed. Given the ordinal nature of the satisfaction scales, Spearman's rank correlation coefficient (r) was calculated.

A binary logistic regression analysis (enter method) was then performed to identify independent predictors of adequate WAI. The dependent variable was derived from the dichotomised WAI score (Adequate vs Inadequate). Independent variables included age, sex, marital status, presence of children, body mass index (BMI), smoking habits, weekly hours spent on caregiving, assistance or educational activities outside of work, and satisfaction with working conditions. All variables were entered simultaneously into the model. Model fit was evaluated using Nagelkerke R^2 and the Hosmer-Lemeshow test. Odds ratios (exp(B)) and corresponding p-values were calculated to assess the strength and significance of associations.

Furthermore, to investigate potential selection biases, the age distribution was compared between nightshift and daytime-only workers using an independent-samples t-test. Levene's test was used to assess the equality of variances, and the appropriate t-statistic was reported accordingly.

All analyses were two-tailed, with statistical significance set at $p<0.05$. IBM/SPSS Statistics for Windows, Version 29.0 (IBM Corp.: Armonk, NY, USA) was used for the analyses.

2.5. Ethical Considerations

The study was approved by the Ethics Committee of the "Area Vasta Emilia Nord" (n. 0017051/2022) and conducted in accordance with the Declaration of Helsinki (Ethical principles for medical research involving human participants, 2024) of the World Medical Association.

3. Results

3.1. Participants Characteristics

The 182 nurses had a mean age of 45.8±11.1 years, with males being younger than females (male M=39.4±10.6 SD years, female M=47.2±11.1 SD years; $p<0.001$). The age distribution shows that 43.4% of the sample were over 50 years old, while 30.8% were between 36 and 50 years old. The

respondents were predominantly female. Table 1 shows the sample characteristics.

Respectively, 43% of males and 48% of females reported spending more than 20 hours per week on non-work-related caregiving, assistance, and educational activities. 26.4% of the sample reported being overweight, while 14.8% reported having obesity of types I-III, with an average BMI of 25.3±4.7 SD and no sex distinctions. Regarding smoking habits, there was a clear prevalence among males (41% vs. 18% of females, p=0.008).

3.2. Job Characteristics and Satisfaction

The vast majority of respondents (98.4%) were employed on a permanent basis. Most worked in medical departments (46.2%) and during daytime shifts (61%), as shown in Table 2. On average, female participants reported significantly greater job seniority compared to males (males 11.7±11.4 SD, female 20.5±12.4 SD; p<0.001). Overall, 61.5% of the sample reported being fairly satisfied with their working conditions.

3.3. Work Ability Index Analysis by Sex

The overall mean WAI score for the study population was 37.2±6.3. When disaggregated by sex, male nurses reported a significantly higher total WAI score than their female counterparts (39.3±5.6 vs. 36.7±6.4, respectively; p=0.039), as shown in Supplemental Material, Table S1.

Table 1. Socio-demographic characteristics and extra-work commitments of the study population (N=182).

Participants characteristics	Total N=182	Male n=32 (17.6%)	Female n=150 (82.4%)	p-value
Age (years, M±SD)	45.8±11.1	39.4±11.0	47.2±10.6	**<0.001**
Educational level				
Professional Nursing Diploma	69 (37.9%)	6 (18.8%)	63 (42%)	0.066
University Diploma in Nursing	18 (9.9%)	3 (9.4%)	15 (10%)	
Nursing Degree	95 (52.2%)	23 (71.9%)	72 (48%)	
Marital status				
Married/Partnered	120 (65.9%)	17 (53.1%)	103 (69.6%)	0.073
Single	62 (34.1%)	15 (46.9%)	47 (31.3%)	
Presence of children in home				
Yes	77 (42.3%)	13 (40.6%)	64 (42.7%)	0.488
No	105 (55.7%)	19 (59.4%)	86 (57.3%)	
Adult caregiving responsibilities				
Yes	48 (26.4%)	6 (18.8%)	42 (28.0%)	0.281
No	134 (73.6%)	26 (81.3%)	108 (72%)	
Extra-work commitments (hours, M±SD)	23.4±17.9	20.2±17.9	24.15±17.9	0.285
Work-life balance				
Good	122 (67%)	23 (71.9%)	99 (66.0%)	0.932
Poor	60 (32.9%)	9 (28.1%)	51 (34.0%)	
Travel time to workplace				
< 30 minutes	141 (77.5%)	27 (84.4%)	114 (77.0%)	0.584
30-60 minutes	37 (20.3%)	5 (15.6%)	32 (21.6%)	
> 60 minutes	2 (1.1%)	0 (0.0%)	2 (1.4%)	

M: Mean; SD: Standard Deviation.

Table 2. Occupational characteristics, work settings, and job satisfaction among the surveyed nurses.

Job variables	Total (N=182)	Male (n=32)	Female (n=150)	p-value
Employment contract				
Permanent	179 (98.4%)	32 (100%)	147 (98%)	1
Temporary	3 (1.6%)	0 (0%)	3 (2%)	
Work setting				
Medical ward	84 (46.2%)	15 (46.9%)	69 (46%)	**0.016**
Surgical ward	31 (17%)	4 (12.5%)	27 (18%)	
Outpatient area	24 (13.2%)	0 (0%)	24 (16%)[a]	
Intensive care unit	22 (12.1%)	9 (28.1%)[a]	13 (8.7%)	
Service area	11 (6%)	2 (6.3%)	9 (6.0%)	
Management area	10 (5.5%)	2 (6.3%)	8 (5.3%)	
Work Shift				
Daytime	111 (61%)	11 (34.4%)	100 (66.7%)	**0.01**
Nighttime	71 (39%)	21 (65.6%)	50 (33.3%)	
Job Seniority (years, M±SD)	18.9±12.7	11.7±11.4	20.5±12.4	**<0.001**
Job Satisfaction*				
Low satisfaction	53 (29.1%)	12 (37.5%)	41 (27.7%)	0.49
Fair satisfaction	112 (61.5%)	17 (53.1%)	95 (64.2%)	
High satisfaction	15 (8.2%)	3 (9.4%)	12 (8.1%)	

** 2 missing data; [a] Adjusted standardized residual > |1.96|, indicating a significant difference in distribution between sexes within this category.*

Data are presented as n (%) or Mean ± Standard Deviation. p-values were calculated using Pearson's Chi-square test, Fisher's exact test (for categorical variables with expected counts < 5), or Independent Samples t-test (for continuous variables). Significant p-values (p<0.05) are highlighted in bold.

Analysis of the seven individual WAI dimensions revealed that the most prominent difference between groups occurred in Dimension 3 (number of diagnosed diseases), where men scored significantly higher than women (4.9±2.0 vs. 3.5±2.4; p=0.003). Furthermore, a borderline significant difference was observed in Dimension 4 (estimated work impairment due to diseases), with higher scores reported by male participants (5.3±0.9 vs. 4.9±1.3; p=0.058).

3.4. Correlation Between Job Satisfaction and Work Ability Dimensions

The analysis revealed significant positive correlations between perceived job satisfaction and work ability. Specifically, overall satisfaction with working conditions was significantly associated with total WAI scores (r=0.259, p=0.001). Furthermore, satisfaction regarding the quantity of work performed was positively correlated with WAI scores (r=0.202, p=0.009), as was the ability to balance work schedules with personal and family commitments (r=0.192, p=0.012).

3.5. Work Ability

As shown in Table 3, 55.5% of our sample demonstrated an adequate level of WA.

47.8% of our sample reported at least three pathologies, with a higher prevalence among females (54% vs. 18.8%). The most common conditions were musculoskeletal disorders (41.8%), including cervical spine (22%), lumbar spine (29%), chronic lumbosciatica (19%), limb disorders (21%), and other

Table 3. Distribution of Work Ability Index (WAI) scores according to four-category and dichotomous classifications.

	Total (N=182)	Male (n=32)	Female (n=150)	p-value
4 WAI Categories				
7-27: Poor	17 (9.3%)	1 (3.1%)	16 (10.7%)	0.201
28-36: Moderate	64 (35.2%)	8 (25.0%)	56 (37.3%)	
37-43: Good	75 (41.2%)	17 (53.1%)	58 (38.7%)	
44-49: Excellent	26 (14.3%)	6 (18.8%)	20 (13.3%)	
2 WAI Categories				
7-36: Inadequate work ability	81 (44.5%)	9 (28.1%)	72 (48.0%)	**0.04**
37-49: Adequate work ability	101 (55.5%)	23 (71.9%)	78 (52.0%)	

Table 4. Prevalence of diagnosed medical conditions and organ-system disorders in the study cohort.

Diagnosis	Total (N=182)	Male (n=32)	Female (n=150)	p-value
Musculoskeletal disorders	76 (41.8%)	8 (25.0%)	68 (45.3%)	0.340
Neurological disorders	43 (23.6%)	4 (12.5%)	39 (26%)	0.103
Metabolic and endocrine disorders	41 (22.5%)	4 (12.5%)	37 (24.7%)	0.135
Cardiovascular diseases	40 (22%)	4 (12.5%)	36 (24.0%)	0.154
Dermatological disorders	37 (20.3%)	5 (15.6%)	32 (21.3%)	0.466
Gastrointestinal disorders	28 (15.4%)	4 (12.5%)	24 (16.0%)	0.618
Respiratory disorders	23 (12.6%)	4 (12.5%)	19 (12.7%)	0.979
Vision and hearing disorders	20 (11%)	1 (3.1%)	19 (12.7%)	0.158
Genitourinary disorders	20 (11%)	**0 (0%)**	**20 (13.3%)**	**0.029**
Anxiety, insomnia	18 (9.9%)	1 (3.1%)	17 (11.3%)	0.158
Oncological disorders	16 (8.8)	1 (3.1%)	15 (10%)	0.212
Blood disorders	14 (7.7%)	1 (3.1%)	13 (8.7%)	0.286
Mental disorders (e.g., severe depression)	4 (2.2%)	1 (3.1%)	3 (2.0%)	0.694

musculoskeletal issues (9%). Beyond musculoskeletal issues, conditions with over 20% prevalence included neurological, metabolic, endocrine, cardiovascular, and dermatological disorders (Table 4).

3.6. Work Ability Among Shift Workers and Non-Shift Workers

Inadequate WA, as measured by the WAI, was significantly more prevalent among nurses who do not work night shifts (Table 5).

Nurses working night shifts, compared to their daytime counterparts, reported lower satisfaction with their working conditions, but seemed to experience less difficulties in achieving a work-life balance.

Moreover, a significant age difference was observed between work-shift categories: nurses in the night-shift rotation were significantly younger than those in daytime-only roles (38.0±10.9 vs. 50.8±8.1 years; $p<0.001$).

3.7. Work Ability Predictors

The multivariable model demonstrated a good fit (Hosmer-Lemeshow: $\chi^2=7.117$, $p=0.524$) and explained 29.3% of the variance (Nagelkerke $R^2=0.293$), correctly classifying 71.1% of cases.

Table 5. Work Ability Index, job satisfaction, and work-life balance in shift and non-shift workers.

		Shift workers	Non-shift workers	p-value
WAI	Inadequate work ability	31%	53%	**0.004**
	Adequate work ability	69%	47%	
Job satisfaction	Low satisfaction	41%	22%	**0.010**
	Fair satisfaction	55%	67%	
	High satisfaction	4%	11%	
Work-life balance	Good	41%	28%	**0.040**
	Poor	59%	72%	

WAI: Work Ability Index.

Three independent predictors of adequate WA were identified. Age was negatively associated with the outcome (OR=0.93, p=0.001), as were the hours spent on extra-work caregiving activities (OR=0.97, p=0.041), indicating that increasing age and domestic burdens significantly reduce the likelihood of maintaining adequate work capacity. Conversely, job satisfaction emerged as a strong protective factor, more than doubling the odds of reporting adequate work ability (OR=2.41, p=0.010). A notable trend was also observed for BMI, with normal-weight nurses more likely to report adequate WA than those in the overweight/obese category (OR=2.28, p=0.065).

Full regression parameters are detailed in Supplemental Material, Table S2.

4. Discussion

The aim of this study was to investigate the prevalence of WA among hospital nurses and explore its association with personal and occupational factors. Almost half of the nurses in our sample (44.5%) reported inadequate WA, a proportion closely mirroring that observed by Garzaro et al. in another Italian university hospital (45.6%) [19]. This rate is, however, higher than those reported in most studies included in the systematic review by Romero-Sánchez et al., where the prevalence of inadequate WA generally ranged between 20% and 40%, with few exceptions in Thailand (53.2%), Germany (56.2%) and Poland (66.6%) [20]. However, it should be noted that most of those studies were conducted before the COVID-19 pandemic, which likely worsened working conditions and may have led to a persistent deterioration in WA among nurses.

A substantial body of evidence indicates that nurses and nursing assistants consistently exhibit poorer WA compared to other healthcare professionals [18, 19, 24].

Hospital nurses, in particular, face intense physical, mental, and psychological demands due to multiple factors: heavy workloads, manual patient handling, responsibility for patient safety, and care of elderly patients with multimorbidity. They also experience various organizational, social, and economic stressors, including night shifts, limited autonomy and control over their work, low pay, and inadequate social support [11, 19, 20, 25]. Furthermore, nurses frequently experience verbal and physical violence from patients and their relatives [26]. The literature has documented a bidirectional association between workplace violence and reduced WA [27]. These conditions contribute to physical strain and psychological distress, both of which are recognised determinants of reduced WA.

Consistent with previous studies, advancing age was the strongest negative predictor of WA in our sample [1, 28]. The progressive ageing of the nursing workforce across Europe, where approximately one in five nurses is aged 55 years or older [29], poses a major sustainability challenge. Although ageing itself cannot be modified, organisational and technological strategies may buffer its impact. In particular, the ongoing digital transformation of healthcare could represent a double-edged sword: while automation, electronic documentation and digital monitoring systems can reduce physical workloads and

increase efficiency, they could also introduce technostress and cognitive strain, especially for older nurses with lower digital literacy. Supporting digital competence through tailored training and mentoring may thus enhance both WA and job satisfaction.

Another important finding was the negative effect of extra-working responsibilities such as caregiving and educational duties. This reflects the increasing prevalence of the so-called 'double duty' among nurses who simultaneously manage the burden of professional and family care roles [30]. As highlighted by many authors, family caregiving among nurses can exacerbate fatigue, stress, and work–life conflict, potentially compromising both self-care and patient safety [31]. The rise of hybrid or remote healthcare models following the pandemic may offer partial solutions by improving flexibility, yet these models can also create new forms of digital overload or professional isolation. Artificial intelligence (AI) and telehealth technologies could be leveraged to redistribute administrative tasks and support nurses' time management, ultimately improving work–life balance [32].

In contrast, satisfaction with working conditions emerged as a protective factor, increasing the likelihood of adequate WA. This is consistent with the Nurse forecasting in Europe (RN4CAST) project findings, which demonstrate strong links between job satisfaction, adequate staffing, and better care outcomes [33, 34]. In the Italian branch of the RN4CAST study, excessive workloads and unfavourable nurse-to-patient ratios were identified as key contributors to job dissatisfaction, burnout and intentions to leave the profession [10]. This evidence aligns with our findings, suggesting that improving nurses' satisfaction with their working conditions may be crucial to maintaining WA. Organisational cultures that promote learning, recognition, and participation, can strengthen both nurses' resilience and retention. Nurse managers play a crucial role in this process by providing visible, supportive leadership, which is known to enhance job satisfaction and reduce errors. As highlighted by Aiken et al. [8], structural interventions that improve hospital work environments and staffing may have a stronger impact on clinicians' well-being and patient safety than individual-level resilience programmes. Our findings further indicate that subjective job satisfaction is not merely a reflection of workplace climate but is significantly correlated with the constituent dimensions of the WAI. The positive association found between satisfaction with work quantity and WAI scores underscores the critical role of perceived workload management. This is consistent with the job demands-resources model [34], suggesting that when nurses perceive their work quantity as manageable and their environment as supportive, their internal resources, as measured by the WAI, are better preserved. These correlations strengthen the validity of using self-reported satisfaction as a reliable proxy for organisational health in nursing settings.

Interestingly, nurses working night shifts displayed higher WA scores than their daytime counterparts, despite reporting poorer job satisfaction. This finding appears counterintuitive, and contrasts with previous studies, which have generally shown lower WA among night or rotating shift workers, consistently associating it with adverse health outcomes, including sleep disturbances, metabolic dysregulation, and increased stress [12]. A possible explanation for this apparent discrepancy may be the 'healthy worker effect', a specific type of survivorship bias where those who remain in night work tend to be younger, healthier, and more resilient, while less healthy workers often move to daytime roles [35]. Our data strictly support this clinical dynamic: nurses in the night-shift rotation were significantly younger than those working exclusively during the day (38.0±10.0 vs. 50.8±8.5 years, respectively; $p<0.001$). This age disparity suggests that the night-shift cohort represents a 'screened' group of younger individuals whose biological resilience likely buffers the stressors of nocturnal work. In contrast, the daytime group includes a higher proportion of ageing staff who may have been transitioned to more regular schedules due to emerging health limitations identified during mandatory health surveillance. This confirms a 'healthy worker effect', where younger, more resilient staff remain in night rotations while older colleagues are transitioned to daytime roles [35]. This dynamic is further reflected in the work-life balance data: night-shift nurses reported a lower prevalence of poor work-life balance (59%) compared to daytime nurses (72%), a

difference that may be attributed to the combined effect of their younger age and the higher proportion of male nurses in the night-shift rotation. Male nurses in our sample were significantly younger and reported fewer weekly hours of extra-work caregiving responsibilities, a pattern consistent with broader evidence that male nurses often carry a lower burden of family caregiving duties compared to their female colleagues [30, 31]. Thus, the observed differences in work-life balance likely reflect demographic selection: younger, predominantly male nurses with fewer domestic responsibilities, rather than a direct protective effect of night work itself.

Moreover, night shifts may be perceived as offering greater autonomy or financial compensation, partially offsetting fatigue. Nonetheless, long-term exposure to irregular schedules remains a recognised risk for sleep disturbance, stress, and impaired performance [25, 36-39]. However, these findings underscore the importance of considering age, sex, and selection bias when interpreting the relationship between shift schedules and work ability. While night work is not without risks, the cross-sectional nature of this study captures a "surviving" cohort of younger, predominantly male nurses whose physiological resilience and, potentially, lower burden of extra-work caregiving responsibilities may temporarily buffer the occupational stressors of shift work. Longitudinal studies are needed to determine whether this cohort maintains its high work ability as it ages or eventually transitions to daytime roles, as observed in the older segment of our sample.

Musculoskeletal disorders were the most frequently reported health condition among our participants, confirming their major role in limiting WA. This is consistent with international evidence showing that 35-80% of nurses experience back injuries during their career, largely due to patient handling and physical overexertion [11, 40]. Musculoskeletal disorders are associated with absenteeism, decreased quality of care, and early exit from the profession [41]. Multicomponent ergonomic interventions combining physical exercise, equipment training and participatory redesign appear the most effective for reducing these risks [42].

The regression analysis highlights that while biological ageing (age) remains a non-modifiable constraint, organisational and personal factors play a decisive role in sustaining work ability. The significant impact of job satisfaction (OR=2.41, p=0.010) suggests that improving the psychosocial work environment can more than double the likelihood of maintaining high work capacity. Furthermore, the significance of extra-work caregiving hours underscores the 'double burden' faced by the nursing workforce, where domestic demands directly interface with professional performance. These findings suggest that interventions to support work-life balance and enhance workplace satisfaction are essential strategies for retaining ageing staff. A trend towards significance was observed for normal-weight nurses (OR=2.28, p=0.065), suggesting that weight management may also contribute to preserving work ability, warranting further investigation.

Beyond its clinical implications, inadequate WA has important organisational consequences, including increased absenteeism, turnover, and reduced patient safety [43, 44]. Studies consistently show that inadequate staffing and poor working environments are associated with higher mortality and readmission rates [6, 45]. Strengthening nurse staffing and improving work environments should therefore be considered not only workforce strategies, but patient-safety imperatives.

The emotional dimension of WA also deserves attention. Over the last century, workplace disorders have become increasingly attributable to cognitive and psychological rather than somatic factors. This shift reflects two interrelated phenomena: the rise of professions requiring sustained mental performance and the progressive decline of physically strenuous work. A study conducted in Germany in 2015 showed that around 20% of retired workers left the labour market due to incapacity for work, relying on disability pensions; however, age-related diseases appear to be influenced more by external determinants such as diet, work type, environment, lifestyle, and genetic predisposition. The high prevalence of inadequate WA in our cohort may partly reflect post-pandemic emotional exhaustion and burnout, now recognised as key contributors to nurse attrition [21, 46, 47]. The concept of sustainable emotional capacity is crucial for understanding WA in nursing, as it encompasses the professional resilience required

to consistently preserve empathetic responsiveness and ethical decision-making despite chronic occupational stress. Integrating moral distress prevention and peer-support programmes into continuing education may help preserve this dimension of WA.

Looking ahead, technological innovation could play a transformative role in safeguarding WA. Predictive analytics and AI applications are beginning to support occupational health surveillance [48], and they could play a role in integrating data from shifts, self-reports and wearable sensors to identify early signs of decline in WA. Embedding such systems into routine occupational monitoring could allow proactive interventions tailored to individual risk profiles. Similarly, promoting "green hospital" design, with natural light, quiet spaces and ergonomic layouts, has been shown to enhance staff well-being and reduce stress. These environmental strategies align with the broader goal of sustainable healthcare and may indirectly contribute to maintaining WA.

This study has some limitations that should be acknowledged. Its cross-sectional design precludes the establishment of causal relationships between WA and the factors identified. In order to clarify whether age, family responsibilities, job satisfaction and other variables act as antecedents or consequences of changes in WA over time, longitudinal designs would be required. Furthermore, data were collected in a single university hospital, which may limit the external validity of the findings.

Another limitation concerns the use of self-reported data, which may be influenced by recall or social desirability bias. However, the anonymous and voluntary nature of participation likely reduced such effects. The absence of objective measures of physical and mental health (e.g. sickness absence, clinical assessments) also limits the ability to triangulate self-perceived WA with actual performance indicators. Given the mean age of the sample and the prevalence of chronic musculoskeletal conditions, medication use could represent a further indicator of disease severity that the standard WAI does not fully capture. Nevertheless, although individual-level triangulation with clinical records was precluded by the anonymized study design, the high prevalence of self-reported musculoskeletal disorders observed in our sample is entirely consistent with the general epidemiological profile and health surveillance trends of the nursing staff within our institution. This alignment reinforces the validity of our findings, suggesting that the self-reported data accurately reflect the objective clinical burden of this professional population. Future studies could integrate administrative and clinical data, or even wearable-sensor metrics, to enhance the precision of WA assessments.

Additionally, this study did not include organisational-level variables such as staffing ratios, team climate, or leadership style, which are known to influence both job satisfaction and WA. Incorporating multi-level data could help capture the complex interactions between individual, team and institutional determinants of WA.

Despite these limitations, the study presents notable strengths. The institutional homogeneity of the sample increases internal consistency and offers a representative insight into the situation of hospital nurses in the Italian public healthcare context. Additionally, the anonymous and voluntary nature of participation likely reduced recall or social desirability bias.

Future research should therefore adopt a multidimensional and mixed-methods approach, combining quantitative modelling with qualitative inquiry into nurses' lived experiences and coping mechanisms. The integration of digital technologies, such as AI-driven predictive tools and occupational health dashboards, could open new avenues for early identification of nurses at risk of declining WA and for tailoring preventive interventions.

Finally, intervention studies are needed to evaluate the effectiveness of strategies aimed at maintaining and improving WA across the career span. These may include targeted physical and ergonomic programmes, flexible scheduling for workers with caregiving responsibilities, and organisational policies promoting emotional sustainability and job satisfaction. Implementing such evidence-based measures could strengthen the resilience and retention of the nursing workforce, contributing to the broader goal of sustainable and high-quality healthcare delivery.

5. Conclusion

In conclusion, our findings highlight the multifactorial nature of WA, shaped by the interplay

between personal characteristics, family responsibilities, organisational culture, and evolving technologies. Nearly half of hospital nurses in our sample experienced inadequate WA, driven by both individual and organisational determinants. Advancing age and external caregiving or educational duties emerged as key challenges, while satisfaction with working conditions acted as a strong protective factor. Addressing these dimensions through coordinated interventions, ranging from ergonomic and psychosocial prevention to digital training, supportive leadership and flexible scheduling, will be essential to sustain nursers' WA, enhance job satisfaction, and ensure both workforce retention and the safety of healthcare systems.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of the "Area Vasta Emilia Nord" (reference number 185/2022/SPER/AOUMO SIRER ID 4136, protocol 0017051/22).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Acknowledgments: We thank the nurses who participated in the survey.

Declaration of Interest: The authors declare no conflict of interest.

Author Contribution Statement: P.F., L.C., L.R., and A.B. contributed to the conception and design of the research. P.F., A.C., and A.B. contributed to the implementation of the research and software management. P.F., A.C., L.C., L.R., and A.B. contributed to the analysis and interpretation of the results. A.M., S.R., and E.R. contributed to the investigation and supervision of the study. P.F. and L.R. were responsible for data curation, while L.C. handled project administration. P.F., A.C., D.C., and A.B. contributed to the writing of the original manuscript, and all authors contributed to the review, editing, and final approval of the manuscript.

References

1. Rypicz Ł, Witczak I, Rosińczuk J, Karniej P, Kołcz A. Factors affecting work ability index among polish nurses working in hospitals - A prospective observational survey. *J Nurs Manag*. 2021;29(3):468-476. Doi: 10.1111/jonm.13192
2. World Health Organization. Global strategic directions for nursing and midwifery 2021-2025. Accessed 16 December 2024, https://www.who.int/publications/i/item/9789240033863
3. Scheffler RM, Arnold DR. Projecting shortages and surpluses of doctors and nurses in the OECD: what looms ahead. *Health Econ Policy Law*. 2019;14(2):274-290. Doi: 10.1017/s174413311700055x
4. OECD/European Union. Health at a Glance: Europe 2022. State of Health in the EU Cycle. [Last Accessed 16 December 2024], https://doi.org/10.1787/507433b0-en
5. Federazione Nazionale Ordini Professioni Infermieristiche. Carenza infermieristica: la buona Università può fare la differenza. Accessed 16 December 2024, https://www.fnopi.it/wp-content/uploads/2024/07/4-luglio-2024-Incontro-FNOPI-CRUI-carenza-infermieristica-la-buona-Universita-puo-fare-la-differenza.pdf
6. McHugh MD, Aiken LH, Sloane DM, Windsor C, Douglas C, Yates P. Effects of nurse-to-patient ratio legislation on nurse staffing and patient mortality, readmissions, and length of stay: a prospective study in a panel of hospitals. *Lancet*. 2021;397(10288):1905-1913. Doi: 10.1016/s0140-6736(21)00768-6
7. Aiken LH, Clarke SP, Sloane DM, Sochalski J, Silber JH. Hospital nurse staffing and patient mortality, nurse burnout, and job dissatisfaction. *Jama*. 2002;288(16):1987-93. Doi: 10.1001/jama.288.16.1987
8. Aiken LH, Sermeus W, McKee M, et al. Physician and nurse well-being, patient safety and recommendations for interventions: cross-sectional survey in hospitals in six European countries. *BMJ Open*. 2024;14(2):e079931. Doi: 10.1136/bmjopen-2023-079931
9. Bagheri Hosseinabadi M, Khanjani N, Etemadinezhad S, Samaei SE, Raadabadi M, Mostafaee M. The associations of workload, individual and organisational factors on nurses' occupational injuries. *J Clin Nurs*. 2019;28(5-6):902-911. Doi: 10.1111/jocn.14699
10. Sasso L, Bagnasco A, Zanini M, et al. The general results of the RN4CAST survey in Italy. *J Adv Nurs*. 2017;73(9):2028-2030. Doi: 10.1111/jan.13066
11. Wang K, Zeng X, Li J, Guo Y, Wang Z. The prevalence and risk factors of work-related musculoskeletal disorders among nurses in China: A systematic review and meta-analysis. *Int J Nurs Stud*. 2024;157:104826. Doi: 10.1016/j.ijnurstu.2024.104826
12. Rosa D, Terzoni S, Dellafiore F, Destrebecq A. Systematic review of shift work and nurses' health. *Occup Med (Lond)*. 2019;69(4):237-243. Doi: 10.1093/occmed/kqz063
13. Ilmarinen J. Work ability – A comprehensive concept for occupational health research and prevention. *Scand J Work Environ Health*. 2009;35(1):1-5. Doi: 10.5271/sjweh.1304

14. Ilmarinen J. The work ability index (WAI). *Occup Med*. 2007;57(2):160. Doi: 10.1093/occmed/kqm008
15. Tuomi K, Työterveyslaitos. *Work ability index*. 2nd rev. ed. Occupational health care, 19. Finnish Institute of Occupational Health; 1998.
16. Tuomi K, Huuhtanen P, Nykyri E, Ilmarinen J. Promotion of work ability, the quality of work and retirement. *Occup Med (Lond)*. 2001;51(5):318-24. Doi: 10.1093/occmed/51.5.318
17. von Bonsdorff MB, Seitsamo J, Ilmarinen J, Nygård CH, von Bonsdorff ME, Rantanen T. Work ability in midlife as a predictor of mortality and disability in later life: a 28-year prospective follow-up study. *Cmaj*. 2011;183(4):E235-42. Doi: 10.1503/cmaj.100713
18. La Torre G, Grima D, Romano F, Polimeni A. Perceived work ability and work-family conflict in healthcare workers: An observational study in a teaching hospital in Italy. *J Occup Health*. 2021;63(1):e12271. Doi: 10.1002/1348-9585.12271
19. Garzaro G, Clari M, Ciocan C, et al. Physical Health and Work Ability among Healthcare Workers. A Cross-Sectional Study. *Nurs Rep*. 2022;12(2):259-269. Doi: 10.3390/nursrep12020026
20. Romero-Sánchez JM, Porcel-Gálvez AM, Paloma-Castro O, et al. Worldwide prevalence of inadequate work ability among hospital nursing personnel: A systematic review and meta-analysis. *J Nurs Scholarsh*. 2022;54(4):513-528. Doi: 10.1111/jnu.12749
21. Loyd LA, Stamler LL, Culross B. Early career nurses and moral distress: An integrative review. *Nurse Educ Pract*. 2023;73:103844. Doi: 10.1016/j.nepr.2023.103844
22. Ronchese F, Ricci F, Peccolo G, et al. Relation of the work ability index to fitness for work in healthcare and public employees in a region of Northeastern Italy. *Int Arch Occup Environ Health*. 2023;96(8):1203-1210. Doi: 10.1007/s00420-023-02001-7
23. Casolari L, Curzi Y, Mastroberardino M, et al. Factors associated with work ability among employees of an Italian university hospital. *BMC Health Serv Res*. 2024;24(1):30. Doi: 10.1186/s12913-023-10465-z
24. D'Ettorre G, Pellicani V, Caroli A, Greco M. Shift work sleep disorder and job stress in shift nurses: implications for preventive interventions. *Med Lav*. 2020;111(3):195-202. Doi: 10.23749/mdl.v111i3.9197
25. Kafle S, Paudel S, Thapaliya A, Acharya R. Workplace violence against nurses: a narrative review. *J Clin Transl Res*. 2022;8(5):421.
26. Magnavita N, Meraglia I. Poor Work Ability Is Associated with Workplace Violence in Nurses: A Two-Wave Panel Data Analysis. *Int J Environ Res Public Health*. 2024;21(9):1118. Doi: 10.3390/ijerph21091118
27. Magnavita N, Meraglia I, Viti G, Borghese L. The Work Ability Index (WAI) in the Healthcare Sector: A Cross-Sectional/Retrospective Assessment of the Questionnaire. *Int J Environ Res Public Health*. 2024;21(3):349. Doi: 10.3390/ijerph21030349
28. World Health Organization. *State of the world's nursing 2025: investing in education, jobs, leadership and service delivery*. 2025. https://www.who.int/publications/i/item/9789240110236/
29. Phillips CS, Dupree G, Kwak J, Thomas Hebdon MC. A Qualitative Study Exploring the Experience of Double-Duty Nurse Caregivers. *West J Nurs Res*. Sep 2025;47(9):836-843.Doi:10.1177/01939459251348135
30. Clendon J, Walker L. Nurses as family caregivers – barriers and enablers facing nurses caring for children, parents or both. *J Nurs Manag*. 2017;25(2):93-101. Doi: 10.1111/jonm.12445
31. Rony MKK, Alrazeeni DM, Akter F, et al. The role of artificial intelligence in enhancing nurses' work-life balance. *J Med Surg Public Health*. 2024;3:100135. Doi: 10.1016/j.glmedi.2024.100135
32. Sermeus W, Aiken LH, Van den Heede K, et al. Nurse forecasting in Europe (RN4CAST): Rationale, design and methodology. *BMC Nurs*. 2011;10:6. Doi: 10.1186/1472-6955-10-6
33. Aiken LH, Sloane DM, Bruyneel L, et al. Nurse staffing and education and hospital mortality in nine European countries: a retrospective observational study. *Lancet*. 2014;383(9931):1824-30. Doi: 10.1016/s0140-6736(13)62631-8
34. Demerouti E. The Job Demands-Resources Model: State of the Art. *J Manag Psychol*. 2007;22:309-328. Doi: 10.1108/02683940710733115
35. Chowdhury R, Shah D, Payal AR. Healthy Worker Effect Phenomenon: Revisited with Emphasis on Statistical Methods – A Review. *Indian J Occup Environ Med*. 2017;21(1):2-8. Doi: 10.4103/ijoem.IJOEM_53_16
36. Zhang H, Wang J, Zhang S, et al. Relationship between night shift and sleep problems, risk of metabolic abnormalities of nurses: a 2 years follow-up retrospective analysis in the National Nurse Health Study (NNHS). *Int Arch Occup Environ Health*. 2023;96(10):1361-1371. Doi: 10.1007/s00420-023-02014-2
37. Di Muzio M, Dionisi S, Di Simone E, et al. Can nurses' shift work jeopardize the patient safety? A systematic review. *Eur Rev Med Pharmacol Sci*. 2019;23(10):4507-4519. Doi: 10.26355/eurrev_201905_17963
38. Bell T, Sprajcer M, Flenady T, Sahay A. Fatigue in nurses and medication administration errors: A scoping review. *J Clin Nurs*. 2023;32(17-18):5445-5460. Doi: 10.1111/jocn.16620
39. Ferri P, Guadi M, Marcheselli L, Balduzzi S, Magnani D, Di Lorenzo R. The impact of shift work on the psychological and physical health of nurses in a general hospital: a comparison between rotating night shifts and day shifts. *Risk Manag Healthc Policy*. 2016;9:203-211. Doi: 10.2147/rmhp.S115326
40. Nelson A, Baptiste AS. Evidence-based practices for safe patient handling and movement. *Online J Issues Nurs*. 2004;9(3):4.

41. Stimpfel AW, Arabadjian M, Liang E, Sheikhzadeh A, Weiner SS, Dickson VV. Organization of Work Factors Associated with Work Ability among Aging Nurses. *West J Nurs Res*. 2020;42(6):397-404. Doi: 10.1177/0193945919866218
42. Krishnanmoorthy G, Rampal S, Karuthan SR, Baharudin F, Krishna R. Effectiveness of Participatory Ergonomic Interventions on Work-Related Musculoskeletal Disorders, Sick Absenteeism, and Work Performance Among Nurses: Systematic Review. *JMIR Hum Factors*. 2025;12:e68522. Doi: 10.2196/68522
43. Ferreira AG, Lopes MRC, Borba A, Marques APO, Alves FAP, Lima BCC. Factors associated with absenteeism in elderly nursing workers. *Rev Gaucha Enferm*. 2022;43:e20210063. Doi: 10.1590/1983-1447.2022.20210063.en
44. Burmeister EA, Kalisch BJ, Xie B, et al. Determinants of nurse absenteeism and intent to leave: An international study. *J Nurs Manag*. 2019;27(1):143-153. Doi: 10.1111/jonm.12659
45. Aiken LH, Simonetti M, Sloane DM, et al. Hospital nurse staffing and patient outcomes in Chile: a multilevel cross-sectional study. *Lancet Glob Health*. 2021;9(8):e1145-e1153. Doi:10.1016/s2214-109x(21)00209-6
46. Dulko D, Kohal BJ. How Do We Reduce Burnout In Nursing? *Nurs Clin North Am*. 2022;57(1):101-114. Doi: 10.1016/j.cnur.2021.11.007
47. Bahlman-van Ooijen W, Malfait S, Huisman-de Waal G, Hafsteinsdóttir TB. Nurses' motivations to leave the nursing profession: A qualitative meta-aggregation. *J Adv Nurs*. 2023;79(12):4455-4471. Doi: 10.1111/jan.15696
48. El-Helaly M. Artificial Intelligence and Occupational Health and Safety, Benefits and Drawbacks. *Med Law*. 2024;115(2):e2024014. Doi: 10.23749/mdl.v115i2.15835

APPENDIX

Supplemental Material

Table S1. Work Ability Index (WAI) scores disaggregated by sex and dimensions.

WAI Dimensions	Total (N=182)	Male (n=32)	Female (n=150)	p-value
Total WAI Score (range 7-49)	37.2 ± 6.3	**39.3 ± 5.6**	**36.7 ± 6.4**	**0.039**
WAI 1: Current WA (range 0-10)	7.4 ± 1.6	7.6 ± 1.3	7.4 ± 1.6	0.512
WAI 2: WA vs job demands (range 2-10)	8.0 ± 1.3	8.3 ± 1.2	7.9 ± 1.3	0.167
WAI 3: Diagnosed diseases (range 1-7)	3.8 ± 2.3	**4.9 ± 2.0**	**3.5 ± 2.4**	**0.003**
WAI 4: Work impairment (range 1-6)	4.9 ± 1.2	5.3 ± 0.9	4.9 ± 1.3	0.058
WAI 5: 12 months sick leave (range 1-5)	3.8 ± 1.0	3.8 ± 1.1	3.8 ± 1.0	0.908
WAI 6: Own 2-year prognosis (range 1-7)	6.1 ± 1.6	6.5 ± 1.4	6.0 ± 1.6	0.092
WAI 7: Mental resources (range 1-4)	3.1 ± 0.7	3.1 ± 0.8	3.1 ± 0.8	0.918

WAI: Work Ability Index; WA: Work Ability.
Data are presented in Mean Scores ± Standard Deviations. Higher WAI scores indicate better work ability. Bold values indicate statistical significance.

Table S2. Multivariable Logistic Regression Model for Predictors of Adequate Work Ability

Predictor	B	S.E.	Wald	p-value	OR (95% CI)
Age	-0.07	0.02	10.43	**0.001**	0.93 (0.89–0.97)
Sex (Female vs Male)	0.44	0.56	0.62	0.431	1.55 (0.52–4.62)
Married/Partnered (Yes vs No)	0.13	0.53	0.06	0.804	1.14 (0.40–3.20)
Children (Yes vs No)	-0.48	0.50	0.91	0.339	0.62 (0.23–1.65)
BMI categories[a]			4.05	0.132	-
Underweight vs Overweight	1.15	0.90	1.64	0.200	3.16 (0.54–18.39)
Normal Weight vs Overweight	0.83	0.45	3.41	0.065	2.28 (0.95–5.49)
Smoking (Yes vs No)	0.55	0.56	0.96	0.328	1.73 (0.58–5.15)
Extra-work caregiving, assistance or educational activities (hours/week)	-0.03	0.01	4.17	**0.041**	0.97 (0.94–0.99)
Job Satisfaction	0.88	0.34	6.56	**0.010**	2.41 (1.23–4.71)
Constant	1.28	1.41	0.83	0.362	3.61

B: regression coefficient; S.E.: standard error; Wald: Wald chi-square statistic; OR: odds ratio; CI: confidence interval. Reference category for the dependent variable: Inadequate work ability. [a] *Reference category for BMI: Overweight/Obese. Model diagnostics: Omnibus model* $\chi^2(9)=31.026$, $p<0.001$; *Nagelkerke* $R^2 = 0.293$; *Hosmer-Lemeshow test:* $\chi^2 = 7.117$, $p=0.524$. *Correct classification rate: 71.1%.*

La Medicina del Lavoro

Short communication

Med. Lav. 2026; 117 (1): 18631
DOI: 10.23749/mdl.2026.18631

The Evolving Landscape of Contact Dermatitis Diagnosis: A Critical Appraisal of Recent Regulatory Constraints

Marco Polonioli[1,*], Marco Dubini[2], Silvia Mariel Ferrucci[3], Paolo Marraccini[2]

[1]Post Graduation School of Occupational Medicine, Università degli Studi di Milano, Milan, Italy
[2]General Medicine, Immunology, and Allergology Unit, IRCCS Foundation Ca' Granda, Ospedale Maggiore Policlinico, Milan, Italy
[3]Dermatology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

Keywords: Occupational Allergic Contact Dermatitis; Allergic Contact Sermatitis; Patch Test; Haptens

Summary

The current limited availability of patch tests for diagnosing Allergic Contact Dermatitis (ACD) and occupational or non-professional diseases, in accordance with AIFA regulations, has significantly affected the diagnostic approach for patients and affected workers. The issue is even more severe for haptens of occupational origin. In occupational medicine, the patch test is crucial for establishing the causal link between the skin disease and the patient's work activities. Accurate diagnosis is essential for occupational physicians both to determine the need for a job change and to assess workers' compensation. Due to limited diagnostics and regulatory restrictions, it remains impossible to diagnose occupational ACD. In this context, occupational doctors will focus on primary prevention by avoiding risk products and replacing them with non-sensitizing or non-cross-reactive alternatives. This paper addresses the challenges posed by the new AIFA (Italian Medicines Agency) diagnostic restrictions and explores potential solutions and future perspectives.

1. Introduction

Allergic contact dermatitis (ACD) is characterized by skin inflammatory processes that account for about 60% of cutaneous eczemas [1], caused by contact with various environmental allergens, aside from occupational ones [2]. Specifically, Occupational Allergic Contact Dermatitis (OACD) is estimated to affect between 6.7% and 10.6% of cases [3], although this data might be underestimated [2]. OACD is responsible for approximately one-third of all occupational diseases in industrialized countries [4]. A wide range of occupations are at risk for skin disease, including bakers, cooks, hairdressers, beauticians, butchers, and other personal service workers [5]. OACD is a well-known Type IV hypersensitivity reaction that occurs in workers with repeated skin exposure to sensitizing haptens. The epicutaneous test (patch test) is an in vivo test and the gold standard for diagnosing OACD, confirming the causal relationship between work and the disease [6]. In the past, we used well-established clinical protocols to diagnose suspected OACD, employing standardized epicutaneous tests combined with occupational history and job analysis. The collaboration between occupational physicians and allergists/dermatologists

Received 01.02.2026 – Accepted 22.04.2026
* Corresponding Author: Marco Polonioli E-mail: marco.polonioli@icloud.com

was straightforward because occupational doctors could request predefined epicutaneous test series from allergists during routine health surveillance. Today, this process is more challenging since these professional series are no longer available on the market. This paper discusses current challenges and the best approaches for diagnosing OACD, starting with the European Guideline on haptens and their Italian transcription [7, 8].

2. Methods

The current regulatory classification of haptens for patch tests as medicinal products dates back to Directive 89/343/EEC, which extended the same obligations to these products as for all medicinal products regarding production, marketing authorization, and clinical use (Autorizzazione Immissione Commercio – AIC). In Italy, the process of regulating allergenic medicines began with the Ministerial Decree Healthcare of December 13, 1991, and experienced a long period of inactivity. Recently, it was resumed with AIFA (Italian Medicines Agency) DG Resolution n. 2130/2017, which established the criteria for completing the process and the possible issuance of the AIC for allergens on the market by law (ope legis): owners of allergen products used for diagnosis (i.e., haptens for patch tests) are required to submit an updated dossier for each hapten. To ensure patients' right to health, it was also necessary to publish a list of haptens temporarily authorized for marketing, attached to AIFA DG Resolution n. 98/2022, which is revised and updated whenever there are production changes or significant literature updates. In conclusion, the allergenic medicines currently on the market in Italy are three types: medicines with regular marketing authorization (AIC), medicines authorized for marketing by law (ope legis), and medicines marketed as specific products for individual patients (Named Patient Products – NPP). The products marketed ope legis (pursuant to the Health Ministerial Decree of December 13, 1991) are legally equivalent to products with an AIC. Products marketed as NPP are medicinal products prepared industrially upon written and unsolicited requests from a doctor, who commits to using the products on a specific patient under their direct and personal responsibility. Patch test haptens cannot be classified as NPP because they are produced through a standardized process for use in a plurality of patients and not nominally intended for a single person.

3. Results

The final process for AIC is currently underway; it involves the regulatory and technical-scientific evaluation of the dossiers filed for the admitted products with the purpose of issuing the AIC. Until this process is completed, the medicines admitted for evaluation will remain on the market as ope legis [9, 11]. Therefore, the conclusion of the first phase and the start of the next phase revealed many critical issues in the sector, creating a situation of unmet clinical need. In particular, regarding patch tests, the Italian Society of Dermatology and Sexually Transmitted Diseases (SIDeMaST) reported serious difficulties in diagnosing ACD or OACD, and in implementing suitable secondary prevention measures, resulting in increased direct costs (therapy for patients) and indirect costs (absence from work) [10, 11, 12]. To identify the best solutions to meet the needs of professionals and patients, and to develop guidelines aligned with the latest scientific standards and regulatory requirements, AIFA Technical Table was established to detect clinical test haptens through AIFA DG Determination n° 134/2022 (updated by AIFA DG Determination n° 447/2022). In occupational medicine, the patch test is essential for establishing the causal link between skin disease and the patient's work activity. Accurate diagnosis of OACD is vital for occupational physicians when deciding on job changes. The lack of recognition of the occupational nature of contact dermatitis prevents worker compensation from Italian Working Compensation Authority (INAIL) and contributes to underestimating the number of reported occupational diseases whose incidence in Italy is already low. Currently, most occupational haptens are not represented by commercially available haptens. In these cases, occupational doctors must use products from commercial or natural sources and resort to the extemporaneous preparation of patch tests. To ensure standardized procedures, a quality assurance

document for these preparations should be developed, updating the information provided by the Official Italian Pharmacopoeia for preparing extemporaneous medicines in pharmacies and radiopharmaceuticals in nuclear medicine. This document is being drafted by experts from the Technical Table and the Secretariat for the Official Pharmacopoeia.

4. Discussion

The limited availability of patch tests for diagnosing ACD and occupational or non-professional diseases, according to AIFA regulations, has significantly impacted how patients and workers are diagnosed. In an unpublished study conducted in 2023 at our center, involving 437 patients, we observed a 44.5% rate of sensitizations compared to 52.1% reported in the literature [13, 14]; this difference may be due to a larger panel of haptens used in other countries where regulatory restrictions were not enforced. Among 14 workers with suspected OACD, 25.6% of sensitizations were identified using haptens without AIC. These cases could be missed with new diagnostic restrictions. Due to the limited supply of AIC tests, the near-future outlook in Italy is not promising. Occupational physicians, allergists, and dermatologists should increase their use of patch tests with products in use, similar to past practices where doctors prepared "at-home" epicutaneous tests. According to recent regulatory proposals, a quality assurance document (currently in progress) should be required, unlike the improvised preparations of the past. Currently, only a few authorized occupational allergology/dermatology centers can ensure standardized preparation procedures. Such an approach requires time and is complex because it demands technical knowledge and supplied materials. Additionally, it's challenging to compile a comprehensive list of chemicals in specific workplaces or review safety data sheets, which are often incomplete due to missing sensitizing compounds. Haptens may also be listed under various names, adding to the complexity. A specialized occupational allergist/dermatologist's expertise, including toxicological knowledge and awareness of industrial production cycles, is essential. Beyond identifying products, allergens, and critical manufacturing phases, the regulatory framework for AIC and related legislation should facilitate case-specific extemporaneous patch testing through more nuanced analysis. Without these developments, limited diagnostics and regulatory restrictions may prevent accurate diagnosis of OACD. In this context, occupational physicians should focus on primary prevention by avoiding hazardous products that could be replaced with non-sensitizing, non-cross-reactive alternatives. If technological or environmental modifications are unfeasible, educational efforts, reduced exposure (such as shift work), and preventive measures (secondary prevention) should be adopted. For example, wearing gloves that are regularly changed and possibly combined with cotton underneath can protect not only hands but also part of the arms. Barrier creams may also be effective depending on the specific task and substances involved, but it is important to note that manual work involving hand rubbing can remove the cream, potentially giving workers a false sense of security.

5. Conclusion

In conclusion, new perspectives are emerging that require more complex analysis. Allergists and dermatologists need to collaborate with occupational doctors to identify new diagnostic tools and empirical approaches in light of stricter regulations. The key is always gaining more knowledge of the processes and identifying critical points. Therapies and health monitoring after implementing preventive measures can be successful, but strong support from specialists is now necessary. New approaches and tailored diagnoses are needed; understanding the problems and solutions from the perspective of expanding diagnosis remains the ultimate goal, which is closely tied to the available haptens [15].

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Declaration of Interest: The authors declare no conflict of interest.

Author Contribution Statement: P.M. conceived the study. M.P., P.M. draft the manuscript. All authors revised and approved the manuscript for intellectual content.

References

1. Nassau S, Fonacier L. Allergic Contact Dermatitis. *Med Clin North Am*. 2020;104(1):61–76.
2. Luckhaupt SE, Dahlhamer JM, Ward BW, et al. Prevalence of dermatitis in the working population, United States, 2010 National Health Interview Survey. *Am J Ind Med.* 2010;56(6):625–634.
3. Mostosi C, Simonart T. Effectiveness of barrier creams against irritant contact dermatitis. *Dermatology*. 2016; 232(3):353–62.
4. Diepgen TL, Coenraads PJ. The epidemiology of occupational contact dermatitis. *Int Arch Occup Environ Health.* 1999;72(8):496–506.
5. Marraccini P. Occupational Allergy. In: Oddone E, editor. Occupational Exposure and Health Risks. New York: Nova Science Publishers; 2016. p. 147–164.
6. American Accademy of Allergy. Asthma and Immunology: American College of Allergy, Asthma and Immunology. Contact dermatitis: a practice parameter. *Ann Allergy Asthma Immunol*. 2006;7(3 Suppl.2):S1–38.
7. D.Lgs 178/1991: recepimento delle direttive della Comunità economica europea in materia di specialità medicinali. (GU Serie Generale n.139 del 15-06-1991)
8. D.Lgs 219/2006: attuazione della direttiva 2001/83/CE (e successive direttive di modifica) relativa ad un codice comunitario concernente i medicinali per uso umano, nonché della direttiva 2003/94/CE. (GU Serie Generale n.142 del 21-06-2006 – Suppl. Ordinario n. 153)
9. AIFA. Available online: www.aifa.gov.it
10. Regulation and clinical use of haptens for patch test rev. 1. Rome: Italian Medicines Agency, 2024. ISBN 979-12-80335-33-3. Available online: www.aifa.gov.it
11. Regolamentazione e uso clinico degli apteni per patch test. Roma: Agenzia Italiana del Farmaco, 2023. Available on: www.aifa.gov.it
12. Relazione annuale dell'Area Autorizzazioni Medicinali. Anno 2022. Avaible on: www.aifa.gov.it
13. Uter W, Schwitulla J, Thyssen JP, et al. The 'overall yield' with the baseline series – a useful addition to the array of MOAHLFA factors describing departmental characteristics of patch tested patients. *Contact Dermatitis*. 2011;65(6):322-8.
14. Uter W, Bauer A, Belloni Fortina A, et al. Patch test results with the European baseline series and additions thereof in the ESSCA network, 2015-2018. *Contact Dermatitis.* 2021;84(2):109–120.
15. Brans R, Skudlik C. Patch testing in occupational dermatology: practical aspects in relation to the conditions in Germany. *Allergol Select.* 2024;8:82–89.