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La Medicina del Lavoro

Editorial

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Reflecting on Success and Looking Towards the Future

Five years ago, *La Medicina del Lavoro* was primarily written in Italian, and the authorship was almost restricted to a few Italian groups. Our journal was available only in part in digital format, and it was accessible only by subscription. Since then, we have made significant strides. The entire collection is now available online and has open access since its foundation in 1901. From 2020 onward, all papers are written in English to reach a broader readership. This evolution is a testament to our progress and a reason to be proud. My heartfelt gratitude goes to all those who implemented new editorial lines: from Authors who have provided original and engaging material to Reviewers and Advisory Board Members who have diligently improved the manuscripts, from the Deputy Editor-in-Chief and Associate Editors to the Editorial Assistants who offered wise advice, diligent reminders, and careful technical editing. Their unique contributions have shaped the journal's trajectory, leading to a broader audience and authorship – thereby enhancing the competition for publication and, hence, the overall journal's quality. Such collective efforts, blending newcomers' willingness to contribute and editors' openness to new contributors, are deeply appreciated and integral to the journal's success. We also gratefully acknowledge the Italian Society of Occupational Medicine's sponsorship of its official journal, which allows us to rely on scientific merit as the sole criterion to decide whether to accept or decline submissions.

Today, as we face the challenges posed by Industry 4.0 and the rapid evolution of artificial intelligence, we are witnessing increased inequalities and deteriorating working conditions. Such conditions undermine workers' ability to secure a healthy and dignified life for themselves and their families. Furthermore, even advancements in the green economy may become problematic if sustainability efforts overlook their implications for the workforce.

European workers who will become unemployed are rejecting an accelerated transition toward a green economy, which is now critically perceived as a new form of fundamentalism even by the population's segments most sensitive to the problems of environmental pollution and the anthropogenic contribution to climate change. The crisis that the automotive sector is going through in Europe results from an abrupt and radical choice for electric engines and the unilateral phasing out of the endothermic ones, which will continue to operate on the rest (i.e., most) of the planet. It is time to reflect on how such a radical choice may not only be inadequate to face environmental challenges. Past experiences teach us that adopting a single strategy to address an old problem risks merely substituting a known, solvable problem with a still unknown solution that may introduce new problems even more challenging to resolve. It has been like that since lead was phased out as a fuel anti-detonant and substituted by benzene and when diesel engines were preferred over gasoline engines, making them economically advantageous. It may happen the same now, banning fossil fuels in favor of electrical engines. Apparent solutions to environmental issues might soon result in a profound political crisis for fragile Western democracies and, in the long run, can result in new, till now conspicuously underestimated, ecological disasters.

Urgent and impactful actions must also be implemented to eliminate forced labor, eradicate modern slavery, and put an end to human trafficking. Ensuring safe and protected work environments for all employees, including migrants, especially female migrants and "invisible" workers in unstable employment situations, should become a priority for our governments, envisioning a role for occupational health to serve workers facing climate change and challenging environmental circumstances.

We cannot forget our roots and will continue pursuing the goal of ensuring the integrity and quality of

Occupational Medicine research while disseminating its scientific results. Our commitment to occupational health is unwavering, even in the face of new epidemics and winds of war that threaten a continent that has lived in peace and prosperity for three-quarters of a century. This commitment is a testament to our determination to overcome the challenges that sometimes unexpectedly arise, and it should reassure all of us about the journal's mission.

Occupational health physicians practicing to serve on the front lines directly impact the health and safety of workers in various work environments. Their insights, experience, and dedication are invaluable in shaping evidence-based practices and policies that promote a healthier and safer workplace. However, the key to our success lies in collaboration. By bridging the gap between academia and the actual challenges in working settings, we can recognize the importance of cooperation between academia and practice. Establishing channels for dialogue, sharing best practices, and integrating academic research with real-world applications will enhance the impact of our collective efforts, driving positive change in occupational health. By fostering collaboration and knowledge sharing among educational institutions and practitioners, we can address emerging issues and nurture the next generation of occupational health professionals. Let's be inspired to work together for a healthier and safer workplace.

Antonio Mutti

La Medicina del Lavoro

Reviews, commentaries, perspectives

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Per- And Poly-Fluoroalkyl Substances (PFAS) Exposure and Risk of Breast, and Female Genital Cancers: A Systematic Review and Meta-Analysis

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Keywords: Breast; Occupational Factors; Endometrial; Female Genital; Malignant; Endocrine Gland; Hormone; Perfluorooctanoic Acid; PFAS; Perfluorooctane Sulfonic Acid

Abstract

Background: *PFASs, synthetic chemicals, can be encountered by humans through occupational or environmental exposure, and some reports suggest that they can disrupt endocrine and hormonal activities. In this comprehensive review and meta-analysis, we explored the connection between exposure to PFASs and the risks of breast and female genital cancers.* **Methods:** *We systematically reviewed the literature from IARC Monographs, ATSDR documents, and PubMed (as of January 2024) for cohort, case-control, and ecological studies on PFAS exposure and breast or female genital cancers. Four reviewers independently screened studies, and data extraction included study design, patient characteristics, and effect size measures. The quality of studies was assessed using the modified version of the Newcastle-Ottawa Scale (NOS). Forest plots of relative risks (RR) were constructed for breast and female genital cancer. Meta-analyses were conducted using random-effects models, stratified analyses, dose-response assessments, and publication bias evaluation.* **Results:** *The meta-analysis included 24 studies, comprising 10 cohort, 13 case-control, and one ecological study. The summary relative risk (RR) of breast cancer for PFOA exposure was 1.08 (95% CI = 0.97-1.20; n=21), and for PFOS was 1.00 (95% CI = 0.85-1.18; n=12). The RR for ovarian cancer and PFAS was 1.07 (95% CI = 1.04-1.09; n=12). The stratification by quality score, year of publication, and exposure source did not reveal any differences. However, analysis by geographical region (p=0.01) and study design (p=0.03) did show differences, particularly in terms of incidence. Stratified analyses of the dose-response relationship did not reveal a trend in the risk of breast cancer or female genital cancers, and no publication bias was found for either cancer type. No results were available for cervical and endometrial cancers.* **Conclusion:** *In summary, our results suggest an association between PFAS exposure and ovarian cancer and a possible effect on breast cancer incidence in some specific groups. However, bias and confounding cannot be excluded and prevent conclusions regarding causality.*

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Abbreviations:

- Agency for Toxic Substances and Disease Registry; ATSDR
- The Environmental Protection Agency; EPA
- The European Chemicals Agency; ECHA
- Endocrine-disrupting chemicals; EDCs
- Human papillomavirus; HPV
- The International Agency for Research on Cancer; IARC
- Nitrogen dioxide; NO2
- Odds ratio; OR
- Risk ratio, rate ratio; RR
- Standardized mortality ratio; SMR
- Standardized incidence ratio; SIR
- Perfluorooctanoic Acid; PFOA
- Per- and poly-fluoroalkyl substances; PFAS
- Perfluorooctane sulfonic acid; PFOS
- Perfluorononanoic acid; PFNA
- Perfluorobutane sulfonate; PFBS
- Perfluorohexanesulfonic acid; PFHxS

1. Introduction

Breast cancer (BC) is the most commonly diagnosed cancer (ASR=46.8 per 100,000) and the leading cause of cancer death (ASMR=12.7 per 100,000) among females worldwide in 2022 [1]. Also, female genital organ cancers (vulva, vagina, cervix, endometrium, ovary) account for approximately 15% of all female cancer cases and fatalities worldwide [1]. Previous studies reported an association between several factors, including demographic, lifestyle, socioeconomic, and infection factors, with the incidence and mortality of these cancers [2, 3]. Furthermore, these studies have been associated with specific occupational and environmental agents, especially those that can impact endocrine glands. These factors include exposure to ionizing and non-ionizing radiation, working night shifts, being exposed to pesticides, asbestos, polycyclic aromatic hydrocarbons (PAH), per- and polyfluoroalkyl substances (PFASs), as well as other job exposure agents [4, 5, 14].

PFASs are a large, complex group of synthetic chemicals that are thermally and chemically stable in the environment [6]. The most commonly used PFAS are perfluorooctane sulfonic acid (PFOS), perfluorooctane sulfonic acid (PFOA), perfluorononanoic acid (PFNA), perfluorobutane sulfonate (PFBS), perfluorohexanesulfonic acid (PFHxS) [8]. These substances have been used in the aerospace, automotive, construction, and electronics industries since the 1940s. They also produce stain- and water-resistant fabrics, firefighting foams, cleaning products, and paints. Humans can be exposed to these substances through occupational and environmental sources such as water, air, and soil [7, 9].

The International Agency for Research on Cancer (IARC) classified PFOA as carcinogenic to humans (Group 1) and PFOS as possibly carcinogenic to humans (Group 2B), mainly based on an association with kidney and testicular cancers [10, 11]. In addition, there is some evidence that other types of cancer, such as breast and female genital cancer, are associated with PFAS exposure, but the evidence remains limited [12-14].

To better clarify the potential effects of PFAS on cancer incidence and mortality, we conducted a systematic review and meta-analysis of occupational and environmental exposures to PFAS and the risk of breast and female genital cancers.

2. METHODS

2.1. Data Sources, Search Strategy, Selection Criteria

First, searches were undertaken on January 23, 2024, for English-language peer-reviewed publications in PubMed and Scopus with no limit according to year of publication to identify more recent studies. Our work included studies on incidence or mortality from all solid and non-solid cancer types other than liver, kidney, and testicular, which were included in a previous report (12), and exposure to different types of PFAS, including PFOA, PFOS, PFDA, and PFNA. Then, we searched the reference lists of the IARC Monograph on PFOA/PFOS (10) and the Agency for Toxic Substances and Disease Registry (ATSDR) Toxicological Profile of PFAS (15). Our study protocol was registered in the PROSPERO database (Registration No. CRD42024560837), and we followed the COSMOS-E and PRISMA-statements to conduct and report systematic reviews and meta-analyses (16,17) (Supplementary Tables 7a, b).

The search strategy utilized the following MeSH terms: ((“PFOA” OR “Perfluorooctanoic Acid” OR “PFOS” OR “Perfluorooctane Sulfonic Acid” OR “PFAS” OR “per and poly-fluoroalkyl substances”) AND (“cancer” OR “malignant” OR “carcinoma” OR “neoplasm” OR “tumor” OR “myeloid” OR “lymphoma” OR “Hematologic”)). The complete search string is reported in Supplementary Table 1.

We only included cohort, case-control, cross-sectional, and ecological human studies of occupational and environmental exposure to PFAS, including studies based on serum level, drinking water, or workplace exposure to PFAS. Studies involving animals or other non-human experimental systems were excluded. Also, we excluded studies in which we needed help finding the full text of the relevant articles. Four reviewers independently screened the titles and abstracts. The final selection was made after thoroughly reviewing the full text of potentially relevant articles. If multiple reports utilized the same database, we only included the most informative article with the most recent update.

The data extraction file contained demographic characteristics of the original studies, such as the author’s name, year of publication, country, study design type (cohort, case-control, ecological), patient characteristics (sex), cancer type, PFAS types, PFAS exposure source (occupational or environmental), duration and level of exposure. We also extracted the effect sizes measures, such as relative risks (RRs), odds ratios (ORs), risk ratios, rate ratio, standardized mortality ratio (SMR), or standardized incidence ratio (SIR), as well as their respective 95% confidence intervals (CI). If results were reported only for subgroups, we combined them using a fixed effect meta-analysis. When RRs or CIs were not reported, we calculated them from the raw data if possible. This strategy led to the identification of 39 independent studies related to different solid and non-solid cancer types other than liver, kidney, and testicular cancer (Figure 1). In this report, our analysis contained 24 studies that addressed breast cancer (24 studies) and also female genital cancer only (6 studies) (Figure 1).

2.2 Quality Assessment

Four independent reviewers critically appraised the eligible studies using a modified version of the Newcastle-Ottawa Scale (NOS) (Supplementary Table 2) [18] for case-control, ecological, and cohort studies.

The scores were divided into two categories: low quality if the study scored less than 8 and high quality if it scored 8 or higher (Table 1).

2.3 Statistical Analysis

In this report, we examined the exposure to total and different types of PFAS and incidence or mortality from breast and female genital (ovarian, cervix, and uterus, the latter comprising endometrium and uterus not otherwise specified) cancers based on the RR and the respective 95% CIs. Heterogeneity among studies was assessed using the Q test, which evaluated variation across studies rather than within them, and the I^2 statistic, which indicates the percentage of variance in a meta-analysis attributable to study heterogeneity [19]. Random-effect models were used for the meta-analysis to

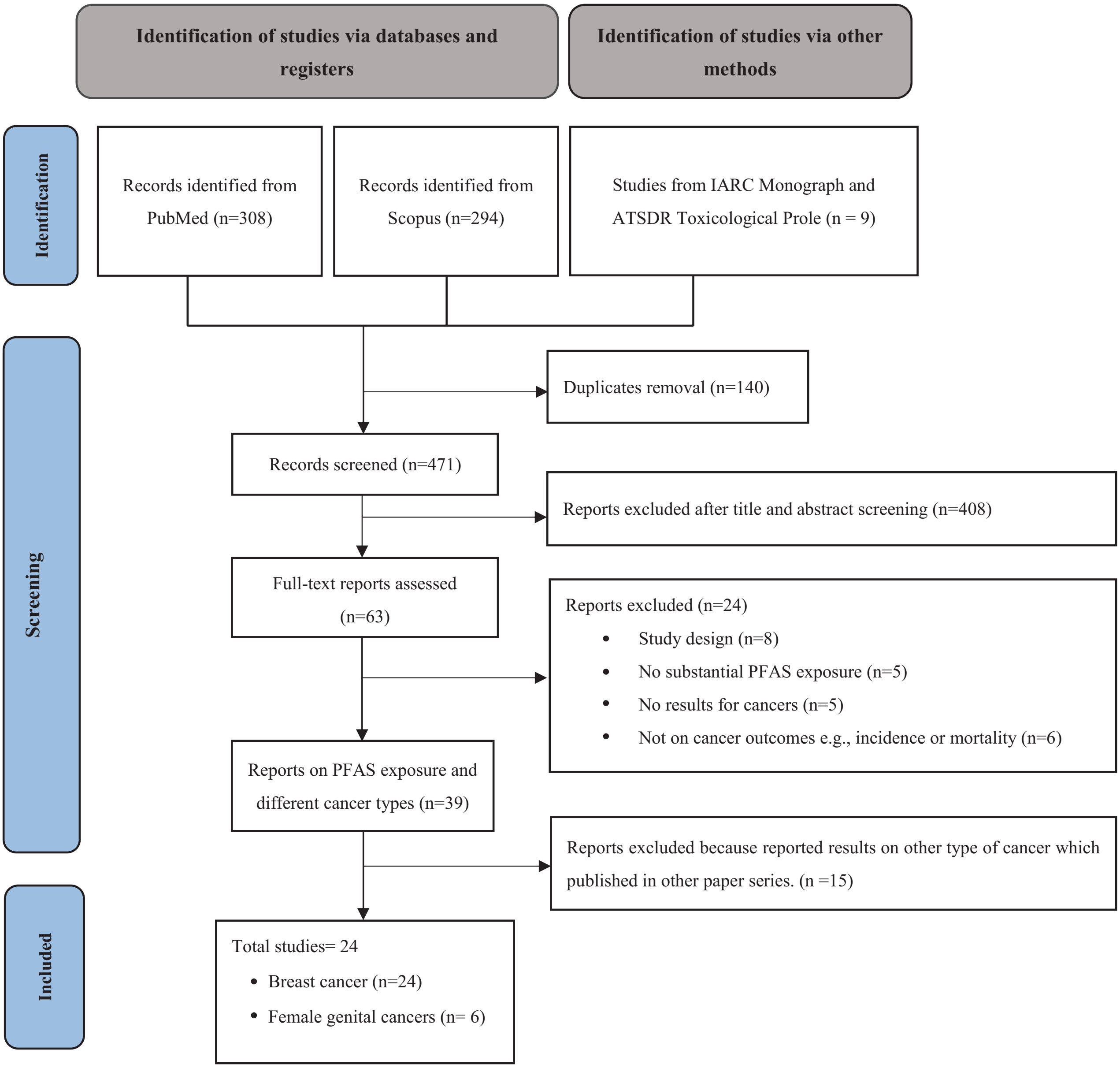

Figure 1. Selection of studies for inclusion in the review and meta-analysis.

account for heterogeneity in the design characteristics of the included studies [20]. We initially performed a meta-analysis including non-overlapping studies for each cancer type (breast and female genitals) separately. We then conducted stratified analyses by region (North America, Europe, and other areas), study design (case-control or cohort), quality score (low quality or high quality), outcome (incidence or mortality), exposure source (environmental, occupational), gender (male/female/both), and year of publication (<2019, >= 2019).

In addition, we performed a meta-regression of the RR on the quality scores. We also extracted dose-response results, including analyses by level of low, medium, or high exposure (Table 2 and Supplementary Tables 5, and 6). We conducted a meta-analysis

Table 1. Selected characteristics of the studies included in the review and meta-analysis.

Ref.	First Author, Year	Country	Study Type	Measure Source	Gender	Exposure Source	Pfas Type	Cancer Type	Outcome	Quality S.
22	Gilliland FD (1993)	US-MN	cohort	Job history	Female	Occupational	PFOA	Breast	Mortality	8
23	Alexander BH (2003)	US-AL	cohort	Serum sample	Both	Occupational	PFOS	Breast	Mortality	6
24	Leonard RC (2008)	US-WV	cohort	Serum sample	Both	Occupational	PFOA	Breast	Mortality	6.5
25	Bonefeld-Jorgensen EC (2011)	GL & CA	case-control	N/A	Female	Environmental	PFOS, PFOA	Breast	Incidence	7.5
26	Steenland K (2012)	US-WV	cohort	Serum sample	Both	Occupational	PFOA	Breast	Mortality	7
27	Barry V (2013)	US-WV	cohort	Serum sample	Both, Female	Occupational & Environmental	PFOA	Breast, Cervix, Ovarian, Uterus	Incidence	8.5
28	Vieira VM (2013)	US-OH & US-WV	case-control	Serum sample	Female	Environmental	PFOA	Breast, Cervix, Ovarian, Uterus	Incidence	7
29	Raleigh KK (2014)	US-MN	cohort	Work records	Both	Occupational	PFOA	Breast	Mortality	8
30	Bonefeld-Jørgensen EC (2014)	DK	case-control	Serum sample	Female	Environmental	PFOS, PFOA, PFNA	Breast	Incidence	8.5
31	Wielsøe M (2017)	GL	case-control	Serum sample	Female	Environmental	PFOS, PFOA, PFNA, PFDA	Breast	Incidence	7
32	Mastrantonio M (2018)	IT	ecological	Drinking water	Both	Environmental	PFAS	Breast	Incidence	6.5
33	Hurley S (2018)	US-CA	case-control	Serum sample	Female	Environmental	PFOA, PFNA, PFOS	Breast	Incidence	8.5
34	Mancini FR (2020)	FR	case-control	Serum sample	Female	Environmental	PFOA	Breast	Incidence	9
35	Tsai MS (2020)	TW	case-control	Serum sample	Female	Environmental	PFOS, PFOA, PFNA, PFDA	Breast	Incidence	7.5
36	Itoh H (2021)	JP	case-control	Serum sample	Female	Environmental	PFOS, PFNA, PFDA, PFOA	Breast	Incidence	7.5
37	Omoike OE (2021)	USA	case-control	Serum sample	Female	Environmental	PFOA, PFOS, PFNA	Breast, Ovarian, Uterus	Incidence	6.5

(*Continued*)

Ref.	First Author, Year	Country	Study Type	Measure Source	Gender	Exposure Source	Pfas Type	Cancer Type	Outcome	Quality S.
38	Velarde MC (2022)	PH	case control	Serum sample	Female	Environmental	PFOS, PFOA, PFNA, PFDA	Breast	Incidence	7
39	Li X (2022)	CN	case control	Serum sample	Female	Environmental	PFOA, PFDA	Breast	Incidence	7.5
40	Feng Y (2022)	CN	cohort	Serum sample	Female	Occupational	PFOA, PFNA, PFDA, PFOS	Breast	Incidence	7
41	Li H (2022)	SW	cohort	Drinking water	Male, Female	Environmental	PFAS	Breast, Cervix, Ovarian, Uterus	Incidence	7.5
42	Cathey AL (2023)	USA	case-control	Serum sample	Female	Environmental	PFOA, PFOS, PFNA,	Breast, Ovarian, Uterus	Incidence	9
43	Law HD (2023)	AU	cohort		Male, Female	Environmental	PFAS	Breast, Ovarian, Uterus	Incidence	6.5
44	Chang VC (2023)	USA	case-control	Serum sample	Female	Environmental	PFOS, PFOA	Breast	Incidence	8
45	Winquist A (2023)	USA	cohort	Serum sample	Female	Environmental	PFNA, PFOA, PFOS	Breast	Incidence	9

*BMI: body mass index, PFAS: per- and poly-fluoroalkyl substances, PFOA: perfluorooctanoic acid, PFNA: perfluorononanoic acid, PFDA: perfluorodecanoic acid, PFOS: perfluorooctanesulfonic acid; Adjusted list other than gender and age, calendar period for each reference if available. Ref. 22: race. Ref. 25: BMI, pregnancy, cotinine, breast-feeding, menopausal status. Ref. 27: smoking, alcohol consumption, education. Ref. 28: diagnosis year, smoking status, insurance provider. Ref. 30: BMI before pregnancy, gravidity, OC use, menarche age, smoking during pregnancy, alcohol intake, maternal education and physical activity. Ref. 31: BMI, cotinine levels, parity, and breastfeeding. Ref. 33: Race/ethnicity, region of residence, date of blood draw, date of blood draw2, season of blood draw, total smoking pack-years, BMI, family history of breast cancer, age at first full-term pregnancy, menopausal status at blood draw, and pork consumption. Ref. 34: Total serum lipids, BMI , smoking status, physical activity, education level, personal history of benign breast disease, family history of breast cancer, parity*age at first full-term pregnancy, age at menarche, age at menopause, use of oral contraceptives, current use of menopausal hormone therapy, score of adherence to the Western diet and to the Mediterranean diet, age at blood draw, BMI at blood draw, menopausal status at blood draw and year of blood draw. Ref. 35: Pregnant history, oral contraception use, abortion, BMI, menopause, and education level. Ref. 36: Residential area, BMI, menopausal status, age at menopause, age at first childbirth, family history of breast cancer, smoking status, physical activity, age at menarche, number of births, breastfeeding duration, alcohol intake, isoflavone intake, and education level, fish and shellfish intake, vegetable intake. Ref. 37: Education, race/ethnicity, PIR, BMI, serum cotinine. Ref. 38: Region of residence, employment status, and monthly income. Ref. 39: BMI, smoking history, age at menarche, age of menopause, parity, breastfeeding duration, use of estrogen or estrogen replacement therapy, family history of breast cancer, education, monthly household income per capita, red meat consumption, pickled, fried, smoked, barbecued food consumption. Ref. 40: BMI, smoking, drinking, marital status, education level, occupation type, batch to enter the cohort, parity, menopausal status, history of mastitis, use of hormone replacement therapy, and family history of cancer. Ref. 42: Natural log-transformed cotinine, poverty-income ratio, race, education, body mass index, and an indicator variable for the NHANES cycle to capture changing exposure and outcome trends over time. Ref. 44: Study center, race/ethnicity, education, age at menarche, age at first live birth and number of live births, age at menopause, duration of MHT use, first-degree family history of female breast cancer, personal history of benign breast disease, MI, smoking status, vigorous physical activity. Ref. 45: Race, education, smoking status, and alcohol consumption.*

Table 2. Meta-analysis of results on the level of PFAS exposure.

Characteristic	PFAS type	Dose category	RR (95% CI)	p trend
Breast	PFOA	Low (9 studies)	0.89 (0.66-1.19)	0.78
		Medium (9 studies)	1.01 (0.81-1.27)	
		High (9 studies)	0.93 (0.69-1.25)	
	PFOS	Low (6 studies)	0.87 (0.60-1.26)	0.81
		Medium (6 studies)	0.97 (0.68-1.39)	
		High (6 studies)	0.81 (0.52-1.25)	
	PFDA	Low (3 studies)	0.69 (0.28-1.69)	0.75
		Medium (3 studies)	1.09 (0.43-2.76)	
		High (3 studies)	1.09 (0.20-5.91)	
	PFNA	Low (5 studies)	0.80 (0.55-1.17)	0.85
		Medium (5 studies)	0.65 (0.35-1.22)	
		High (5 studies)	0.74 (0.41-1.34)	
Female genital	PFAS + PFOA	Low (2 studies)	0.95 (0.85,1.06)	0.20
		High (2 studies)	1.13 (0.89,1.42)	

** The p-value of the test for linear trend.*
PFAS: per- and polyfluoroalkyl substances, PFOA: perfluorooctanoic acid, PFNA: perfluorononanoic acid, PFDA: perfluorodecanoic acid, PFOS: perfluorooctanesulfonic acid.

for each exposure category and performed a meta-regression of the linear trend using weights 1, 2, and 3 for the respective exposure categories. Lastly, we assessed publication bias by creating a funnel plot and applying a regression asymmetry test [21]. Finally, a sensitivity analysis (e.g., removing one study at a time) was performed to identify potential outliers and influential studies. All statistical analyses were completed using the STATA version 17 (Stata, College Station, TX, USA).

3. RESULTS

Figure 1 shows the flow diagram for literature search and study selection. We included 24 independent studies [22-45].

The review comprised 10 cohort studies [22- 24, 26, 27, 29, 40, 41, 43, 45], 13 case-control studies [25, 28, 30, 31, 33-39, 42, 44], and one ecological study [32]. All studies had individual-level assessments of PFAS exposure except for three studies in which the assessment was not mentioned [32, 41, 43]. Details on these studies are provided in Table 1.

The studies reported 52 risk estimates for breast cancer and 27 for female genital cancer. When looking at the subgroup analysis for each PFAS type considering cancer incidence (46 risk estimates) or mortality (6 risk estimates), the summary RR of breast cancer incidence for PFOA exposure was 1.09 (95% CI = 0.98-1.21; I^2=88.5%, p-het=0.000; n=16). The subgroup analysis for PFOS for breast cancer incidence reveals the summary RR to be 1.00 (95% CI = 0.84-1.18; I^2 = 83.1%, p-het= 0.000; n=11) (Figure 2 and Supplementary Table 3).

The summary RR of different female genital cancer types included: 1) RR of cervical cancer was 0.94 (95% CI = 0.79-1.12; I^2 = 0.0%; p-het=0.858, n= 3); 2) RR of ovarian cancer was 1.07 (95% CI = 1.04-1.09; I^2 = 99.3%; p-het = 0.000, n=12); and 3) RR of uterus cancer was 0.93 (95% CI = 0.84-1.04; I^2 = 100.0%; p-het = 0.000, n=12) (Figure 3, Supplementary Table 4).

The results of stratified meta-analyses are reported in Supplementary Tables 3 and 4. No differences by type of PFAS were detected for breast cancer overall or by different outcomes. The stratification by quality score, year of publication, and

A Incidence

B Mortality

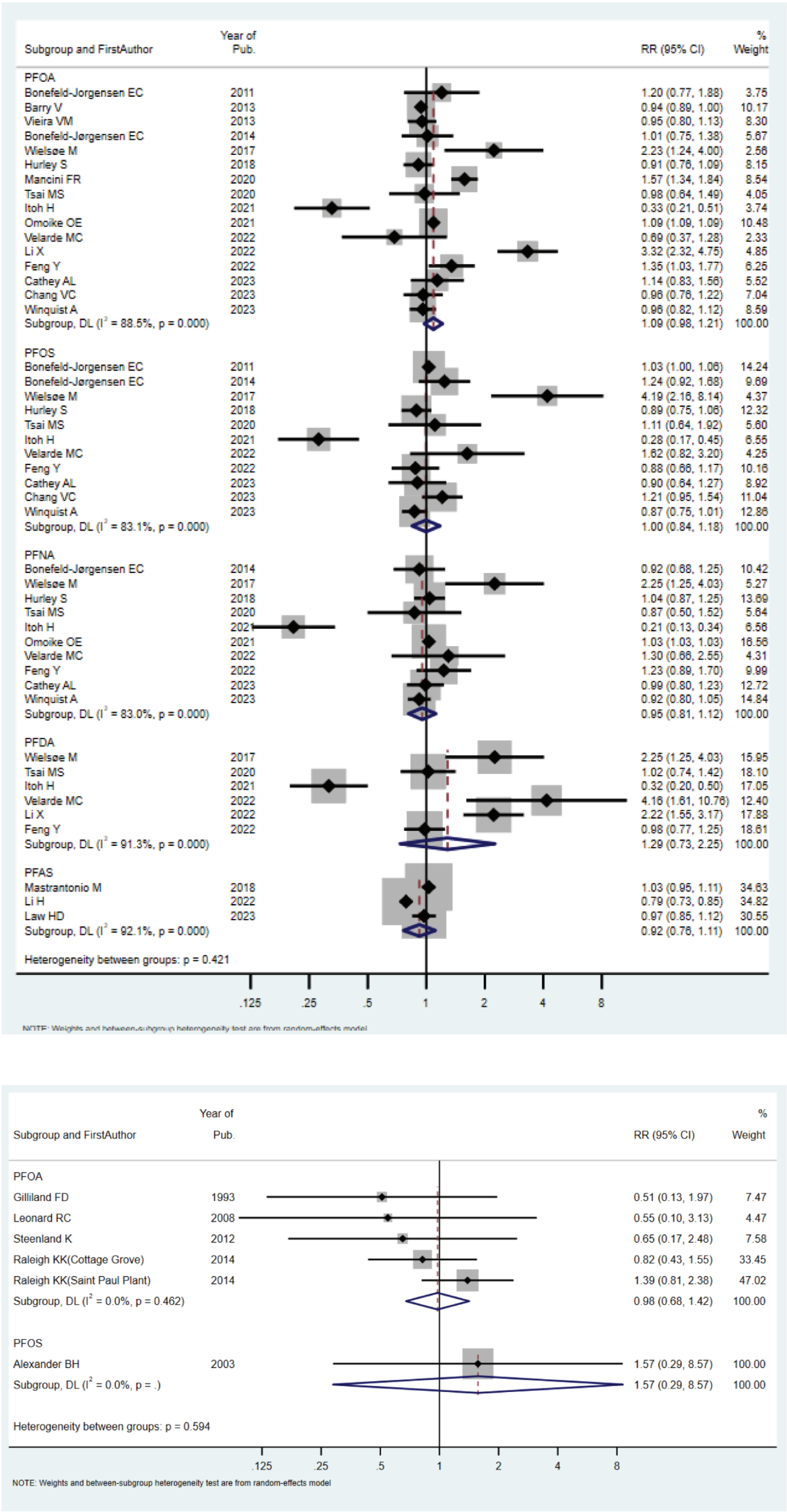

Figure 2: Forest plot (random-effects model) of results on the association between PFAS exposure and breast cancer by outcome a) incidence, b) mortality.

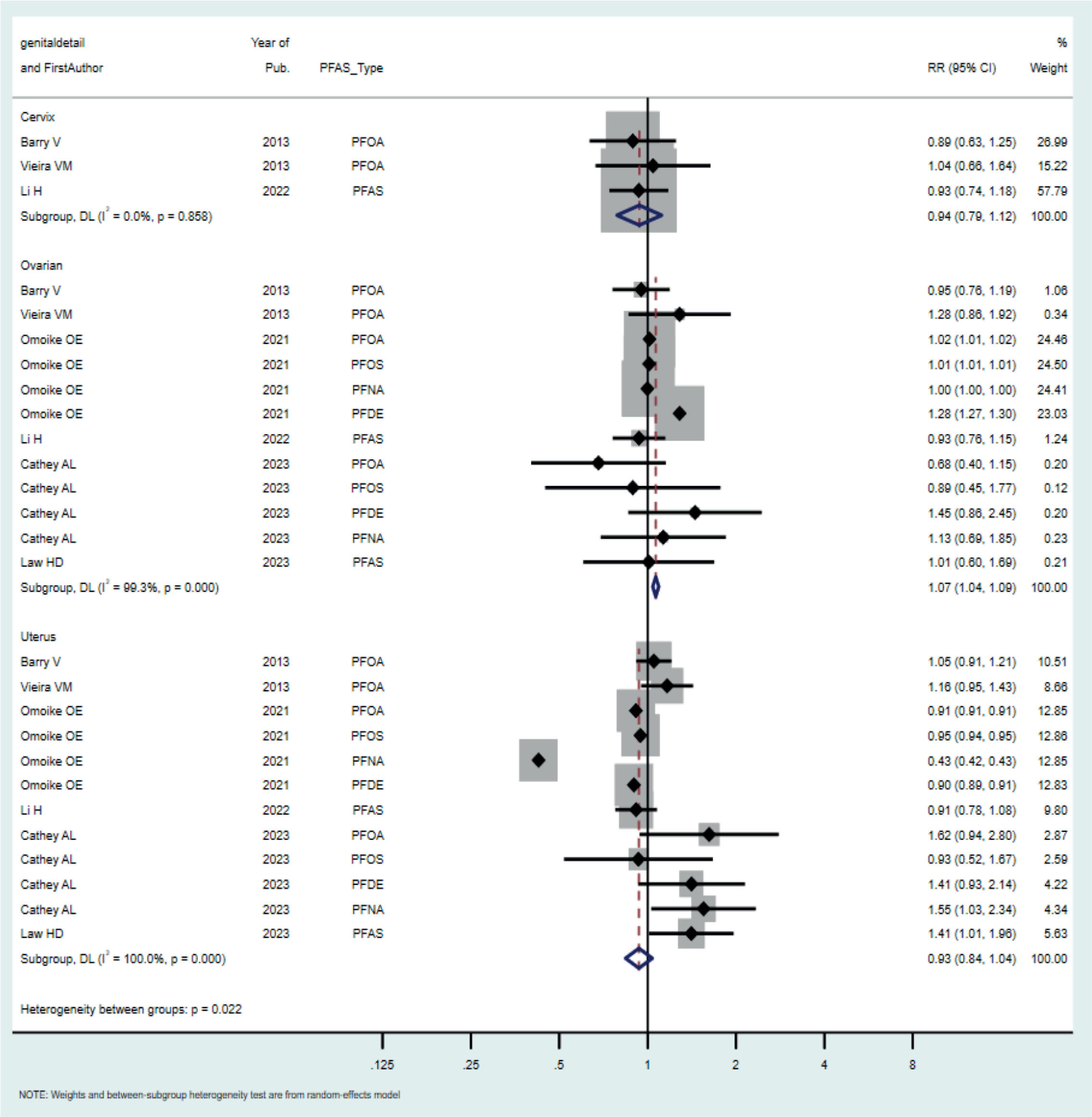

Figure 3: Forest plot (random-effects model) of results on the association between PFAS exposure and female genital cancers (cervix, ovarian, uterus) incidence.

exposure source did not show any differences in breast cancer overall or in terms of incidence and mortality. However, when considering both outcomes together, stratification by geographical region (p=0.01) and study design (p=0.03) did reveal differences with a focus on studies among European countries RR=1.36(95%CI=1.09, 1.71)and case-control design. RR=1.05 (95%CI=1.01-1.09). These results were consistent when we only looked at the incidence. Regarding mortality, all the studies were from North America and used a cohort study design (Supplementary Table 3). When we focused solely on PFOA exposure for stratification analysis, the results aligned with the overall exposure findings (Supplementary Table 3).

For ovarian cancer, stratification by geographical region, study design, outcome, quality score, year of publication, and exposure type did not reveal

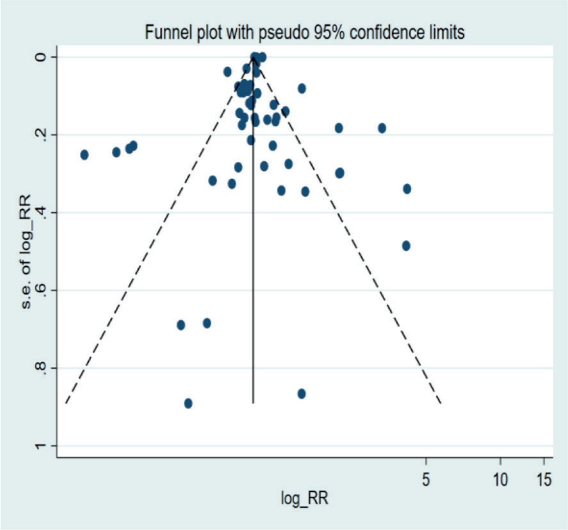

Figure 4: Funnel plot of results on the association between PFAS exposure and breast cancer. P = 0.30.

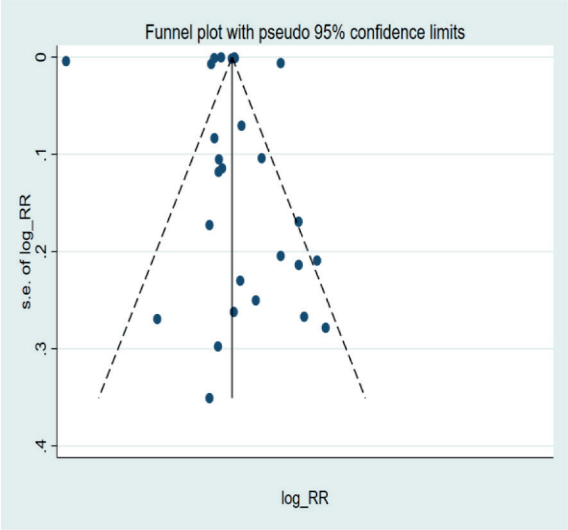

Figure 5: Funnel plot of results on the association between PFAS exposure and female genital cancers (cervix, ovarian, uterus). P = 0.55.

heterogeneity. However, the association between the North American region, case-control studies, and incidence outcomes was more effective. The results by kind of PFAS demonstrate heterogeneity ($p<0.001$), with emphasis on PFOS [RR=1.01 (95% CI =1.01, 1.02)], and PFDA [RR=1.28 (95% CI =1.27,1.30)]. For uterus cancer, stratification by study design, quality score, and type of PFAS did not reveal heterogeneity. However, stratification by geographical region (p=0.05) and year of publication (p=0.02) did.

Thirteen studies reported results on the levels (low, medium, and high) of different PFAS exposures. These results are summarized in Supplementary Tables 5 and 6. The meta-analysis of these results didn't reveal a trend in breast cancer or female genital cancer risk (Table 2). No publication bias was found for breast cancer (p=0.30) or female genital cancers (p=0.55). The funnel plots are shown in Figures 4 and 5.

In leave-one-out sensitivity analyses, pooled effect estimates for breast cancer incidence ranged from 1.02 to 1.07 (Supplementary Figure 1a), 0.76 to 1.04 for breast cancer mortality (Supplementary Figure 1b), and 0.99 to 1.3 for female genital cancer incidence (Supplementary Figure 1c), indicating that no single study substantially influenced the pooled estimate.

4. Discussion

In our systematic review and meta-analysis, we identified an association between ovarian cancer and overall PFAS exposure, as well as specific subtypes of PFOS and PFDA. However, we did not find a similar association for the cervix and uterus cancer. Additionally, we presented evidence suggesting a possible link between overall PFAS exposure, especially PFOA, and the incidence of breast cancer. Compared to others, this association was observed in specific subgroup analyses, such as studies conducted in European countries or those employing case-control study designs.

Based on previous epidemiological and experimental research, it has been consistently demonstrated that exposure to different types of PFAS through environmental or occupational sources can impact health and the activities of various organs in the human body [46]. Mechanisms such as oxidative stress and epigenetics contribute to the development of renal disorders [47, 48]. Moreover, these mechanisms can interfere with lipid metabolism, causing non-alcoholic fatty liver disease and ultimately leading to the subsequent development of cancer [49, 50]. Furthermore, the impact of PFAS on the human body remains an ongoing topic of discussion, especially concerning its adverse effects on the endocrine and immune systems. Different endocrine glands and hormones may be targeted in this process, resulting in reproductive repercussions for both males and females [51].

Consequently, glands such as the thyroid, ovary, and testicular, as well as organs like the breast, are influenced by hormones and can potentially lead to the development of diseases and cancers. This is because the PFASs interact with nuclear receptors, specifically estrogen receptors (ERs) and androgen receptors (ARs), according to the in vivo and in vitro studies [52, 53, 54]. Moreover, additional studies have indicated that PFASs, as a group of endocrine-disrupting chemicals (EDCs), may increase estrogen levels or mimic its effects, potentially contributing to the development of conditions such as breast and ovarian cancer [39]. Future research could focus on different types of breast cancer (luminal A, luminal B, HER2-positive, and triple-negative) to deepen our understanding of this relationship [63].

Several studies have indicated that the activity of PFAS on endocrine organs can be influenced by the length of the chain [55]. Long-chain PFASs such as PFOA, PFOS, PFNA, and PFDA are considered more significant. However, it is worth noting that certain short-chain PFASs, like PFHxS, can have a more negative effect [55]. Aside from chain length, the potential impact of PFAS also depends on various exposure factors, including concentration, functional group type, half-life, duration, route of exposure, and more. Additionally, factors such as age, sex, ethnicity, health status, and genetic predisposition play a role in determining the effects of PFAS exposure [56, 57]. Our study found PFOA, PFOS, and PFDA to be the most effective PFAS types. However, we should recognize that more studies focus on these subsites than others, which should be considered in future studies. Furthermore, PFAS exposure reduces mammary differentiation, induces malignant transformation of normal breast epithelial cells, and increases mammary fibroadenomas in vitro [64]. Finally, maternal PFAS exposure causes adverse birth outcomes [65], which is shown by some evidence that in-utero exposure to PFASs has been linked to breast cancer risk [66].

A recent case-control study (n=102 cases) reported a sizable, statistically significant association between in-utero exposure to EtFOSSA (a precursor to PFOS) and the risk of breast cancer in the presence of high maternal perinatal total cholesterol [67]. This result is consistent with the hypothesis that breast cancer originates in utero. Larger population-based studies are urgently needed to confirm or refute these preliminary findings.

As mentioned above, several factors related to agents and individuals can affect results. However, there are also confounding risk factors associated with outcomes. Regarding breast cancer, major risk factors include age at menarche, age at the first pregnancy, age at menopause, hormone use, alcohol consumption, obesity, and nulliparity [58]. Concerning female genital cancers, particularly the cervix, ovary, and uterus, we can mention human papillomavirus (HPV), low socioeconomic status, smoking, genetics, family history, hormone replacement therapy, nulliparity, and dietary fat [59, 60]. Of 24 studies, around 17 included in our analysis used adjusted models considering important confounders. Most of the adjusted reporters were related to the case-control studies that showed a stronger association than cohort studies.

The regional stratification analysis showed significant heterogeneity, with European and American countries differing notably from other locations, particularly concerning Asian countries, in terms of breast cancer. It is possible to interpret this phenomenon as being attributable to the elevated quantity and prolonged duration of occupational and environmental sources of pollution within these regions. Although agencies such as the Environmental Protection Agency (EPA) and the European Chemicals Agency (ECHA) have started preparing action plans to control PFAS pollution, it will take time to see beneficial results [61, 62].

To the best of our knowledge, this systematic review and meta-analysis represents the first comprehensive examination of the potential link between environmental and occupational exposure to PFAS and breast and female genital cancers. However, it is essential to acknowledge that our review has certain limitations. One major constraint is the limited number of available studies, particularly those investigating the effects of exposure to specific PFAS compounds other than PFOA. Additionally, there is a scarcity of studies reporting results from regions outside of North America and Europe, such as East Asia and sub-Saharan Africa, especially related to female genital cancers. It is worth noting that only one study focused on male breast cancer; thus, conducting stratified analyses by gender was not efficient for breast cancer. Furthermore, the number of studies examining female genital cancers other than those affecting the ovary and uterus was also limited.

5. Conclusion

In summary, our research has suggested a link between general PFAS exposure, which is known as a possible EDC, and the development of ovarian and possibly breast cancer. Specifically, evidence appears to be stronger for PFOA, PFOS, and PFDA. In addition, our findings yielded no definitive results regarding the cervix and uterus.

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Data Availability Statement: The data supporting this study's findings are available from the corresponding author upon reasonable request.

Author Contributions: PB, TZ, and MSS conceived and designed the study; MSS, EK, and SZ selected the studies and extracted the data; MSS conducted the statistical analysis; MSS and EK drafted the manuscript; SZ, TZ, and PB provided substantial comments to the results and manuscript.

Conflicts of Interest: PB acted as an expert in litigation involving PFAS exposure, which is unrelated to the present work. Other authors declare no conflict of interest.

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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.
2. Sun YS, Zhao Z, Yang ZN, et al. Risk Factors and Preventions of Breast Cancer. *Int J Biol Sci*. 2017;13(11): 1387-1397.
3. Lee CO. Gynecologic cancers: Part. I – Risk factors. *Clin J Oncol Nurs*. 2000;4(2):67-71.
4. Fenga C. Occupational exposure and risk of breast cancer. *Biomed Rep*. 2016;4(3):282-292.
5. Weiderpass E, Labrèche F. Malignant tumors of the female reproductive system. *Saf Health Work*. 2012;3(3): 166-80.
6. Li Y, Fletcher T, Mucs D, et al. Half-lives of PFOS, PFHxS and PFOA after end of exposure to contaminated drinking water. *Occup Environ Med*. 2018;75(1): 46-51.
7. Gaines LGT. Historical and current usage of per- and polyfluoroalkyl substances (PFAS): A literature review. *Am J Ind Med*. 2023;66:353-378.
8. Langenbach B, Wilson M. Per- and Polyfluoroalkyl Substances (PFAS): Significance and Considerations within the Regulatory Framework of the USA. *Int J Environ Res Public Health*. 2021;18(21):11142.
9. Panieri E, Baralic K, Djukic-Cosic D, Buha Djordjevic A, Saso L. PFAS Molecules: A Major Concern for the Human Health and the Environment. *Toxics*. 2022;10(2):44.
10. International Agency for Research on Cancer. PFOA. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, vol. 110. Some Chemicals Used as Solvents and in Polymer Manufacture. Lyon, IARC, 2017, pp. 37-110.
11. Zahm S, Bonde JP, Chiu WA, et al.Carcinogenicity of perfluorooctanoic acid and perfluorooctanesulfonic acid. *Lancet Oncol*. 2024;25(1):16-17.
12. Seyyedsalehi MS, Boffetta P. Per- and Poly-fluoroalkyl Substances (PFAS) Exposure and Risk of Kidney, Liver, and Testicular Cancers: A Systematic Review and Meta-Analysis. *Med Lav*. 2023;114(5): e2023040.
13. Ding N, Harlow SD, Randolph JF Jr, Loch-Caruso R, Park SK. Perfluoroalkyl and polyfluoroalkyl substances (PFAS) and their effects on the ovary. *Hum Reprod Update*. 2020; 26:724-752.
14. Chang ET, Adami HO, Boffetta P, Cole P, Starr TB, Mandel JS. A critical review of perfluorooctanoate and perfluorooctanesulfonate exposure and cancer risk in humans. *Crit Rev Toxicol*. 2014 May;44 Suppl 1:1-81.
15. Agency for Toxic Substances and Disease Registry. Toxicological Profile for Perfluoroalkyls. Atlanta, GA, ATSDR, 2021.
16. Dekkers OM, Vandenbroucke JP, Cevallos M, Renehan AG, Altman DG, Egger M. COSMOS-E: guidance on conducting systematic reviews and meta-analyses of observational studies of etiology. *pLoS Med*. 2019;16.

17. Moher D, Liberati A, Tetzlaff J, Altmann DG. The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *Ann Intern Med.* 2009;151:264-69.
18. Stang A, Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol*. 2010; 25:603–605.
19. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*. 1986;7:177-88.
20. Higgins J.P, Thompson, S.G. Quantifying heterogeneity in a meta-analysis. *Stat Med*. 2002, 21, 1539–1558.
21. Egger M, Davey Smith G, Schneider M, Minder CE. Bias in meta-analysis detected by a simple, graphical test. *BMJ*. 1997; 315:629-34.
22. Gilliland FD, Mandel JS. Mortality among employees of a perfluorooctanoic acid production plant. *J Occup Med*. 1993;35(9):950-4.
23. Alexander BH, Olsen GW, Burris JM, Mandel JH, Mandel JS. Mortality of employees of a perfluorooctanesulphonyl fluoride manufacturing facility. *Occup Environ Med*. 2003;60(10):722-9.
24. Leonard RC, Kreckmann KH, Sakr CJ, Symons JM. Retrospective cohort mortality study of workers in a polymer production plant including a reference population of regional workers. *Ann Epidemiol*. 2008; 18(1):15-22.
25. Bonefeld-Jorgensen EC, Long M, et al. Perfluorinated compounds are related to breast cancer risk in Greenlandic Inuit: a case control study. *Environ Health*. 2011;10:88.
26. Steenland K, Woskie S. Cohort mortality study of workers exposed to perfluorooctanoic acid. *Am J Epidemiol*. 2012;176(10):909-17.
27. Barry V, Winquist A, Steenland K. Perfluorooctanoic acid (PFOA) exposures and incident cancers among adults living near a chemical plant. *Environ Health Perspect*. 2013;121(11-12):1313-8.
28. Vieira VM, Hoffman K, Shin HM, Weinberg JM, Webster TF, Fletcher T. Perfluorooctanoic acid exposure and cancer outcomes in a contaminated community: a geographic analysis. *Environ Health Perspect*. 2013;121(3):318-23.
29. Raleigh KK, Alexander BH, Olsen GW, et al. Mortality and cancer incidence in ammonium perfluorooctanoate production workers. *Occup Environ Med*. 2014;71(7): 500-6.
30. Bonefeld-Jørgensen EC, Long M, Fredslund SO, Bossi R, Olsen J. Breast cancer risk after exposure to perfluorinated compounds in Danish women: a case-control study nested in the Danish National Birth Cohort. *Cancer Causes Control*. 2014;25(11):1439-48.
31. Wielsøe M, Kern P, Bonefeld-Jørgensen EC. Serum levels of environmental pollutants is a risk factor for breast cancer in Inuit: a case control study. *Environ Health*. 2017;16(1):56.
32. Mastrantonio M, Bai E, Uccelli R, Cordiano V, Screpanti A, Crosignani P. Drinking water contamination from perfluoroalkyl substances (PFAS): an ecological mortality study in the Veneto Region, Italy. *Eur J Public Health*. 2018;28(1):180-185.
33. Hurley S, Goldberg D, Wang M, et al. Breast cancer risk and serum levels of per- and poly-fluoroalkyl substances: a case-control study nested in the California Teachers Study. *Environ Health*. 2018;17(1):83.
34. Mancini FR, Cano-Sancho G, Gambaretti J, et al. Perfluorinated alkylated substances serum concentration and breast cancer risk: Evidence from a nested case-control study in the French E3N cohort. *Int J Cancer*. 2020;146(4):917-928.
35. Tsai MS, Chang SH, Kuo WH, et al. A case-control study of perfluoroalkyl substances and the risk of breast cancer in Taiwanese women. *Environ Int*. 2020;142:105850.
36. Itoh H, Harada KH, Kasuga Y, et al. Serum perfluoroalkyl substances and breast cancer risk in Japanese women: A case-control study. *Sci Total Environ*. 2021; 800:149316.
37. Omoike OE, Pack RP, Mamudu HM, Liu Y, Wang L. A cross-sectional study of the association between perfluorinated chemical exposure and cancers related to deregulation of estrogen receptors. *Environ Res*. 2021;196:110329.
38. Velarde MC, Chan AFO, Sajo MEJV, et al. Elevated levels of perfluoroalkyl substances in breast cancer patients within the Greater Manila Area. *Chemosphere*. 2022;286(Pt 1):131545.
39. Li X, Song F, Liu X, et al. Perfluoroalkyl substances (PFASs) as risk factors for breast cancer: a case-control study in Chinese population. *Environ Health*. 2022; 21(1):83.
40. Feng Y, Bai Y, Lu Y, et al. Plasma perfluoroalkyl substance exposure and incidence risk of breast cancer: A case-cohort study in the Dongfeng-Tongji cohort. *Environ Pollut*. 2022;306:119345.
41. Li H, Hammarstrand S, Midberg B, et al. Cancer incidence in a Swedish cohort with high exposure to perfluoroalkyl substances in drinking water. *Environ Res*. 2022;204(Pt C):112217.
42. Cathey AL, Nguyen VK, Colacino JA, Woodruff TJ, Reynolds P, Aung MT. Exploratory profiles of phenols, parabens, and per- and poly-fluoroalkyl substances among NHANES study participants in association with previous cancer diagnoses. *J Expo Sci Environ Epidemiol*. 2023;33(5):687-698.
43. Law HD, Armstrong BK, D'este C, et al. Relative rates of cancers and deaths in Australian communities with PFAS environmental contamination associated with firefighting foams: A cohort study using linked data. *Cancer Epidemiol*. 2023;82:102296.
44. Chang VC, Rhee J, Berndt SI, et al. Serum perfluorooctane sulfonate and perfluorooctanoate and risk of postmenopausal breast cancer according to hormone

receptor status: An analysis in the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial. *Int J Cancer*. 2023;153(4):775-782.
45. Winquist A, Hodge JM, Diver WR, et al. Case-Cohort Study of the Association between PFAS and Selected Cancers among Participants in the American Cancer Society's Cancer Prevention Study II LifeLink Cohort. *Environ Health Perspect*. 2023;131(12):127007.
46. Fenton SE, Ducatman A, Boobis A, et al. Per- and Polyfluoroalkyl Substance Toxicity and Human Health Review: Current State of Knowledge and Strategies for Informing Future Research. *Environ Toxicol Chem*. 2021; 40:606-630.
47. Wen LL, Lin CY, Chou HC, Chang CC, Lo HY, Juan SH. Perfluorooctanesulfonate mediates renal tubular cell apoptosis through PPARgamma inactivation. *PLoS One*. 2016;11: e0155190.
48. Stanifer JW, Stapleton HM, Souma T, Wittmer A, Zhao X, Boulware LE. Perfluorinated chemicals as emerging environmental threats to kidney health: A scoping review. *Clin J Am Soc Nephrol*. 2018; 13:1479-1492.
49. Wan HT, Zhao YG, Wei X, Hui KY, Giesy JP, Wong CK. PFOS-induced hepatic steatosis, the mechanistic actions on beta-oxidation and lipid transport. *Biochim Biophys Acta*. 2012; 1820:1092-1101.
50. Hui Z, Li R, Chen L. The impact of exposure to environmental contaminant on hepatocellular lipid metabolism. *Gene*. 2017; 622:67-71.
51. Mokra K. Endocrine Disruptor Potential of Short- and Long-Chain Perfluoroalkyl Substances (PFASs)-A Synthesis of Current Knowledge with Proposal of Molecular Mechanism. *Int J Mol Sci*. 2021;22(4):2148.
52. Kranthi Kumar K, Uma Devi B, Neeraja P. Integration of in silico approaches to determination of endocrine disrupting perfluorinated chemicals binding potency with steroidogenic acute regulatory protein. *Biochem Biophys Res Commun*. 2017; 491:1007–1014.
53. Kar S, Sepulveda MS, Roy K, Leszczynski J. Endocrine-disrupting activity of per- and polyfluoroalkyl substances: Exploring combined approaches of ligand and structure-based modeling. *Chemosphere*. 2017;184:514–523.
54. Kang J, Choi J, Park J. Transcriptional changes in steroidogenesis by perfluoroalkyl acids (PFOA and PFOS) regulate the synthesis of sex hormones in H295R cells. *Chemosphere*. 2016; 155:436–443.
55. Mokra K. Endocrine Disruptor Potential of Short- and Long-Chain Perfluoroalkyl Substances (PFASs)-A Synthesis of Current Knowledge with Proposal of Molecular Mechanism. *Int J Mol Sci*. 2021;22(4):2148.
56. Kaiser AM, Zare Jeddi M, Uhl M, Jornod F, Fernandez MF, Audouze K. Characterization of Potential Adverse Outcome Pathways Related to Metabolic Outcomes and Exposure to Per- and Polyfluoroalkyl Substances Using Artificial Intelligence. *Toxics*. 2022; 10(8):449.
57. Park SK, Peng Q, Ding N, Mukherjee B, Harlow SD. Determinants of per- and polyfluoroalkyl substances (PFAS) in midlife women: Evidence of racial/ethnic and geographic differences in PFAS exposure. *Environ Res*. 2019; 175:186-199.
58. Singletary SE. Rating the risk factors for breast cancer. *Ann Surg*. 2003;237(4):474-82.
59. Ali AT, Al-Ani O, Al-Ani F. Epidemiology and risk factors for ovarian cancer. *Prz Menopauzalny*. 2023;22(2): 93-104.
60. Kashyap N, Krishnan N, Kaur S, Ghai S. Risk Factors of Cervical Cancer: A Case-Control Study. *Asia Pac J Oncol Nurs*. 2019;6(3):308-314.
61. European Chemicals Agency (ECHA). Per- and polyfluoroalkyl substances (PFAS). Available on line at: https://echa.europa.eu/hot-topics/perfluoroalkyl-chemicals-pfas (Last Accessed 09-10-2024)
62. Key EPA Actions to Address PFAS. Available on line at: https://www.epa.gov/pfas/key-epa-actions-address-pfas (Last updated on October 1, 2024)
63. Mohammed AA. The clinical behavior of different molecular subtypes of breast cancer. *Cancer Treat Res Commun*. 2021; 29:100469.
64. Pierozan P, Jerneren F, Karlsson O. Perfluorooctanoic acid (PFOA) exposure promotes proliferation, migration and invasion potential in human breast epithelial cells. *Arch Toxicol*. 2018;92(5):1729-1739.
65. Gui SY, Chen YN, Wu KJ, et al. Association Between Exposure to Per- and Polyfluoroalkyl Substances and Birth Outcomes: A Systematic Review and Meta-Analysis. *Front Public Health*. 2022;10:855348.
66. Cohn BA, La Merrill MA, Krigbaum NY, et al. In utero exposure to poly- and perfluoroalkyl substances (PFASs) and subsequent breast cancer. *Reprod Toxicol*. 2020 Mar;92:112-119.
67. Gui SY, Chen YN, Wu KJ, et al. Association Between Exposure to Per- and Polyfluoroalkyl Substances and Birth Outcomes: A Systematic Review and Meta-Analysis. *Front Public Health*. 2022;10:855348.
68. Cohn BA, La Merrill MA, Krigbaum NY, et al. In utero exposure to poly- and perfluoroalkyl substances (PFASs) and subsequent breast cancer. *Reprod Toxicol*. 2020;92:112-119.

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Supplementary Table 1. Detailed search strategy used on the different databases.

Database	Search String
PubMed	((“PFOA”[Text Word] OR “Perfluorooctanoic Acid”[Text Word] OR “PFOS”[Text Word] OR “Perfluorooctane Sulfonic Acid”[Text Word] OR “PFAS”[Text Word] OR “per and poly fluoroalkyl substances”[Text Word]) AND (“cancer”[Text Word] OR “malignant”[Text Word] OR “carcinoma” [Text Word] OR “neoplasm”[Text Word] OR “tumor”[Text Word] OR “myeloid”[Text Word] OR “lymphoma”[Text Word] OR “Hematologic”[Text Word])) AND (humans[Filter])
Scopus	(TITLE-ABS-KEY (“PFOA”) OR TITLE-ABS-KEY (“Perfluorooctanoic Acid”) OR TITLE-ABS-KEY (“pfosa”) OR TITLE-ABS-KEY (“Perfluorooctane Sulfonic Acid”) OR TITLE-ABS-KEY (“pufas”) OR TITLE-ABS-KEY (“per and poly fluoroacyl substances”)) AND (TITLE-ABS-KEY(“cancer”) OR TITLE-ABS-KEY(“malignant”) OR TITLE-ABS-KEY(“carcinoma”) OR TITLE-ABS-KEY(“neoplasm”) OR TITLE-ABS-KEY(“tumor”) OR TITLE-ABS-KEY(“myeloid”) OR TITLE-ABS-KEY(“lymphoma”) OR TITLE-ABS-KEY(“Hematologic”)) 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”))

Supplementary Table 2. NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE.

CASE CONTROL STUDIES (maximum score: 9)

Note: A study receives one star for each numbered item within the Selection and Exposure categories. For comparability, a maximum of two stars can be awarded.

Selection

1. **Is the case definition adequate?**
   a. yes, with independent validation **(1)**
   b. yes, e.g., 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 based on 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 records (e.g., 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 statement **(0)**

(*Continued*)

COHORT STUDIES (maximum score: 10)

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability.

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, e.g., nurses and 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 records (e.g., surgical records) **(1)**
   b. structured interview **(1)**
   c. written self-report **(0.5)**
   d. no description **(0)**
4. **Demonstration that the outcome of interest was not present at the start of the study**
   a. yes **(1)**
   b. no **(0)**

Comparability

1. **Comparability of cohorts based on 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 the 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
   c. adequate %) follow up, or description provided of those lost) between 60-90% **(0.5)**
   d. follow-up rate < ____% (select an adequate %) and no description of those lost under 60% **(0)**
   e. no statement **(0)**

Supplementary Table 3. Results of the meta-analyses of breast cancer stratified by region, study design, quality score, outcome, gender, year of publication, exposure type, and PFAS type.

Characteristic	RA, No.	RR (95% CI)	p- het.	RA, No.	RR (95% CI)	p-het.	RA, No.	RR (95% CI)	p-het.
		Overall			**Incidence**			**Mortality**	
Overall	52	1.01 (0.98-1.04)		46	1.01 (0.98-1.04)		6	1.00 (0.70-1.43)	
				Region					
North America	23	1.01 (0.97-1.04)	0.01	17	1.01 (0.97-1.04)	0.02	6	1.00 (0.69-1.43)	-
Europe	10	1.36 (1.09, 1.71)		10	1.36 (1.09-1.70)		0	-	
Other regions	19	0.93 (0.71,1.23)		19	0.93 (0.71-1.23)		0	-	
				Study design					
Case-control	35	1.05 (1.01-1.09)	0.03	35	1.05 (1.02- 1.09)	0.04	0	-	-
Cohort	16	0.94 (0.87-1.05)		10	0.94 (0.87-1.02)		6	1.00 (0.69-1.43)	
Ecological	1	1.03 (0.95-1.11)		1	1.03 (0.95-1.11)		0	-	
				Quality score					
Low (< 8)	33	1.01 (0.98-1.05)	0.95	30	1.01 (0.98-1.05)	0.93	3	0.79 (0.32-1.96)	0.65
High (>= 8)	19	1.01 (0.93-1.09)		16	1.01 (0.93-1.09)		3	1.00 (0.62-1.63)	
				Years of publication					
<2019	21	1.05 (0.98-1.13)	0.25	15	1.05 (0.97-1.14)	0.29	6	1.00 (0.69-1.43)	-
>=2019	31	1.00 (0.96-1.04)		31	1.00 (0.97-1.04)		0	-	
				Gender					
Men	1	0.53 (0.19-1.47)	0.13	1	0.53 (0.19-1.47)	0.12	0	-	0.31
Women	43	1.02 (0.99-1.05)		42	1.02 (0.98- 1.05)		1	0.51 (0.13-1.97)	
Both	10	0.94 (0.85-1.03)		5	0.93 (0.84-1.03)		5	0.93 (0.84-1.03)	
				Exposure					
Occupational	10	1.07 (0.93-1.23)	0.4	4	1.09 (0.89-1.32)	0.43	6	1.00 (0.69-1.43)	-
Environmental	44	1.01 (0.98-1.03)		44	1.01 (0.98-1.03)		0	-	
				Type of PFAS					
PFOA	21	1.08 (0.97-1.20)	0.56	16	1.09 (0.98-1.21)	0.42	5	0.98 (0.68- 1.42)	0.59
PFOS	12	1.00 (0.85-1.18)		11	1.00 (0.84-1.18)		1	1.57 (0.29-8.57)	
PFNA	10	0.95 (0.81-1.12)		10	0.95 (0.81-1.12)		0	-	
PFDA	6	1.29 (0.73-2.25)		6	1.29 (0.73-2.25)		0	-	
PFAS	3	0.92 (0.76-1.11)		3	0.92 (0.76-1.11)		0	-	
				PFOA					
				Region					
North America	13	0.99 (0.91-1.08)	0.15	8	0.99 (0.91-1.08)	0.15	5	0.98 (0.68-1.42)	-
Europe	3	1.45 (1.00-2.10)		3	1.45 (1.00-2.10)		0	-	
Other regions	5	1.01 (0.48-2.11)		5	1.01 (0.48-2.11)		0	-	
				Study design					
Case-control	13	1.10 (0.93-1.30)	0.35	13	1.10 (0.93-1.30)	0.48	0	-	-
Cohort	8	1.00 (0.88-1.13)		3	1.02 (0.87-1.18)		5	0.98 (0.68-1.42)	

(*Continued*)

Characteristic	RA, No.	RR (95% CI)	p- het.	RA, No.	RR (95% CI)	p-het.	RA, No.	RR (95% CI)	p-het.
Quality score									
Low (< 8)	11	1.09 (0.85-1.41)	0.76	9	1.13 (0.87-1.46)	0.65	2	0.61 (0.21-1.76)	0.40
High (>= 8)	10	1.05 (0.91-1.21)		7	1.05 (0.90-1.23)		3	1.00 (0.62-1.63)	
Years of publication									
<2019	11	0.98 (0.89-1.08)	0.27	6	0.99 (0.88-1.11)	0.33	5	0.98 (0.68-1.42)	-
>=2019	10	1.11 (0.91-1.35)		10	1.11 (0.91-1.35)		0	-	
Gender									
Men	0	-	0.05	0	-	0.04	0	-	0.32
Women	15	1.11 (0.95-1.29)		14	1.12 (0.96-1.31)		1	0.51 (0.13-1.97)	
Both	6	0.94 (0.89-1.00)		2	0.94 (0.89-0.99)		4	1.03 (0.70-1.51)	
Exposure									
Occupational	6	1.16 (0.89-1.51)	0.57	1	1.35 (1.03-1.77)	0.13	5	0.98 (0.68-1.42)	-
Environmental	15	1.07 (0.96-1.20)		15	1.07 (0.96-1.20)		0	-	

PFAS: per- and polyfluoroalkyl substances, PFOA: perfluorooctanoic acid, PFNA: perfluorononanoic acid, PFDA: perfluorodecanoic acid, PFOS: perfluorooctanesulfonic acid.

Supplementary Table 4. Results of the Female genital cancer (ovarian, uterus) meta-analyses stratified by region, study design, quality score, outcome, gender, year of publication, and PFAS type.

Characteristic	N risk estimates	RR (95% CI)	p heterogeneity
		Ovarian	
Region			
North America	10	1.07(1.04-1.09)	0.44
Europe	1	0.93(0.76-1.15)	
Other regions	1	1.01(0.60-1.69)	
Study design			
Case-control	9	1.07(1.04-1.09)	0.11
Cohort	3	0.95(0.82-1.09)	
Quality score			
Low quality (<8)	7	1.07(1.04-1.09)	0.40
High quality (>= 8)	5	0.98(0.81-1.19)	
Years of publication			
<2019	2	1.05(0.80-1.39)	0.93
>=2019	10	1.07(1.04-1.09)	
Outcome			
Incidence	12	1.07(1.04-1.09)	-
Mortality	0	-	
Type of PFAS			
PFOA	4	1.00(0.90-1.11)	<0.0001
PFOS	2	1.01(1.01-1.01)	
PFNA	2	0.99(0.99-1.00)	
PFDA	2	1.28(1.27-1.30)	
PFAS	2	0.94(0.78-1.14)	
		Uterus	
Characteristic	**N risk estimates**	**RR (95% CI)**	**p heterogeneity**
Region			
North America	10	0.91(0.81-1.02)	0.05
Europe	1	0.91(0.78-1.07)	
Other regions	1	1.41(1.01-1.96)	
Study design			
Case-control	9	0.89(0.79-1.01)	0.14
Cohort	3	1.05(0.88-1.27)	
Quality score			
Low quality (< 8)	7	0.85(0.76-0.96)	0.003
High quality (>= 8)	5	1.23(0.99-1.52)	
Years of publication			
<2019	2	1.08(0.97-1.22)	0.02
>=2019	10	0.90(0.80-1.01)	

(*Continued*)

Characteristic	N risk estimates	RR (95% CI)	p heterogeneity
Outcome			
Incidence	12	0.93(0.84-1.04)	-
Mortality	0	-	
Type of PFAS			
PFOA	4	1.05(0.89-1.24)	0.63
PFOS	2	0.94(0.94-0.95)	
PFNA	2	0.80(0.22-2.83)	
PFDA	2	1.07(0.69-1.65)	
PFAS	2	1.11(0.72-1.69)	

RR: relative risk, N: number.

Supplementary Table 5. The list of individual studies that included in the analysis of breast cancer by level of PFAS exposure.

PFAS type	First Author, year	Exposure level	Dose detail	RR (95% CI)
PFNA	#Bonefeld-Jørgensen EC (2014)	Low	0.32-0.42	1.1(0.6,2.02)
		Medium	0.42-0.50	0.75(0.41,1.4)
		High	0.50-0.64	1.08(0.58,1.99)
		Very high	>0.64	0.8(0.43,1.47)
	*Wielsøe M (2017)	Low	2nd Tertile	2.43(1.07,5.51)
		High	3rd Tertile	2.07(0.9,4.76)
	*Hurley S (2018)	Medium	N/A	1.043(0.808,1.345)
		High	N/A	1.037(0.798,1.348)
	Itoh H (2021)	Low	2.01–2.79 (2.32)	0.38(0.18,0.82)
		Medium	2.80–3.79 (3.22)	0.15(0.06,0.35)
		High	3.81–22.37 (4.56)	0.12(0.05,0.32)
	Velarde MC (2022)	Low	1.29–1.79	1.28(0.4,4.11)
		Medium	1.79–4.48	1.33(0.42,4.3)
		High	2.31–7.91	1.29(0.4,4.1)
	Feng Y (2022)	Low	0.55, 0.79	1.08(0.68,1.7)
		Medium	0.80, 1.06	1.3(0.84,2.02)
		High	≥1.07	1.38(0.89,2.13)
	Winquist A (2023)	Low	0.450-<0.630	0.66(0.46,0.94)
		Medium	0.630-<1.000	0.57(0.39,0.82)
		High	>=1.000	0.81(0.55,1.19)
PFOS	#Bonefeld-Jørgensen EC (2014)	Low	20.42-25.31	1.51(0.81,2.71)
		Medium	25.31-30.20	1.51(0.82,2.84)
		High	30.20-39.07	1.13(0.59,2.04)
		Very high	>39.07	0.9(0.47,1.7)
	*Wielsøe M (2017)	Low	2nd Tertile	3.13(1.2,8.15)
		High	3rd Tertile	5.5(2.19,13.84)
	*Hurley S (2018)	Medium	N/A	0.88(0.69,1.12)
		High	N/A	0.89(0.69,1.16)
	Itoh H (2021)	Low	10.29–14.27 (12.2)	0.38(0.18,0.82)
		Medium	14.27–19.24 (16.27)	0.31(0.14,0.69)
		High	19.28–377.33 (24.67)	0.15(0.06,0.39)
	Velarde MC (2022)	Low	2.20–3.02	1.36(0.42,4.52)
		Medium	3.05–3.82	1.25(0.38,4.17)
		High	3.90–23.03	2.38(0.81,7.31)
	Feng Y (2022)	Low	6.39, 10.35	0.75(0.47,1.19)
		Medium	10.36, 15.66	1.05(0.66,1.67)
		High	≥15.67	0.87(0.54,1.39)

(*Continued*)

PFAS type	First Author, year	Exposure level	Dose detail	RR (95% CI)
	Chang VC (2023)	Low	N/A	1.21(0.84,1.74)
		Medium	N/A	1.3(0.96,1.99)
		High	N/A	1.1(0.77,1.79)
	Winquist A (2023)	Low	13.000-<18.000	0.66(0.45,0.97)
		Medium	18.000-<25.000	0.84(0.57,1.23)
		High	>=25.000	0.7(0.48,1.01)
PFDA	*Wielsøe M (2017)	Low	2nd Tertile	2.14(0.94,4.91)
		High	3rd Tertile	2.36(1.04,5.36)
	Itoh H (2021)	Low	0.56–0.77 (0.65)	0.31(0.15,0.64)
		Medium	0.78–1.07 (0.90)	0.46(0.21,0.99)
		High	1.07–3.84 (1.26)	0.18(0.07,0.47)
	Velarde MC (2022)	Low	0.56–0.74	1.62(0.33,9.17)
		Medium	0.74–0.99	4.09(1.03,21)
		High	1.00–6.57	9.26(2.54,45.1)
	Feng Y (2022)	Low	0.35, 0.54	0.94(0.61,1.45)
		Medium	0.55, 0.80	1.18(0.76,1.82)
		High	≥0.81	1.02(0.65,1.6)
PFOA	*Steenland K (2012)	Low	<1,520 ppm-years	1.49(0.18,5.39)
		High	≥1,520 ppm-years	0.87(0.02,4.83)
	#Raleigh KK (2014)	Low	N/A	0.8(0.26,1.86)
		Medium	N/A	0.88(0.18,2.56)
		High	N/A	0.73(0.09,2.62)
		Very high	N/A	1.02(0.03,5.69)
	#Bonefeld-Jørgensen EC (2014)	Low	3.69-4.59	0.97(0.53,1.75)
		Medium	4.59-5.42	1.02(0.56,1.89)
		High	5.42-6.53	1.14(0.62,2.12)
		Very high	>6.53	0.94(0.51,1.76)
	*Wielsøe M (2017)	Low	2nd Tertile	1.86(0.8,4.31)
		High	3rd Tertile	2.64(1.17,5.97)
	*Hurley S (2018)	Medium	N/A	0.901(0.705,1.152)
		High	N/A	0.925(0.715,1.197)
	Mancini FR (2020)	Low	13.6-17.3 ng/mL	1.78(1.37,2.34)
		Medium	17.3-22.5 ng/mL	1.48(1.12,1.97)
		High	22.5-85.3 ng/mL	1.44(1.09,1.89)
	Itoh H (2021)	Low	4.00–5.57 (4.71)	0.37(0.19,0.73)
		Medium	5.57–7.62 (6.46)	0.39(0.18,0.84)
		High	7.64–62.98 (9.31)	0.2(0.08,0.51)
	Velarde MC (2022)	Low	1.50–1.77	0.64(0.21,1.9)
		Medium	1.77–2.30	1.05(0.38,2.93)
		High	2.31–8.46	0.44(0.14,1.36)

PFAS type	First Author, year	Exposure level	Dose detail	RR (95% CI)
	Feng Y (2022)	Low	0.84, 1.18	0.88(0.56,1.39)
		Medium	1.19, 1.79	1.28(0.8,2.04)
		High	≥1.80	1.69(1.05,2.7)
	Chang VC (2023)	Low	N/A	0.91(0.64,1.3)
		Medium	N/A	1(0.73,1.55)
		High	N/A	1.01(0.66,1.55)
	Winquist A (2023)	Low	3.850-<5.100	0.8(0.56,1.15)
		Medium	5.100-<6.300	0.75(0.52,1.09)
		High	>=6.300	0.82(0.57,1.17)
	#Vieira VM (2013)	Very high	600–4,679μg/L-year	1.4(0.9,2.3)
		High	198–599μg/L-years	0.7(0.5,1)
		Medium	89–197μg/L-years	1.1(0.8,1.5)
		Low	3.9–88μg/L-years	0.9(0.7,1.2)

PFAS: per- and polyfluoroalkyl substances, PFOA: perfluorooctanoic acid, PFNA: perfluorononanoic acid, PFDA: perfluorodecanoic acid, PFOS: perfluorooctanesulfonic acid.

**Studies with only two categories (low and high, without any results for medium category excluded from analysis): Wielsøe M (2017), Hurley S (2018), Steenland K (2012).*

#If a study reported four categories, we used high and very high to calculate one category as the high group: Bonefeld-Jørgensen EC (2014), Vieira VM (2013), Raleigh KK (2014).

Supplementary Table 6. The list of individual studies that included in the analysis of female genital cancer by the level of PFAS exposure.

PFAS type	First Author, year	Cancer type	Exposure level	Dose detail	RR (95% CI)
PFOA	Vieira VM (2013)	Cervix	Low	N/A	0.87(0.48,1.57)
			High	N/A	1.33(0.66,2.70)
		Uterus	Low	N/A	1.04(0.81,1.34)
			High	N/A	1.41(1.00,2.00)
		Ovarian	Low	N/A	1.03(0.59,1.81)
			High	N/A	1.62(0.90,2.90)
PFAS	Li H (2022)	Cervix	Low	N/A	0.97(0.73,1.26)
			High	N/A	0.81(0.45,1.33)
		Uterus	Low	N/A	0.94(0.77,1.13)
			High	N/A	0.82(0.55,1.17)
		Ovarian	Low	N/A	0.87(0.68,1.11)
			High	N/A	1.12(0.72,1.65)

PFAS: per-poly-fluoroalkyl alkyl substances, PFOA: perfluorooctanoic acid.

Supplementary Table 7a. PRISMA Checklist.

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	
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.	
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	
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.	
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.	
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.	
	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.	
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.	
Effect measures	12	Specify the effect measure(s) (e.g., risk ratio, mean difference) used in synthesizing or presenting results for each outcome.	
Synthesis methods	13a	Describe the processes 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)).	
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling missing summary statistics or data conversions.	

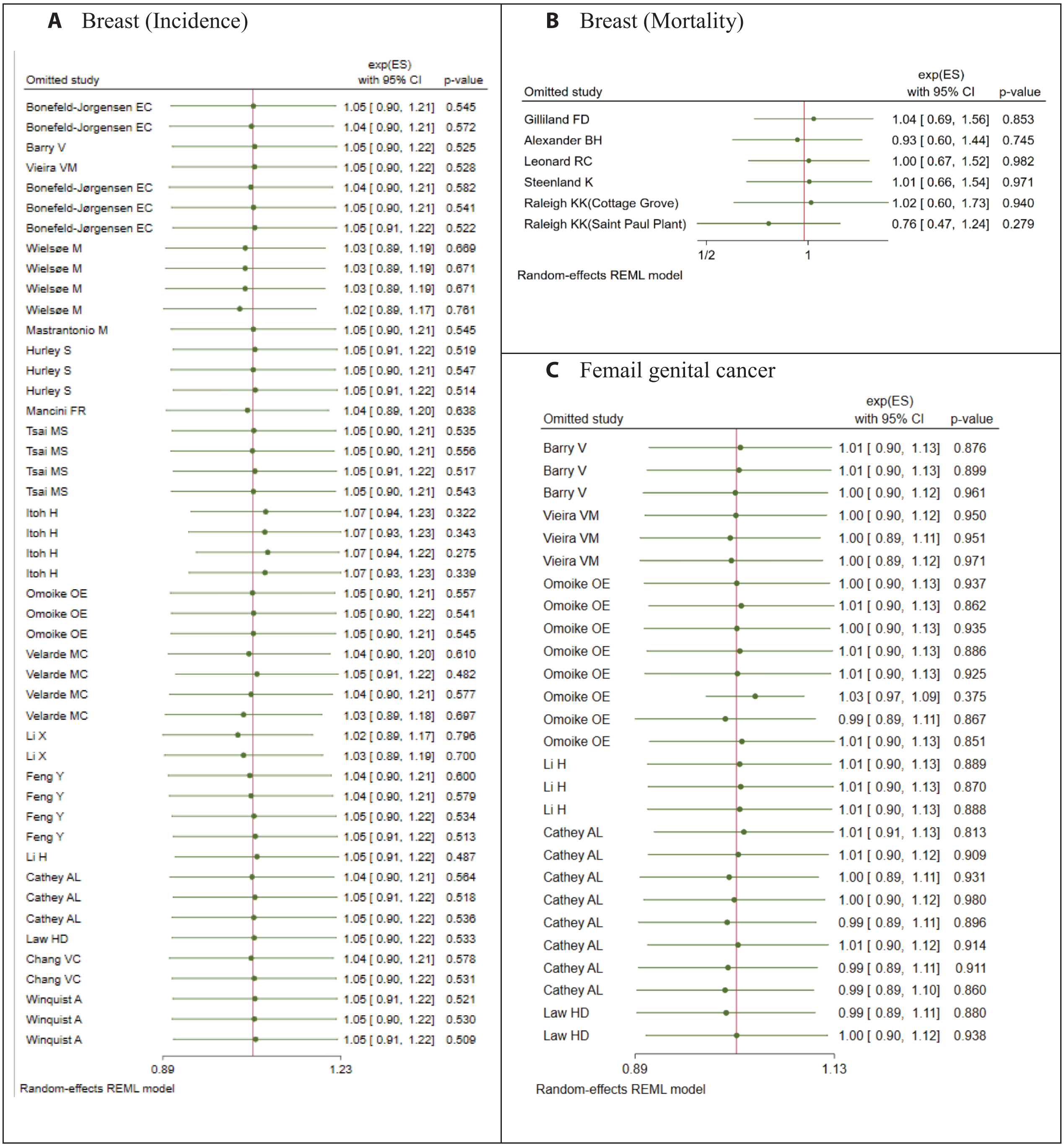
(*Continued*)

Section and Topic	Item #	Checklist item	Location where item is reported
	13c	Describe any methods used to tabulate or visually display the results of individual studies and syntheses.	
	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.	
	13e	Describe any methods to explore possible causes of heterogeneity among study results (e.g., subgroup analysis, meta-regression).	
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of 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.	
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	
Study characteristics	17	Cite each included study and present its characteristics.	
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	
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.	
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	
	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.	
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	

Section and Topic	Item #	Checklist item	Location where item is reported
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	
	23b	Discuss any limitations of the evidence included in the review.	
	23c	Discuss any limitations of the review processes used.	
	23d	Discuss implications of the results for practice, policy, and future research.	
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.	
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	
Competing interests	26	Declare any competing interests of review authors.	
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.	

Supplementary Table 7b. PRISMA Abstract Checklist.

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	
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.	
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	
Synthesis of results	6	Specify the methods used to present and synthesise results.	
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	
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).	
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	
Interpretation	10	Provide a general interpretation of the results and important implications.	
OTHER			
Funding	11	Specify the primary source of funding for the review.	
Registration	12	Provide the register name and registration number.	



Supplementary Figure 1: Leave-one-out meta-analysis for the association between Per- and poly-fluoroalkyl Substances (PFAS) exposure and risk of breast a) incidence, b) modtality, and c) female genital cancers incidence.

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Human Exposure to Asbestos in Central Asian Countries and Health Effects: A Narrative Review

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Keywords: Asbestos; Chrysotile; Asbestos-Related Diseases; Exposure Assessment; Mesothelioma

Summary

The discovery of the detrimental effects of asbestos on human health came long after its widespread use, with the first scientific evidence of asbestos-related diseases emerging in the late 19th and early 20th centuries. Despite efforts to ban its use, asbestos continues to be mined and used in Central Asia (as well as in Russia, China, and other countries). To gain a deeper understanding of the situation in Central Asia, we have conducted a review of scientific literature on the use of asbestos, exposure assessment, and health consequences of asbestos exposure in this geographic area. This review encompasses studies about exposure assessments, epidemiological data, and biochemical or clinical surveys conducted in Kazakhstan, Uzbekistan, Tajikistan, Turkmenistan, and Kyrgyzstan. A total of 18 articles met the inclusion criteria, and their content is summarised in this review, which represents the first attempt to systematically examine research on asbestos and its impact on the health of workers and the general population in Central Asia countries, including literature published in Russian and English. The findings here highlighted the substantial limitations of the currently available knowledge about the impact of asbestos on health in this geographical area.

1. Introduction

Asbestos is the name given to six silicate minerals: chrysotile (the only one belonging to the serpentines) and amphiboles (amosite, crocidolite, asbestos anthophyllite, asbestos tremolite, and asbestos actinolite) [1]. Asbestos has been considered a valuable resource in various industrial sectors for a long time owing to its exceptional physical and chemical properties. These properties include, but are not limited to, fire resistance, electrical, thermal, and acoustic insulation, and mechanical robustness. As such, asbestos has been extensively utilized in a wide range of manufactured goods, such as building materials (roofing, ceiling and floors, and asbestos cement products), automobile parts, heat-resistant fabrics, and the war industry [2].

Exposure to any form of asbestos poses an increased risk of developing asbestos-related diseases (ARDs) [3]. These diseases can be divided into

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non-malignant conditions, such as pleural plaques and asbestosis, and malignant ones, lung cancer, pleural and peritoneal mesothelioma, laryngeal and ovarian cancer, and, with lower levels of evidence, other cancers [3, 4]. Malignant mesothelioma is a highly aggressive cancer arising from the mesothelial linings of pleural, pericardial, peritoneal, and testicular cavities [5]. It has given rise to clinical manifestations for several decades since the beginning of exposure [6, 7]. Different levels of exposure and risk exist, with certain occupations and proximity to asbestos mines or factories posing higher risks [7, 8].

Asbestos-related diseases cause around 255,000 deaths annually worldwide [9]. Many countries have banned asbestos production and use, aligning with the C162 Asbestos WHO reports published in 2006 and 2007, the Basel Convention [10, 11], and national prohibition laws [12]. Nevertheless, there are several countries, among which Russia, China, Kazakhstan, and India, who continue asbestos mining and use. Other countries, including Central Asia (CA), such as Kyrgyzstan, Tajikistan, Turkmenistan, and Uzbekistan, are still large importers and consumers of chrysotile, even if they do not have asbestos mines. On these bases, the present paper provides an overview of the existing knowledge on asbestos use, exposure, and consequences in CA (and precisely in Kyrgyzstan, Kazakhstan, Tajikistan, Uzbekistan, and Turkmenistan), aiming to understand the current situation in these countries, where asbestos-containing materials are still highly diffused.

2. Methods

2.1. Data Sources and Search Strategy

We reviewed available publications to identify articles on asbestos and ARDs in CA countries. We searched international repositories (Google Scholar, PubMed, Web of Science, Scopus, and Elibrary.ru [13]) using the keywords reported in Table S1 in the Supplementary materials.

Articles published in English and Russian from 2008 to 2022 were collected as electronic publications. All references were imported into EndNote X20. The PRISMA Flow Diagram [14, 15] created a review flowchart. In addition, we used the Russian-language version of the Elibrary.ru database (an electronic library of scientific publications from Russia and CA countries integrated with the Russian Science Citation Index (RSCI) to search for all available Russian journals. Data were also collected from the Scientific Production Association 'Preventive Medicine' in Kyrgyzstan and the national statistical agencies of each CA country [16]. In addition, data was taken from open online sources, such as export and import statistics, production quantities, and data concerning the consumption of asbestos in CA [17].

2.2. Selection Criteria

During this search, we reviewed the articles by selecting them by title and abstract, then by full text and review results. After removing duplicate articles, we screened each study based on the inclusion and exclusion criteria.

The papers were included if they contained sufficient and relevant information concerning the following topics: asbestos, occupational and environmental exposure to asbestos, production, use of asbestos-containing products, asbestos-related diseases, and mesothelioma. They were included if they were available as complete texts, written in English or Russian, and focused on CA Countries.

The screening process and quality assessment of the selected articles were conducted separately (and double-checked) by different authors (ZK, KD, AS, CC) to reduce operator-related errors. The four investigators independently extracted the information from the included studies using a predefined datasheet (first author, geographic area, year of publication, industry sector, type of asbestos, and outcome). Articles that could not provide sufficient data or information or that were related to laboratory studies on asbestos in chemistry and geology sciences and studies published in languages other than English and Russian, reviews, and articles unavailable as full text were excluded from the study. Excluded studies were checked for any relevant information not delivered in the selected publications. Any disagreement or discrepancy in the study selection and data extraction processes was resolved by consensus among the authors.

2.3. Data Extraction

The full text of each study was categorized by its title, first author, date of publication, journal, study period, keywords, and strand use. This data was then used to build a database using an Excel spreadsheet.

3. Results

3.1. Data Acquisition and Analysis

In total, 105 relevant research articles were found using the repositories outlined in Figure S1 (Supplementary materials), which summarises the PRISMA [14, 15] flow diagram selection process.

The main findings of the selected articles were tabulated in a data extraction Excel form. Table S2 (Supplementary materials) summarises the study's key findings, the year of publication, and the language used. After applying the inclusion and exclusion criteria to all 105 articles, 18 papers were left (a summary is presented in Table S1). CA countries are former members of the Soviet Union; therefore, they predominantly publish in Russian (78% of the 18 selected articles were written in Russian). As for the country addressed, most of the studies (88.9%) concerned Kazakhstan. Only 5.6% concerned Kyrgyzstan, another 5.6% concerned Uzbekistan, and none concerned Turkmenistan and Tajikistan. The thematic content of the 18 articles can be summarised as follows:

- Only one reviewed paper [18] was about asbestos exposure in workplace environments.
- Only one paper [19] addresses outdoor air pollution from asbestos production.
- Nine studies [20–28] are based on biological samples from individuals working with asbestos and conducting clinical examinations, including biochemical and histological tests.
- Two studies [19, 29] contained additional information concerning asbestos dust pollution at the workplace.
- The other two [30, 31] described tests conducted on laboratory animals (rats).
- One [32] addressed Uzbekistan's economic and public health-related disadvantages of asbestos use.
- Three studies [23, 26, 30] concerned non-malignant ARDs.
- Two articles [19, 33] contained epidemiological studies on the links between mesothelioma and chrysotile asbestos.
- One article [34] focused on developing risk management strategies to minimize health risks in workers.
- Only one study [35] investigated the morbidity with temporary disability (MTD) among workers in the asbestos factory.

In addition to peer-reviewed journals, we also examined the occupational disease registries of the various CA countries, non-peer-reviewed reports, conference proceedings, and internal government documents, such as the report of the Scientific and Production Association "Preventive Medicine" under the Ministry of Health of the Kyrgyz Republic.

3.2. Overview of Asbestos Production and Corresponding Industries in CA Countries

Three countries—Russian Federation, China, and Kazakhstan—still produce more than 2 million metric tons of asbestos annually. Currently, 25 countries, including all the CA countries: Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan, and Uzbekistan, consume at least 1,000 metric tons of asbestos annually (Table 1) [36].

3.2.1. Asbestos Mining and Producing Asbestos-Contained Commodities Industries in Kazakhstan.

Kazakhstan is the largest country in CA, with a population of 18,879,552 [37]. The country is rich in deposits of various minerals, including chrysotile. Today, Kostanay Minerals Enterprise (KME) is the only company mining asbestos in the country [38]. The KME works the Zhitikara chrysotile deposit in the Kostanay region and employs around 2,000 people. This deposit ranks fourth in the world in terms of reserves, and the company exports to other countries of CA and beyond. Annually, the KME produces over 200,000 tons of asbestos as a raw material [38]. In addition to this company, three linked companies within the mining industry produce

Table 1. Export and import of asbestos (excluding asbestos products) to CA countries from 2017-2021. Adapted from https://www.trademap.org/, accessed on 26.12.2022.

Years	Countries	Kazakhstan	Uzbekistan	Tajikistan	Turkmenistan	Kyrgyzstan
2017	Exported asbestos (tons)	182,304	0	0	0	0
	Imported asbestos (tons)	130	87,403	4,968	6,405	9,601
2018	Exported asbestos (tons)	184,830	0	0	0	0
	Imported asbestos (tons)	44	129,032	9,616	6,438	9,319
2019	Exported asbestos (tons)	217,839	0	0	0	0
	Imported asbestos (tons)	12	94,168	14,818	8,786	9,847
2020	Exported asbestos (tons)	209,784	0	0	0	15
	Imported asbestos (tons)	407	116,654	15,493	13,324	9,616
2021	Exported asbestos (tons)	232,366	0	0	0	0
	Imported asbestos (tons)	20	126,115	23,711	13,130	12,013

asbestos-cement goods, employing about 6,000 additional people [29].

3.2.2. Industries of Kyrgyzstan Produce Asbestos-Containing Commodities

Kyrgyzstan is another of the former Soviet republics in CA, with a population of 6.936,2 million [39]. The first enterprise in Kyrgyzstan to produce chrysotile-cement products is the Kant Pipe and Slate Enterprise (PSE) [40], which has been operating since 1967 and remains open today. The enterprise is located in Kant town, 22 km from the capital, Bishkek, and employs around 300 workers. Raw asbestos is imported from Kostanay Minerals JSC (Kazakhstan) and Ural Asbest OJSC [41] (Russia). Annually, the company sells 5 million units of asbestos-containing products. In 2020, a branch of Kant PSE was opened in the city of Kyzyl-Kyia, in the south of Kyrgyzstan, with a production capacity of 3.7 million units of 8-wave slate per year and employing around 150 workers. This production capacity is designed to meet the demand in the south of Kyrgyzstan, and it is exported to Uzbekistan and Tajikistan [40]. The second plant to open in Kyrgyzstan producing chrysotile products is Kant Kurulush LLC [42], founded in 2013 in the city of Kant in the north of Kyrgyzstan. They produce non-pressure pipes and couplings as well as 8-wave slate. The primary raw material used is Russian chrysotile (asbestos), imported from Ural Asbest OJSC, Russia [42].

3.2.3. Industries of Uzbekistan Producing Asbestos-Containing Commodities

Uzbekistan is the most highly populated country in the CA region, with a population of 36,024,946 [43]. In 2020, Uzbekistan imported $37 million worth of asbestos, making it the 3rd largest asbestos importer in the world. In the same year, asbestos was Uzbekistan's 132nd most imported commodity. Uzbekistan imports asbestos mainly from the following countries: Kazakhstan ($29.2 million); Russia ($7.63 million), China ($104 thousand), and Kyrgyzstan ($2.29 thousand) [44]. There are 44 enterprises in the country producing asbestos goods [45]. However, the total quantity of asbestos products manufactured by Uzbekistan is unknown.

3.2.4. Industries in Tajikistan Producing Asbestos-Containing Commodities

Tajikistan's population is around 9,700,000 [46]. In 2020, Tajikistan imported $6.19 million worth of asbestos, becoming the ninth-largest asbestos importer in the world. Asbestos is ranked 138th among Tajikistan's most imported commodities. Tajikistan imports asbestos mainly from Kazakhstan ($4.54 million) and China ($1.65 million) [44].

However, information regarding the number of enterprises producing asbestos products is not publicy available.

3.2.5. Industries in Turkmenistan Producing Asbestos-Containing Commodities

Turkmenistan has a population of 6,341,855 [47]. In 2020, it imported $4.52 million worth of asbestos, making it the 10th largest asbestos importer globally. In the same year, asbestos was Turkmenistan's 147th most imported commodity. Turkmenistan imports asbestos mainly from Kazakhstan ($4.52 million) [44]. Again, the number of enterprises using asbestos is unavailable.

3.3 Detailed Overview of the Results

3.3.1. Physical and Chemical Characteristics of Asbestos Used in CA

Ibraev and colleagues described the physical and chemical characteristics of chrysotile mined and extracted from Zhitikara ore [48]. The study used a scanning electron microscope (Tescan Vega\LSU) with an energy-dispersive spectroscopy microprobe (INCA-PentaFET-x3). Notwithstanding, the authors do not present any EDS spectra, only SEM images (compatible with pure chrysotile) and a table containing the percentage of elements included in the analyzed points. The results showed the different values of the outer diameter of the chrysotile fibers, which range from 94 to 167 nm (no data about the lengths of the fibers were presented).

3.3.2. Asbestos Concentrations in the Workplace and the Environment

Amanbekova and co-workers (2014) [29] found that the average daily dust concentration at workplaces in "Kostanay minerals" JSC in Kazakhstan was equal to 6 mg/m^3 in 2014, which was higher than the maximum permissible concentration (MPC) of Kazakhstan's legislation where the MPC is equal to 0,5 mg/m^3 (for dust containing more than 20% of asbestos) and 1 mg/m^3 (for dust containing less than 20% of asbestos) [49]; however, they did not specify whether the MPC of one-time exposure or average daily exposure, moreover there was no description of the measurement method used for determining the dust concentration. The following year (2015), Ibraev et al. [18] measured the level of dust in 2015 in the same industry; the average daily results ranged from 0.2 to 1 mg/m^3, which did not exceed the MPC limits of Kazakhstan. This study used a gravimetric method to measure the asbestos concentration. This method is considered obsolete for measuring asbestos contamination since it does not count only the number of asbestos fibers but the whole dust dust collected, thereby not providing a fiber-specific concentration.

Both studies did not mention the implementation of specific environmental control actions between 2014 and 2015. The decrease in reported dust levels by Ibraev et al. (2015) could imply some intervention to reduce dust levels. However, with explicit details, we can conclusively link the decrease in fiber concentration to any particular control measures.

The Centre for Environmental Medicine and Human Ecology also studied air pollution in one industry that produced asbestos-containing commodities (Kant PSE, Kyrgyzstan) from 2019 to 2020 [16]. In total, 340 measurements were made at 162 points during the day and 18 points at night. The dust content in the air was determined through the gravimetric method. The dust dispersion and particle size characteristics were determined using a light trinocular microscope equipped with an ocular micrometer and software (BioVision, Austria). According to the results of the study, the average daily dust level in the air at the workplaces varied from 1.34 mg/m^3 to 1.45 mg/m^3 [16], which exceeds the national regulations on acceptable MPC limits of dust containing asbestos in industries, where average daily MPC is equal to 0,5 mg/m^3 (for dust containing more than 20% of asbestos) and 1 mg/m^3 (for dust containing less than 20% of asbestos) [50]. The authors did not report the determination of weight concentrations of asbestos.

However, it should be noted that the studies' findings do not comply with the European Union's occupational exposure limits or Kazakhstan's or Kyrgyzstan's MPCs. Additionally, the gravimetric method is obsolete for measuring asbestos contamination since it is impossible to count the number of asbestos fibers (and thus obtain a quantitative and specific value for airborne asbestos concentrations) [3, 51].

Korotenko et al. (2011) studied the environmental emissions caused by Kant Pipe and Slate Enterprise (PSE) in Kyrgyzstan [19]. They highlighted that the industry released ten pollutants into the surrounding atmosphere, with 0.515 tonnes of asbestos-containing dust emitted in 2010. This amount of asbestos did not exceed the allowed annual emission of asbestos-containing dust in Kyrgyzstan, which is 1.47 tonnes. However, the authors did not elaborate further on their findings.

3.3.3. Research on Asbestos Industry Workers

3.3.3.1. Morbidity

Ibraev et al. (2014) [34] studied working conditions and health risks in chrysotile extraction at JSC "Kostanai Minerals", revealing hazard levels of 3.3-3.4 at the enrichment complex (EC) and 3.3 at mining and transport enterprises (MTE). Occupational disease rates were 55.9 per 10,000 workers at EC and 34.9 at MTE, with temporary morbidity causing 1127.3 days of incapacity at EC and 1144.6 days at MTE. The authors analyzed morbidity using the WHO's "International Classification of Diseases, Injuries, and Causes of Death" (1996) but did not specify the exact diseases, such as mesothelioma or lung cancer. However, the authors emphasized the need for strict chrysotile use control, safety standards, risk management, and preventive measures to protect workers' health and ensure compliance with safety regulations.

Ibraev et al. (2018) [35] investigated the temporary disability/morbidity among workers involved in chrysotile production at JSC "Kostanai Minerals," focusing on ore enrichment. Two groups were compared: control (administrative and technical workers, n=299) and main (ore preparation and enrichment workers, n=917). The control group faced fewer harmful factors, while the main group suffered high noise levels, dust exposure, and poor working conditions. Morbidity rates were higher in the main group, with men showing 21.2±2.2 cases of disability/morbidity and 514.1 days of incapacity per 100 workers, compared to 9.1±0.2 cases and 203.1 days in the control group. Women's rates were slightly lower but still significant. The main group's overall morbidity was 69.2±8.4 cases and 1127.3 days per 100 workers, versus 46.0±2.6 cases and 677.3 days in the control group. The highest morbidity was among workers with less than 9 years of experience, and respiratory diseases were the most common ailment. The study highlights the significant impact of production factors on worker health, with a higher morbidity level in the leading group, indicating the need for improved working conditions and health monitoring. Notably, the work did not address specifically asbestos-related diseases.

3.3.3.2. Radiological Findings

A study by Ibraev et al. (2008) examined 47 employees of Kostanay Minerals JSC in 2008 [23]. An X-ray examination of 20 workers with more than 20 years of work experience showed an increase in the vascular picture, minor perivascular and peribronchial pneumofibrosis in the median zones of the lungs in 60% of cases, and moderately expressed perivascular and peribronchial pneumofibrosis in the media zones in 13 cases (40%).

3.3.3.3. Pulmonary Function and Respiratory Findings (PFR)

In the same study, the respiratory function of these 47 employees was analyzed, revealing that six workers suffered from chronic bronchitis and disorders of pulmonary ventilation function. Twenty-five percent of cases among them had respiratory obstruction, with some cases also showing hypoxemia [23]. Interestingly, no cases of pulmonary restriction were observed.

Additional cytological examination of the nasal and oral epithelium of 65 workers [22] and 108 workers [27] of Kostanay Minerals JSC (2015) showed a high frequency of destructive changes of the cells of the nasal mucosa in samples of workers with occupational exposure from 5 to 20 years. In these studies, authors investigated cellular changes in the nasal mucosa and buccal epithelium among workers exposed to asbestos. Cytological examinations were performed to detect potential signs of cellular damage or early disease states related to asbestos exposure.

The results indicated that for workers with more than 20 years of exposure, the cellular alterations were similar to those observed in individuals without exposure (the control group). This was contrary to expectations since long-term asbestos exposure is typically associated with cellular damage. The authors interpreted these findings to suggest that over time, the bodies of these long-term exposed workers may have adapted to the presence of asbestos fibers. This implied, in the Authors' view, some form of physiological or cellular adjustment that resulted in reduced observable damage in the nasal and buccal epithelial cells. However, it should be noted that no evidence exists of a possible biological adaptation to carcinogens. Therefore, the most logical answer to the problem posed by these findings is simply that asbestos does not cause the cellular alterations that were searched for by these authors. For sure, asbestos is a known carcinogen, and the most diffused and accepted understanding is that the risk of disease increases with the duration and intensity of exposure, with some differences for mesothelioma.

3.3.3.4. Immunological Markers

Amanbekova et al. (2012) studied the cell and humoral immunity of 106 workers in the Kostanay Minerals JSC, examining the "shortened" panel of monoclonal antibodies (mAbs), immunoglobulins (IgA, IgM, IgG) and secretory immunoglobulin A (SIgA) through an ELISA test [24]. They reported decreased functional activity of the T-lymphocytes in a proportion of all immune cells, accompanied by a reduced number of CD3 cells in workers who had worked more than 20 years — 58.7±0.41% ($p<0.01$), compared to the control group (71,2±0,52%). A similar picture was reported in CD4 cells - 40.9±0.85% (control group 45,2±0,26), CD20 cells - 6.1±0.39% (control 12,7±1,09), and IgA 1.35±0.57 g/l (control group 2,85 ± 0,27 g/l), and an increase of IgG - 19,27±0,57 g/l (control group 11,27±0,14 g/l) of the employees who worked more than 20 years, respectively. Workers exposed to chrysotile asbestos over 20 years had decreased the mucous barrier of the nasal secretion in IgA - 0.16±0.03 g/l ($p<0.01$), compared with a control group (0.34±0.07 g/l).

In another study on 125 workers in the Kostanay Minerals JSC, Koigeldinova et al. (2022) found changes in the number of CD4+ T-cells [28]. In employees' occupational exposure of more than 15 years, the number of CD4+ T-cells was significantly lower than in those who had been working for less than 15 years. The levels of CD8+ T-cells were similar in these two examined groups. They concluded that most healthy workers with a longer occupational exposure to chrysotile have increased neutrophil phagocytic activity and a decreased total number of CD3+ T and CD4+ T cells but an increased number of CD8+ T-cells with a lower immunoregulating index of CD4+8+. Koigeldinova et al. (2015) also found that the workers of Kostanay Minerals JSC with longer occupational exposure to asbestos fibers have an increased activity of lipid peroxidation, which was more pronounced in the workers of the processing complex than the drivers and miners [21].

3.3.3.5. Biochemical and Cytological Changes

Ibraev et al. (2015) found that workers of Kostanay Minerals JSC showed destructive changes in the nasal mucosa and buccal epithelium cells. Notably, the alterations were primarily observed in the workers with less than 20 years of exposure, while in workers with more than 20 years of exposure, the pathological changes were not different, for incidence and entity, to those observed in the control group [26]. On the other hand, blood plasma analysis revealed elevated alveomucin 3EG5 levels ($p<0.05$), a marker of lung fibrosis, in workers with over 20 years of exposure compared to controls. They recommended measuring lipid peroxidation products and alveomucin 3EG5 levels in blood plasma as biomarkers of the initial stage of pneumoconiosis caused by chrysotile exposure.

3.3.3.6. Longitudinal Studies and Cellular Membrane Changes

A 7-year longitudinal study by Ibraev et al. (2016) revealed adaptive changes in cell membrane constituents, such as an increase in sphingomyelin (SM) and a decrease in phosphatidylcholine (PC) in workers with longer occupational exposure to asbestos-containing dust [20]. According to the authors ' opinion, these changes in the cell membrane, involving both the plastic and energy state of cells and the level of catecholamines, occurred due to adaptation to asbestos exposure at the workplace. Differences in the body's functional state were revealed in workers involved directly in the production for 4 to 5 years and in employees of the mining and transport department who had worked for between 5 and 6 years. For workers directly involved in the production, the authors regarded a working period of 5 years as a risk for developing occupational disease, while for employees of the mining and transport department, this risk began from 6 years.

3.3.3.7. Chromosomal and Genetic Findings

In a cytogenetic blood study of workers in chrysotile-asbestos production, Amanbekova et al. (2012) revealed structural disorders of chromosomes represented by aberrations of chromosome and chromatid types [25]. The authors observed higher rates of such induced chromosomal abnormalities in workers with more than 25 years of asbestos exposure. The frequency of cells with chromosomal aberrations in the peripheral blood lymphocytes of the leading group significantly exceeded the control values.

3.3.3.8. Morphological and Pathological Assessments

Ibraev et al. (2022) studied the morphological parameters and the dust content in lung tissue taken from autopsy material of 343 deceased individuals (including workers at Kostanay Minerals JSC and a control group composed of residents of Zhitikara who never worked at Kostanay Minerals JSC) [52]. They observed severe sclerosis and dust particles in the form of grains (pigments) of black color. These black dust particles were found in the lung sections of 33.3% of the workers of Kostanay Minerals and 44.6% of non-exposed residents of Zhitikara. Such particles, however, cannot be regarded as a specific consequence of asbestos exposure since they are different from asbestos bodies that appear as brown or dark yellow corpuscles at light microscopy. Moreover, the authors found more pronounced fibrotic changes, sometimes with the obliteration of alveoli, in the lung sections of Kostanay Minerals JSC workers compared to the controls, in which non-specific inflammation prevailed. The authors concluded that chrysotile occupational exposure does not increase the risk of developing pathologic changes in the lung tissue (RR-1.9 CI=0.68).

3.3.4. Epidemiological Studies

An epidemiological study by Altynbekov et al. (2018) investigated the prevalence of mesothelioma in Kazakhstan and examined the potential relationship between chrysotile asbestos exposure and the development of mesothelioma [33]. From 2012 to 2016, 17 mesothelioma cases were reported in Kazakhstan. The majority (95.7%) was represented by pleural mesothelioma, the remaining by peritoneal and pericardial mesothelioma. The age at diagnosis was between 40 and 70 years. Notably, in only 7.5% of diagnosed cases, there was a documented history of occupational asbestos exposure. The authors concluded from this data that there was no evident relationship between exposure to chrysotile asbestos and the development of mesothelioma. This was based on the low percentage of cases with documented occupational exposure. The study also reported some data regarding the geographical distribution of the cases, with 15.2% of cases coming from the Almaty region, 12.8% from the Kostanay region, and 10.5% from the Karaganda region. This is interesting as Almaty and Karaganda regions are not known for asbestos-producing facilities. While the study highlights the low incidence of occupational exposure in mesothelioma cases, it does not provide detailed environmental exposure data or a comprehensive description of asbestos-related work activities in Kazakhstan. It is essential to consider both occupational and environmental exposures when assessing the risks associated with asbestos because secondary or non-occupational exposures can also contribute to disease.

As already mentioned in the introduction, Kazakhstan has industries engaged in mining and producing asbestos-containing commodities. For instance, the Kostanay Minerals Enterprise is mentioned as the primary company involved in asbestos mining. Additionally, asbestos is used in various industries, including asbestos-cement goods manufacturing. Altynbekov et al.'s assertion that "no relationship between chrysotile asbestos exposure and mesothelioma" is controversial, given the widely recognized carcinogenicity of all forms of asbestos, including chrysotile. The International Agency for Research on Cancer (IARC) and other health authorities have concluded that all types of asbestos fibers are causally linked to mesothelioma and other asbestos-related diseases.

Only one study on pleural mesothelioma was conducted in Kyrgyzstan by Golovachev in 2008 [53]. He examined 12 patients with a newly diagnosed pleural mesothelioma at the National Centre of Oncology (NCO) in 2000-2005. Among these, seven were male (58.4%), and five female (41.6%); their average age was 44. The incidence rate of pleural mesothelioma in Kyrgyzstan was 0.14 per 100,000 men and 0.1 per 100,000 women in the same period. Histologically, malignant mesothelioma was confirmed in six patients (50%). In three patients (25%), the diagnosis remained histologically unverified due to their refusal to conduct diagnostic and therapeutic thoracoscopy. The rest (25%) were finally diagnosed with other types of malignant neoplasms. The patient's history showed occupational exposure to asbestos in five patients who had worked with asbestos insulation and asbestos-cement materials. The verification of the diagnosis was based on histological methods only, an immunohistochemical assay was never performed.

Comprehensive studies that account for all potential exposure routes, latency periods, and detailed work histories are essential for a more accurate assessment of the relationship between asbestos exposure and mesothelioma. The data should include occupational, environmental, and secondary exposures to give a complete picture of the asbestos-related health burden.

Even with the lack of studies in CA regarding ARDs, after an extensive search, we found some data on occupational diseases among workers only in the Bureau of National Statistics of the Republic of Kazakhstan database. According to them, "pneumoconiosis caused by asbestos and other minerals" (J61, ICD-10) was registered in 1 case in 2006, 10 cases in 2015, and 1 case in 2021 [37], with an age range predominantly from 30-45. Such data reflect the deficient reporting of ARDs. However, the findings of Chen et al. for Kazakhstan indicate a significant burden of asbestos-related diseases, with the country experiencing the highest age-standardized mortality rate (ASMR) and age-standardized DALY rate (ASDR) among the four countries studied: Russia, Brazil, China, Kazakhstan). Specifically, Kazakhstan's ASMR peaked at 4.89 per 100,000 population in 2015, while the ASDR reached a high of 123.75 per 100,000 in the same year. Between 1990 and 2019, Kazakhstan's ASMR and ASDR declined significantly, with a reduction of approximately -48.62% in ASMR and -54.06% in ASDR in men, represented by estimated annual percentage changes (EAPC) of -3.09 and -3.69, respectively. Despite these reductions, tracheal, bronchus, and lung (TBL) cancers remained the leading causes of asbestos-related mortality and DALYs, contributing to the sustained high disease burden [54]. At the same time, it is worth mentioning that the incidences of mesothelioma in CA countries, according to the WHO, are low compared to the European ones: 0.28/100,000 in Kazakhstan, 0.06/100,000 in Kyrgyzstan, 0.12/100,000 in Uzbekistan, 0.02/100,000 in Tajikistan, 0.15/100,000 in Turkmenistan compared to 1.7 for males and 0.4 for females in Europe [55].

4. Discussion

This review presents the available data about asbestos in CA countries, including epidemiology, exposure assessment, and experimental studies.

First, it is essential to note the need for more accurate data on the number of workers occupationally exposed to asbestos in Central Asia. For instance, it is known that Kazakhstan's Kostanay Minerals Enterprise, a significant asbestos producer in the region, employs approximately 2000 workers and produces substantial quantities of asbestos-containing materials. In contrast, countries like Kyrgyzstan, Uzbekistan, Tajikistan, and

Turkmenistan, while importing large amounts of asbestos (see Table 1) for manufacturing asbestos-containing products, must provide comprehensive data on their workforce engaged in these activities.

The absence of precise data concerning the number of workers engaged in asbestos processing presents significant constraints. One of the primary obstacles posed by this need for more information is the need for reliable denominators for statistical analysis and the difficulty in creating profiles of asbestos exposure among workers based on jobs, tasks, working time, etc., and determining ARD incidence among asbestos workers. Comprehensive studies that collect accurate occupational data, including the number of workers involved in asbestos-related industries, are imperative. Such efforts are essential for accurately assessing health risks associated with asbestos exposure, developing targeted public health strategies, improving worker safety standards, and advocating for the cessation of asbestos use in the region.

Even though incomplete, the existing data about occupational exposure to asbestos in Central Asia reveals alarming health outcomes reflective of outdated safety practices and inadequate regulatory frameworks. Studies at Kostanay Minerals JSC show high morbidity rates among workers, primarily due to respiratory diseases such as chronic bronchitis and pneumofibrosis [9]. Radiological findings by Ibraev et al. (2008) showed significant lung damage among workers with over 20 years of exposure, including perivascular and peribronchial pneumofibrosis [23]. These findings are evident from the elevated exposure levels at the workplace, which was reported by Amanbekova et al. (2014), showing that the daily dust concentrations were significantly higher than the maximum permissible concentration (MPC) in Kazakhstan [24]. This is concerning compared to Europe and other Western countries, where stringent occupational safety measures have been adopted. For example, the recent European directive (EU) 2023/2668 has established to modify the former OELV (8-hour time-weighted average (TWA) – PCM analysis) 0.1 ff/ml established by Directive 2009/148/EC, reducing it to 0.01 ff/ml (within 20 December 2029 – electron microscopy analysis) and then progressively to 0.002 ff/ml (from 21 December 2029 – electron microscopy analysis) [56]. In contrast, the average daily dust concentrations at Kostanay Minerals JSC, as reported by the studies mentioned above, were significantly higher, even considering the difficulties in comparison due to different analytical approaches, often exceeding national and international permissible limits [49, 56].

Other findings in CA literature were based on laboratory experiments performed on animals; the above-cited studies demonstrated the development of asbestos-related pneumofibrosis, which can lead to neoplasms. However, sufficient and relevant studies on cancers related to asbestos have just been published in CA. This can be explained by the need for well-established methods or equipment for applying the most internationally accepted approaches, sometimes due to insufficient financial support. Another issue that should be reported is that Occupational Health is not well-developed in CA countries. In Kyrgyzstan, for instance, only a few specialists in occupational diseases are active across the country, and the medical examination of workers is among the duties of general practitioners, who often lack the occupational health skills necessary to manage the health surveillance of workers [16]. It should be stressed, however, that awareness and consideration of the problem of asbestos hazards are generally evident in CA countries through the work of scientists in the corresponding fields.

Interestingly, countries with comprehensive asbestos regulations, such as those in the European Union, showed a decline in recognized cases of ARDs between 2013 and 2021. Specifically, there was a 26% decrease in the overall index of recognized occupational diseases, and in this frame, pneumoconiosis due to asbestos and other mineral fibers saw a 52% reduction.

Despite reductions over time, the findings by Chen et al. highlight that Kazakhstan continues to bear a high burden of asbestos-related diseases, mainly due to TBL cancers, which account for the majority of asbestos-related deaths and DALYs. Kazakhstan's peak ASMR and ASDR in 2015 and the highest values among the countries studied suggest that the population is still experiencing significant health impacts from asbestos exposure [54]. This indicates that while the EU has seen progress in controlling occupational diseases, CA countries face ongoing but under-recognized challenges, potentially due to differences in regulatory approaches, recognition of occupational diseases, and prevention measures taken [57, 58].

Even though all types of asbestos are known to be carcinogenic, the literature reports differences in the pathogenic potential according to asbestos type. However, there is no agreement about the lower neoplastic potential of chrysotile compared to amphiboles [59, 60]. In addition, most previous studies about fiber content in the lungs of asbestos workers non-occupationally exposed patients, and the general population has been conducted in Europe, the US, Canada, and Australia on subjects exposed to a mixture of chrysotile and amphiboles [61-63].

Instead, in CA, only chrysotile is mined and used, even though there is currently no sufficient evidence to prove that amphiboles do not contaminate the chrysotile ores here exploited. Chrysotile is considered less carcinogenic for the mesothelium than amphiboles; however, its association with mesothelioma has been described in some studies conducted in Italy and China [64, 65]. Recent research has significantly advanced our understanding of the health risks associated with asbestos exposure, particularly chrysotile, a topic of considerable debate. A comprehensive case-control study published in 2020 in the USA (investigating exposures that occurred from 1975 to 1980) suggests that both chrysotile alone and mixtures containing amphiboles pose significant risks of developing mesothelioma [66], contradicting the previously held view that chrysotile might be less hazardous than other forms of asbestos [59]. The study found that exposure to pure chrysotile was significantly associated with mesothelioma, even with a risk magnitude lower than amphiboles. The research underscores the heterogeneity in the risk of different fiber types and lengths, suggesting a nuanced approach to asbestos regulation and control strategies.

Despite the well-known hazardousness of chrysotile, in CA countries, there is a lack of epidemiological data on lung cancer. On the other hand, the incidence of mesothelioma, according to the available literature, appears to be as low as 0,28/100.000 in Kazakhstan and 0,06/100.000 in Kyrgyzstan; this unbelievably low incidence of mesothelioma (much lower compared to countries where asbestos has been banned for decades) might be due both to the type of asbestos used (maybe pure chrysotile) and perhaps to significant under-reporting of the diseases, owed, on one hand, to the lack of a sound diagnostic protocol and, on the other hand, to insufficient health surveillance of workers, which is recommended, in case of asbestos exposure, even after retirement. The protocol for mesothelioma diagnosis adopted in CA countries needs to be explained in detail in any of the consulted sources, and it does not include immunohistochemistry [67]. A suitable histopathologic protocol accompanied by an immunohistochemistry assessment is an essential tool in the differential diagnosis of this neoplasm, which could also be difficult for a very experienced pathologist.

Moreover, the scientific literature concerning asbestos exposure in CA needs to provide sufficient data to understand if workers and the general population are exposed to pure chrysotile substances or if amphibole contaminations occur. The available data described above have been produced using outdated and imprecise methods, lacking the accuracy of the widely shared updated recommendations. For instance, with a fiber-specific sampling method (and applicable, consistent exposure limits), industrial hygiene experts can fully understand the complex exposure picture for asbestos in CA. This means they cannot wholly and accurately evaluate the health risks of asbestos in the workplace. Asbestos has been recognized as different from other dust or fibers; thus, appropriate sampling and analysis techniques should be used to obtain data applicable to the industrial hygiene field. The microscopic method (e.g., ISO 14966-2019) has been used for many years to count and identify "respirable" asbestos fibers in fiber and dust samples collected on a filter. Moreover, recent analyses emphasize the importance of understanding the fiber type, length, and exposure duration when assessing health risks. Longer and thinner fibers are more persistent in lung tissue and, thus, more likely to cause mesothelioma and other lung diseases. This complexity is crucial for developing practical occupational health standards and protective measures.

Integrating the detailed exposure assessments from recent studies with regional insights can enhance our understanding of asbestos-related risks. Any safe exposure level is highly questionable and historical and current data should inform ongoing efforts to eliminate asbestos use and improve public health outcomes.

Our review delves into the impact of asbestos in Central Asia, shedding light on the widespread use and health consequences of heavy asbestos use in the region. Despite global banning policies, we show the ongoing production and use of asbestos, emphasizing the critical need for comprehensive exposure assessments and epidemiological data to guide public health measures.

Epidemiological and postmortem lung content studies are needed to address the above-summarized lack of data. Determining asbestos exposure, asbestos inhalation at the workplace and in both urban and rural environments, and asbestos persistence in the lungs, as well as the link between asbestos exposure (occupational and non-occupational) and neoplasms (malignant pleural mesothelioma, lung cancer, etc.), is an urgent and unmet public health issue in CA.

5. Conclusion

This is the first review of asbestos and its impact on the health of workers and the general population of CA countries, including also studies published in Russian. We emphasize that the arbitrary presentation of the results of reviewed studies and their notable incompleteness do not allow a clear understanding of the situation. The picture of asbestos-related issues in CA countries strongly needs to be improved. Several topics require attention: in the CA area, there are only a few studies on asbestos's impact on health, and almost no occupational and environmental exposure assessments are conducted adopting modern and internationally accepted methods. In particular, outdated techniques are often used to assess exposure in the cited studies. These methods are unsuitable for determining the composition of the revealed dust and distinguishing between asbestos and non-asbestos components. There is also a need for studies addressing the actual nature of asbestos mined in Kazakhstan, as well as the link between mesothelioma risk and chrysotile exposure. CA might offer the opportunity to study the effects of exposures to chrysotile alone (if the absence of amphibole contamination were confirmed with suitable methods) and would help solve the still open problem regarding the capacity of chrysotile to pose a significant risk of pleural mesothelioma. Overall, a shortage of analytical foundations results in a substantial scarcity of inquiries and sizeable gaps in the few existing investigations. To fill this gap, more studies must be conducted according to updated and validated methods to address the currently open issues, investigating the amount of asbestos exposure and the impact of asbestos mining and use on public health. For sure, the situation in CA regarding asbestos represents a chance to conduct research, fill the existing knowledge gap, and improve the general knowledge regarding the toxicity of specific types of asbestos fibers.

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Supplemetary Material: Figure S1. The inclusion and exclusion criteria for published articles on asbestos and asbestos-related diseases in CA Countries.

Table S1. Searching keywords and strings in international repositories.

Table S2. Summarized details of the selected articles.

References

1. Schulte PS, Trout D, Zumwalde RD. Asbestos fibers and other elongate mineral particles; state of the science and roadmap for research. NIOSH current intelligence bulletin 62; DHHS publication no. (NIOSH) 2011-159. Published online 2011. https://stacks.cdc.gov/view/cdc/5892 (Last Accessed October 2, 2023.)
2. Wachowski L, Domka L. Sources and effects of asbestos and other mineral fibres present in ambient air. *Pol J Environ Stud*. 2000;9(6):443-454.
3. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Arsenic, metals, fibres, and dusts. *IARC Monogr Eval Carcinog Risks Hum*. 2012; 100(Pt C):11-465.
4. Mensi C, Riboldi L, De Matteis S, Bertazzi PA, Consonni D. Impact of an asbestos cement factory on mesothelioma incidence: global assessment of effects of occupational, familial, and environmental exposure. *Environ Int.* 2015;74:191-199. Doi: 10.1016/j.envint.2014.10.016
5. Zucali PA, Ceresoli GL, De Vincenzo F, et al. Advances in the biology of malignant pleural mesothelioma. *Cancer Treat Rev.* 2011;37(7):543-558. Doi: 10.1016/j.ctrv.2011.01.001
6. Kazan-Allen L. Asbestos and mesothelioma: worldwide trends. *Lung Cancer.* 2005;49 Suppl 1:S3-8. Doi: 10.1016/j.lungcan.2005.03.002
7. Marinaccio A, Binazzi A, Cauzillo G, et al. Analysis of latency time and its determinants in asbestos-related malignant mesothelioma cases of the Italian register. *Eur J Cancer.* 2007;43(18):2722-2728. Doi:10.1016/j.ejca.2007.09.018
8. Darcey DJ, Feltner C. Occupational and environmental exposure to asbestos. In: Oury TD, Sporn TA, Roggli VL, eds. Pathology of Asbestos-Associated Diseases. *Springer Berlin Heidelberg*. 2014:11-24. Doi: 10.1007/978-3-642-41193-9_2
9. Furuya S, Chimed-Ochir O, Takahashi K, David A, Takala J. Global Asbestos Disaster. *Int J Environ Res Public Health*. 2018;15(5). Doi: 10.3390/ijerph15051000
10. International Labour Organisation. C162 - Asbestos Convention, 1986 (No. 162). 1986. Accessed November 18, 2022. https://www.ilo.org/dyn/normlex/en/f?p=NORMLEXPUB:12100:0::NO::P12100_ILO_CODE:C162
11. International Labour Organisation. Safety in the Use of Asbestos: An ILO Code of Practice.; Geneva, ILO, 1984. https://www.ilo.org/sites/default/files/wcmsp5/groups/public/%40ed_protect/%40protrav/%40safework/documents/normativeinstrument/wcms_107843.pdf (Last Accessed October 31, 2024)
12. Laurie Kazan-Allen. Current Asbestos Bans. 2022. (Last Accessed November 18, 2022). http://ibasecretariat.org/alpha_ban_list.php
13. eLIBRARY.RU – electronic library of scientific publications. Accessed October 7, 2023. https://www.elibrary.ru/defaultx.asp (Available in Russian)
14. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Syst Rev.* 2021;10(1):89. Doi: 10.1186/s13643-021-01626-4
15. Page MJ, McKenzie JE, Bossuyt PM, et al. Updating guidance for reporting systematic reviews: development of the PRISMA 2020 statement. *J Clin Epidemiol*. 2021;134:103-112. Doi: 10.1016/j.jclinepi.2021.02.003
16. Scientific Production Association "Preventive Medicine. Hygiene Assessment of the Working Conditions of Workers Engaged in the Production of Asbestos-Cement Products. Ministry of Health of the Kyrgyz Republic; 2020:68. (Available in Russian)
17. Trade Map – Trade statistics for international business development. Accessed December 26, 2022. https://www.trademap.org/Index.aspx
18. Ibraev SA, Otarov Ez, Zharylkasyn Z, Koigeldinova Sh S, Kulov DB, Kalishev MG. The possibility of predicting the pathology of the lungs in terms of the allowable work experience with chrysotile. *Med Tr Prom Ekol*. 2015;(3):8-11. (Available in Russian)
19. Korotenko VA, Kirilenko AV, Kurokhtin AV, Neronova TI, Vashneva NS, Yakovlev MV. Asbestos: the practice of application in Kyrgyzstan, problems and recommendations. *Survey study*. Published online 2011. (Available in Russian)
20. Ibraev SA, Pankin YN, Koygeldinova SS, et al. [Longitudinal study of differences between functional state of the body in workers at the chrysotile asbestos plant]. *Gig Sanit*. 2016;95(10):961-965. (Available in Russian)
21. Koigeldinova SS, Ibraev SA, Kasymova AK. State of lipid peroxidation in workers engaged into chrysotile-asbestos production. *Meditsina truda i promyshlennaia ekologiia*. 2015;(3):5-8. (Available in Russian)
22. Baselyuk LT, Bekpan AZ. Cytological analysis of smears of the nasal mucosa and buccal epithelium of the cheeks in workers of the chrysotile-asbestos production of JSC Kostanay Minerals. *Toxicological Bulletin*. 2011; (2 (107)):20-23. (Available in Russian)
23. Ibraev SA, Kazimirova OV, Eshmagambstova JA, Sydyrmanova TV, Kasymova AK. Clinical and functional characteristics of the state of the bronchopulmonary system under the influence of chrysotile-asbestos dust. *Russ J Occup Heralth Indust. Ecol*. 2008;(2):30-33. (Available in Russian)
24. Amanbekova AU, Azhimetova GN, Gazizov OM, Bekpan AZ. Characteristics of the immune system of the organism of workers in chrysotile-asbestos production. Bulletin of Karaganda University. Published online 2012:61.
25. Amanbekova AU, Ibrayeva LK, Azhimetova GN, Zhumabekova GS. Identification of induced

mutagenesis by method of accounting of chromosomal aberrations at the workers of chrysotile asbestos production. *Bulletin of Karaganda University*. 2012;66(2): 12-16.
26. Ibraev SA, Zharylkasyn ZZ, Otarov EZ, et al. Biochemical indicators in interstitial pneumofibrosis in workers with chrysotile. *Bulletin of the Ural Medical Academic Science*. 2015;(2):53-55. (Available in Russian)
27. Kurkin AV, Abaevna DZ, Khabibullaevna RD. Cytological study of buccal epithelium with different work experience in chrysotile-asbestos production. *Russ. J Occup Heralth Indust Eco.* 2015;(3):16-18. (Available in Russian)
28. Koigeldinova S, Alexeyev A, Zharylkassyn Z, et al. Immune Status of Workers with Professional Risk of Being Affected by Chrysotile Asbestos in Kazakhstan. *Int J Environ Res Public Health.* 2022;19(21):14603.
29. Amanbekova AU, Sakiev KZ, Ibraeva LK, Otarbaeva MB. [Main results of research concerning asbestos-related diseases in Kazakhstan Republic]. *Med Tr Prom Ekol.* 2014;(8):13-18. (Available in Russian)
30. Koigeldinova SS, Ibraev SA, Bazelyuk LT, Kasymova AK, Talaspayeva AE. Phagocytosis of alveolar macrophages in experimental animals exposed to chrysotile-asbestos dust. *Hygiene and Sanitation*. 2021;100(1):73-76. (Available in Russian)
31. Ainagulova G, Bulgakova O, Ilderbayev O, Manekenova K, Tatayeva R, Bersimbaev R. Molecular and immunological changes in blood of rats exposed to various doses of asbestos dust. *Cytokine*. 2022;159:156016. Doi: 10.1016/j.cyto.2022.156016
32. Akhmadaliev MA, Askarov IR, Turdiboev IHU. Mineral-basalt fibers instead of carcinogenic asbestos-containing composite materials. *Universum: engineering sciences*. 2021;(8-2 (89)):17-20. (Available in Russian)
33. Altynbekov MB, Sembaev Z, Salimbaeva BM. Regional assessment of mesothelioma incidence in the Republic of Kazakhstan. In: State budgetary educational institution of higher professional education Tver State Medical Academy of the Ministry of Health of the Russian Federation; 2018:58-61. (Available in Russian)
34. Ibraev SA, Otarov EZ, Zharylkasyn LJ, Koigeldinova S. Controlled use of chrysotile through occupational risk development. *Medicine of Kyrgyzstan*. 2014;(4):88-90. (Available in Russian)
35. Ibraev S, Alekberov M, Zharylkassyn Z, Otarov E, Tilemisov M. [analysis of morbidity with temporary disability of workers in the ore beneficiation on chrysotile production]. *Georgian Med News*. 2018;(283): 104-108. (Available in Russian)
36. Allen, Lucy P, Baez, Jorge, Stern, Mary Elizabeth C & George, Frank. (2017). Asbestos: economic assessment of bans and declining production and consumption. World Health Organization. Regional Office for Europe. https://iris.who.int/handle/10665/344114
37. Agency for Strategic planning, reforms of the Republic of Kazakhstan Bureau of National Statistics. Agency for Strategic planning and reforms of the Republic of Kazakhstan Bureau of National statistics. Published online 2022. (Available in Russian)
38. Kostanay Minerals JSC. Accessed November 18, 2022. https://km.kz/en/%D0%B3%D0%BB%D0%B0%D0%B2%D0%BD%D0%B0%D1%8F-english/
39. National Statistical Committee of the Kyrgyz Republic. The Population of Kyrgyzstan. Book II. Census, 2022. National Statistical Committee; 2023. (Available in Russian)
40. Kant Pipe - Slate Enterprise. About the company. Accessed November 18, 2022. https://kantslate.kg/en/about
41. About company | Industrial complex "Uralasbest." Accessed October 19, 2023. https://www.uralasbest.ru/en/about-company
42. Kant Kurulush. Kant Kurulush. Accessed February 10, 2023. http://www.kurulush.kg/. (Available in Russian)
43. Agency on statistics under the President of the Republic of Uzbekistan. Permanent population. Accessed February 13, 2023. https://stat.uz/en/
44. The Observatory of Economic Complexity. Bilateral-product. Asbestos. Accessed February 13, 2023. https://oec.world/en/profile/bilateral-product/asbestos/reporter/
45. The Association of building materials industry enterprises of Uzbekistan. Database of building materials manufacturers. Asbestos-cement products.
46. Agency on statistics under the President of the Republic of Tajikistan. Population. Accessed February 13, 2023. https://www.stat.tj/en. (Available in Russian)
47. The World Bank Group. Country. Turkmenistan. Accessed February 13, 2023. https://data.worldbank.org/
48. Ibraev SA, Otarov EJ, Zeynidenov AK. Some data on the physicochemical properties of the surface of chrysotile-asbestos fiber. *Bulletin of Karaganda University.* 2011;2(62):3-7. (Available in Russian)
49. Ministry of Health of the Republic of Kazakhstan R of K. On Approval of Hygienic Standards for Atmospheric Air in Urban and Rural Settlements, in the Territories of Industrial Organizations; 2022. (Available in Russian)
50. Government of the Kyrgyz Republic. Hygienic Standards "Maximum Permissible Concentrations of Harmful Substances in the Air of the Working Zone."; 2016. Accessed February 1, 2023. http://cbd.minjust.gov.kg/act/view/ky-kg/11958?cl=ky-kg. (Available in Russian)
51. World Health Organization. Determination of Airborne Fibre Number Concentrations: A Recommended Method, by Phase Contrast Optical Microscopy (Membrane Filter Method). World Health Organization; 1997:53.
52. Ibraev SA, Zharylkasyn ZhZh, Alekseev AV, Sokharev EYu. Lung tissue and the content of chrysotile dust in persons living in Zhitikara, in the section. In: NAO "MEDICAL UNIVERSITY OF KARAGANDY".; 2022:85-87. (Available in Russian)

53. Golovachev SV. Some epidemiological aspects of malignant pleural mesothelioma. *Vestnik KRSU*. 2008;8(4):93. (Available in Russian)
54. Chen J, Wang C, Zhang J, et al. A comparative study of the disease burden attributable to asbestos in Brazil, China, Kazakhstan, and Russia between 1990 and 2019. *BMC Public Health*. 2022;22(1):2012. Published 2022 Nov 3. Doi: 10.1186/s12889-022-14437-6
55. Ferlay J, Lam F, Colombet M, et al. EM. Global Cancer Observatory: Cancer Today. 2020. [Last Accessed January 27, 2023]. https://gco.iarc.fr/today
56. Directive (EU) 2023/2668 amending Directive 2009/148/EC on the protection of workers from the risks related to exposure to asbestos at work – European Sources Online. Accessed June 22, 2024. https://www.europeansources.info/record/proposal-for-a-directive-amending-directive-2009-148-ec-on-the-protection-of-workers-from-the-risks-related-to-exposure-to-asbestos-at-work/
57. Occupational diseases statistics - Statistics Explained. Accessed June 22, 2024. https://ec.europa.eu/eurostat/statisticsexplained/index.php?title=Occupational_diseases_statistics&oldid=623809
58. Eurogip. EUROPEAN FORUM of the Insurance against Accidents at Work and Occupational Diseases Enquiry Report. Published online 2006. Accessed June 22, 2024. www.eurogip.fr
59. Gibbs GW, Berry G. Mesothelioma and asbestos. *Regul Toxicol Pharmacol*. 2008;52(1 Suppl):S223-31. Doi: 10.1016/j.yrtph.2007.10.003
60. Smith AH, Wright CC. Chrysotile asbestos is the main cause of pleural mesothelioma. *Am J Ind Med*. 1996; 30(3):252-266. doi:10.1002/(SICI)1097-0274(199609)30:3<252::AID-AJIM2>3.0.CO;2-0
61. Visonà SD, Capella S, Bodini S, et al. Inorganic Fiber Lung Burden in Subjects with Occupational and/or Anthropogenic Environmental Asbestos Exposure in Broni (Pavia, Northern Italy): An SEM-EDS Study on Autoptic Samples. *Int J Environ Res Public Health*. 2021;18(4). Doi: 10.3390/ijerph18042053
62. Casali M, Carugno M, Cattaneo A, et al. Asbestos Lung Burden in Necroscopic Samples from the General Population of Milan, Italy. *Ann Occup Hyg*. 2015;59(7):909-921. Doi: 10.1093/annhyg/mev028
63. Barbieri PG, Somigliana A, Chen Y, Consonni D, Vignola R, Finotto L. Lung Asbestos Fibre Burden and Pleural Mesothelioma in Women with Non-occupational Exposure. *Ann Work Expo Health*. 2020;64(3):297-310. Doi: 10.1093/annweh/wxaa009
64. Mirabelli D, Calisti R, Barone-Adesi F, Fornero E, Merletti F, Magnani C. Excess of mesotheliomas after exposure to chrysotile in Balangero, Italy. *Occup Environ Med*. 2008;65(12):815-819. Doi: 10.1136/oem.2007.037689
65. Lin S, Wang X, Yu ITS, et al. Cause-specific mortality in relation to chrysotile-asbestos exposure in a Chinese cohort. J Thorac Oncol. 2012;7(7):1109-1114. Doi: 10.1097/JTO.0b013e3182519a60
66. Wong JYY, Rice C, Blair A, Silverman DT. Mesothelioma risk among those exposed to chrysotile asbestos only and mixtures that include amphibole: a case-control study in the USA, 1975-1980. *Occup Environ Med*. Published online October 21, 2020. Doi: 10.1136/oemed-2020-106665
67. Republic of Kazakhstan. Pleural mesothelioma > Clinical protocols of the Ministry of Health of the Republic of Kazakhstan - 2017 (Kazakhstan). MedElement. November 10, 2017. Accessed November 13, 2023. https://diseases.medelement.com/disease/%D0%BC%D0%B5%D0%B7%D0%BE%D1%82%D0%B5%D0%BB%D0%B8%D0%BE%D0%BC%D0%B0-%D0%BF%D0%BB%D0%B5%D0%B2%D1%80%D1%8B-2017/15485

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Supplementary material

Asbestos in Central Asian Countries: Exposure Assessment and Health Consequences: A review

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Supplementary material

Table S1. Searching keywords and strings in international repositories.

Search string or keywords	Asbestos use and asbestos-related diseases in CA and	Database(s)
Keywords	"Asbestos"; "Chrysotile"; "Asbestosis OR asbestos-related diseases OR Mesothelioma"; "Asbestos AND Kyrgyzstan"; "Asbestos AND Uzbekistan"; "Asbestos AND Tajikistan"; "Asbestos AND Turkmenistan"; "Asbestos AND Kazakhstan"; and "Asbestos AND Central Asia"	PubMed, Google Scholar, Web of Science, Scopus and Elibrary.ru (in Russian)

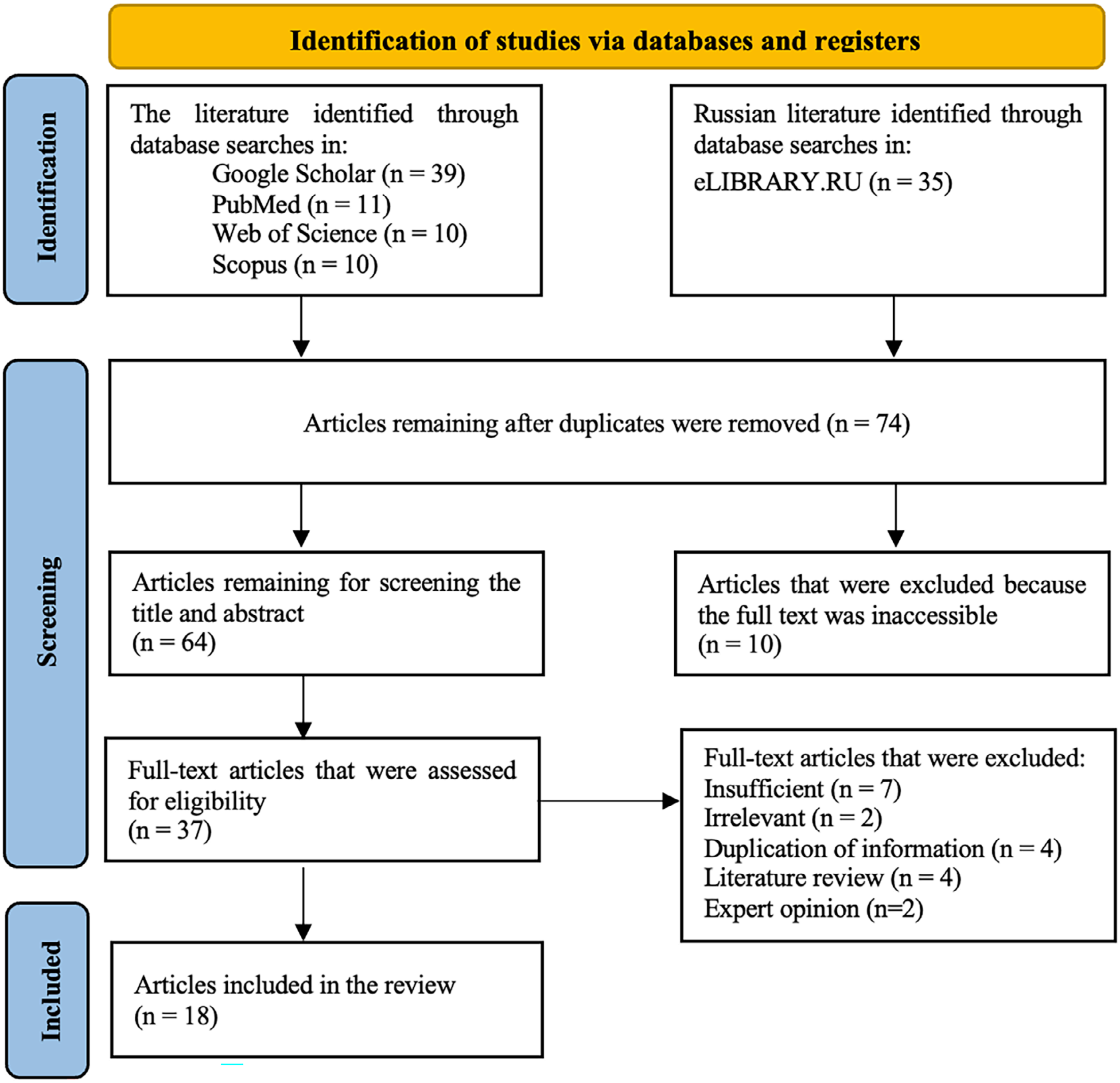

Figure S1. The inclusion and exclusion criteria for published articles on asbestos and asbestos-related diseases in CA Countries.

Table S2. Summarized details of the selected articles.

#	Authors	Language	Method	Sample	Samples size	Dust pollution at the workplace	Human data (stat data)	Biological samples from human and clinical examination	Studies on lab animals	Non-malignant ARDs -pneumoconiosis, pleural plaques	Asbestos-related Mesothelioma (ARM)	Asbestos-related Lung cancer (ARL)
1.	Altynbekov et al., (2018) Kazakhstan, [33]	Russian	analysis of the incidence of mesothelioma in the country for 2012-2016, survey	statistical data, questionnaires	257 human's data	no	yes	no	no	no	yes	no
2.	Ibraev et al., (2016) Kazakhstan, [20]	Russian	The longitudinal study (every year for 7 years, the same group of workers were examined)	blood	85 humans	no	no	yes	no	no	no	no
3.	Koigeldinova et al., (2015) Kazakhstan, [21]	Russian	biochemical analysis	blood	207 humans	no	no	yes	no	no	no	no
4.	Ibraev et al., (2015) Kazakhstan [18]	Russian	Calculation of the allowable length of service based on indicators of the average shift concentration of chrysotile-asbestos dust	dust	unknown	yes	no	no	no	no	no	no
5.	Amanbekova et al., (2014) Kazakhstan, [29]	Russian	review of own previous studies	n/a	n/a	yes	yes	no	no	no	no	no
6.	Ibraev et al., (2014) Kazakhstan [34]	Russian	assessment of occupational disease risk	statistical data	5 years	no	yes	no	no	no	no	no

Table S2 (*Continued*)

#	Authors	Language	Method	Sample	Samples size	Dust pollution at the workplace	Human data (stat data)	Biological samples from human and clinical examination	Studies on lab animals	Non-malignant ARDs -pneumoconiosis, pleural plaques	Asbestos-related Mesothelioma (ARM)	Asbestos-related Lung cancer (ARL)
7.	Baselyuk et al., (2011) Kazakhstan, [22]	Russian	cytomorphological study of cells of the nasal mucosa and buccal epithelium of the cheeks	the nasal mucosa and buccal epithelium of the cheeks	65 humans	no	no	yes	no	no	no	no
8.	Ibraev et al., (2008) Kazakhstan, [23]	Russian	analysis of the function of external respiration, the study of the gas composition of arterial blood, plain radiography of the chest	human	47 humans	no	no	yes	no	yes	no	no
9.	Amanbekova et al., (2012) Kazakhstan, [24]	English	observational cohort studies	nasal mucosa	106 humans	no	no	yes	no	no	no	no
10.	Amanbekova et al., (2012) Kazakhstan, [25]	English	observational cohort studies	blood	85 humans	no	no	yes	no	no	no	no
11.	Koigeldinova et al., (2021) Kazakhstan, [30]	Russian	study of cytotoxic effect	asbestos dust	30 rats	no	no	no	yes	yes	no	no
12.	Ibraev et al., (2015) Kazakhstan, [26]	Russian	X-ray of chest and blood, aeration function of the lungs	human	119 humans	no	no	yes	no	yes	no	no
13.	Kurkin et al., (2015) Kazakhstan, [27]	Russian	Buccal epithelium cytograms	the nasal mucosa and buccal epithelium of the cheeks	108 humans	no	no	yes	no	no	no	no

14.	Ainagulova et al., (2022) Kazakhstan, [31]	English	Immunity monitoring	blood	40 rats	no	no	no	yes	no	no	no
15.	Koigeldinova et al., (2022) Kazakhstan, [28]	English	multiplex immunological assay	blood	125 humans	no	no	yes	no	no	no	no
16.	Ibraev et al., (2018) Kazakhstan, [35]	Russian	retrospective analysis of morbidity	statistical data	1216 human	no	yes	no	no	no	no	no
17.	Korotenko et al., (2011) Kyrgyzstan, [19]	Russian	various	statistical data	n/a	yes	yes	no	no	no	yes	no
18.	Akhmadaliev et al., (2021) Uzbekistan, [32]	Russian	review of the situation in the country	n/a	n/a	n/a	n/a	n/a	n/a	no	no	no

n/a – not applicable

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Original article

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COVID-19 Pandemic's Effects on Occupational Health and Perceived Work Ability of a Large Group of Italian Banking Employees

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Keywords: Asthenopia; Musculoskeletal Disorders; Work-Related Stress; Work Ability; Tertiary

Abstract

Background: *The COVID-19 pandemic compelled changes to the structure and organization of many occupational sectors that may impact workers' well-being and work-related symptoms.* **Objective:** *To evaluate the effects of work-related modifications associated with the COVID-19 pandemic on occupational health outcomes and work ability (WA) among a large group of Italian banking employees.* **Methods:** *2,859 employees visited during health surveillance in 2021 were divided into two job groups: front-office (FO) and back-office (BO) workers. Data on conditions associated with office work, psychological distress, WA, and fitness-to-work judgment were analyzed and compared with available pre-COVID (2018–2019) studies.* **Results:** *After lockdown, a 28% increase in asthenopia was found in BO, while a 22% and 9% increase in musculoskeletal symptoms was found in BO and FO, respectively. Moreover, a 28% rise in stress-related symptoms and a 17% increase in psychotropic drug consumption were found in both groups. After lockdown, the prevalence of WAI scores moderate/poor decreased by 17% in each group, but no evidence of significantly improved WA emerged for either group. Fitness-to-work judgment without limitations prevalence remained unchanged.* **Conclusion:** *The study showed a reduced prevalence of analyzed outcomes compared to that found in the literature at pre-COVID and post-lockdown evaluation. A slight worsening in all outcomes examined post-lockdown was also highlighted in our study. It can be speculated that these results are linked to the measures the Institute took to support employees during the COVID-19 pandemic. Indeed, a comprehensive integration between occupational safety and health promotion practices is recommended to ensure the highest level of safeguarding for workers' well-being.*

1. Introduction

During the COVID-19 pandemic in Italy, business continuity was ensured by forcing changes to the structure and organization of various occupational sectors. This was done in compliance with regulations protecting public health [1, 2] to contrast the virus's spread.

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Throughout the "4.0" tertiary sector, which includes the banking industry, the widespread adoption of "smart" working (SW)—which was encouraged from the start of the nationwide lockdown to May 2020 and continued in many organizations until the end of the pandemic emergency—has had a substantial impact on workers' exposure to traditional work-related risk factors, potentially affecting work-related symptoms and employees' psychological well-being [3].

Data from Sondtel (Economic survey on industrial and service companies) [4] indicates that during the pandemic, particularly during the first and second waves (spring 2020 and winter 2020-2021), the relevance of SW in Italy significantly increased (the percentage of companies applying agile work increased from 28.7% in 2019 to 82.3% in 2020).

SW appeared to have beneficial effects such as improved job performance and focus at work; however, it was also linked to adverse effects such as increased social isolation of home workers, decreased free time for personal activities, and an overlap of work and family life [5].

Indeed, the COVID-19 pandemic has resulted in many workers being required to work from home, often in cramped and restricted spaces, using tablets, laptops, and smartphones. As a result of these changes, new risk factors are gradually emerging alongside the two major occupational risk factors historically linked to the office work setting: oculo-visual overload (associated with prolonged use of a video terminal or other digital devices) and posture risk (concerning using a workstation that is not ergonomic or spending a lot of time stationary). The growing usage of SW during COVID-19 highlighted that operators in the tertiary sector must maintain a constant connection with "information and communication technologies" (ICT), which have evolved into essential instruments for job performance. Prolonged use of tablets, smartphones, and other electronic devices—often after regular business hours—might pose psychosocial risks due to issues with learning new software, data overload, hyperreactivity, and a blurring of the lines between personal and professional life (cognitive ergonomics). Furthermore, the development of ICT has the potential to affect workers' health significantly if it is not controlled or appropriately regulated, leading to excessive and compulsive use and an increased risk of digital addiction [8].

Additionally, the ongoing engagement with clients and the corresponding handling of disputes (which may involve physical or verbal abuse) in the banking industry may contribute to a high prevalence of psychological symptoms among Italian bank workers [9, 10], particularly for those who carried on providing in-person services to clients throughout the COVID-19 pandemic [11].

Psychological distress in tertiary workers can also contribute to a decline in perceived work ability (WA), which is the extent to which an employee believes he is physically and mentally capable of handling the demands of his job and workplace [12, 13]. A systematic review found that high mental work demands, a lack of decision-making autonomy, and an unsuitable work environment are among the factors most likely associated with poor WA in older age [14]. A poor WA raises the possibility that employees may intend to leave work early due to illness, stress, or depression, as well as the number of absences caused by these conditions [13].

Occupational physicians and other professionals involved in worker safety and health protection must oversee all these aspects, which are especially important in the "4.0" tertiary sector. This study aims to evaluate the effects of organizational restrictions and working changes related to the COVID-19 pandemic on occupational health (including asthenopia-like symptoms, musculoskeletal problems, stress-related symptoms, and psychotropic drug consumption) and WA among a large group of Italian banking employees divided into two job sub-groups: front-office (FO) and back-office workers (BO).

2. Methods

The study was conducted in a prime financial institution with over 95,000 employees, with branches throughout northern and southern Italy. Out of them, around one-third were subject to routine medical examinations by occupational physicians for exposure to occupational risks, as indicated by law. The study sample consisted of 2,859 workers who were examined during a health surveillance program in 2021 (roughly one year after the national COVID-19 lockdown) and had a clinical examination documented in the electronic medical database two years before the COVID pandemic (2018-2019). The study was conducted as a repeated cross-sectional study, also known as repeated measures or longitudinal study [15], comparing the prevalence of the outcomes of interest between the post-lockdown period and pre-COVID biennium (2018-2019). The mean interval between the two medical exams was 32,8 months.

The study cohort included 2,859 workers (mean age 50 years±4.24 SD; 1,391 males, 1,468 females). As shown in Table 1, about 64% of the workers performed BO activities; specifically, men were more prevalent than females (54.0% vs. 46.0%), while most FO workers (60.9%) were women. Compared to BO workers, FO workers had a higher average age (51.1 vs. 49.4 years). About 45% of the subjects in the BO group had college degrees (vs 25.6% of FO). Respectively, 8.1% of BO and 19.2% of FO reported having had a COVID-19 infection at the 2021 health surveillance examination.

The study cohort was classified into two main groups according to the primary activities conducted by the workers during lockdown: employees with FO activities (1,030 workers) who continued to work in person to guarantee the availability of "essential" services by government directives [1], and employees with remote BO activities (1,829 workers), such as online branches and administrative staff, who worked exclusively from home during the emergency phase and continued to work primarily remotely in the months that followed the pandemic.

The study analyzed data from the health surveillance program managed by the Occupational Physicians, looking into the prevalence of (i) conditions associated with office work, such as asthenopic symptoms and musculoskeletal disorders; (ii) signs of psychological distress, such as stress-related symptoms (e.g., asthenia, headaches, anxiety, depression, sleep disturbances, epigastralgia, and stomach pain) and consumption of psychotropic drugs (e.g., antidepressants, anti-anxiety medications and mood stabilizers); (iii) perceived WA; (iv) fitness to work judgment as result of health surveillance examination performed by Occupational Physicians.

Table 1. Characteristics of the employees in BO and FO groups.

	Back-office (N=1,829)	Front-office (N=1,030)
Gender		
F	841 (46.0%)	627 (60.9%)
M	988 (54.0%)	403 (39.1%)
Age		
18-30	63 (3.4%)	4 (0.4%)
31-40	212 (11.6%)	72 (7.0%)
41-50	514 (28.1%)	317 (30.8%)
51-60	1003 (54.8%)	615 (59.7%)
>60	37 (2.0%)	22 (2.1%)
Scholarly level		
Middle School	33 (1.8%)	27 (2.6%)
High School	882 (48.2%)	731 (71.0%)
Professional School	21 (1.1%)	4 (0.4%)
Bachelor Degree	48 (2.6%)	10 (1.0%)
Master's Degree	835 (45.7%)	253 (24.6%)
Others	10 (0.5%)	5 (0.5%)
COVID status in 2021		
Infected	149 (8.1%)	187 (18.2%)
Not infected	1680 (91.9%)	843 (81.8%)

Twelve Occupational Physicians were involved in health surveillance. Furthermore, periodic meetings to discuss the most complex cases and the presence of two occupational medical coordinators allowed for homogeneity in the criteria used by occupational physicians for recording symptoms and managing cases.

The Occupational Physicians used a targeted questionnaire [6] to gather data on the prevalence and the degree of asthenopia during medical examination. The questionnaire assesses the frequency of asthenopia symptoms while using video terminals. A score of 0 denotes the lack of abnormalities, a score of 1 to 3 indicates the presence of not significant asthenopia, and a score of more than 4 indicates the presence of asthenopia (mild degree between 4 and 6, moderate degree from 7 to 9, and severe if higher than 9). The Occupational Physicians also conducted targeted anamnesis to gather data on musculoskeletal disorders and stress-related symptoms. To study stress-related symptoms, Occupational Medical Coordinators listed several conditions that are most frequently reported by employees in Literature, including mental asthenia, headaches, anxiety, depression, sleep disturbances, epigastralgia, and stomach pain [9]. These symptoms were investigated during the health surveillance examinations.

The Work Ability Index (WAI) questionnaire assessed perceived work ability [16]. The WAI is composed of seven items that correspond to one or more questions: (i) current ability to work with the best in life (work ability score), (ii) ability to work with job requirements, (iii) number of current illnesses diagnosed by a physician, (iv) estimated work loss because of illness, (v) absence from work in the previous year, (vi) self-prognosis of work ability in 2 years, and (vii). mental resources. The index is calculated by the sum of the points on each item, ranging from 7 to 49 points. Work ability is then classified as poor (7 to 27 points), moderate (28 to 36 points), good (37 to 43 points), or excellent (44 to 49 points).

The data was gathered through health surveillance medical examinations, anonymously extracted from the medical records, and then analyzed in compliance with the most recent privacy protection laws.

2.1. Statistical Analysis

The analysis was performed on 2,859 records, including information about employee demographics, job characteristics, and the study outcomes. All the variables were recorded on a categorical scale and reported using counts and percentages. Longitudinal regression models [17] were used to evaluate changes in outcome prevalences between pre-COVID and post-lockdown periods for BO and FO. To this end, logistic regression models were fitted, with time (pre-COVID or post-lockdown) and occupational category (BO or FO) as covariates and log links. The models were fitted using the Generalized Estimating Equations (GEE) method to account for the longitudinal design [18].

The hypothesis of parallelism was first assessed; in case the null hypothesis was not rejected, tests on time and group effects were performed [17]. It is worth noting that since the time variable can assume only two distinct values, the hypothesis of parallelism is equivalent to the hypothesis of having the same change in the prevalence of outcome within BO and FO groups.

Results were reported using estimated prevalence ratios (post-lockdown vs. pre-COVID) with respective 95% Confidence Intervals. Estimates of prevalence ratios adjusted for gender, age, scholarly, time between pre-COVID and post-lockdown evaluation, and infection status in 2021 were reported to account for potential confounding effects.

Finally, the *"mosaic matrix"* technique [19] was used to evaluate the association between the pre-COVID outcomes—except for the WAI score, which was recorded only in a subset of the cohort. All the analyses were performed using the software R release 4.2.3 [20] with the package geepack [21] added.

3. Results

Figure 1 displays the prevalences of the analyzed occupational outcomes for BO and FO workers during the pre-COVID and post-lockdown periods.

Tables 2 and 3 show the results of longitudinal analysis focused on comparing the prevalences between the above periods.

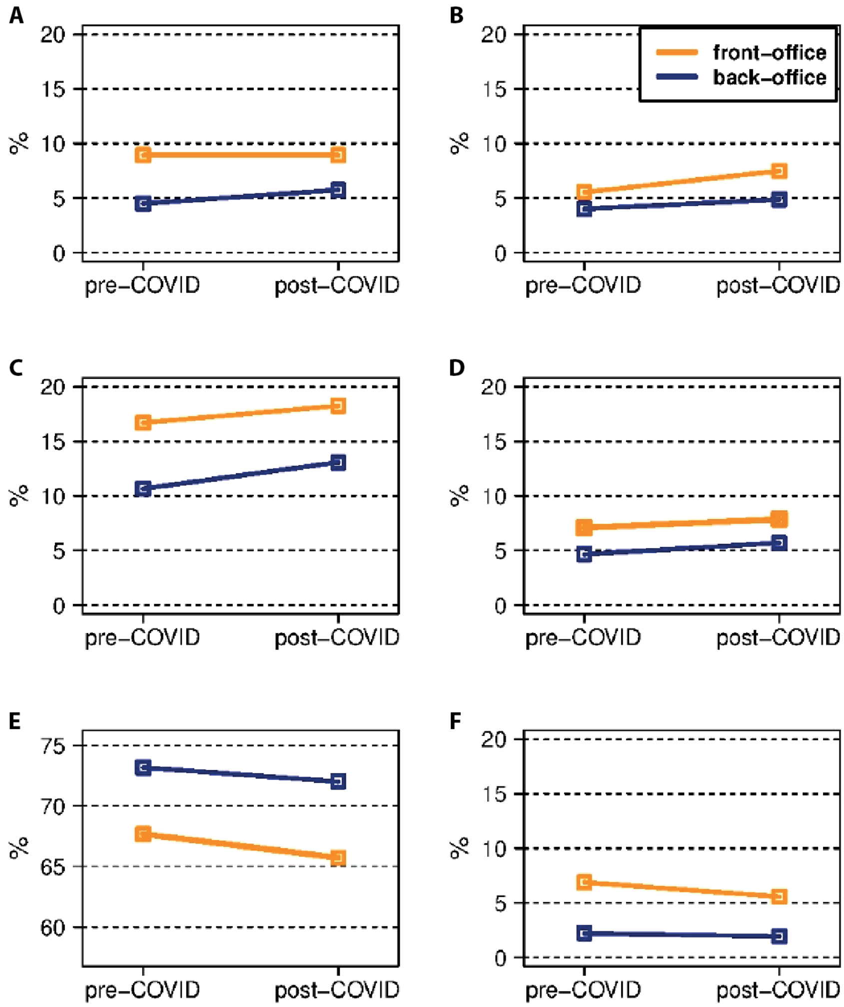

Figure 1. Prevalence of occupational outcomes at pre-COVID and post-lockdown evaluations for front and back office workers.

Regarding ocular-visual system disorders, non-negligible asthenopia (score>3) was reported by 4.5% of BO workers and 8.9% of FO workers during the pre-COVID period. During post-lockdown, the prevalence increased by 28% in the BO group (according to a prevalence ratio equal to 1.28), while it remained unchanged in the FO group (prevalence ratio: 1.00). Evidence was found of a non-null difference between the above prevalence ratios (p=0.0046; Table 3), suggesting a more significant increase of asthenopia in the BO group.

Musculoskeletal disorders were reported by 10.7% of BO workers and 16.7% of FO workers during pre-COVID-19 evaluation. An increase in these symptoms during the post-lockdown period was observed in both BO and FO workers (23% and 9%, respectively). Lumbar (40% of FOs and 48% of BOs) and cervical spine (40% of FOs and 33% of BOs) were the affected segments. The two groups exhibited a difference in prevalence ratios (1.23 and 1.09 for BOs and FOs, respectively), with a more significant increase in musculoskeletal symptoms in BOs post-lockdown (p=0.0305, Table 3).

The figure shows the prevalences of the outcomes considered in this work, represented by colored squares. The segments connect the prevalences, thus

Table 2. Estimated prevalence ratios for assessing outcomes changes for pre-COVID and post-COVID period in back-office and front-office employees.

OUTCOME	Occupational group	Time	Prevalence		Unadjusted prevalence ratio	Adjusted+ prevalence ratio
			Observed	Estimate, 95% CI.	Estimate, 95% CI.	Estimate, 95% CI.
Asthenopy	back-office	pre-COVID	4.5%	4.5% (3.6%, 5.5%)	1.28 (1.12, 1.47)	1.28 (1.12, 1.46)
	front-office	post-COVID	5.7%	5.7% (4.8%, 6.9%)	1.00 (0.90, 1.11)	1.00 (0.90, 1.11)
		pre-COVID	8.9%	8.9% (7.3%, 10.9%)		
		post-COVID	8.9%	8.9% (7.3%, 10.9%)		
Musculoskeletal symptoms	back-office	pre-COVID	10.7%	10.7% (9.3%, 12.2%)	1.23 (1.14, 1.32)	1.22 (1.14, 1.32)
	front-office	post-COVID	13.1%	13.1% (11.6%, 14.7%)	1.09 (1.02, 1.17)	1.09 (1.02, 1.17)
		pre-COVID	16.7%	16.7% (14.6%, 19.1%)		
		post-COVID	18.3%	18.3% (16.0%, 20.8%)		
Stress-related symptoms	back-office	pre-COVID	4.0%	3.8% (3.1%, 4.8%)	1.28 (1.15, 1.41)	1.28 (1.15, 1.41)
	front-office	post-COVID	4.9%	4.9% (4.0%, 6.0%)	1.28 (1.15, 1.41)	1.28 (1.15, 1.41)
		pre-COVID	5.5%	5.8% (4.6%, 7.3%)		
		post-COVID	7.5%	7.4% (6.0%, 9.2%)		
Psychotropic drugs consumption	back-office	pre-COVID	4.6%	4.8% (4.0%, 5.8%)	1.17 (1.08, 1.27)	1.17 (1.08, 1.27)
	front-office	post-COVID	5.7%	5.6% (4.7%, 6.8%)	1.17 (1.08, 1.27)	1.17 (1.08, 1.27)
		pre-COVID	7.1%	6.8% (5.5%, 8.5%)		
		post-COVID	7.9%	8.0% (6.5%, 9.8%)		
Fitness to work without limitation	back-office	pre-COVID	73.2%	73.3% (71.3%, 75.3%)	0.98 (0.96, 1.00)	0.96 (0.95, 0.98)
	front-office	post-COVID	72.0%	71.9% (69.9%, 73.9%)	0.98 (0.96, 1.00)	0.96 (0.95, 0.98)
		pre-COVID	67.7%	67.4% (64.8%, 70.1%)		
		post-COVID	65.7%	66.1% (63.5%, 68.7%)		
WAI poor-moderate	back-office	pre-COVID	2.2%	2.3% (1.5%, 3.3%)	0.83 (0.67, 1.03)	0.83 (0.67, 1.03)
	front-office	post-COVID	1.9%	1.9% (1.2%, 2.8%)	0.83 (0.67, 1.03)	0.83 (0.67, 1.03)
		pre-COVID	6.9%	6.8% (5.1%, 9.1%)		
		post-COVID	5.6%	5.7% (4.2%, 7.7%)		

Prevalence ratios were defined as post-lockdown prevalence versus pre-COVID prevalence.
+*Adjusted for: gender, age, scholarity, infection state and time between pre-COVID and post lockdown evaluation.*

Table 3. Comparison of prevalence ratios of outcomes between groups (parallelism hypothesis) and outcome prevalences between times and between groups.

Outcome	Null hypothesis	χ^2	df	p
Asthenopy	Equal variation of prevalence between groups	8.05	1	0.0046
Musculoskeletal symptoms	Equal variation of prevalence between groups	4.68	1	0.0305
Stress-related symptoms	Equal variation of prevalence between groups	0.94	1	0.3312
	No difference in prevalence between periods	22.28	1	<0.0001
	No difference in prevalence between groups	7.58	1	0.0059
Psychotropic drugs consumption	Equal variation of prevalence between groups	1.36	1	0.2428
	No difference in prevalence between periods	13.70	1	0.0002
	No difference in prevalence between groups	6.10	1	0.0135
Fitness to work without limitation	Equal variation of prevalence between groups	0.30	1	0.5867
	No difference in prevalence between periods	3.36	1	0.0668
	No difference in prevalence between groups	13.06	1	0.0003
WAI poor-moderate	Equal variation of prevalence between groups	0.10	1	0.7500
	No difference in prevalence between periods	2.97	1	0.0850
	No difference in prevalence between groups	21.48	1	<0.0001

df = degrees of freedom

highlighting the differences between pre-COVID and post-lockdown periods. Outcomes: A) asthenopia; B) stress symptoms; C) musculoskeletal symptoms; D) consumption of psychotropic drugs; E) fitness to work; F) WAI low/moderate. Orange: front office; blue: back office.

Four point zero percent of BO workers and 5.5% of FO workers reported experiencing stress-related symptoms. During post-lockdown evaluation, the prevalence of these symptoms increased by 28% for both FO and BO workers (p<0.0001, Table 3). Additionally, there was evidence of a non-null difference in the prevalence of stress-related disorders between the two job groups in each period, with a greater prevalence of these symptoms in FOs both during the pre-COVID and post-lockdown period (p=0.0059).

Psychotropic drug consumption was reported by 4.6% of BO and 7.1% of FO, with an increase of 17% in both groups during post-lockdown evaluation. The comparison between the pre-COVID and post-lockdown periods showed evidence of a non-null difference in both groups (p=0.0002). Both in the pre-COVID and post-lockdown periods, the consumption of these drugs was more significant in the FO group compared to the BO group (p=0.0135).

Fitness to work judgment without limitations was expressed by Occupational Physicians for 73.2% of BOs and 67.7% of FOs during pre-COVID examinations, with no change in prevalence in both groups. Longitudinal analysis showed a greater prevalence of fitness to work judgment without limitations in BOs compared to FOs (p=0.0003) in both periods.

WAI questionnaire results were available for more than half of the workers (57.7% of the total) involved in the study (1650 employees out of 2859; 820 M – 830 F, mean age 50.3±2.8 SD, min-max range 20-64 years). This workers' cohort did not exhibit any notable dissimilarities in characteristics with the total study's cohort.

At the pre-COVID evaluation, most of the cohort (57%) scored "excellent," and more than a third of them (39%) scored "good". Four point four percent of employees received an insufficient rating (scoring "moderate" in 3.2% of cases and "poor" in 11 cases). A moderate/poor WAI score was registered by 2.2% of BO workers and 6.9% of FO workers. During post-lockdown evaluation, both groups showed improvements in the perceived WAI, and the prevalence of moderate/poor scores decreased by 17% in each group (according to a prevalence ratio of 0.83), even though this last finding was not evident (p=0.0850). Longitudinal analysis showed, both in pre-COVID and post-lockdown evaluation, a greater prevalence of moderate/poor scores in FOs when compared to BOs (p<0.0001).

For each outcome, the adjusted estimates of prevalence ratios in Table 2 were very close to the unadjusted ones, suggesting a negligible impact of the confounding variables on the latter ones.

Finally, Figure 2 shows the results of the "mosaic matrix" technique, used to evaluate the relationships between the analyzed outcomes during the pre-COVID examination. A slight association was highlighted between fitness to work judgment and the other outcomes. Among those, the strongest association was found with asthenopia (Cramer V=0.17).

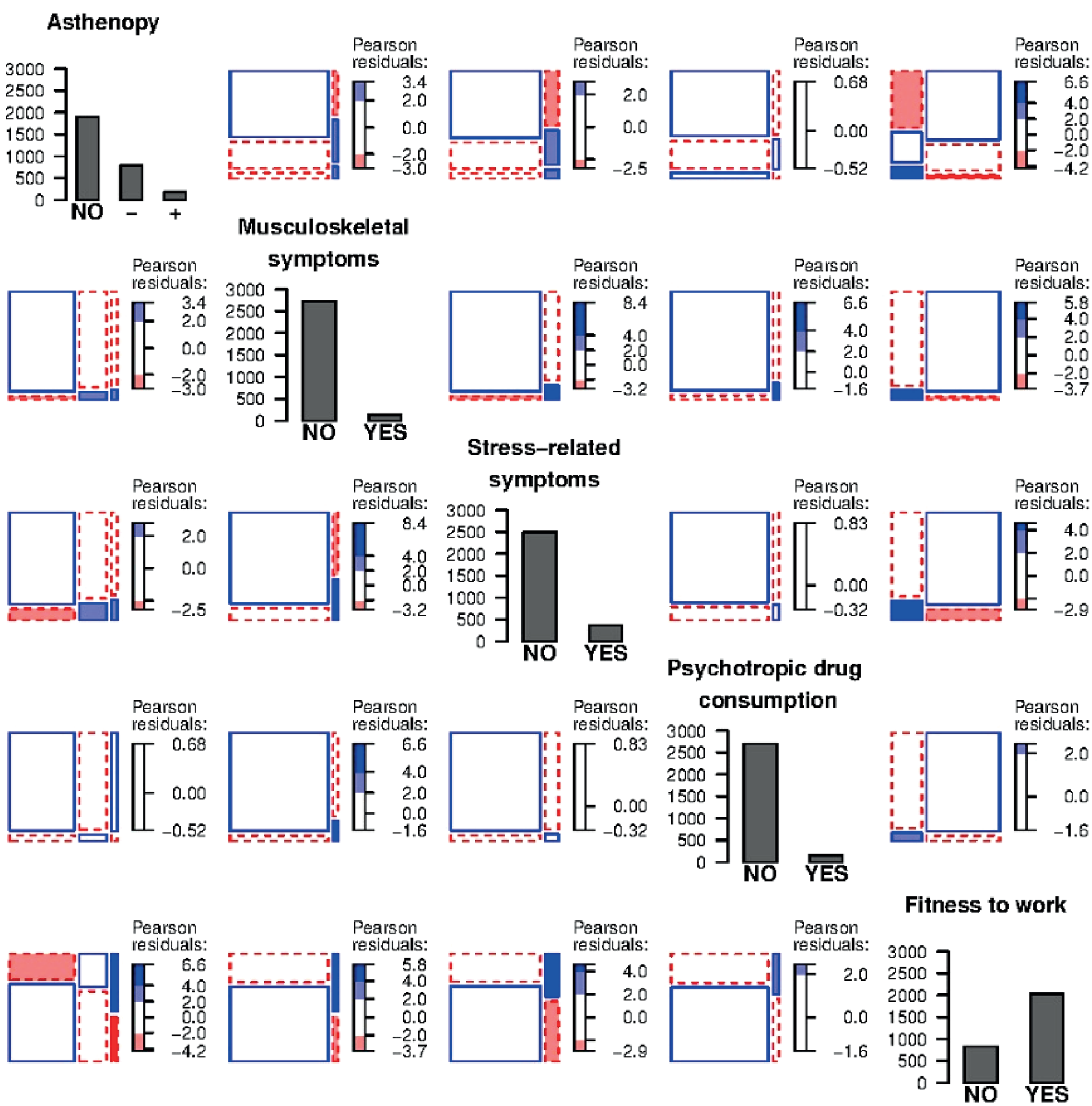

Figure 2. Associations between the examined occupational outcomes at the pre-COVID time in the study population.

In this case, the proportion of subjects with non-negligible asthenopia was higher among employees evaluated as “not fully fit to work” (fitness to work judgment with limitation) than employees with fitness to work judgment without constraints. Additionally, there was a slight positive association (Cramer V=0.17) between musculoskeletal and stress-related symptoms: workers who experience stress-related symptoms may also have musculoskeletal symptoms, and vice-versa. Lastly, we found a slight positive correlation between the use of psychotropic drugs and the occurrence of stress symptoms (V=0.13) but not with musculoskeletal symptoms (V=0.02). As a result, individuals using psychotropic medications may experience symptoms of stress and vice-versa.

Diagonal panels: bar plots showing the total counts of employees within each modality of the outcomes. Asthenopy was labeled as NO (absent), - (negligible), and + (light or moderate or severe); Fitness to work was labeled as NO (not fitting or fitting with limitations) and YES (fitness without limitations. Non-diagonal panels: mosaic plots showing the association between each outcome. A rectangle is drawn for each combination of outcome modalities within each mosaic plot. Color shading reflects the values of the Pearson residuals from the chi-square statistic; therefore, colored rectangles denote specific combinations of modalities with a higher or a lower frequency (blue and red color) compared to the expected frequencies under the assumption of independence. In conclusion, the greater the number of colored rectangles found within the graph and the intensity of the color, the greater the association between the variables considered.

4. Discussion

Our study aimed to assess the potential effects of the COVID-19 pandemic on work-related symptoms and perceived work ability (WA) of a large workforce in the banking industry. This working reality is important because, in the context of the COVID-19 emergency, the Italian government classified it as one of the “essential services” [1, 2]. As a result, these activities were kept on even during the lockdown, being instead subject to significant organizational changes. These measures were implemented to ensure that the activity could be carried out in person safely and to reduce the risk of spreading infection.

Specifically, the study examined the prevalence of occupational outcomes traditionally linked to video terminal activity, such as asthenopia and musculoskeletal disorders, in the selected population after the COVID-19 lockdown (post-lockdown). Additionally, we investigated the occurrence of stress-related symptoms and the use of psychotropic drugs in the study population. Lastly, an evaluation of the WAI questionnaire results, which the workers filled in during the occupational medicine examination, was carried out. Data from the post-lockdown period were compared to pre-COVID data from the same cohort to determine whether there had been any notable changes.

Regarding ocular-visual system disorders, our study highlighted asthenopia (mild, moderate, or severe) in 4.5% of BO and 8.9% FO, with a 28% rise in these symptoms in BOs during post-lockdown evaluation. Despite rising during the COVID-19 pandemic, the prevalence of these disorders was still lower than the primary published data on the topic. In a population of 191 video terminal operators, Taino et al. found a prevalence of non-negligible asthenopia greater than 30% [22]. Das et al. found that, out of 319 office workers, 89,4% had asthenopic symptoms, with more than 8 out of 10 subjects reporting the co-presence of at least one visual and musculoskeletal symptom. Prolonged working hours and an incorrect distance between the operator’s position and the screen were major contributors to asthenopic symptoms [23].

Regarding the traditional ergonomic risk associated with office work, a cross-sectional study conducted on video terminal operators between 2017 and 2020 found that 37.9% of the population had musculoskeletal disorders, with cervical/lumbar spine and shoulders being the most commonly affected [24]. In our study, musculoskeletal disorders were reported by 10.7% of BO workers and 16.7% of FO workers. Even though a 22% and 9% increase in these symptoms’ prevalence was found in the BO and FO groups during the post-lockdown period, their prevalence remains lower than that found in

Literature. The fact that musculoskeletal disorders had a more significant increase in the BO working population compared to the FO group could be attributed to the possibility that, in some cases, BOs did not use ergonomic workstations at home. Our study showed that the cervical and lumbar spines were the main areas of involvement, as reported in the literature [24].

Stress-related symptoms were experienced by less than 6% of our workers' cohort, with a 28% increase after the lockdown. This growth trend is consistent with data from the literature. According to a survey of 670 workers from various industries, including manual labor, healthcare, education, and other areas, stress-related symptoms increased during the COVID-19 pandemic. These symptoms were specifically linked to increased workload and, for over half of the participants, to a fear of getting infected at work [25]. Additionally, an Italian National Institute of Health survey [26] among over 55,000 interviews conducted between 2018 and 2020 revealed a rise in the prevalence of depressive symptoms among Italian adults (19-69 years old) during the two-month lockdown of March–April 2020 (7.1% vs. 6.1% in 2018-19), which was followed by a decrease (4.4%) in the two months following the end of pandemic restrictions (May-June 2020). Several factors may have contributed to the onset of these symptoms, including fear of infection in situations where the continuation of in-person work activity was necessary [11], as well as organizational changes related to the implementation of remote work activity with numerous subsequent forceful requests for workplace adaptations, with a significant impact on people's quality of life and general well-being. In all of the pandemic's phases, Orfei et al. showed how the overwhelming requests for employees to adjust to an unprecedented work-from-home mode and family routine had been a significant source of stress [27].

Regarding the use of psychotropic drugs, the Eurispes (Italian Institute of Research) survey conducted in 2021 found that the percentage of Italians consuming these drugs was 19%, a 20% increase from the pre-lockdown period [28]. The data collected in our study showed that, in the post-lockdown period, both job groups consumed fewer psychotropic drugs than the general population (5.6% for BO workers and 8% for FO workers), despite a slight increase when compared to the pre-COVID period.

Regarding the perceived work ability (WA), the overwhelming majority (>90%) of the cohort under investigation in our study reported good or excellent WAI scores before the COVID-19 pandemic, indicating a high level of occupational well-being among the study cohort. Additionally, there were no notable changes in scores during the post-lockdown period in our study's cohort. Similar data emerged in a study that examined how the COVID-19 pandemic affected the psychosocial characteristics and perceived work ability of 1211 Brazilian workers. Over 75% of employees reported good to excellent work ability at baseline evaluation and during the follow-up conducted in October 2021—more than a year after the COVID pandemic started [29]. Another study highlighted the possibility that work's intrinsic characteristics could significantly impact WA. In the Zgombic et al. study, banking operators (21 men and 75 women) were split into three groups: those with mostly front-office (FO) activities, those with primarily customer-facing activities within the office, and those with mostly back-office (BO) activities. The group of FO workers had lower WAI scores, whereas the operators who did not deal directly with customers had higher WAI scores; this difference between the groups was evident [30]. In agreement with Zgombic et al., our study found an apparent difference in WAI scores between the BO and FO groups both during pre-COVID and post-lockdown evaluation time. Furthermore, we found no notable changes in both groups' WAI scores comparing pre-COVID and post-lockdown evaluation data. In a recent study conducted in Finland, Kyrönlahti assessed the working capacity trend of a cohort of Scandinavian university employees after the COVID-19 pandemic's organizational and structural restrictions. This study also showed that, for the majority (75%) of the population, the perceived working capacity remained stable during follow-up, with an improvement affecting up to 17% of the workers and evidence of a worsening WA in only 8% of those interviewed [31].

Our research revealed a slight worsening in all examined occupational health outcomes after the post-lockdown period. Furthermore, the prevalence of our study's highlighted outcomes was consistently lower than the published data for the same topics.

It should be noted that all of these results could be related to the COVID-19 pandemic itself, as well as to the new work practices that have recently been growing in the tertiary sector and the measures that Companies have taken to support employees during this period of change. Indeed, during the past few years, the tertiary sector has undergone a "natural" and progressive transformation of the workplace that has impacted both the nature of the job itself and how it is organized, with modifications to the standard workday and workspace. Physical ergonomics (related to workstation characteristics and electronic/video terminal devices use) and cognitive ergonomics (that focuses on how well the use of innovative work tools matches the mental capabilities of workers) are affected by these changes [32]. The COVID pandemic has led to a notable acceleration of these changes, linked to the growing use of SW [33] and the mandatory changes to the workspaces and workstations (e.g., working in open spaces and sharing tools with coworkers guaranteeing the absence of risk of contagious, allocating work hours and places according to the kind of the activity being done and putting up barriers and equipment to lower the risk of infection transmission when engaging in public-facing activities).

Due to the nature and characteristics of the research that we conducted, we cannot investigate the causes that may have influenced the results of our study. However, we can speculate about the hypothesis of the involvement of preventive measures that the Financial Institute took to support all employees during this transitional period accelerated by the pandemic. In particular, these include: (i) the formation of a "task force" consisting of physicians that constantly work on COVID-19-related issues; (ii) the design of a psychological help desk to provide knowledgeable, experienced, and free assistance available 24/7; (iii) the distribution of information about adopting ergonomic postures and managing the workstation ergonomically at home; (iv) the distribution of content on meditation, mindfulness, and emotional well-being via the Institutional intranet; (v) an online application available to promote physical activity, as well as information and assistance regarding healthy lifestyle choices, with a focus on the worker's family-work balance. While the purpose of this study was not to assess the efficacy of these measures, it is possible to hypothesize that these good practices could have some role in reducing the impact of the COVID-19 pandemic on analyzed worker occupational health outcomes. While more research is required in this regard, it is essential to emphasize the necessity of a more comprehensive integration between the Occupational Physician and all other Occupational Safety personnel's activity, not only in the context of preventing occupational risks but also regarding health promotion, to ensure the highest level of safeguarding for workers' well-being.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki and the ethical principles of research conducted with human participants in Italy. Ethical review and approval were waived for this observational study because data were obtained during a mandatory health surveillance program and participants' data were anonymously processed. Observational studies like this do not need to get ethical approval.

Informed Consent Statement: The data were gathered through health surveillance medical examinations, anonymously extracted from the medical records, and then analyzed in compliance with the most recent privacy protection laws.

Author Contribution Statement: MM and PC conceived and designed the analysis; MM and ML collected the data; MM performed da-ta mining; GM performed the analysis; MM and ML wrote the first version of the paper; MM and GM revised the paper; DR, MC, EB, PC contributed to paper revision; PC supervised all phases of research activity planning. All Authors reviewed the results and approved the final version of the manuscript.

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

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References

1. Italian Government, Decree of the Prime Minister 8th march 2020 "Ulteriori disposizioni attuative del decreto-legge 23 febbraio 2020, n. 6, recante misure urgenti in materia di contenimento e gestione dell'emergenza epidemiologica da COVID-19". (available at: https://www.gazzettaufficiale.it/eli/id/2020/03/08/20A01522/sg; Last Accessed: 04.01.2024.)
2. Italian Government, Law Decree Apr 22 2021, n. 52 "Misure urgenti per la graduale ripresa delle attività economiche e sociali nel rispetto delle esigenze di contenimento della diffusione dell'epidemia da COVID-19. (available at: https://www.gazzettaufficiale.it/eli/id/2021/04/22/21G00064/sg; Last Accessed: 04.01.2024.)
3. Meyer B, Zill A, Dilba D, Gerlach R, Schumann S. Employee psychological well-being during the COVID-19 pandemic in Germany: A longitudinal study of demands, resources, and exhaustion. *Int J Psychol*. 2021;56(4):532-550. Doi: 10.1002/ijop.12743
4. Basso G, Formai S, "Il lavoro da remoto in Italia durante la pandemia: le imprese del settore privato," Banca d'Italia, 2021. (available at: https://www.bancaditalia.it/pubblicazioni/note-covid-19/2021/Nota_Covid_2_GBSF.pdf; Last Accessed: 04.01.2024.)
5. La Torre G, Chiappetta M, Mazzalai E, et al. Smart working perception in banking companies' employees during the COVID-19 pandemic: A cross-sectional pilot study. *Work*. 2022;73(2):363-376. Doi: 10.3233/WOR-211152
6. SIML – Italian Society of Occupational Medicine "Linee guida per la sorveglianza sanitaria degli addetti ad attività lavorativa con videoterminali", 2013. (available at: https://www.repertoriosalute.it/wp-content/uploads/2017/02/Linee_Guida_VDT_SIMLII.1.pdf; Last Accessed: 04.01.2024.)
7. SIML – Italian Society of Occupational Medicine, "Linee guida per la formazione continua e l'accreditamento del medico del lavoro: attività lavorativa con VDT". 2020. (available at: https://uploads-ssl.webflow.com/5e314724ceeebbf011927853/5e314724ceeebb0d99927a2b_Funzione%20visiva%20ed%20uso%20occupazionale%20di%20videoterminali%20orientamenti%20ed%20indicazioni%20pratico-applicative%20per%20l'attività%20professionale%20del%20medico%20del%20lavoro%20e%20del%20medico%20competente%20-%20Documento%20di%20orientamento%20professionale.pdf ; Last Accessed: 04.01.2024.)
8. European Agency for Safety and Health at Work. Foresight on new and emerging occupational safety and health risks associated with digitalisation by 2025 – final report. 2018. (available at: https://op.europa.eu/en/publication-detail/-/publication/dce30031-1946-11e9-8d04-01aa75ed71a1/language-en; Last Accessed: 04.01.2024.)
9. Giorgi G, Arcangeli G, Perminiene M, et al. Work-Related Stress in the Banking Sector: A Review of Incidence, Correlated Factors, and Major Consequences. *Front Psychol*. 2017;8:2166. Published 2017 Dec 12. Doi: 10.3389/fpsyg.2017.02166
10. Mannocci A, Marchini L, Scognamiglio A, et al. Are Bank Employees Stressed? Job Perception and Positivity in the Banking Sector: An Italian Observational Study. *Int J Environ Res Public Health*. 2018;15(4):707. Published 2018 Apr 10. Doi: 10.3390/ijerph15040707
11. Gerding T, Davis KG, Wang J. An Investigation into Occupational Related Stress of At-Risk Workers During COVID-19. *Ann Work Expo Health*. 2023;67(1):118-128. Doi: 10.1093/annweh/wxac076
12. Bethge M, Radoschewski FM, Müller-Fahrnow W. Work stress and work ability: cross-sectional findings from the German sociomedical panel of employees. *Disabil Rehabil*. 2009;31(20):1692-1699. Doi: 10.1080/09638280902751949
13. Garzaro G, Sottimano I, Di Maso M, et al. Work Ability among Italian Bank Video Display Terminal Operators: Socio-Demographic, Lifestyle, and Occupational Correlates. *Int J Environ Res Public Health*. 2019;16(9):1653. Published 2019 May 12. Doi: 10.3390/ijerph16091653
14. van den Berg TI, Elders LA, de Zwart BC, Burdorf A. The effects of work-related and individual factors on the Work Ability Index: a systematic review. *Occup Environ Med*. 2009;66(4):211-220. Doi :10.1136/oem.2008.039883
15. Checkoway H, Pearce N, & Kriebel D. Research methods in occupational epidemiology (Vol. 34). Monographs in Epidemiology and Biostatistics. 2004.
16. Ilmarinen, Juhani. The work ability index (WAI). *Occupational medicine.* 57.2(2007):160-160.
17. Fitzmaurice GM, Laird NM, Ware JH. (2012). Applied longitudinal analysis. John Wiley & Sons.
18. Zeger SL, Liang KY, Albert PS. (1988). Models for longitudinal data: a generalized estimating equation approach. *Biometrics*, 1049-1060.
19. Friendly, M. (1999). Extending mosaic displays: Marginal, conditional, and partial views of categorical data. Journal of Computational and graphical Statistics, 8(3), 373-395.
20. R Core Team (2023). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/
21. Højsgaard, S., Halekoh, U. & Yan J. (2006). The R Package geepack for Generalized Estimating Equations, Journal of Statistical Software, 15, 2, pp1—11
22. Taino G, Ferrari M, Mestad IJ, Fabris F, Imbriani M. Astenopia e lavoro al videoterminale: studio di una popolazione di 191 lavoratori esposti al rischio mediante somministrazione di questionario anamnestico mirato e valutazione oftalmologica [Asthenopia and work at video display terminals: study of 191 workers exposed to

the risk by administration of a standardized questionnaire and ophthalmologic evaluation]. *G Ital Med Lav Ergon*. 2006;28(4):487-497.
23. Das A, Shah S, Adhikari TB, et al. Computer vision syndrome, musculoskeletal, and stress-related problems among visual display terminal users in Nepal. *PLoS One*. 2022;17(7):e0268356. Published 2022 Jul 19. Doi: 10.1371/journal.pone.0268356
24. Putsa B, Jalayondeja W, Mekhora K, Bhuanantanondh P, Jalayondeja C. Factors associated with reduced risk of musculoskeletal disorders among office workers: a cross-sectional study 2017 to 2020. *BMC Public Health*. 2022;22(1):1503. Published 2022 Aug 6. Doi: 10.1186/s12889-022-13940-0
25. Gerding T, Davis KG, Wang J. An Investigation into Occupational Related Stress of At-Risk Workers During COVID-19. *Ann Work Expo Health*. 2023;67(1):118-128. Doi: 10.1093/annweh/wxac076
26. Gigantesco A, Minardi V, Contoli B, Masocco M. Depressive symptoms among adults in 2018-2019 and during the 2020 COVID-19 pandemic in Italy. *J Affect Disord*. 2022;309:1-8. Doi: 10.1016/j.jad.2022.04.131
27. Orfei MD, Porcari DE, D'Arcangelo S, et al. COVID-19 and Stressful Adjustment to Work: A Long-Term Prospective Study About Homeworking for Bank Employees in Italy. *Front Psychol*. 2022;13:843095. Published 2022 Mar 17. Doi: 10.3389/fpsyg.2022.843095
28. Eurispes. "Risultati del Rapporto Italia 2021." (available at: https://eurispes.eu/news/risultati-del-rapporto-italia-2021/ ; Last Accessed: 04.01.2024.)
29. Andrade MA, Castro CSM, Batistão MV, Mininel VA, Sato TO. Occupational Profile, Psychosocial Aspects, and Work Ability of Brazilian Workers During COVID-19 Pandemic: IMPPAC Cohort. *Saf Health Work*. 2022;13(1):104-111. Doi: 10.1016/j.shaw.2021.11.004
30. Zgombić J. The impact of workplace on the health and work ability of bank staff. *Sigurnost: časopis za sigurnost u radnoj i životnoj okolini*, 2014,56.4:303-313.
31. Kyrönlahti S, Neupane S, Nygård CH, Oakman J, Juutinen S, Mäkikangas A. Perceived Work Ability during Enforced Working from Home Due to the COVID-19 Pandemic among Finnish Higher Educational Staff. *Int J Environ Res Public Health*. 2022;19(10):6230. Published 2022 May 20. Doi: 10.3390/ijerph19106230
32. Van Steenbergen EF, van der Ven C, Peeters MCW, Taris TW. Transitioning Towards New Ways of Working: Do Job Demands, Job Resources, Burnout, and Engagement Change?. *Psychol Rep*. 2018;121(4):736-766. Doi: 10.1177/0033294117740134
33. Galanti T, Guidetti G, Mazzei E, Zappalà S, Toscano F. Work From Home During the COVID-19 Outbreak: The Impact on Employees' Remote Work Productivity, Engagement, and Stress. *J Occup Environ Med*. 2021; 63(7): e426-e432. Doi: 10.1097/JOM.0000000000002236

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Immediate Effects of Whole Body Vibration on Proprioception and Upper Extremity Reaction Speed in Young Adult Students

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Keywords: Whole Body Vibration; Acute Effect; Speed of Movement; Reaction Time; Joint Position Sense

Abstract

Background: *There is limited information on the immediate effects of whole-body vibration (WBV) on the upper limb. This study aims to determine the immediate effects of WBV on reaction speed and proprioception in young adult students' upper extremities.* **Methods:** *In total, 62 students participated in the study. WBV was applied to the participants, and its immediate effects on proprioception and upper extremity reaction speed were examined. Participants' proprioception and perception of joint position at 30-60 degrees of shoulder flexion, shoulder abduction, and elbow flexion angles were measured with absolute error degrees. Reaction rates were evaluated with the Ruler-Drop Test and the mobile application SWAY.* **Results:** *A decrease was observed in the absolute error level of the participants' joint position perception at 30-60 elbow and shoulder position degrees, measured after immediate WBV application (p <0.05). After the RDT application, a decrease in the length of catching the target was observed (p <0.05). The SWAY test determined that they moved the smartphone in a shorter time (p <0.05). Right and left RDT scores showed that the distance to catch the ruler was significantly lower in male individuals before the application. In comparison, the distance to catch the ruler was lower after the application (right/left p<0.05).* **Conclusions:** *The study found that applying WBV improved upper extremity proprioception perception and reaction speed in young adults. This information can guide clinicians in applying WBV to healthy individuals and those with symptoms.*

1. Introduction

Vibration is a mechanical stimulus that produces oscillatory motion and is used for therapeutic purposes to trigger various physiological responses [1]. Whole-body vibration (WBV) is a neuromuscular training method clinicians have recently used as a rehabilitation tool [2]. The application involves transmitting mechanical stimuli to the whole body through the individual's feet or upper extremities on a vibrating platform [3].

The WBV device produces vibrations that can affect the individual's musculoskeletal system. Neuromuscular muscle spindles and the skin, joints, and

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secondary nerve endings detect these vibrations. This stimulation is believed to lead to more effective muscle and nerve function. This effect of WBV on muscle and joint mechanoreceptors is a significant factor in its relationship with proprioception [4]. Proprioception is the sense that detects internal sensory information, including the position of different body parts in space, movement, and joint position [5]. These sensations arise from signals from sensory receptors in joints, muscles, and skin. Proprioception allows for perceiving limb movements, weight, forces, and positions. Furthermore, it controls static and dynamic joint stability and precise movements of the upper extremities [6]. Loss of proprioception may result in neuromuscular dysfunctions, an increased risk of injury, and poor segmental stability [6].

Functional gains following whole-body vibration (WBV) applications are associated with neuromuscular and joint deep sensory systems adaptations, improved neural activation, and muscle mobilization [7]. This explains how WBV affects the neuromuscular system and proprioception. It can be inferred that WBV potentially affects individuals' reaction speeds. Reaction time is defined as the time it takes to initiate a behavioral response after the presentation of a sensory stimulus [8]. Reaction time impairments are associated with poor reaction time and limb performance [9].

It is emphasized that WBV applications improve the functions of the trunk muscles [10] and enable the activation of the lumbar and abdominal muscles [11]. In addition to these potential benefits, it is argued that it can also improve proprioception [6, 7, 12]. The studies in the literature also contain gender comparisons of WBV effects, mainly on the lower limbs and trunk muscles [13, 14]. Very few studies compare the immediate effects of WBV application on proprioception and reaction speed of the upper extremity according to gender [15].

Based on the literature, the immediate effects of whole-body vibration on upper limb proprioception and reaction speed have yet to be discovered. This study aims to determine the immediate effects of whole-body vibration on reaction speed and upper extremity proprioception in young adult students. Our secondary findings were to compare the immediate effects of WBV on proprioception and reaction speed according to gender. The study's findings regarding the immediate effects of WBV on reaction speed and proprioception may guide clinicians working with patients and contribute to a better understanding of the complex effects of WBV on human health, injury risk, and performance.

2. Methods

2.1. Participants

This study is an experimental study in which pretest and post-test were evaluated. The study was conducted at the measurement and evaluation laboratory of the Department of Physiotherapy and Rehabilitation at Gaziantep Islam Science and Technology University. All of the participants were university students aged between 18 and 35 years. Those who had no orthopedic or neurological upper extremity problems, no cardiac problems, and who agreed to participate in the study were included. Those with vertigo were excluded. Out of 63 volunteers, one individual was excluded due to vertigo. In this study, the Declaration of Helsinki was complied with, and written consent was obtained from the individuals in the survey stating that they participated voluntarily.

According to the power analysis conducted using the G-Power 3.1.7 program, based on a previous study, the number of samples required for the research was 62 ($a = 0.05$, $1\text{-}b = 0.95$) [16].

2.2. Procedure and Measurements

The study began by measuring demographic characteristics, upper extremity proprioception, and hand reaction speed. Afterward, WBV was applied using the Compex Winplate (Novotec Medical GmBH, Germany) device. The application protocol of whole-body vibration is in the push-up position with a frequency of 30 Hz. The amplitude was 2 mm, 1 minute of application, and 1 minute of rest for five sets [17]. Immediately after the WBV application, a second evaluation was made, and hand reaction speed and upper extremity proprioception measurements were repeated. The procedure and measurements are presented in Figure 1.

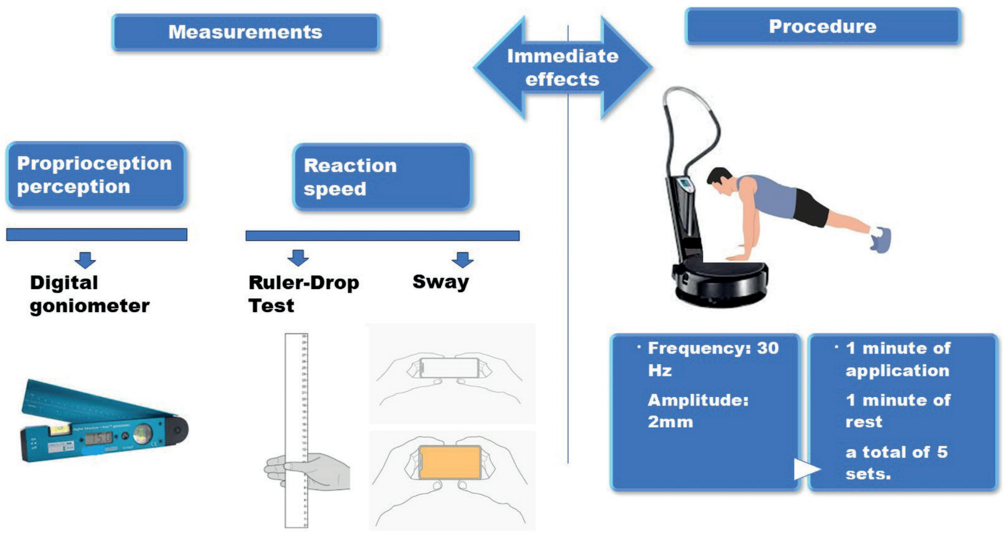

Figure 1. Procedure and measurements.

Proprioception perception was assessed in the upper extremities, specifically in the shoulder and elbow regions. The evaluation included measuring proprioception at 30 and 60-degree shoulder flexion, 30-60-degree shoulder abduction, and 30-60-degree elbow flexion angles. Before the review, the starting position was adjusted to the desired angle value, and participants were instructed to remember this position at the end of the movement. Next, the patient was asked to return the limb to the neutral position by closing their eyes and placing it in the remembered position. The passive and remembered positions were measured using a digital goniometer (Baseline®, USA), and the absolute degree of error in joint position perception was recorded [18].

The Ruler-Drop Test (RDT) is a method used to evaluate hand reaction speed. During the test, the participant is asked to sit comfortably in a chair with their forearm and hand resting on the table. The tips of their thumb and index finger should be positioned 8-10 cm away from the table, with the tops of the thumb and index finger parallel to each other. The tester then instructs the individual to hold the ruler between their thumb and index finger. Simultaneously, the participant was asked to fixate on the midpoint of the ruler while holding it between their fingers. They were instructed to grasp the ruler with their thumb and forefinger immediately upon release. The ruler was then released, and the numerical centimeter value on the upper edge of the participant's thumb, where they grasped the ruler, was recorded. This process was repeated ten times, and the results were averaged for data analysis [8].

The SWAY smartphone application is designed to evaluate upper extremity reaction speed. Users are instructed to sit comfortably on a chair, hold the smartphone with their thumbs on both sides and quickly turn the phone screen in the desired direction when the orange screen appears. A trial test is conducted to familiarize users with the application. The reaction rate was calculated by applying the procedure three times and taking the average time of these three applications [19].

2.3. Data Analysis

The data were analyzed using SPSS version 25 (IBM, Inc., Chicago, IL, USA). The Shapiro-Wilk test and histogram were used to assess the suitability of the normal distribution. Descriptive data are presented as mean and standard deviation (SD). Wilcoxon signed-rank test was used to compare the measurements before and after the WBV application. Figures were created using the GraphPad

Prism 8 program. Mann Whitney U test was used to compare between groups according to gender. A value of $P < 0.05$ was considered statistically significant.

3. RESULTS

Table 1 presents the demographic characteristics of the 62 individuals (26 females, 36 males) who participated in the study.

Figure 2 presents a statistical comparison of the measurements before and after the application is presented the visual comparison.

A decrease in the absolute error level of joint position perception was observed after the application in the participants' 30 to 60-degree flexion and abduction positions of both shoulders (Figure 2). There was a decrease in the average value after the RDT application, which evaluates hand reaction speed. (Figure 2). This meant that the participants caught the target at a shorter distance. The SWAY test, which assesses the upper extremity reaction speed, determined that the participants moved the smartphone in a shorter time as an immediate effect after the application (Figure 2). The statistical comparison of the measurements before and after WBV application according to gender is presented visually in Figure 3. There was no statistically significant difference in comparing proprioception deviation values of male and female participants before and after the application ($p > 0.05$). Right and left RDT scores showed that the distance to catch the ruler was significantly lower in male individuals before the application (Figure 4). In comparison, the distance to catch the ruler was significantly lower after the application (right/left $p<0.001$/$p=0.043$, respectively, Figure 4). No significant difference was observed in SWAY measurement values before and after WBV application according to gender ($p>0.05$, Figure 4).

Table 1. Demographic characteristics.

	X±SD	Min-Max
Age (years)	20.6±2.6	18-34
Weight (kg)	68.8±16.2	40-130
Height (cm)	172.5±9.2	155-193
BMI (kg/m2)	22.96±4.2	15-36
	n	
Gender (female/male)	26/36	
Dominant side (right/left)	59/3	

BMI: Body mass index.

4. DISCUSSION

During the application of WBV, skeletal muscles undergo minor changes in length. This vibration elicits a response known as the 'tonic vibration reflex,' which includes the activation of muscle spindles, modulation of neural signals by Ia afferents, and muscle fibers' activation via large α-motor neurons. The tonic vibration reflex can also increase the recruitment of motor units through the activation of muscle spindles and polysynaptic pathways [20]. The input of proprioceptive pathways (Ia, IIa, and IIb) plays an essential role in the occurrence of isometric contractions [21, 22]. Increasing isometric strength after WBV training with extensive sensory stimulation may result from more efficient use of the positive proprioceptive feedback loop [23]. Muscle functions can be improved with whole-body vibration. WBV also has the potential to provide proprioception training by modifying muscle stiffness, joint stability, and mechanoreceptor activity through gamma efferent stimulation [24].

According to the literature, WBV training on a vibrating balance board has been shown to improve proprioception in patients with knee osteoarthritis [23]. In a study by Fontana et al., adding whole-body vibration to a simple weight-bearing exercise increased lumbosacral position sensation after a single 5-minute session [25]. Although the study used hand vibration as the stimulus, which differs from recent vibration studies, Tripp et al. demonstrated that it reduces the variability of elbow joint position sense [26]. The authors suggested that vibration provides additional afferent input to the sensorimotor system, which may facilitate joint position sense. It has been suggested that vibration increases joint stiffness by activating joint mechanoreceptors and stimulating gamma efferents, which is closely related to improved joint position sense [25]. In this study, 32 students received WBV training

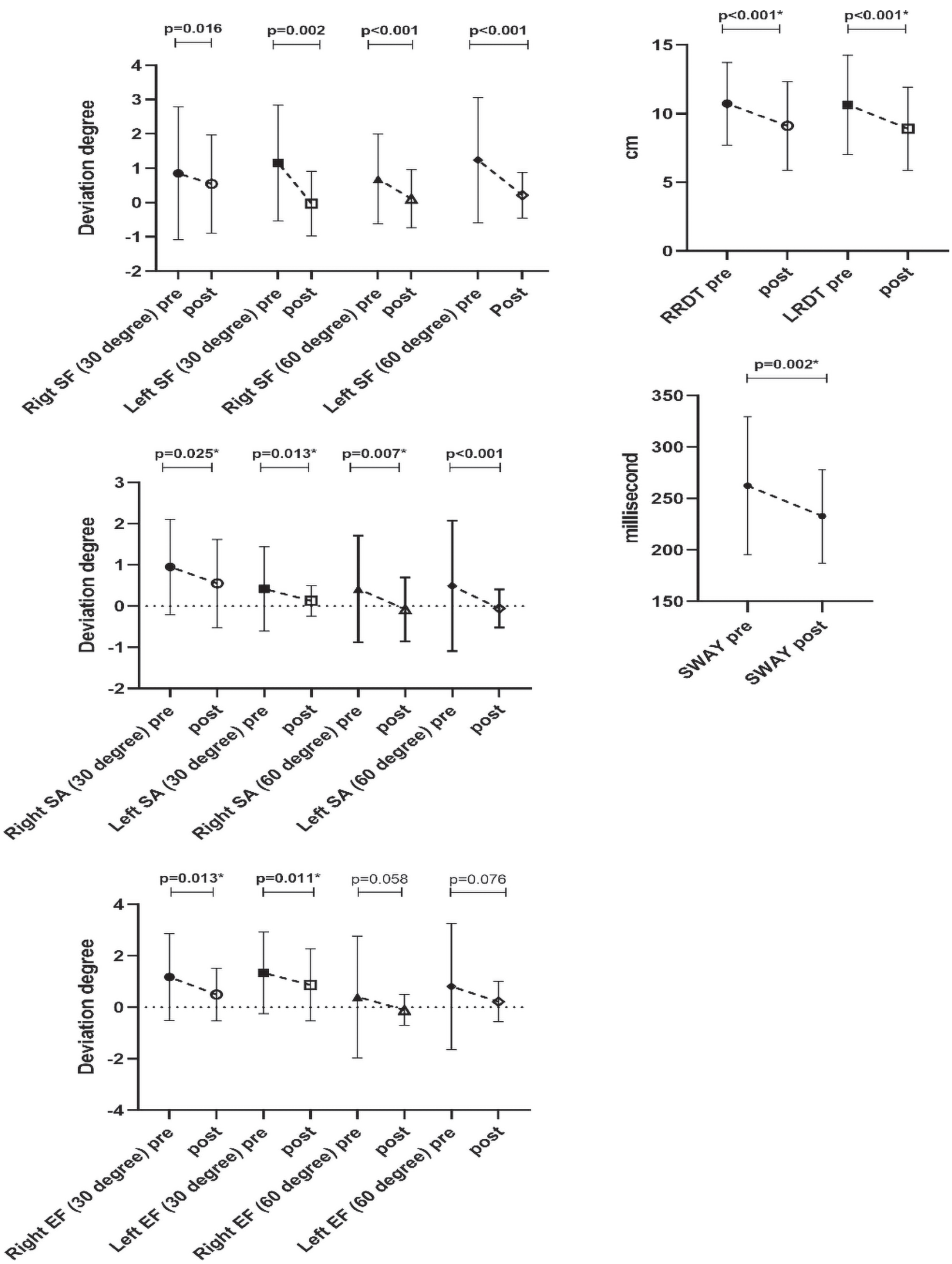

Figure 2. Comparison of proprioception and reaction speed of all participants before and after WBV application. (SF:shoulder flexion, SA:shoulder abduction, EF: elbow flexion, RRDT and LRDT: rigt and left side Ruler-Drop Test, SWAY: mobil application).

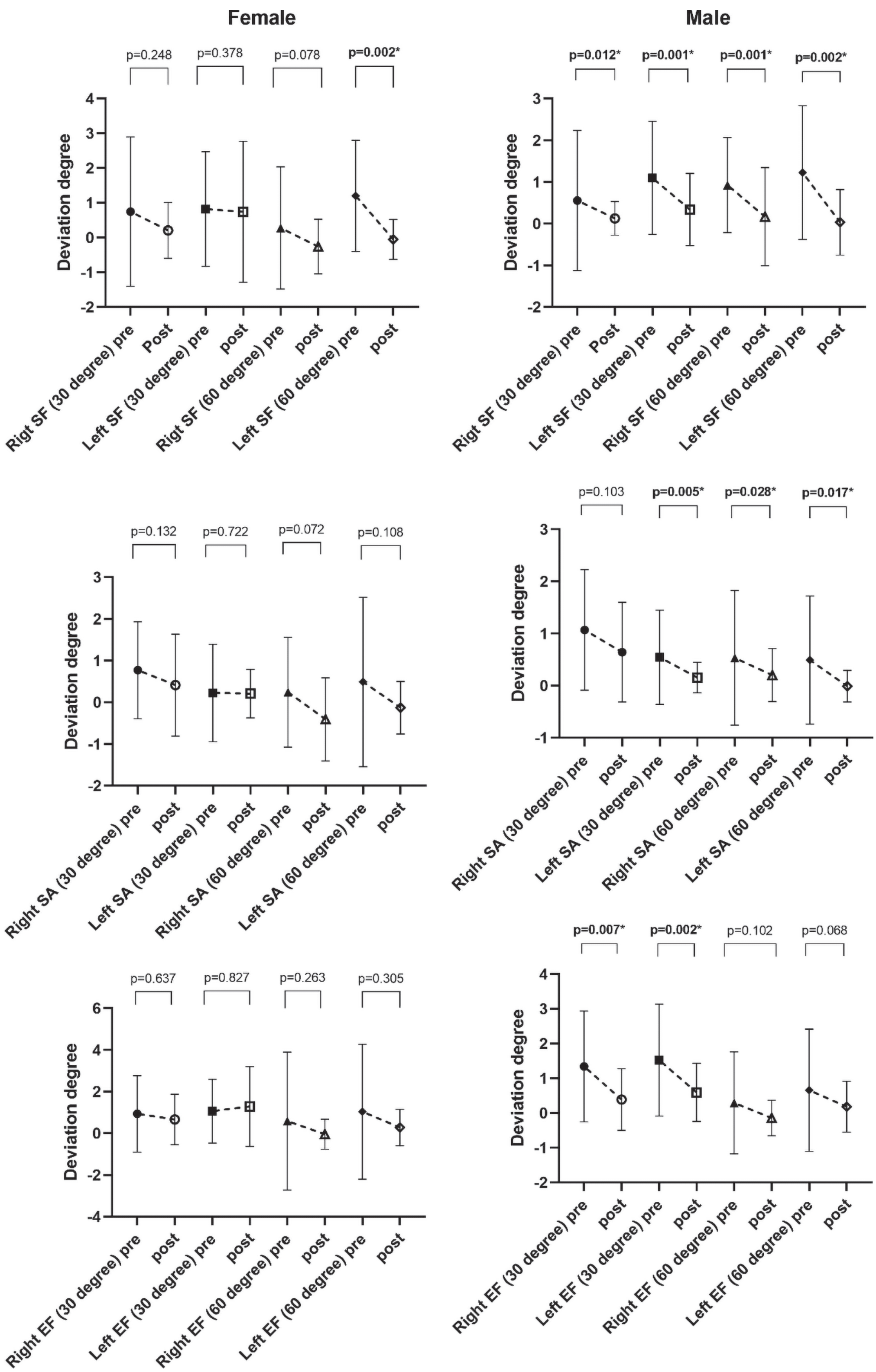

Figure 3. Comparison of proprioception before and after WBV application according to gender (SF:shoulder flexion, SA:shoulder abduction, EF: elbow flexion).

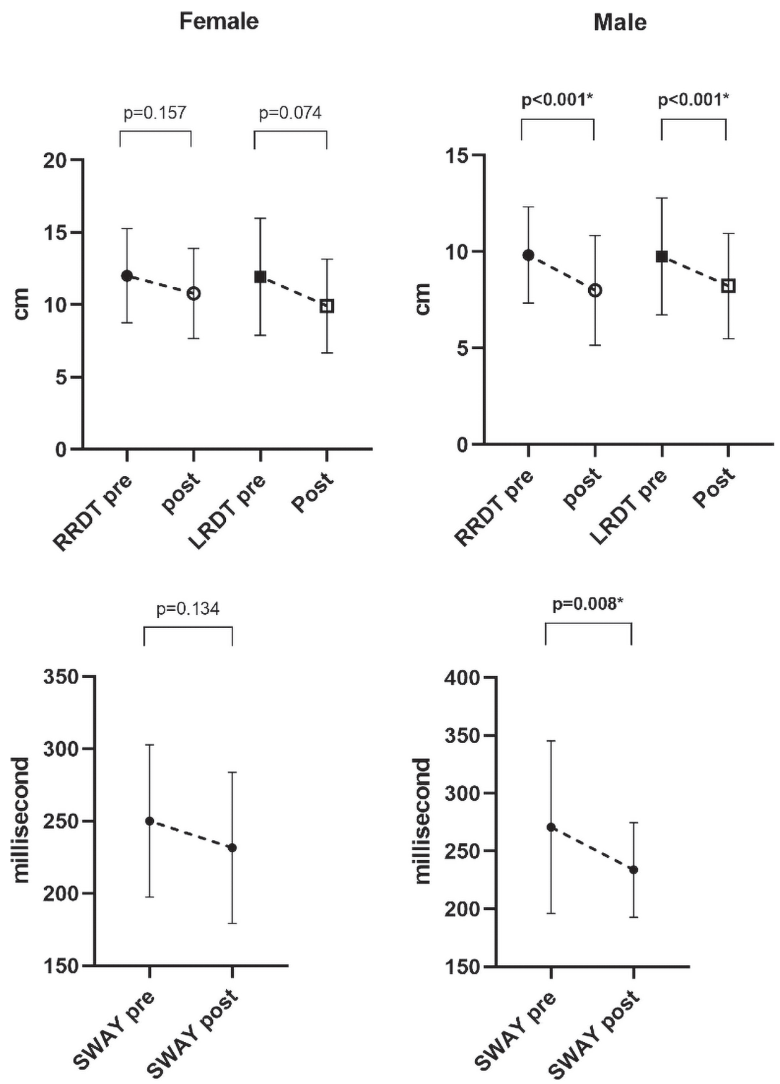

Figure 4. Comparison of reaction speed before and after WBV application according to gender (RRDT and LRDT: rigt and left side Ruler-Drop Test, SWAY: mobil application).

in three positions: control (no vibration), push-up with a straight elbow, and push-up for 2 minutes with 30-minute intervals. The results significantly improved angle repositioning in all three positions [27]. The present study observed that WBV resulted in an immediate decrease in the absolute degree of error in bilateral upper extremity proprioception. This development, in line with the literature, is believed to occur due to vibration providing additional afferent input to facilitate joint position sense.

It has been found that WBV improves muscle performance parameters such as strength and endurance [28]. Therefore, WBV may impact reaction time by influencing muscle nerve activity. However, there is limited literature on the effects of WBV on reaction time, particularly in the upper extremity muscles [29]. In a study of forty healthy young women, timing parameters were measured in the intervention (WBV) group using reaction time, premotor time, motor time, and pre- and post-vibration

EMG. The same protocol was used for the control group (without WBV) but without flicker. The results showed that whole-body vibration did not significantly affect lower extremity reaction rate [29]. WBV immediately positively affected reaction time in both groups: the intervention group with lumbar lordosis and the control group without lumbar lordosis. Another study on Parkinson's patients showed improvements in reaction time with WBV, but no apparent effect was observed compared to the control group. The study suggested that this lack of effect may be due to the age of the participants [30]. Our study found a decrease in hand-holding reaction distance in the RDT, which evaluates WBV reaction speed. Additionally, we observed a parallel reduction in phone movement time in the SWAY evaluation. This suggests that the nerve activity of WBV may be affected, potentially impacting reaction speed.

Structural and functional differences exist between the upper and lower extremities. According to these anatomical differences, the central nervous system plays a more active role in hand and arm functions than in foot and leg functions [31]. It has also been suggested that there is a more significant decrease in reaction time and movement time in the lower extremities than in the upper extremities with age, as they are the most frequently used areas [32]. The variations in the outcomes of the studies mentioned above may be attributed to the varying effects of WBV in different body regions and the influence of factors such as age and gender on reaction time. More extensive research in the literature is crucial for generalizing the results.

Hormonal differences in males and females play a critical role in understanding the effects of WBV on proprioceptive and motor responses [33]. In a study investigating the difference in shoulder position sense according to gender, it was reported that the calculation of shoulder absolute repositioning error did not show a significant difference between males and females. The same study also reported that men had significantly more variable error than women, i.e., there was more variability in position sensation [34]. The present study showed no significant difference in shoulder and elbow joint position sense before WBV application. The decrease in the proprioception error margin of men after the application explains more changes in their position sense. Research on upper limb reaction speed by gender shows that males generally have shorter reaction times than females. This is due to biological differences such as males' muscle mass, strength levels, and nerve conduction velocities [35]. In our current study, the difference between RDT scores in favor of males before the WBV application supports previous studies. We think that the lack of difference in SWAY scores before and after the application according to gender may be because young adults have shown similar familiarity with the use of smartphones, which may affect the reaction speed. However, further studies are needed to confirm this.

A study comparing the effect of WBV application on upper extremity reaction speed according to gender is quite limited. In a study on lower extremity muscle activity, women showed higher hamstring activity than men in the pre-application test, especially before 50 milliseconds. However, this difference was reported to disappear after WBV [13]. The significant difference in RDT scores after WBV application in our study may have been due to biological differences according to gender. Additional studies are needed to determine the generalizability of this information.

The main limitation of our study is the need for a control group and randomization. The lack of a control group limited the results. In addition, examining immediate effects at different frequencies would have been more helpful in understanding the effects of frequencies on proprioception and reaction rates. In addition, testing proprioception and reaction with more sensitive measurement methods could have given more objective results. Analyzing WBV effects according to age groups may help to understand age-related biological differences. This study was limited to flexion and abduction movements of the shoulder. Studies evaluating the multidirectional joint movements of the shoulder are needed.

5. CONCLUSION

Our study showed an improvement in upper extremity proprioception and reaction speed of young university students with the acute effect of WBV.

As a result of this study, the immediate effects of WBV on upper extremity proprioception and reaction speed may guide clinicians who will work on patients and contribute to a better understanding of the complex effects of WBV application on human health and performance. Studies evaluating the effects of WBV on proprioception and reaction speeds on a gender basis are lacking. While the current findings reveal general effects, further controlled research is needed to examine gender differences.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Gaziantep Islam Science and Technology University, Non-Interventional Clinical Research Ethics Committee (Protocol No: 2023/266, June 2023) and registered at ClinicalTrials.gov (NCT06172244).

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

Declaration of Interest: The authors declare no conflict of interest

Author Contribution Statement: ÇM: conceptualization, methodology, data curation, formal analysis, writing original draft, project administration, writing review, and editing. DGK, GE: conceptualization, methodology, writing, review, and editing. FBK, HY, MG: investigation, data curation, resources, writing, review, and editing. SY: methodology, supervision, writing – review, and editing.

Declaration on the use of AI: None.

References

1. Alam MM, Khan AA, Farooq M. Effect of whole-body vibration on neuromuscular performance: A literature review. *Work.* 2018;59(4):571-583. Doi: 10.3233/wor-182699
2. Wang Z, Wei Z, Li X, Lai Z, Wang L. Effect of whole-body vibration on neuromuscular activation and explosive power of lower limb: A systematic review and meta-analysis. *Plos one.* 2022;17(12):e0278637. Doi: 10.1371/journal.pone.0278637
3. Alashram AR, Padua E, Annino G. Effects of whole-body vibration on motor impairments in patients with neurological disorders: a systematic review.*Am J Phys Med Rehabil*. 2019;98(12):1084-1098. Doi: 10.1097/phm.0000000000001252
4. Albasini A, Krause M, Rembitzki I. Using whole body vibration in physical therapy and sport. Clinical practise and treatment exercises. London: Churchill Livingstone Elservier; 2010. Doi: 10.1016/b978-0-7020-3173-1.00002-8
5. Héroux ME, Butler AA, Robertson LS, Fisher G, Gandevia SC. Proprioception: a new look at an old concept. *J Appl Physiol*. 2020;132(3):811-814. Doi: 10.1152/japplphysiol.00809.2021
6. Hong J, Velez M, Moland A, Sullivan J. Acute effects of whole body vibration on shoulder muscular strength and joint position sense. *J Hum Kinet*. 2010;25(2010):17-25. Doi: 10.2478/v10078-010-0027-0
7. Ameer M, Al Abbad A. Acute effect of upper body vibration on shoulder joint internal and external active position sense in healthy female university students. *Phys educ stud.* 2023;27(5):221-229. Doi: 10.15561/20755279.2023.0501
8. Del Rossi G, Malaguti A, Del Rossi S. Practice effects associated with repeated assessment of a clinical test of reaction time. *J Athl Train.* 2014;49(3):356-359. Doi: 10.4085/1062-6059-49.2.04
9. Gray HN, Williams RM, Valovich McLeod TC, Bay RC. Establishing reliability of a reaction time testing battery in high school athletes. *Athl Train Sports Health Care*. 2021;13(4):e168-e175. Doi: 10.3928/19425864-20200310-01
10. Ye J, Ng G, Yuen K. Acute effects of whole-body vibration on trunk muscle functioning in young healthy adults. *J Strength Cond Res.* 2014;28(10):2872-2879. Doi: JSC.0000000000000479
11. Dong Y, Wang H, Zhu Y, et al. Effectsof whole body vibration exercise on lumbar-abdominal muscles activation for patients with chronic low back pain. *BMC sports sci med. rehabil*. 2020;12:1-10. Doi: 10.1186/s13102-020-00226-4
12. Salami A, Roostayi MM, Naimi SS, Shadmehr A, Baghban AA. The immediate effects of whole body vibration on cervical joint position sense in subjects with forward head posture. *Muscles Ligaments Tendons J.* 2018;8(2).
13. Sañudo B, Feria A, Carrasco L, de Hoyo M, Santos R, Gamboa H. Gender differences in knee stability in response to whole-body vibration. *J Strength Cond Res*. 2012;26(8):2156-2165. Doi: 10.1519/JSC.0b013e31823b0716.
14. Shibata N, Ishimatsu K, Maeda S. Gender difference in subjective response to whole-body vibration under standing posture. *Int Arch Occup Environ Health*. 2012;85:171-179. Doi: 10.1007/s00420-011-0657-0
15. Bosco C, Cardinale M, Tsarpela O. Influence of vibration on mechanical power and electromyogram activity in human arm flexor muscles. *Eur J Appl Physiol*. 1999;79:306-311.
16. Kaçoğlu C. An investigation of the effects of acute whole body vibration training on unilateral static body

balance. *Gaziantep Üniversitesi Spor Bilimleri Dergisi*. 2019;4(1):144-156. Doi:10.31680/gaunjss.528141

17. Pozo-Cruz BD, Adsuar JC, Parraca JA, Pozo-Cruz JD, Olivares PR, Gusi N. Using whole-body vibration training in patients affected with common neurological diseases: a systematic literature review. *J Altern Complement Med.* 2012;18(1):29-41. Doi: 10.1089/acm.2010.0691
18. Juul-Kristensen B, Lund H, Hansen K, Christensen H, Danneskiold-Samsøe B, Bliddal H. Poorer elbow proprioception in patients with lateral epicondylitis than in healthy controls: a cross-sectional study. *J Shoulder Elbow Surg.* 2008;17(1):72-81. Doi: 10.1016/j.jse.2007.07.003
19. VanRavenhorst-Bell HA, Muzeau MA, Luinstra L, Goering J, Amick RZ. Accuracy of the SWAY mobile cognitive assessment application. *Int J Sports Phys Ther*. 2021;16(4):991. Doi: 10.26603/001c.24924
20. Işler AK. Effects of vibration on performance. *Hacettepe J of Sport Sciences*. 2007;18(1):42-56.
21. Delecluse C, Roelants M, Verschueren S. Strength increase after whole-body vibration compared with resistance training. *Med Sci Sports Exerc.* 2003;35(6):1033-1041. Doi: 10.1249/01.MSS.0000069752.96438.B0
22. Roelants M, Delecluse C, Verschueren SM. Whole-body-vibration training increases knee-extension strength and speed of movement in older women. *J Am Geriatr Soc*. 2004;52(6):901-908. Doi: 10.1111/j.1532-5415.2004.52256.x
23. Trans T, Aaboe J, Henriksen M, Christensen R, Bliddal H, Lund H. Effect of whole body vibration exercise on muscle strength and proprioception in females with knee osteoarthritis. *The knee.* 2009;16(4):256-261. Doi: 10.1016/j.knee.2008.11.014
24. Lee TY, Chow DH. Effects of whole body vibration on spinal proprioception in normal individuals. In 2013 35th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, 4989-4992. Doi: 10.1109/EMBC.2013.6610668
25. Fontana TL, Richardson CA, Stanton WR. The effect of weight bearing exercise with low frequency, whole body vibration on lumbosacral proprioception: A pilot study on normal subjects. *Aust J Physiother.* 2005;51(4):259-263. Doi: 10.1016/S0004-9514(05)70007-6
26. Tripp BL, Faust D, Jacobs P. Elbow joint position sense after neuromuscular training with handheld vibration. *J Athl Train.* 2009;44(6):617-623. Doi: 10.4085/1062-6050-44.6.617
27. Forouhideh F, Naeimi S, Khademi Kalantari K, Rahimi A, Farhadi A. The short term effects of one-session of whole body vibration training on isokinetic strength of rotator cuff and shoulder proprioception in young healthy subjects. *Sci J Kurdistan Univ Med Sci.* 2011;15(4):52-64.
28. Hopkins T, Pak JO, Robertshaw AE, Feland JB, Hunter I, Gage M. Whole body vibration and dynamic restraint. *Int J Sports Med.* 2007;424-428.
29. Ashnagar Z, Shadmehr A, Hadian MR, Talebian S, Jalaei S. The immediate effects of whole body vibration on timing parameters in the upper extremity muscles of healthy young women. *Mod Rehabil*. 2012;6(1).
30. Dincher A. Effects of Whole Body Vibration on reaction time in Parkinson's Disease Patients A pilot study. *Neurodegener Dis Cur Res*. 2021;1:1-6.
31. Li Y, Mc Colgin C, Van Oteghen SL. Comparisons of psychomotor performance between the upper and lower extremities in three age groups. *Percept Mot Skills*. 1998;87(3):947-952. Doi: 10.2466/pms.1998.87.3.94
32. Kauranen K, Vanharanta H. Influences of aging, gender, and handedness on motor performance of upper and lower extremities. *Percept Mot Skills.* 1996;82(2):515-525. Doi: 10.2466/pms.1996.82.2.515
33. Cochrane DJ. The potential neural mechanisms of acute indirect vibration. *J Sports Sci Med*. 2011;10(1):19-30.
34. Vafadar AK, Côté JN, Archambault PS. Sex differences in the shoulder joint position sense acuity: a cross-sectional study. *BMC Musculoskelet. Disord.* 2015;16:1-7. Doi: 10.1186/s12891-015-0731-y
35. Slopecki M, Messing K, Côté JN. Is sex a proxy for mechanical variables during an upper limb repetitive movement task? An investigation of the effects of sex and of anthropometric load on muscle fatigue. *Biol Sex Differ.* 2020;11:60. Doi:10.1186/s13293-020-00336-1

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Reliability and Validity of the Turkish Version of the Work-Related Questionnaire for Upper Extremity Disorders (WORQ-UP)

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Keywords: Upper Extremity; Musculoskeletal Disorders; Work-Related Questionnaire for Upper Extremity Disorders; WORQ-UP

Abstract

Background: *The Work-Related Questionnaire for Upper Extremity Disorders (WORQ-UP) is a patient-reported outcome measure to identify work-related limitations in individuals with upper extremity musculoskeletal disorders. This study aims to adapt the WORQ-UP into Turkish and evaluate its validity and reliability.* **Methods:** *The Turkish WORQ-UP, along with the previously validated Turkish Quick Disabilities of the Arm, Shoulder, and Hand (Quick-DASH), were administered to 136 patients at the Department of Orthopedics in Nigde Omer Halisdemir Education and Training Hospital. The Quick-DASH evaluates upper extremity disorders by assessing physical function, pain, and psychosocial impact. The Turkish WORQ-UP was administered twice within 7-14 days to determine test-retest reliability. Reliability was evaluated using internal consistency measures and the intraclass correlation coefficient (ICC). The Spearman correlation coefficient was calculated between the Turkish WORQ-UP and the Quick-DASH to assess validity, and explanatory (EFA) and confirmatory factor analysis (CFA) was performed.* **Results:** *In the reliability analysis, items 11, 12, 13, 15, and 16, which did not meet the criterion of item-total score correlation coefficient >30, were excluded, resulting in a 12-item Turkish WORQ-UP with satisfactory validity and reliability outcomes. The Cronbach's alpha and ICC were calculated as 0.895 and 0.879, respectively, while the SEM and MDC were determined to be 0.93 and 1.85. In the EFA, the Kaiser-Meyer-Olkin measure (0.895) and Bartlett's tests were both significant ($p < 0.001$). Additionally, the CFA indicated an acceptable fit with two factors. The goodness of fit indices, including $\chi 2/df = 2.09$, CFI = 0.934, TLI = 0.918, and RMSEA = 0.08, confirmed the adequacy of the model. The 12-item Turkish WORQ-UP showed a significant and moderately strong correlation ($r = 0.754$; $p < 0.001$) with Quick DASH.* **Conclusion:** *The Turkish version of WORQ-UP with 12 items had proper psychometric properties to identify work-related limitations in individuals with upper extremity musculoskeletal disorders.*

1. Introduction

Musculoskeletal disorders are highly prevalent in Europe, ranking as the foremost occupational diseases and affecting a significant workforce across diverse industries [1]. These conditions have profound personal and societal implications, including limitations in daily activities, increased healthcare expenses, income loss, and work disability. Companies also grapple with adverse consequences such

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as decreased productivity and heightened absenteeism [2]. Upper-extremity musculoskeletal disorders have emerged as a significant health concern among the working population, with many cases linked to occupational factors, both physical and psychosocial [3]. Addressing and minimizing exposure to these work-related factors could prevent many disorders. Research on the epidemiology of these disorders has identified various contributing factors, with global prevalence rates ranging from 2% to 53% for point prevalence and 2% to 41% for 12-month prevalence [6]. In 2019, in France, over 80% of officially recognized occupational diseases were upper-extremity musculoskeletal disorders, totaling more than 40,500 cases. In England, a significant portion of the population reported pain or sensory symptoms in the upper extremities or neck, with one-week prevalence rates of 24% for neck pain, 36% for upper limb pain, and 27% for sensory symptoms [7]. In Turkiye, the prevalence of musculoskeletal pain is high among computer-using office workers, with 82.6% reporting pain in the past 12 months, particularly in the neck (32.7%), upper limbs (25.3%) and lower back (24.7%) [8].

The primary occupational factors contributing to upper extremity musculoskeletal disorders include a fast-paced work environment, repetitive motion patterns, inadequate recovery time, lifting heavy loads, engaging in forceful manual activities, maintaining awkward postures for extended periods, exposure to mechanical pressure, the use of vibrating hand tools, and job-related stress [9-13]. These factors can lead to persistent symptoms for patients, impacting their ability to perform basic daily activities and potentially resulting in job loss, symptoms of depression, and disruptions within the family [14]. Prolonged sickness absence is also associated with lower quality of life ratings over time, highlighting the importance of early intervention and considering the role of work in the diagnosis and treatment of upper extremity disorders [15]. Therefore, the Work-Related Questionnaire for Upper Extremity Disorders (WORQ-UP), a patient-reported outcome measure (PROM), was developed in 2017 to assess the work-related limitations faced by individuals with upper extremity musculoskeletal disorders. The Disabilities of the Arm, Shoulder, and Hand (DASH), or quick DASH questionnaires, are frequently used by clinicians and researchers to assess disability after upper limb injuries. However, the DASH does not include occupational impairments; it assesses general upper limb function [16].

The 17-item WORQ-UP was developed in consultation with patients from the target population and experts in the field, including physiotherapists, insurance physicians, occupational health physicians, rehabilitation physicians, and orthopedic surgeons. Its validity and reliability study was conducted with patients with musculoskeletal disorders of the upper extremities attending an orthopedic outpatient clinic at Amphia Hospital in the Netherlands. This questionnaire is a standardized tool for documenting or eliciting work-related limitations in patients with upper extremity conditions. It facilitates consistent communication between healthcare professionals and allows the specific nature and extent of the patient's work-related limitations to be recorded [17, 18].

The WORQ-UP has demonstrated strong measurement properties in terms of internal consistency and a four-factor structure: exertion, dexterity, tools and equipment, and mobility. The WORQ-UP can be valuable in work-related rehabilitation scenarios by assessing the degree and severity of a patient's work limitations. This information allows adjustments to the patient's treatment and rehabilitation plan, ensuring a more patient-centered approach [17, 18]. Therefore, this study aims to translate and culturally adapt the WORQ-UP into Turkish and to assess its validity and reliability in patients with upper extremity musculoskeletal disorders.

2. Methods

2.1. Study Design and Participants

This observational measurement study adopted a test-retest and validity design, following the guidelines outlined in the reporting of reliability and agreement studies (GRRAS) and Consensus-based standards for the selection of health measurement instruments (COSMIN) [19, 20]. Written permission was obtained from the original developer of the WORQ-UP for its translation into Turkish. Ethical approval was secured from the Health Sciences Ethics Committee of Mugla Sitki Kocman University (Protocol No: 230152, Decision No: 3). The study complied with the Declaration of Helsinki. Participants were fully briefed on the study, and those who volunteered to participate signed an informed consent form.

The study was conducted on individuals seeking treatment at the orthopedic outpatient clinic of Nigde Omer Halisdemir Education and Research Hospital in Türkiye between February 2024 and April 2024.

The inclusion criteria were as follows:

- Aged between 18 and 65 years.
- Diagnosed with an upper extremity musculoskeletal disorder.
- At least one year of experience in a job involving the use of upper limbs/extremities and currently employed.
- Proficient in Turkish with a minimum literacy level.
- Signed informed consent document.

The exclusion criteria were as follows:

- Diagnosed with cervical spine disease or neurological disorders (e.g., multiple sclerosis, vestibular disorders, stroke).
- Previous upper extremity trauma (e.g., bone fracture, surgery).
- Ongoing psychological problems such as depression, anxiety, and bipolar disorders (information obtained from medical reports by the orthopedic doctor).

2.2. Translation and Cultural Adaptation of the WORQ-UP

The standard "forward-backward" procedure outlined by Beaton was applied to translate the questionnaire from English to Turkish [21]. Two native Turkish speakers (A.C.P and C.D), proficient in English and familiar with the relevant test terminology, translated the original English version into Turkish. These translators collaborated to merge the individual Turkish translations into a single version. The resulting Turkish version was independently translated back into English by two native English translators (T.K. and E.K.) who were not associated with the study. A committee comprising four translators and Turkish linguists compared the final translation with the initial one, ensuring the equivalence of the original and Turkish versions of the WORQ-UP. Item 6, initially "Performing rapid and repetitive arm movements (e.g., sorting the post or doing assembly line work)," has been replaced with "Performing rapid and repetitive arm movements (e.g., placing products on shelves)".

- In item 16, initially, "Using heavy equipment that causes vibration (e.g., a hammer drill or demolition hammer)" was replaced with "Using heavy equipment that causes vibration (e.g., a concrete breaker)."

Lastly, 20 healthy individuals were surveyed to assess the clarity of the Turkish translation. After completing the test, each participant was questioned about difficulties in understanding. Their interpretations of each item were documented, leading to the creation of the final version of the Turkish WORQ-UP. The subsequent phase involved investigating its validity and reliability.

2.3. Data Collection and Psychometric Properties of the Turkish WORQ-UP

Data were collected through face-to-face interviews with 136 participants using a 17-item Turkish WORQ-UP and an 11-item Quick-DASH. On average, the entire data collection form took 10 to 15 minutes to complete. Patients completed the questionnaire themselves and then returned it to the coordinator. The coordinator carefully checked for missing items. If any items remained unanswered, the coordinator asked the patient to complete them. Therefore, no data were missing from the questionnaire.

The Turkish WORQ-UP's reliability was gauged through test-retest reliability and internal consistency tests. To evaluate internal consistency, Cronbach's alpha was interpreted [22]. For the test-retest reliability, a subset of 40 patients who initially completed the questionnaire were re-interviewed within 7-14 days, and the Turkish WORQ-UP was re-administered.

Criterion validity evaluates how well the cumulative scores of a measurement align with the scores of another measure, guided by theoretical assumptions about the construct being assessed. In the original study, the WORQ-UP demonstrated strong positive correlations with the Quick DASH [17]. Therefore, Quick DASH was utilized to affirm the construct validity of the Turkish WORQ-UP. Our hypothesis assumed a positive and significant correlation between the Turkish WORQ-UP and Quick DASH. Subsequently, construct validity was investigated by performing factor analysis to determine the items' factor loadings and subgroups.

2.3.1. WORQ-UP

The 17-item original version of the WORQ-UP encompasses a range of work-related tasks that may be impacted by musculoskeletal issues in the upper extremities. These tasks are categorized into four primary domains: exertion, dexterity, handling tools and equipment, and mobility. Participants must assess the difficulty they experience while performing these work-related tasks due to complaints about their upper extremities. Responses are rated on a five-point Likert scale ranging from 1 (not at all) to 5 (extremely/I can't do this), with the option of selecting 0 (not applicable) if a specific activity is not relevant to their job. The WORQ-UP scoring system ranges from 0 to 85 points. A lower score indicates that the individual experiences fewer difficulties while working, whereas a higher score reflects increased difficulty encountered during work [17, 18].

2.3.2 Quick DASH

The DASH is a self-administered outcome instrument to measure upper-extremity disability and symptoms. The Quick-DASH is a condensed version of the original 30-item DASH questionnaire comprising 11 items. It evaluates upper extremity disorders by assessing physical function, pain, and psychosocial impact. Scores on the Quick-DASH range from 0 to 100, with lower scores indicating lesser disability and higher scores indicating more significant disability. Research has demonstrated that the Quick-DASH maintains excellent reliability and validity compared to the original 30-item DASH while being convenient for respondents due to its reduced length [23].

2.4. Sample Size and Statistical Analysis

In validation studies, international guidelines recommend a respondent-item ratio of 5:1 to 10:1 (e.g., 50 participants for a 10-item survey), 15:1, or 30:1 when determining the sample size. The 5:1 or 10:1 ratio is commonly utilized [24]. Therefore, the goal was to enroll a minimum of 85 and a maximum of 170 participants for the 17-item WORQ-UP.

The data were analyzed using SPSS version 22.0. The normality of continuous variables was assessed visually and analytically. Descriptive statistics were used to present categorical variables as numbers (n) and percentages (%), while continuous variables were expressed as mean ± standard deviation or median (interquartile range). A significance level of $p < 0.05$ was considered statistically significant.

Internal consistency and test-retest reliability were examined to evaluate instrument reliability. Cronbach's alpha value higher than 0.70 [25] and item-rest correlation higher than 0.30 [26] indicate homogeneity and internal consistency. Test-retest reliability of the Turkish WORQ-UP was determined using the intraclass correlation coefficient (ICC) between the initial and subsequent evaluations. An ICC ranging from 0.75 to 1 suggests excellent reliability, 0.4 to 0.75 indicates moderate reliability and less than 0.4 indicates poor reliability [27]. Reproducibility was assessed using the measurement of the standard error ($SEM=SD\sqrt{[1-ICC]}$) and Minimal Detectable Change (MDC = 1.96 x SEM x square root of 2) [28].

Both construct and criterion validity were assessed to evaluate instrument validity. Exploratory Factor Analysis (EFA) and Confirmatory Factor Analysis (CFA) were utilized for construct validity. A Kaiser-Meyer-Olkin (KMO) value above 0.5 and a significant Bartlett's test with a p-value below 0.05 were considered appropriate for factor analysis.

Factor extraction was performed using maximum likelihood extraction and Oblimin rotation. Criteria such as Scree Plot inflection, Eigenvalue greater than 1.0, and variance exceeding 10% were used to determine factors [29]. In the subsequent stage, model fit was evaluated through Confirmatory Factor Analysis (CFA) of the factors identified in EFA. CFA was conducted using Jamovi Statistical Software (Version 1.6.23.0). Various indices were examined to assess model fit, including Chi-square statistics ($\chi2$), root mean square error of approximation (RMSEA), comparative fit index (CFI), and normed fit index (NFI) [30]. Criterion validity was determined by calculating Spearman's correlation coefficients (r) between the total score of Turkish WORQ-UP and the Quick DASH. Correlation coefficient (r) values categorized as "weak" (.00–.19), "mild" (.20–.39), "moderate" (.40–.59), "moderately strong" (.60–.79), and "strong" (.80–1.0) relationships [31].

3. Results

3.1. Characteristics of Participants

A total of 136 patients who met the inclusion criteria were enrolled in the study. Most patients (94.1%) were right dominant, and most participants (52.9%) reported correct upper extremity disorders. Among the participants, 72 (52.9%) had shoulder injuries, 19 (14%) had elbow or forearm disorders, and 45 (33.1%) had hand or wrist disorders. The mean and standard deviation of the Turkish WORQ-UP total score were 36.1 (13.2), and for the Quick DASH, they were 31.3 (8.7) (Table 1).

Table 1. Characteristics of participants (n = 136).

	Median (IQR)
Age (years)	**41.00 (25)**
Gender	**n (%)**
Female	64 (47.1%)
Male	72 (52.9%)
Dominant upper extremity	8 (5.9%)
Left	128 (94.1%)
Right	
Affected upper extremity	64 (47.1%)
Left	72 (52.9%)
Right	
Smoker	43 (31.6%)
Yes	93 (68.4%)
No	
Trauma Region	72 (52.9%)
Shoulder or humerus disorders	19 (14%)
Elbow or forearm disorders	45 (33.1%)
Hand or wrist disorders	
	Mean (S.D.)
Turkish WORQ-UP (0-85)	36.1 (13.2)
Quick DASH (0-100)	31.3 (8.7)

IQR: Interquartile Range. SD: Standard Deviation. WORQ-UP: The WOrk-Related Questionnaire for UPper extremity disorders. Quick DASH: Quick Disabilities of the Arm, Shoulder, and Hand.

3.2. Initial Reliability and Validity Analysis for 17-Item Turkish WORQ-UP

The test-retest analysis showed that the ICC values for individual items of the 17-item Turkish WORQ-UP ranged from 0.829 to 0.896, with a total score ICC value of 0.864. These ICC values indicate excellent test-retest reliability. The 17-item Turkish WORQ-UP also demonstrated high internal consistency with a Cronbach's alpha coefficient of 0.864. Deleting items resulted in Cronbach's alpha values ranging from 0.849 to 0.871, indicating strong relationships among the questionnaire items. However, items 11, 12, and 13 did not meet the >0.30 criterion for item-rest correlations (Table 2). These items were interpreted as being unrelated to the questionnaire.

The suitability of the data for factor analysis was confirmed with a KMO value of 0.840 and Bartlett's test of sphericity ($\chi2$ = 1224.018, $p < 0.001$). The Principal Component Analysis for the 17-item Turkish WORQ-UP revealed a four-factor solution. The E.V. for the factors were as follows: factor 1=6.00, factor 2=2.53, factor 3=1.77, and factor 4=1.25. The four factors accounted for 68.08% of the total variance, with the first, second, third, and fourth factors explaining 35.32%, 14.93%, 10.44%, and 7.38% of the total variance, respectively. However, for these structures to be considered genuine factors, they needed to meet the criteria of E.V.> 1.0, along with explaining > 10% of the variance.

Table 2. Reliability Statistics of Turkish WORQ-UP.

	Reliability Statistics of Turkish WORQ-UP with 17-Item		**Reliability Statistics of Turkish WORQ-UP with 14-Item**	
	Item-rest correlation	**Cronbach's α If item dropped**	**Item-rest correlation**	**Cronbach's α If item dropped**
Item1	0.687	0.849	0.740	0.859
Item2	0.669	0.849	0.697	0.861
Item3	0.608	0.852	0.635	0.864
Item4	0.498	0.857	0.519	0.870
Item5	0.627	0.851	0.668	0.862
Item6	0.618	0.852	0.650	0.864
Item7	0.588	0.854	0.629	0.865
Item8	0.509	0.856	0.507	0.870
Item9	0.562	0.854	0.599	0.866
Item10	0.646	0.849	0.651	0.863
Item11	**0.279**	0.867	Item11 was deleted	
Item12	**0.295**	0.866	Item12 was deleted	
Item13	**0.167**	0.871	Item13 was deleted	
Item14	0.426	0.860	0.411	0.874
Item15	0.320	0.867	**0.287**	0.885
Item16	0.374	0.862	**0.278**	0.881
Item17	0.507	0.856	0.458	0.873

**Values not meeting the item-rest correlation (<0.30) are shown in bold. WORQ-UP: The WOrk-Related Questionnaire for UPper extremity disorders.*

Therefore, the fourth factor, which explained only 7.38% of the total variance, was not accepted (Table 2).

When examining the fit indices for the four-factor solution in the CFA, the results did not show acceptable outcomes. The ratio of chi-square to degrees of freedom ($\chi 2/df$) yielded a value of 2.43, below the threshold of 5, indicating a satisfactory fit. However, other fit indices (RMSEA = 0.103, CFI = 0.856, and TLI = 0.831) did not reach acceptable values. Upon removing items 11, 12, and 13 with inappropriate item-rest correlation, the CFA revealed acceptable values for the three-factor structure of the 14-item Turkish WORQ-UP. The CFA results for a 14-item, three-factor Turkish WORQ-UP were $\chi 2/df = 2.12$, RMSEA = 0.09, CFI = 0.914, and TLI = 0.894. Upon reevaluating the reliability and validity results for the 14-item Turkish WORQ-UP, Cronbach's alpha was 0.877, and the test-retest ICC was 0.890. However, the total-item correlation value for items 15 and 16 of the 14-item Turkish WORQ-UP did not meet the criterion of > 0.30.

3.3. Final Reliability and Validity Analysis for 12-Item Turkish WORQ-UP

After removing items 11, 12, 13, 15, and 16 from the 17-item Turkish WORQ-UP, the 12-item Turkish WORQ-UP demonstrated reliability. The item-rest correlation coefficients of all items were above 0.30. The Cronbach's alpha, ICC, SEM, and MDC values for the total score of the 12-item Turkish WORQ-UP were 0.895, 0.901, 0.936, and 1.85, respectively. The outcomes of internal consistency and homogeneity are outlined in Tables 3 and 4.

The criterion validity of the 12-item Turkish WORQ-UP was evaluated through correlation analysis with Quick DASH, demonstrating a significant and moderately strong correlation (r = 0.754; p < 0.001) between the two assessment tools, indicating the criterion validity of the 12-item Turkish WORQ-UP (Table 5).

The 12-item Turkish WORQ-UP showed a two-factor structure in the EFA and explained 62.54% of the total variance (Factor 1: E.V. = 1.74 and 47.91%; Factor 2: E.V. = 1.74 and 14.57%) (Table 5). In the EFA, the KMO measure (0.895) and Bartlett's tests were both significant ($\chi 2$= 904.551; p < 0.001). The CFA results for a 12-item and two-factor Turkish WORQ-UP were $\chi 2$/df = 2.09, RMSEA = 0.08, CFI = 0.934, and TLI = 0.918. According to the CFA results, the excellent fit of the model confirmed the factor structures. The first factor (Items 1, 2, 3, 4, and 5) was labeled as "function," and the second factor (Items 6, 7, 8, 9, 10, 11, 12) was labeled as "dexterity".

Table 3. Reliability Statistics of Turkish WORQ-UP with 12-Item.

	Reliability Statistics of Turkish WORQ-UP with 12-Item	
	Item-rest correlation	Cronbach's α If item dropped
Item1	0.770	0.878
Item2	0.718	0.880
Item3	0.669	0.883
Item4	0.475	0.893
Item5	0.682	0.882
Item6	0.688	0.882
Item7	0.672	0.883
Item8	0.535	0.890
Item9	0.662	0.883
Item10	0.623	0.887
Item11	0.459	0.893
Item12	0.392	0.898

WORQ-UP: The WOrk-Related Questionnaire for UPper extremity disorders.

4. Discussion

This study aimed to translate and culturally adapt the WORQ-UP into Turkish and evaluate its psychometric properties. The results indicate that the 12-item Turkish WORQ-UP is a valid and reliable tool for assessing work-related limitations in patients with upper extremity injuries. To date, only a Persian version of the WORQ-UP has been developed, and the findings of this study have been compared with the results of both the original WORQ-UP [17, 18] and the Persian version [32].

In the current study, the mean total score of the Turkish WORQ-UP was 36.1, and for the Quick DASH, it was 31.3. Although no established cut-off values exist for either questionnaire, scores approaching the total maximum suggest that patients experience work-related limitations due to upper extremity problems.

The KMO and Bartlett's tests confirmed that the sample size of the current study was adequate for factor analysis. The Turkish WORQ-UP was administered to 136 participants, compared to 150 in the original survey and 181 in the Persian version [17, 32]. The original WORQ-UP demonstrated a four-factor structure in EFA, with factors labeled as effort, hand skills, tools and equipment, and mobility. This four-factor structure was deemed

Table 4. Reliability and criterion validity results of the 12-item Turkish WORQ-UP.

12-Item Turkish WORQ-UP	Cronbach alfa	Test-retest reliability ICC (95 % CI)	SEM	MDC	Spearman Correlation with Quick DASH
Total Score	0.895	0.879 (0.790–0.888)	0.936	1.85	0.754
Factor 1 (function)	0.893	0.812 (0.765–0.855)	0.477	0.96	
Factor 2 (dexterity)	0.836	0.814 (0.722–0.868)	0.572	1.49	

WORQ-UP: The WOrk-Related Questionnaire for UPper extremity disorders. Quick DASH: Quick Disabilities of the Arm, Shoulder, and Hand. SEM: Standard Error of Measurement. MDD: Minimal Detectable Change

Table 5. Principal Component Analysis of 12-Item Turkish WORQ-UP.

Total Variance Explained						
	Initial Eigenvalues			Extraction Sums of Squared Loadings		
Component	**Total**	**% of Variance**	**Cumulative %**	**Total**	**% of Variance**	**Cumulative %**
1	5.757	47.971	47.971	5.757	47.971	47.971
2	1.749	14.577	62.548	1.749	14.577	62.548
3	.963	8.022	70.570			
4	.683	5.690	76.261			
5	.558	4.652	80.913			
6	.529	4.407	85.319			
7	.435	3.621	88.941			
8	.352	2.936	91.876			
9	.319	2.660	94.536			
10	.267	2.228	96.764			
11	.205	1.707	98.470			
12	.184	1.530	100.000			

Extraction Method: Principal Components Analysis.

appropriate. However, although the initial 17-item Turkish WORQ-UP also exhibited a four-factor structure, it was ultimately reduced to three factors because the fourth factor explained less than 10% of the total variance. The remaining items revealed a two-factor structure after excluding items 11, 12, 13, 15, and 16 due to reliability issues. The WORQ-UP includes various activities requiring upper extremity effort. The differences in results between the Turkish version and the original may be attributed to the less frequent performance of these five items in Turkey.

According to the COSMIN guidelines, a minimum of 30 participants is recommended for investigating test-retest reliability and measurement error [22]. Therefore, in this study, test-retest reliability was assessed with 40 individuals. The original study examined test-retest reliability with 28 patients from a sample group of 150 individuals [17]. It can be concluded that the test-retest reliability analyses in the current study were conducted with sufficient participants. In the original study, the ICC value for test-retest reliability of the WORQ-UP was reported to be 0.88 (0.75 to 0.94) [17], and in the Persian version, it was 0.85 (0.69 to 0.92) [32]. In the present study, the ICC value for the 12-item Turkish WORQ-UP was determined to be 0.87 (0.79–0.88). Consequently, it can be inferred that the results are consistent with the original study and the Persian version, suggesting that WORQ-UP exhibits stability over time.

In the original study, although Cronbach's alpha value for the total score was not reported, it was found to be 0.970 in the Persian version, while in the current study, it was found to be 0.899 [32]. Additionally, in the original study, Cronbach's alpha values for the subgroups were 0.88, 0.74, 0.87, and 0.66, respectively, whereas in the current study, they were found to be 0.893 and 0.836 [17,18]. Consistent with these studies, it can be observed that the 12-item Turkish WORQ-UP demonstrates internal consistency. Item-rest correlation coefficients, another important reliability indicator, ranged from 0.484 to 0.710 for the 12-item Turkish WORQ-UP [17,18]. The literature suggests that for Cronbach's alpha to be higher than 0.70 [25] and for the item-rest correlation to be adequate, the minimum correlation coefficient required is 0.30 [26]. Therefore, when the five items with inadequate item-rest correlations were removed, the item homogeneity of the 12-item Turkish WORQ-UP was demonstrated. It was proven that all items were associated with the questionnaire.

Although the criterion validity of WORQ-UP was not investigated in the original study, the current study, similar to the Persian version, examined the relationship between Quick DASH and WORQ-UP. A moderately strong correlation ($r = 0.754$; $p < 0.001$) was found between Quick DASH and WORQ-UP in the current study, similar to the Persian version (0.630; $p < 0.001$) [32]. Quick DASH is commonly used to assess activity limitations following upper extremity injuries; however, it does not encompass specific activities like WORQ-UP. Therefore, establishing the Turkish validity and reliability of WORQ-UP, which includes more specific work-related activities, can be highly beneficial for clinicians and researchers in this field as an alternative to Quick DASH.

One strength of this study is the utilization of CFA and the validation of the obtained factor structure. As emphasized in the original work, WORQ-UP can assess the severity of work-related limitations in vocational rehabilitation cases and identify changes in work limitations over time. The omission of this aspect from the current study is a limitation. This limitation underscores the necessity for future research to evaluate the sensitivity and reproducibility of this PROM. Such investigations would contribute to a more comprehensive understanding of the WORQ-UP's utility in vocational rehabilitation settings and its capacity to capture changes in work-related limitations.

5. CONCLUSIONS

The 12-item Turkish version of WORQ-UP has demonstrated suitable psychometric properties for identifying work-related limitations in individuals with upper extremity musculoskeletal disorders. WORQ-UP showed a significant and moderately strong correlation with the Quick DASH, confirming its effectiveness in assessing work-related limitations in patients with upper extremity injuries. The total score or clinical subscores of WORQ-UP can guide clinical decision-making and intervention planning in occupational rehabilitation or health. Further studies are needed to evaluate the psychometric properties of WORQ-UP in other health conditions, particularly in populations with mental health issues or multiple comorbidities, and in preventive activities.

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Author Contribution Statement: M.K. and C.D. designed and directed the research, C.D and E.K.B collected the necessary data for the research, M.K., B.B. and K.B. checked the data, M.K. performed the statistical analyses. M.K., C.D. and B.B. checked the results and made the necessary edits. All authors took part in writing the article.

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REFERENCES

1. de Kok J, Vroonhof P, Snijders J, Roullis G, Clarke M, Peereboom K. Work-related MSDs: prevalence, costs and demographics in the E.U. European Agency for Safety and Health at Work (EU-OSHA). 2019: Page 18.
2. Rapicault C, Roquelaure Y, Bodin J, Fouquet N, Bertrais S. Development and validation of a work-related risk score for upper-extremity musculoskeletal disorders in a French working population. *Scand J Work Environ Health*. 2023;49(8):558-568. Doi: 10.5271/sjweh.4119
3. Roquelaure Y, Ha C, Rouillon C, et al. Risk factors for upper-extremity musculoskeletal disorders in the working population. *Arthritis Rheum*. 2009;61(10): 1425-1434. Doi: 10.1002/art.24740
4. Nambiema A, Bodin J, Stock S, et al. Proportion and Number of Upper-Extremity Musculoskeletal Disorders Attributable to the Combined Effect of Biomechanical and Psychosocial Risk Factors in a Working Population. *Int J Environ Res Public Health*. 2021;18(8):3858. Doi: 10.3390/ijerph18083858
5. Nambiema A, Bodin J, Fouquet N, et al. Upper-extremity musculoskeletal disorders: how many cases

can be prevented? Estimates from the COSALI cohort. *Scand J Work Environ Health*. 2020;46(6):618-629. Doi: 10.5271/sjweh.3911

6. Huisstede BM, Bierma-Zeinstra SM, Koes BW, Verhaar JA. Incidence and prevalence of upper-extremity musculoskeletal disorders. A systematic appraisal of the literature. *BMC Musculoskelet Disord*. 2006;7:7. Doi: 10.1186/1471-2474-7-7
7. Walker-Bone K, Palmer KT, Reading I, Coggon D, Cooper C. Prevalence and impact of musculoskeletal disorders of the upper limb in the general population. *Arthritis Rheum*. 2004;51(4):642-651. Doi: 10.1002/art.20535
8. Aytutuldu KG, Birinci T, & Tarakcı E. Musculoskeletal pain and its relation to individual and work-related factors: a cross-sectional study among Turkish office workers who work using computers. *Int J Occup Saf Ergon*. 2022;28(2); 790-797. Doi: 10.1080/10803548.2020.1827528
9. National Research Council, The National Academy of Sciences. Musculoskeletal disorders and the workplace: low back and upper extremity musculoskeletal disorders. Washington (D.C.): National Academy; 2001.
10. Punnett L, Wegman DH. Work-related musculoskeletal disorders: the epidemiologic evidence and the debate. *J Electromyogr Kinesiol*. 2004;14(1):13-23. Doi: 10.1016/j.jelekin.2003.09.015
11. Bernard BP. Musculoskeletal disorders and workplace factors: a critical review of epidemiologic evidence for work-related musculoskeletal disorders of the neck, upper-extremity, and low back. Cincinnati (O.H.): U.S. Health and Human Services; 1997.
12. Bongers PM, Kremer AM, ter Laak J. Are psychosocial factors, risk factors for symptoms and signs of the shoulder, elbow, or hand/wrist?. A review of the epidemiological literature. *Am J Ind Med*. 2002;41(5):315-342. Doi: 10.1002/ajim.10050
13. Bongers PM, Ijmker S, van den Heuvel S, Blatter BM. Epidemiology of work-related neck and upper limb problems: psychosocial and personal risk factors (part I) and effective interventions from a bio behavioural perspective (part II). *J Occup Rehabil*. 2006;16(3):279-302. Doi: 10.1007/s10926-006-9044-1
14. Morse TF, Dillon C, Warren N, Levenstein C, Warren A. The economic and social consequences of work-related musculoskeletal disorders: the Connecticut Upper-Extremity Surveillance Project (CUSP). *Int J Occup Environ Health*. 1998;4(4):209-216. Doi: 10.1179/oeh.1998.4.4.209
15. Ekberg K, Wildhagen I. Long-term sickness absence due to musculoskeletal disorders: the necessary intervention of work conditions. *Scand J Rehabil Med*. 1996;28(1):39-47.
16. Beaton DE, Wright JG, Katz JN. Upper Extremity Collaborative Group. Development of the QuickDASH: comparison of three item-reduction approaches. *J Bone Joint Surg Am*. 2005;87(5):1038-1046. Doi: 10.2106/JBJS.D.02060
17. Aerts BRJ, Kuijer PPFM, Beumer A, Eygendaal D, Frings-Dresen MHW. Development of a novel Work-Related Questionnaire for UPper extremity disorders (WORQ-UP). *Int Arch Occup Environ Health*. 2017;90(8):823-833. Doi: 10.1007/s00420-017-1246-7
18. Aerts BR, Kuijer PP, Beumer A, Eygendaal D, Frings-Dresen MH. WOrk-Related Questionnaire for UPper extremity disorders (WORQ-UP): Factor Analysis and Internal Consistency. *Arch Phys Med Rehabil*. 2018;99(9):1818-1826. Doi: 10.1016/j.apmr.2018.03.013
19. Kottner J, Audige L, Brorson S, et al. Guidelines for Reporting Reliability and Agreement Studies (GRRAS) were proposed. *Int J Nurs Stud*. 2011;48(6):661-671. Doi: 10.1016/j.ijnurstu.2011.01.016
20. Mokkink LB, Terwee CB, Gibbons E, et al. Inter-rater agreement and reliability of the COSMIN (Consensus-based Standards for the selection of health status Measurement Instruments) checklist. *BMC Med Res Methodol*. 2010;10:82. Published 2010 Sep 22. Doi: 10.1186/1471-2288-10-82
21. Beaton DE, Bombardier C, Guillemin F, Ferraz MB. Guidelines for the process of cross-cultural adaptation of self-report measures. *Spine* (Phila Pa 1976). 2000; 25(24): 3186-3191. Doi: 10.1097/00007632-200012150-00014
22. Mokkink LB, Prinsen CA, Bouter LM, Vet HC, Terwee CB. The COnsensus-based Standards for the selection of health Measurement Instruments (COSMIN) and how to select an outcome measurement instrument. *Braz J Phys Ther*. 2016;20(2):105-113. Doi: 10.1590/bjpt-rbf.2014.0143
23. Beaton DE, Wright JG, Katz JN. Upper Extremity Collaborative Group. Development of the QuickDASH: comparison of three item-reduction approaches. *J Bone Joint Surg Am*. 2005;87(5):1038-1046. Doi: 10.2106/JBJS.D.02060
24. Tsang S, Royse CF, Terkawi AS. Guidelines for developing, translating, and validating a questionnaire in perioperative and pain medicine. *Saudi J Anaesth*. 2017;11(Suppl 1): S80-S89. Doi: 10.4103/sja.SJA_203_17
25. Cronbach LJ, & Shavelson RJ. My Current Thoughts on Coefficient Alpha and Successor Procedures. *Educ Psychol Meas*. 2004;64(3):391-418. Doi: 10.1177/0013164404266386

26. Field A. Discovering Statistics Using SPSS. 2nd ed. London: Sage, 2005.
27. Enderlein G, Fleiss, JL. The Design and Analysis of Clinical Experiments. Wiley, New York – Chichester – Brislane – Toronto – Singapore 1986. Doi: 10.1002/bimj.4710300308
28. Weir JP. Quantifying test-retest reliability using the intraclass correlation coefficient and the SEM. *J Strength Cond Res*. 2005;19(1):231-240.
29. Tinsley HE, Workman KR, Kass RA. Factor analysis of the domain of client expectancies about counseling. *J Couns Psychol*. 1980;27(6):561.
30. The jamovi project. Jamovi (Version 1.6.23.0) [Computer Software]. Avaible Online: https://www.jamovi.org (accessed on 10.04.2024)
31. Schober P, Boer C, Schwarte LA. Correlation Coefficients: Appropriate Use and Interpretation. *Anesth Analg*. 2018;126(5):1763-1768. Doi: 10.1213/ANE.0000000000002864
32. Shariyate MJ, Beumer A, Kachooei AR. Validity and Reliability of the Persian Version of WOrk-Related Questionnaire for UPper Extremity Disorders (WORQ-UP). *J Hand Surg Asian Pac Vol*. 2023;28(1):102-107. Doi: 10.1142/S2424835523500030

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Adapting the HSE-MS Indicator Tool for Academia: A Psychometric Evaluation of the Academic Teacher Stress Indicator Tool for Italian University Teachers

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Keywords: Work-Related Stress; Stress Assessment; Academic Teaching Staff

Abstract

Background: *The assessment of work-related stress is mandatory in Italy, according to Legislative Decree 81/2008. The Academic Teacher Stress Indicator Tool (ATS-IT) was developed to address stress in academic teaching staff by adapting the Health and Safety Executive Management Standards Indicator Tool (HSE-MS IT).* **Methods:** *An online ATS-IT survey was administered to all teaching staff at the University of Trieste, yielding 334 valid responses. The survey also included a measure of psychosomatic complaints and demographic questions. Confirmatory factor analysis (CFA) was performed to test the six-factor structure, and reliability was assessed using Cronbach's alpha.* **Results:** *CFA confirmed an excellent fit for the six-factor structure (CFI = .99; TLI = .99; RMSEA = .034). Reliability analysis mainly showed acceptable values (Cronbach's α ranging from .66 to .91). Significant gender differences were found in the Demands and Control scales, with additional differences based on age and academic role across multiple scales. The ATIS-IT scales were significantly intercorrelated and negatively correlated with psychosomatic complaints.* **Conclusions:** *The ATS-IT demonstrates good potential as a valid and reliable instrument for assessing work-related stress among Italian academic teaching staff. Its use can facilitate better stress management and intervention strategies in educational institutions.*

1. Introduction

In Italy, the assessment of work-related stress is mandatory in every workplace, according to Legislative Decree 81/2008 [1]. This emphasizes the importance of reliable and valid tools to evaluate stress levels across professional sectors. The Italian National Institute for Insurance against Accidents at Work (INAIL) in 2010 [2] suggested using the British Health Safety Executive stress model [3] to assess work-related stress. It handled the Italian translation of the Health and Safety Management Standards Indicator Tool (HSE-MS IT) questionnaire [4, 5].

The original HSE-MS IT was designed for broader occupational contexts. Still, specific ad-hoc versions have been developed to assess the risk of work-related stress in particular sectors, such as defense, oil and gas industry, and healthcare [6-8], to represent distinctive stress factors overlooked in the original version but relevant in specific organizational structures. Similarly, in 2015, we adapted the Italian version of the HSE-MS IT to the needs of the Italian academic teaching staff, developing the Academic Teacher Stress Indicator Tool (ATS-IT) [9]. We preliminarily conducted focus groups and interviews with academic teaching staff from Italian

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public universities to refine the HSE-MS IT to reflect the specific challenges academic teaching staff encounter in their work environment. In particular, the Manager Support dimension, which does not apply to the typically non-hierarchical structure of academic institutions, has been replaced with Responsibilities, recognizing the critical aspects of decision-making and accountability in academic roles. This dimension, indeed, includes items that highlight the significant responsibilities of academic teachers, such as the need to make crucial decisions that may have substantial implications for others (e.g., students or colleagues) and the possibility that mistakes could cause harm to individuals or their institution [10]. This pressure to perform accurately, coupled with the weight of accountability for one's actions, has been reported as a source of considerable stress for academic staff. Additionally, item wording was adjusted to resonate more accurately with the experiences of academic staff in Italy. The final version of the ATS-IT, as discussed in the previous literature, comprises 27 items that assess six critical areas of work-related stress: Demands, Control, Relationships, Peer support, Responsibilities, and Change [9, 11].

While the ATS-IT conceptual framework and preliminary application have been discussed in previous literature [9], an evaluation of its psychometric properties has not been conducted yet, except from a study published in the gray literature [11], which supported the six-factor structure of the ATS-IT and demonstrated that the six areas are significantly correlated with perceived occupational stress, as well as a set of psychophysical issues commonly associated with stress. The present study attempts to fill this gap by testing the validity and reliability of the ATS-IT as an instrument for assessing work-related stress among Italian academic teaching staff, thus contributing to better stress management and intervention strategies in educational institutions.

2. Methods

2.1. Participants and Procedure

The study was conducted as part of the mandatory periodic work-related stress assessment required by Italian law [1]. Therefore, Ethical Committee approval was not needed. The study adhered to the principles outlined in the Helsinki Declaration and the Italian Association of Psychology (AIP) ethical code. Participants were informed that their participation was voluntary, that they could refuse to participate or withdraw at any time without giving any reason, that all measurement instruments were anonymous, and that only aggregated data would be reported. By completing the questionnaire, participants indicated their acceptance of participating in the work-related stress assessment.

On March 27th, 2023, all teaching staff (full professors, associate professors, and researchers) employed at the University of Trieste received an email briefly introducing the study and its aims, along with a link to an online survey form to be completed before April 30th. A reminder was sent on April 28th: 340 questionnaires were completed, with a response rate of 44% for full professors, 45% for associate professors, and 51% for researchers.

2.2. Measures

The online survey was organized into three sections. The first section presented the ATS-IT, which considers a six-month time window before the assessment and consists of 27 items tapping the following six scales: Demands (7 items), Control (4 items), Relationships (6 items), Peer support (4 items), Responsibilities (3 items), and Change (3 items). Answers were provided on a five-point scale, ranging from 1 (never) to 5 (always). Consistent with the original HSE-MS IT, the ATS-IT is a risk indicator of work-related stress. This means that, unlike other tools that measure stress intensity [12], the ATS-IT measures employees' exposure to a set of organizational dimensions, which, if not correctly managed, could lead to psychological distress [5, 13]. Higher scores on the ATS-IT scales indicate a better performance in organizational dimensions and, therefore, a lower risk of work-related stress and vice-versa. The ATS-IT items are reported in Supplementary Material A.

The second section included seven items measuring the prevalence of psychosomatic complaints commonly associated with work-related stress (palpitations, sleep disorders, depression, irritability, anxiety, physical and mental tiredness, and headaches) [14, 15]. Participants reported the prevalence of these complaints over the last six months using a five-point scale ranging from 1 (never) to 5 (always). A global measure of psychosomatic complaints was obtained by aggregating the seven items, with higher scores indicating a higher frequency of psychosomatic problems. Cronbach's α for this measure was .82. The final section included demographic questions (gender, age group, and academic role).

2.3. Data Analysis

The factor structure of the ATS-IT items was tested using confirmatory factor analysis (CFA) with diagonally weighted least squares estimation method. The following fit indices were employed: Comparative Fit Index (CFI), Tucker-Lewis Index (TLI), and Root Mean Square Error of Approximation (RMSEA). Values higher than .95 for CFI and TLI and lower than .08 for RMSEA indicated an acceptable fit to the data [16]. Cronbach's α was used to estimate the reliability of the scales, with values ≥ .80 indicating good reliability and values ≥ .70 acceptable reliability. Pearson correlation coefficients were used to examine the association with psychosomatic complaints. Standard inferential tests (t-test and ANOVA) were performed to analyze whether the ATS-IT scales scores differed across the participants' age groups, genders, and academic roles. Statistical analyses were conducted using Jamovi software.

3. Results

Data from six participants were removed from the analyses due to having five or more missing values in the ATS-IT items, leaving a final sample of 334 participants. All remaining missing values were replaced using the EM imputation algorithm.

The results of the CFA showed excellent fit for the hypothesized six-factor structure (CFI = .99; TLI = .99; RMSEA = .034, 95% CI = .026-.042). The factor loadings are reported in Supplementary Material B. Reliability analysis revealed acceptable values. Cronbach's α was .80 for Demands, .79 for Control, .85 for Relationships, .91 for Peer support, .79 for Responsibilities, and .66 for Change.

Descriptive statistics for the whole sample and divided for demographic variables are reported in Table 1.

Table 1. Descriptive statistics of the ATS-IT scales (means, standard deviations in brackets) by demographic variables.

Demographic Variables (N)	Demands	Control	Relationships	Peer Support	Responsibilities	Change
Gender						
M (218)	2.74 (0.57)	3.83[a] (0.64)	3.94 (0.65)	3.54 (0.81)	2.66 (0.77)	3.30 (0.71)
F (112)	2.55 (0.56)	3.65 (0.69)	3.91 (0.62)	3.55 (0.91)	2.70 (0.82)	3.31 (0.59)
Age group						
<30 years (67)	2.63 (0.54)	3.76 (0.61)	3.95 (0.59)	3.67 (0.81)	3.03 (0.76)[a]	3.22 (0.72)
30 – 40 years (84)	2.55 (0.48)[a]	3.72 (0.67)	3.87 (0.64)	3.55 (0.78)	2.60 (0.70)[b]	3.15 (0.60)[a]
41 – 50 years (94)	2.62 (0.64)	3.68 (0.67)	3.84 (0.69)	3.44 (0.93)	2.60 (0.73)[b]	3.31 (0.71)
51 – 60 years (61)	2.85 (0.57)[b]	3.85 (0.64)	4.11 (0.54)	3.57 (0.75)	2.62 (0.85)[b]	3.49 (0.62)[b]
>60 years (25)	2.98 (0.56)[b]	3.96 (0.83)	3.91 (0.79)	3.48 (1.07)	2.44 (0.88)[b]	3.58 (0.68)[b]
Academic role						
Researcher (112)	2.78 (0.55)[a]	3.85 (0.55)	4.03 (0.62)[a]	3.70 (0.86)[a]	3.05 (0.74)[a]	3.31 (0.68)
Associate professor (156)	2.51 (0.57)[b]	3.73 (0.74)	3.81 (0.69)[b]	3.40 (0.88)[b]	2.52 (0.72)[b]	3.20 (0.70)[a]
Full professor (66)	2.86 (0.52)[a]	3.69 (0.66)	4.01 (0.55)	3.55 (0.73)	2.40 (0.77)[b]	3.50 (0.55)[b]

Note. Different superscript letters indicate significant differences in the Tukey post-hoc test, all Ps < .05.

Table 2. Pearson correlations among the ATS-IT scales and psychosomatic complaints.

	Demands	Control	Relationships	Peer Support	Responsibilities	Change
Demands	-					
Control	.38***	-				
Relationships	.49***	.38***	-			
Peer Support	.28***	.32***	.62***	-		
Responsibilities	.38***	.24***	.23***	.12*	-	
Change	.56***	.46***	.62***	.44***	.16***	-
Psychosomatic complaints	-.56***	-.42***	-.42***	-.33***	-.14*	-.48***

*Note. * P < .05 ** P < .01 *** P < .001.*

As for gender differences, females were found to be more at risk in the Demands (t(328) = 2.81, P = 0.005) and Control (t(328) = 2.38, P = 0.018) dimensions compared to males. Significant differences between age groups emerged in the Demands (F(4,116) = 4.78, P = 0.001), Responsibilities (F(4,114) = 4.60, P = 0.002), and Change (F(4,116) = 4.00, P = 0.004) dimensions. Significant differences between academic roles were found in the Demands (F(2,174)=12.28, P<0.001), Relationships (F(2,132) = 4.52, P = 0.012), Peer support (F(2,180) = 4.03, P=0.019), Responsibilities (F(2,166)= 22.29, P<0.001), and Change (F(2,184)=5.75, P = 0.004) dimensions. Tukey post-hoc tests (reported in Table 1) revealed that the significant differences were coherent with expected patterns (e.g., less Responsibilities for researchers compared to associate and full professors).

Table 2 reports Pearson correlations between the ATS-IT scales and psychosomatic complaints. The ATS-IT scales were significantly intercorrelated, as in the HSE-MS IT from which they are derived, and significantly negatively correlated with psychosomatic complaints, with Demands, Relationships, and Change displaying the most robust associations (-.56, -.49, and -.48, respectively).

4. Discussion

Confirmatory factor analysis supported the hypothesized six-factor structure [9, 11] with excellent fit indices, corroborating the tool's construct validity. The reliability analysis confirmed the internal consistency, revealing acceptable values for all dimensions except Change. This result aligns with previous research using the HSE-MS IT [5], from which the ATS-IT is derived, where Change emerged as the weakest subscale.

The negative correlations between the ATS-IT scales and psychosomatic complaints validate the tool, showing concurrent associations with expected stress-related health outcomes [17]. Higher scores in organizational dimensions, indicating lower stress, were associated with fewer psychosomatic problems, consistent with the broader literature on the HSE-MS IT, which showed significant associations among its dimensions and stress-related outcomes, such as job satisfaction, anxiety, and depression [18, 19], highlighting the importance of assessing the risk of occupational stress to mitigate these adverse outcomes. Similarly, our results emphasize the practical relevance of the ATS-IT in identifying organizational stressors in the Italian academic environment.

Significant differences among demographic variables underscore the ATS-IT's sensitivity to individual differences, including specific academic roles. This is consistent with recent research [20] that found that organizational factors and demographic differences can influence work-related stress profiles, particularly during times of crisis. Our findings align with this result, showing that academic teaching staff face distinct stressors depending on their role within the institution, and interventions should be designed accordingly.

Overall, the results of this study are consistent with previous studies validating the HSE-MS IT in occupational settings [18, 21], and indicate that the ATS-IT shows good potential as a valid and reliable instrument for assessing work-related stress among Italian academic teaching staff.

This study has several limitations that should be acknowledged. First, the sample was drawn from a single university with relatively few participants. Second, the overall low response rate may limit the generalizability of the findings. Moreover, we adopted a cross-sectional design, which does not allow for the assessment of causality, and there is a risk that negative affectivity could have influenced the self-reported data. Furthermore, while the Responsibilities dimension was included to capture academic teaching roles' decision-making and accountability aspects, it showed the weakest association with psychosomatic complaints. A possible explanation for this finding is that the relationship between responsibility and stress may not be linear. For example, both low levels of responsibility (which may reduce work engagement and meaning) and high levels (which may increase stress due to the weight of accountability) could contribute to adverse outcomes. Future research should investigate the role of responsibilities, exploring how different levels impact strain and work engagement in academic settings.

5. Conclusion

The ATS-IT shows promise as a valuable tool for assessing work-related stress in Italian academic teaching staff. Its six dimensions provide a focused measure of key stressors relevant to the academic teaching context. Thus, the ATS-IT can serve as a valuable instrument for developing tailored stress management strategies, contributing to the well-being and productivity of academic teaching staff. Further research should investigate longitudinal applications of the ATS-IT to assess its effectiveness over time and explore the role of the Responsibilities dimension.

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Institutional Review Board Statement: The study was conducted following the Declaration of Helsinki guidelines and the Italian Association of Psychology (AIP) ethical code. Ethics committee approval was not required, as the study was part of the mandatory work-related stress assessment (Legislative Decree 81/2008). Data were handled in compliance with privacy laws and under European Union Regulation 679/2016 (GDPR).

Informed Consent Statement: Participants indicated their informed consent by returning the questionnaire.

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

Author Contribution Statement: F.M., D.F. and L.D.B. and contributed to the design of the research; F.M. and F.L.F. contributed to the implementation of the research; F.M. contributed to the analysis of the results; all the authors contributed to the writing of the manuscript.

References

1. Ministry of Labour and Social Policies. Decreto Legislativo 9 aprile 2008, n. 81: Attuazione dell'articolo 1 della legge 3 agosto 2007, n. 123, in materia di tutela della salute e della sicurezza nei luoghi di lavoro. Gazzetta Ufficiale della Repubblica Italiana, Serie Generale, n. 101. Available online at: https://www.gazzettaufficiale.it/eli/id/2008/04/30/008G0104/sg. (Last Accessed: July 28, 2024).
2. INAIL. La metodologia per la valutazione e gestione del rischio stress lavoro-correlato. Available online at: https://www.inail.it/portale/it/inail-comunica/pubblicazioni/catalogo-generale/catalogo-generale-dettaglio.2017.10.la-metodologia-per-la-valutazione-e-gestione-del-rischio-stress-lavoro-correlato.html. (Last Accessed: July 28, 2024).
3. MacKay CJ, Cousins R, Kelly PJ, Lee S, McCaig RH. 'Management Standards' and work-related stress in the UK: policy background and science. *Work Stress*. 2004;18(2):91-112. Doi: https://doi.org/10.1080/02678370410001727474
4. Cousins R, Mackay CJ, Clarke SD, et al. Management standards and work-related stress in the UK: Practical development. *Work Stress*. 2004;18(2):113-136. Doi: 10.1080/02678370410001734322
5. Magnavita N. Validation of the Italian version of the HSE Indicator Tool. *Occup Med* (*Lond*). 2012;62(4):288-294. Doi: https://doi.org/10.1093/occmed/kqs025
6. Wattie SC, Bridger RS. Work-related stress indicator surveys in UK Ministry of Defence. *BMJ Mil Health*. 2019;165(2):128-132. Doi: https://doi:10.1136/jramc-2018-000963

7. Bergh LIV, Hinna S, Leka S, Jain A. Developing a performance indicator for psychosocial risk in the oil and gas industry. *Safety Sci*. 2014;62:98-106. Doi: https://doi:10.1016/j.ssci.2013.07.029
8. Zeinolabedini M, Motlagh ME, Heidarnia A, Shakerinejad G, Zeidi IM. Revision and validation of the Health and Safety Executive Management Standards Indicator Tool among health care workers. Available online at: https://assets-eu.researchsquare.com/files/rs-4230780/v1/2c3c4048-0c9d-46e8-9ee6-701774a995b3.pdf?c=1712824436. (Last accessed: July 28, 2024).
9. Sclip G, Marcatto F, Larese Filon F, Negro C, Ferrante D. La valutazione dello stress lavoro-correlato nell'università pubblica italiana: dall'obbligo di legge a un protocollo operativo. *ISL. IGIENE & SICUREZZA DEL LAVORO*. 2015;19(6):319-326.
10. Hall AT, Royle MT, Brymer RA, Perrewé PL, Ferris GR, Hochwarter WA. Relationships between felt accountability as a stressor and strain reactions: The neutralizing role of autonomy across two studies. *J Occup Health Psychol*. 2006;11(1):87. Doi: https://psycnet.apa.org/doi/10.1037/1076-8998.11.1.87
11. Marcatto F, Sclip G, Di Blas L, Ferrante D. La misura dello stress e la valutazione soggettiva: un'indagine sul personale docente dell'Università degli Studi di Trieste. Trieste, Italy: EUT Edizioni Università di Trieste; 2016.
12. Marcatto F, Di Blas L, Luis O, et al. The perceived occupational stress scale: A brief tool for measuring workers' perceptions of stress at work. *Eur J Psychol Assess*. 2022;38:293-306. Doi: https://doi:10.1027/1015-5759/a000677
13. Marcatto F, Colautti L, Filon FL, et al. Work-related stress risk factors and health outcomes in public sector employees. *Saf Sci*. 2016;89:274-278. Doi: https://doi.org/10.1016/j.ssci.2016.07.003
14. Marcatto F, Patriarca E, Bramuzzo D, Lucci E, Filon FL. Investigating the role of organizational stress in nurses' psychosomatic complaints: Evidence from a study in northeastern Italy. *AIMS Public Health*. 2024;11(2):420-431.Doi:https://doi:10.3934/publichealth.2024021.
15. Nieuwenhuijsen K, Bruinvels D, Frings-Dresen M. Psychosocial work environment and stress-related disorders, a systematic review. *Occup Med*. 2010;60:277-286. Doi: https://doi:10.1093/occmed/kqq081
16. Hu LT, Bentler PM. Cut-off criteria for fit indexes in covariance structure analysis: Conventional criteria versus new alternatives. *Struct Equ Modeling Multidiscip J*. 1999; 6(1):1-55.
17. Marcatto F, Di Blas L, Ferrante D. Diagnostic utility of the Perceived Occupational Stress scale. *Eur J Psychol Assess*. 2023; Advance online publication. Doi: https://doi: 10.1027/1015 5759/a000789.
18. Kerr R, McHugh M, McCrory M. HSE Management Standards and stress-related work outcomes. *Occup Med* (*Lond*). 2009;59(8):574-579. Doi: https://doi.org/10.1093/occmed/kqp146
19. Marcatto F, Ferrante D. Beyond the assessment of work-related stress risk: the management standards approach for organizational wellbeing. *G Ital Med Lav Ergon*. 2021;43(2):126-30.
20. Charzyńska E, Habibi Soola A, Mozaffari N, Mirzaei A. Patterns of work-related stress and their predictors among emergency department nurses and emergency medical services staff in a time of crisis: a latent profile analysis. *BMC Nurs*. 2023;22(1):98. Doi: https://doi.org/10.1186/s12912-023-01241-9
21. Marcatto F, Colautti L, Larese Filon F, Luis O, Ferrante D. The HSE Management Standards Indicator Tool: concurrent and construct validity. *Occup Med* (*Lond*). 2014;64(5):365-71. Doi: https://doi:10.1093/occmed/kqu038

Supplementary material A

Academic Teacher Stress Indicator Tool – Italian version

Di seguito le verranno presentate delle affermazioni che descrivono possibili situazioni lavorative, indichi quanto frequentemente le ha vissute negli ultimi sei mesi.

1	Ricevo delle richeste che mi è difficile soddisfare*	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
2	Le relazioni sul lavoro sono tese e difficili*	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
3	Sono soggetto a prepotenze e vessazioni*	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
4	Posso scegliere i miei ritmi di lavoro	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
5	Il mio lavoro è soggetto a cambiamenti che non dipendono da me*	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
6	Ricevo dai miei colleghi l'aiuto e il sostegno che mi servono	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
7	Mi ritrovo ad affrontare sgraditi cambiamenti lavorativi*	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
8	Devo lavorare molto intensamente*	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
9	Posso decidere quando fare una pausa	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
10	Devo svolgere più attività contemporaneamente*	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
11	Il mio ruolo prevede molte responsabilità*	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
12	Nel mio lavoro posso scegliere cosa fare	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
13	Vengo trattato/a con rispetto	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
14	Ricevo pressanti richieste che mi costringono a rivedere le mie priorità lavorative*	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
15	Riesco a rispettare le scadenze	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
16	Devo prendere decisioni che hanni implicazioni importanti per le altre persone*	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
17	Mi capita di essere trattato in modo ingiusto*	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
18	Un mio errore potrebbe causare danni ad altri/alla struttura*	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
19	Nelle situazioni difficili mi sento supportato/a dei miei colleghi	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
20	Ho a che fare con persone irritanti*	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐

(*Continued*)

21	Mi capita di trascurare alcune attività perché ho troppo da fare*	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
22	Comprendo e condivido le ragioni alla base dei cambiamenti a cui è soggetto il mio lavoro	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
23	Posso decidere in che modo svolgere il mio lavoro	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
24	Se emergono difficoltà sul lavoro posso contare sull'aiuto dei miei colleghi	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
25	Mi capita di discutere animatamente con le altre persone*	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
26	I miei colleghi mi ascoltano quando parlo dei miei problemi di lavoro	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐
27	Mi capita di dedicare al lavoro più tempo di quanto avevo previsto*	mai ☐	raramente ☐	qualche volta ☐	spesso ☐	sempre ☐

*Note. Items marked with an * must be reverse-scored.*

Supplementary material B

Academic Teacher Stress Indicator Tool – CFA factor loadings.

ATIS-IT items	Demands	Control	Relationships	Peer Support	Responsibilities	Change
Item1	0.788					
Item8	0.576					
Item10	0.560					
Item14	0.779					
Item15	0.252					
Item21	0.662					
Item27	0.577					
Item4		0.788				
Item9		0.576				
Item12		0.560				
Item23		0.779				
Item2			0.815			
Item3			0.738			
Item13			0.674			
Item17			0.788			
Item20			0.748			
Item25			0.381			
Item6				0.855		
Item19				0.936		
Item24				0.900		
Item26				0.702		
Item11					0.878	
Item16					0.785	
Item18					0.626	
Item5						0.670
Item7						0.643
Item22						0.555

Note. All factor loadings P < 0.001.

La Medicina del Lavoro

Letter to the Editor

Med. Lav. 2024; 115 (6): e2024039

Fatal Accidents

Sir,

We have read the article published in "La Medicina del Lavoro" titled *Two Decades of Fatal Workplace Accidents in Milan and Monza, Italy: Trends, Work Sectors, and Causes from Autopsy Data*. It has raised some concerns for us.

The subject of workplace fatalities is of utmost importance for public health and safety, as acknowledged in the article itself, and it requires strong societal commitment to adopt the necessary measures to prevent them. However, these claims are not substantiated in the description of the work carried out.

The topic is approached solely from the perspective of the injury, which is merely the starting point for further investigations that lead to reconstructing the dynamics of the event, analyzing the risk factors that caused the chain of events, and ultimately assigning any responsibilities. All this knowledge cannot emerge solely from the autopsy and the "administrative" information provided.

In the case of fatal or serious workplace accidents, certain legal procedures are triggered: investigations begin with an immediate inspection of the accident site, collecting testimonies from any witnesses, followed by all necessary technical assessments. These actions require expertise and professionalism and are carried out under the delegation of the judiciary by PSAL (Workplace Health and Safety Services) staff, in collaboration with other bodies such as law enforcement, the labor inspectorate, and the fire department.

For several years now, the ASLs (Local Health Authorities) have contributed to a national surveillance system known as Infor.MO (https://www.inail.it/nsol-informo/home.do?tipoEvento=1), reconstructing the dynamics of the investigated accidents and the associated factors that caused them. Analyzing these factors, together with reconstructing the incidents, allows for targeted prevention interventions to eliminate risk factors through specific prevention plans and research into solutions.

The article makes no mention of these essential activities, and they are not even cited in the bibliography, nor are international surveillance systems on fatal accidents, such as FACE (https://www.cdc.gov/niosh/face/default.html), managed by NIOSH.

Yet, prevention interventions can only be planned if we come to understand the risk factors (and not just the accident) that caused the event.

To better understand contextual aspects, particularly organizational ones, which increasingly feature among the causes of workplace accidents, a project has been launched by DORS in recent years in which accident investigations are transformed into "stories" narrated by the operators who conducted the investigations (https://www.storiedinfortunio.dors.it/le-storie/). Narrating the events is a tool for knowledge and training, particularly aimed at the public and especially workers.

Perhaps it would have been much more useful to reflect on other information that emerged from the autopsy exams. For example, the article states that alcohol consumption and a history of drug abuse had no influence on the occurrence of the accident. This is a statement that invites reflection, considering that the legislation on alcohol and drugs assumes that such habits are a cause of accidents: was the lack of influence due to the controls introduced by the legislation, or were the claims made in the past for the introduction of these regulations merely statements of principle without any objective evidence?

Lalla Bodini, Susanna Cantoni, Giovanni Falasca, Tino Magna

Occupational Health Physicians, Milan, Italy

Authors' Reply

Sir,

We appreciated the correspondence from Bodini et al., which shows interest in our work among specialists in the field. We all concur that it is urgent to investigate and critically assess the most effective tools for understanding the causes and preventive strategies to address the epidemic of fatal work accidents.

The "concerns" expressed by colleagues are fundamentally two: (i) our paper would lead one to assume that the inspection investigation is not essential; (ii) our investigation would lead to underestimating the impact of substance abuse on the occurrence of fatal work accidents.

In either case, however, Bodini et al. have quite overinterpreted our paper. Our intention was only to discuss whether the autopsy apparatus, with the information collected for its purpose (which, as we mention in our introduction—see page 2 of our paper—is always ordered by the judiciary in the context of a more complex investigation), is or is not a potentially helpful complementary tool (adding value) for describing the phenomenon of fatal workplace accidents.

In no portion of our work is it intended to present the autopsy act as the only valuable resource or, in some way, as a substitute for the in-depth analyses and investigations that "must ultimately assign any responsibilities " nor to forget "the expertise and professionalism required" for these in-depth analyses.

Secondly, the statement that "alcohol consumption and a history of drug abuse did not influence the occurrence of the accident" does not appear in the body of our publication since we are aware of the numerous epidemiological studies that correlate unsafe behaviors with this occupational risk. We only reported statistical data that showed that (see results page 4) "concerning alcohol consumption and history of drug abuse, we didn't find any differences among fatal accident types". We believe that the interpretation of this data is attributable to (as highlighted in the limitations of the discussion section of our paper) the probable lack of information in the autopsy report. Not everyone is subjected to toxicological testing, and data collected posthumously from relatives is frequently unreliable.

We sincerely appreciate your recommendation and citation of the INAIL Infor.MO repository (https://www.inail.it/nsol-informo/home.do?tipoEvento=1). It contains indications that are undoubtedly useful for understanding the phenomenon. Unfortunately, it is available only in Italian. Moreover, it does not give the user an overall view of the aggregate data or summary statistics INAIL produces in the periodic report.

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New Prospects for Rural Health Collaboration

Milan (Italy), Regione Lombardia Building, October 23rd, 2024

Organized by the International Association of Rural Health and Medicine (IARM)

Rural areas worldwide continue to face significant disadvantages compared to urban areas, both in developing and transitional countries and the so-called developed world. This situation highlights a strong need for initiatives to promote the development of various actions required to enhance the well-being of rural populations and workers. To address this issue and initiate an internal renewal process, the International Association of Rural Health and Medicine (IARM) organized a one-day hybrid meeting featuring participation from key associations active in rural areas and input from the World Health Organization and the International Labor Office.

The event was a satellite of the Region of Lombardy's celebrations of the European Week for Health and Safety at the Workplace. It was organized with the support of Drs. Nicoletta Cornaggia and Francesca Pregnolato (Region of Lombardy) and Professors Carrer and Bonzini on behalf of the Coordination of the Regional Hospital units of Occupational Medicine.

Professors Petar Bulat (IARM), Claudio Colosio (IARM, ICOH), Hajo Hannich (IARM), Sara de Matteis (ICOH), Istvan Szilard (IARM), Drs. Sashikala Chandrasekar (ICOH) and István Kiss (IARM) attended in person. Drs. John Wynn Jones (WONCA Rural Party), Ferdinando Petrazzuoli (EURIPA), Shengli Niu (ILO), Ngajilo, Dorothy Amaleck (WHO), Satoshi Izawa (IARM), Khuseyn Egamnazarov (IARM), Burat Kurt (IARM), Ashok Vikke Patil (IARM), Hanifa Denny (ICOH), Roman Kolmatov (IARM), and Zhang Min (IARM) participated remotely.

Prof. Petar Bulat opened the meeting by outlining the IARM activities. Prof. Claudio Colosio presented a new scenario for Primary Health Care in rural areas, discussing prospects for collaboration and the role of international organizations. Dr. John Wynn Jones delivered a presentation on the "Blue Print," the EURIPA Lincoln statement, and the European Academic Rural Health Network proposal. Dr. Ferdinando Petrazzuoli discussed recent developments in EURIPA activities and potential collaboration among organizations. Dr. Shengli Niu presented the priorities and objectives for OHS in agriculture from the ILO's perspective. Dr. Dorothy Amaleck Ngajilo addressed WHO's views on the importance of global health coverage in the third millennium and the challenges rural areas face. Prof. Hanifa Denny shared insights from the ICOH Scientific Committee on Rural Health regarding primary occupational health care in rural areas and essential occupational health services.

A deep debate followed addressing rural areas' significant disadvantages regarding access to welfare structures, education, employment, income, and, particularly, healthcare systems. In this context, all the participants emphasized the need for collaboration among various subjects and organizations involved in Rural Health, including social service providers, healthcare professionals at all levels, stakeholders, and policymakers, as well as the potential for improvement. Collaboration also uses new technologies, which allow organizing virtual meetings. In the view of the participants, the key aspect of the increase of coverage in rural areas is represented by a sound collaboration among local communities and their representatives, employers' and employees' organizations, rural GPs, and rural occupational physicians, which is crucial for creating structures that enhance access for rural citizens and workers within the healthcare system. This is part of a global public health project that, particularly in rural areas, must adopt a "one health" or even "Planetary Health" approach, linking human, animal, and environmental health. This goal can only be achieved by enhancing primary healthcare, which serves as the first point of contact for citizens with the healthcare system.

The primary actors in rural primary health care include rural GPs, rural occupational physicians, and rural nurses, alongside structures promoting increased coverage, such as the currently running "Basic Healthcare Centres (BAHCs)" and "Basic Occupational Health Services (BOHSs)" in certain countries. BAHCs and BOHSs can vary in organization and complexity, ranging from elementary structures with few personnel to more complex, well-structured, and equipped units. BAHCs should also provide dental care. Other professionals, such as rural veterinarians and environmental health specialists, should be involved in the project, with particular attention given to supplying essential pharmaceuticals, including vaccines. Organizations like WONCA Rural Party and EURIPA address primary health care in rural areas, while ICOH handles specific aspects of occupational health. However, there is a lack of an organization focused on the public health challenges, particularly in rural areas, which may become the main task of the renewed IARM. Since its founding on July 12, 1961, IARM has required a profound renovation process. After extensive debate, participants reached the following agreement points: a strong collaboration is necessary among the organizations active in Rural Health. This can be achieved both through the invitation to the decisional bodies of the Organizations and members of the other Organizations as observers. Since its first board meeting after the publication of these minutes, IARM will invite members of different organizations to its board meeting. A second level of coordination will be organizing periodic moments of debate among representatives of the Organizations. IARM representatives will also participate in the Rural Heath Annual Forum organized by EURIPA.

Government organizations (WHO and ILO) will continuously be informed about rural health activities.

IARM representatives will participate in the European Academic Rural Health Network founded by EURIPA and propose specific areas of research and training.

Under the proposal of WONCA and EURIPA, IARM will evaluate the possibility of changing its name to ensure clarity regarding its role, which is not linked to care provision.

IARM will periodically organize and propose collaborations with other organizations and conduct specific training and education initiatives through online webinars. It will also invite independent experts to discuss the different problems of rural areas. Themes of particular relevance are zoonoses and heat stress.

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