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Systematic Review

The Quality of Life and the Bio-Molecular Profile in Working Environment: A Systematic Review

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Abstract: Working life is characterised by various requirements and degrees of control in meeting these demands. The imbalance of these elements with workers' resources can result in work-related stress involving the repeated activation of stress response systems. Modifications in the bio-molecular profile may represent a biological signature of individuals' life experiences and provide evidence on pathways through which such stressors can result in health outcomes. The aim of our systematic review is to characterize the quality of life (QOL) and the bio-molecular profile in the working population, to highlight if the alteration observed might be related to the working conditions. The article query was performed on PubMed, Embase, and Cochrane CENTRAL and results have been presented according to three molecular pathways involved in the stress response: oxidative stress, inflammation, and neuroendocrine activation. The epidemiological sample has been sub-grouped into "clinical" and "non-clinical" populations according to the presence of a diagnosis of psychological disorders. Besides some critical issues, the review highlights the importance of developing a valid array of biological indicators, measurable in non-invasive matrices, sensitive to both derangements from physiological conditions and stress reduction, useful for identifying those groups at higher risk of health outcomes and, eventually, promoting workers' wellbeing.

Keywords: stress-related outcomes; biomarkers; quality of life; wellbeing; working conditions

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1. Introduction

Working life is characterised by different requirements, both physical and mental, and by various degrees of control in meeting these demands, according to the occupation and the job grade achieved [1]. To better understand the overall impact of working conditions on workers' health, the traditional analysis of occupational exposures, concerning mainly biological, physical, and chemical hazards, has been enriched with the investigation of adverse psychosocial work environment consequences [2]. In this scenario, emergency first responders and tactical operators represent an extreme condition, being required to complete physically and psychologically demanding tasks over and over again for extended periods and to make difficult decisions, thus exacerbating the role of physical, physiological, cognitive, and psychological stressors to which they are exposed [3].

Challenges exceeding the individual's ability to cope can lead to a shift from tolerable to toxic stress and, in turn, to repeated activation of stress response systems without sufficient buffering factors, in a condition known as allostatic load [4,5]. In the short term, biological responses to stress can deal with circumstances, promoting the adaptation, maintenance of homeostasis, and survival via neuroendocrine, cardiovascular, autonomic, immune, and metabolic systems [6]. The maintenance of elevated levels of stress hormones,

such as glucocorticoids and catecholamines, for longer than is optimal for health can evolve into chronic stress [6–8]. This condition can lead to a derangement in biological pathways, underlying the association between stress and health impairments and exacerbating pathophysiological consequences [4,9]. Indeed, the hallmarks of the allostatic state are high levels of stress hormones, interruption of metabolic regulation, and a shift towards a pro-inflammatory state, all conditions that are able to promote the onset of various chronic symptoms [7].

The departure from physiological conditions can be assessed as a modification in the biomolecular profile that may represent a biological signature of individuals' life experiences and provide evidence on pathways through which such stressors can result in health outcomes [4,10,11]. Thus, from an epidemiological perspective, biomarker levels may represent an early warning system for future adverse health outcomes, and their assessment can help in the prevention of chronic diseases [11,12].

Specifically, in occupational settings, this imbalance between demands and workers' resources can lead to so-called work-related stress [13]. This condition is also an important risk factor for many chronic impairments, such as cardiovascular diseases [14], sleep disorders, anxiety, depression, post-traumatic stress disorders [15], burnout [16], and musculoskeletal disorders [17]. Notably, work-related stress can result in sickness absence even without formal psychiatric diagnosis [18].

Thus, even though the various facets of the association have not been completely clarified yet, job characteristics and working context may evidently affect the workers' overall quality of life (QOL) [19].

The World Health Organisation (WHO) defines this indicator as "a person's perception of his/her position in life within the context of the culture and the value system in which he/she lives and in relation to his/her goals, expectations, standards, and concerns" [20]. This broad concept incorporates many elements, each of them able to influence the QOL perception, such as a person's health, psychological state, level of independence, social relationships, personal beliefs, and relationship to salient features of the environment [20]. A similar construct is the health-related quality of life (HRQOL) concept, described by the Centre for Disease Control and Prevention (CDC) as "an individual's or group's perceived physical and mental health over time", in an attempt to entangle into a single definition all those aspects able to play a role in affecting health, either physically or mentally [21]. The huge variability in HRQOL has been reported in the professionally active US population even after adjusting for sociodemographic and health behaviour factors, highlighting the importance of considering the role of occupation in research concerning this peculiar indicator [19]. All the elements previously described can be summarised in the framework of workers' well-being, which can be defined as "an integrative concept that characterises quality of life with respect to an individual's health and work-related environmental, organizational, and psychosocial factors. Well-being is the experience of positive perceptions and the presence of constructive conditions at work and beyond that enables workers to thrive and achieve their full potential" [22].

The promotion of stress-reducing strategies to improve workers' ability and wellbeing is thus a topical issue nowadays, with economic and social benefits for companies, workers, and society [23]. A recent review highlighted a considerable financial burden on society due to work-related stress, estimating the total cost of work-related stress in the US at $221.13 million to $187 billion, with 70–90% due to productivity-related losses [24].

In this context, the aim of our systematic review is to characterise the QOL and biomolecular profile in the working population, highlighting, when possible, if the alteration observed in these subjective and objective indicators might be related to the quality of working conditions.

2. Materials and Methods

The present study is in accordance with the PRISMA 2020 Statement [25] and registered on the PROSPERO database (Protocol n. CRD42020210876). Due to the PROSPERO working

group's necessity to focus on COVID-19 submissions, the registration of this protocol underwent only the basic automated checks for eligibility.

2.1. Study Selection

The query of original research articles investigating the bio-molecular profile and QOL in working environments was launched the 3 March 2022 in PubMed, Cochrane CENTRAL, and Embase.

The search string included the following terms: "Oxidative Stress", "Hydrocortisone", "Malondialdehyde", "8-Hydroxy-2'-Deoxyguanosine", "F2-Isoprostanes", "C-Reactive Protein", "Interleukin-6", "Interleukin-8", "Interleukin-1", "Tumor Necrosis Factor-alpha", "Melatonin", "Quality of Life", "Work", "Employment", "Occupations", "Job Satisfaction", "Occupational Stress", "Occupational Exposure", "Occupational Health", "Occupational Groups". Full details are given in Appendix A.

2.2. Inclusion and Exclusion Criteria

All those articles, in English or Italian, concerning adult workers (18+ years) and reporting a quantification of both QOL and bio-molecular profile were considered potentially eligible, regardless of age, sex, occupation, and qualification.

The exclusion criteria were (i) unemployed subjects or workers under 18 years old; (ii) review articles; (iii) editorials or commentaries; (iv) protocols; (v) conference abstracts.

Two reviewers performed the selection of the articles in a blind process according to the eligibility criteria previously described. Eventual disagreements were submitted to a third reviewer.

2.3. Data Extraction

Two independent reviewers completed the data extraction process. Missing data were requested from the original study investigators. Data extracted included: authors, year of publication, title, journal, country, study characteristics (setting, design, composition, and sample size), sample characteristics (age, gender, eventual disorders or pathologies, ethnicity, lifestyle), quality of life assessment (the type of questionnaire employed), working activity characteristics (the type of working activity, working years, working condition assessment), bio-molecular profile assessment (the type of biomarker, analytical method, biological specimen), outcome measurements, co-factors/confounding factors measured, adjusted relative risk or odds ratio, suggested mechanisms of action, suggested interventions, limitations, and conclusions, eventual conflict of interest. Data reported by graphs in the original studies were extracted by the WebPlotDigitizer software (https://apps.automeris.io/wpd/) (accessed on 17 May 2022).

2.4. Quality Assessment

Two independent reviewers assessed the risk of bias in a blind process, employing the appropriate Critical Appraisal Checklist according to the study design of original research: cross-sectional studies and randomised controlled trials were evaluated by the specific Joanna Briggs Institute (JBI) checklist, while before-after studies by the proper NIH Quality Assessment Tool. The only N-to-1 study included was evaluated with the JBI checklist for case series, considering only the appropriate questions. Each study was awarded a Completeness of Reporting (COR) score according to the number of the checklist items satisfied. The COR score of each study was calculated as COR (%) = ("satisfied"/("satisfied" + "not satisfied/unclear")) $\times$ 100). Quality was then defined according to the COR score as "poor" (if <50% of items were met), "moderate" (if 50–74% of items were met), or "high" (if $\geq$75% of items were met) [26]. Only studies with a "moderate" or "high" quality were included in the review.

2.5. Statistical Analysis

Categorical variables have been reported as frequency (n), while continuous variables have been reported as mean ± standard deviation (SD) or mean ± standard error of the mean (SEM) or median and interquartile range (IQR). Graphs were created by R Studio (RStudio Team (2020). RStudio: Integrated Development for R. RStudio, PBC, Boston, MA, USA).

3. Results

3.1. Search Results

The query provided 10,375 results from the three databases selected. Among the 7413 records obtained after duplicate removal, we excluded 7310 results according to title and abstract screening and the comparison with our inclusion/exclusion criteria. The study selection process is summarised in Figure 1. In summary, we identified 23 articles [27–49] fulfilling our inclusion criteria, which were included in the present review. Among them, 12 (52.2%) were awarded with a "high" quality score, while 11 (47.8%) were awarded with a "moderate" quality score.

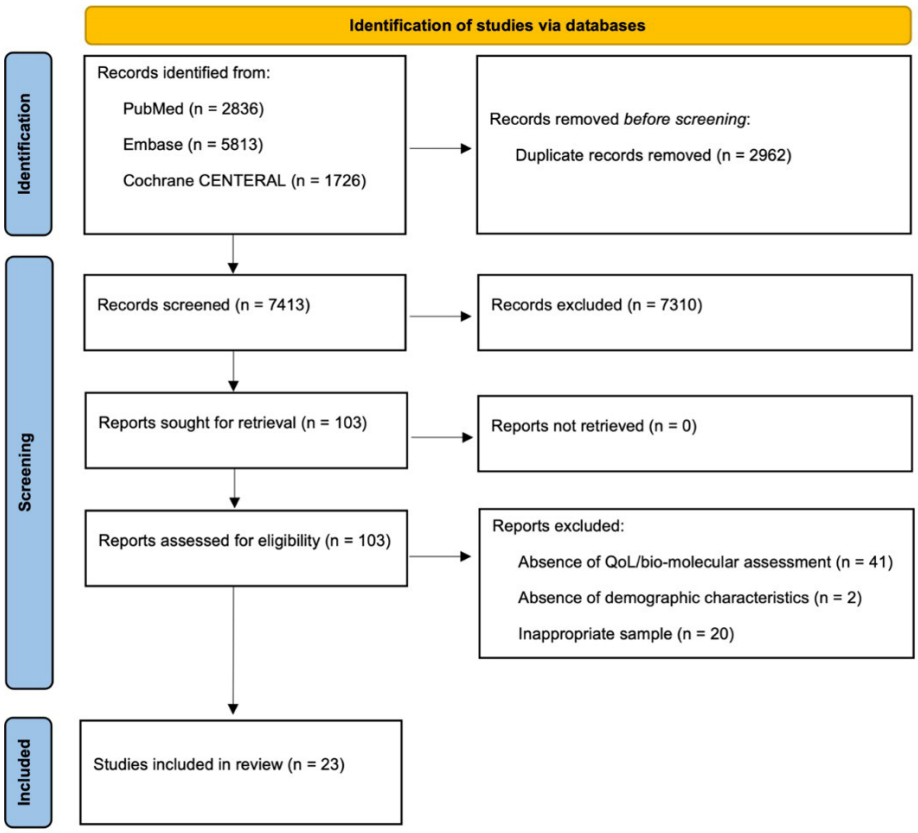

Figure 1. PRISMA flow diagram summarising the literature query and the study selection process.

3.2. Epidemiological Sample

The 23 selected studies are characterised, as expected, by a high diversity in terms of the characteristics of the subjects and occupation type. In order to preserve the original value of the data reported in the included articles, we split the epidemiological sample into "clinical" and "non-clinical" populations. By "clinical population" we meant those subjects having received a diagnosis for psychological disorders that could be related to working activities. 775 subjects have been included in the clinical sample, and 3155 subjects in the non-clinical sample. A brief synopsis of the included studies in each group is reported in Tables 1 and 2. A more detailed description can be found in the Supplementary Materials. As specified, in some studies, biological analyses were performed only in subsamples.

Table 1. Summary of studies, epidemiological sample characteristics, and results as originally reported in the included articles ascribed to the "*Clinical population group*". Quality assessment was performed according to the study design.

Authors, Year	Country	Sample Population and Diagnosis	QOL Questionnaire	Biological Matrix and Biomarkers	Quality Assessment
Devoto et al., 2017 [27]	US	Active duty military personnel; Traumatic Brain Injury	SF-36	Blood—TNF-α; IL-6; IL-10	High
Gill et al., 2014 [28]	US	Active duty military personnel; PTSD, Depression, Traumatic Brain Injury	SF-36	Blood—IL-6; CRP	High
Heinzelmann et al., 2014 [29]	US	Military personnel; Insomnia, Depression, PTSD	RAND-36	Blood—IL-6; CRP	Moderate
Kanefsky et al., 2019 [30]	US	Active duty military personnel; Traumatic Brain Injury	SF-36	Blood—IL-6; IL-10; TNF-α	Moderate
Knuth et al., 2016 [31]	BR	Community Health Agents; Depression	WHOQOL-Bref	Saliva—Cortisol	Moderate
Nieuwenhuijsen et al., 2017 [32]	NL	Professionally active adults; Neurasthenia	SF-36	Hair—Cortisol	Moderate
Sandstrom et al., 2011 [33]	SE	Workers with work-related exhaustion; Burnout	WHOQOL-Bref	Urine—Cortisol Saliva—Cortisol Blood—IL-1β, TNF-α, IL-1Ra, IL-6	High
Schaffler et al., 2013 [34]	D	Professionally active adults; Asthenia/Fatigue	WHO-5	Saliva—Cortisol	Moderate

TNF-α = Tumour Necrosis Factor alpha; IL = Interleukin; CRP = C Reactive Protein; IL-1Ra = Interleukin 1 Receptor Antagonist.

Table 2. Summary of studies, epidemiological sample characteristics, and results as originally reported in the included articles ascribed to the "*Non-clinical population group*". Quality assessment was performed according to the study design.

Authors, Year	Country	Sample Population	QOL Questionnaire	Biological Matrix and Biomarkers	Quality Assessment
Devoto et al., 2017 [27]	US	Active-duty personnel	SF-36	Blood—TNF-α; IL-6, IL-10	High
Ebata et al., 2017 [35]	J	Public employees, Nurses, Office workers	SF-8	Blood—d-ROM; BAP	Moderate
Everding et al., 2016 [36]	US	Sworn officers	Unhealthy Days	Blood—IL-6; IL-10; TNF-α; IL-1β; IL-4; IL-8; TGF-α; TNF-β	High

Table 2. *Cont.*

Authors, Year	Country	Sample Population	QOL Questionnaire	Biological Matrix and Biomarkers	Quality Assessment
Feicht et al., 2013 [37]	D	Insurance company employees	WHO-5	Saliva—Cortisol; α-amylase	Moderate
Giessing et al., 2020 [38]	DE	Patrol police officer	SF-36; WHO-5	Saliva—Cortisol; α-amylase	High
Harris et al., 2007 [39]	NO	Nursing staff	SF-36	Saliva– Cortisol	High
Jordakieva et al., 2021 [40]	AT	Hospital workers	WHOQOL-Bref	Blood—CRP; IL-6	High
Kanefsky et al., 2019 [30]	US	Active duty military personnel	SF-36	Blood—IL-6; IL-10; TNF-α	Moderate
Kasemy et al., 2020 [41]	EG	Physicians; Nurses; Non-Health Care Workers	WHOQOL-Bref	Blood—IL-6; TNF-α	High
Nickel et al., 2007 [42]	A	Blue collar; white-collar; self-employed	SF-36	Saliva—Cortisol	Moderate
Özyürek et al., 2020 [43]	TR	Nurses	SF-36; SWLS	Blood—TOS; TAS; Cortisol	High
Pandaran Sudheeran et al., 2016 [44]	IND	Private company employees	SF-36	Blood—CAT; SOD; GPx; Glutathione; MDA	High
Poon et al., 2018 [45]	HK	Jockeys	WHOQOL-Bref	Blood—Cortisol	Moderate
Rector et al., 2014 [46]	D	Employees	SF-12	Blood—CRP Saliva—Cortisol	Moderate
Rosemberg et al., 2019 [47]	US	Hotel housekeepers	SF-12	Blood—Allostatic Load Index; CRP; Cortisol	High
Sadowska et al., 2020 [48]	PL	Professional caregivers	WHOQOL-Bref	Blood—IL-6; CRP; Cortisol	Moderate
Vlahoyiannis et al., 2022 [49]	GR	Nurses	SF-36	Saliva—Melatonin	High

TNF-α = Tumour Necrosis Factor alpha; IL = Interleukin; dROM = diacrons Reactive Oxygen Metabolic; BAP = Biological Antioxidant Potential; TGF-α = Transforming Growth Factor alpha; TNF-β = Tumor Necrosis Factor beta; CRP = C Reactive Protein; TOS = Total Oxidant Status; TAS = Total Antioxidant Status; CAT = Catalase; SOD = Superoxide Reductase; GPx = Glutathione Peroxidases; MDA = Malondialdehyde.

3.3. Biomarker Selection

As can be seen in Figure 2, 22 biomarkers had been assessed in the articles included in the review. The biological matrices employed were blood, saliva, hair, and urine.

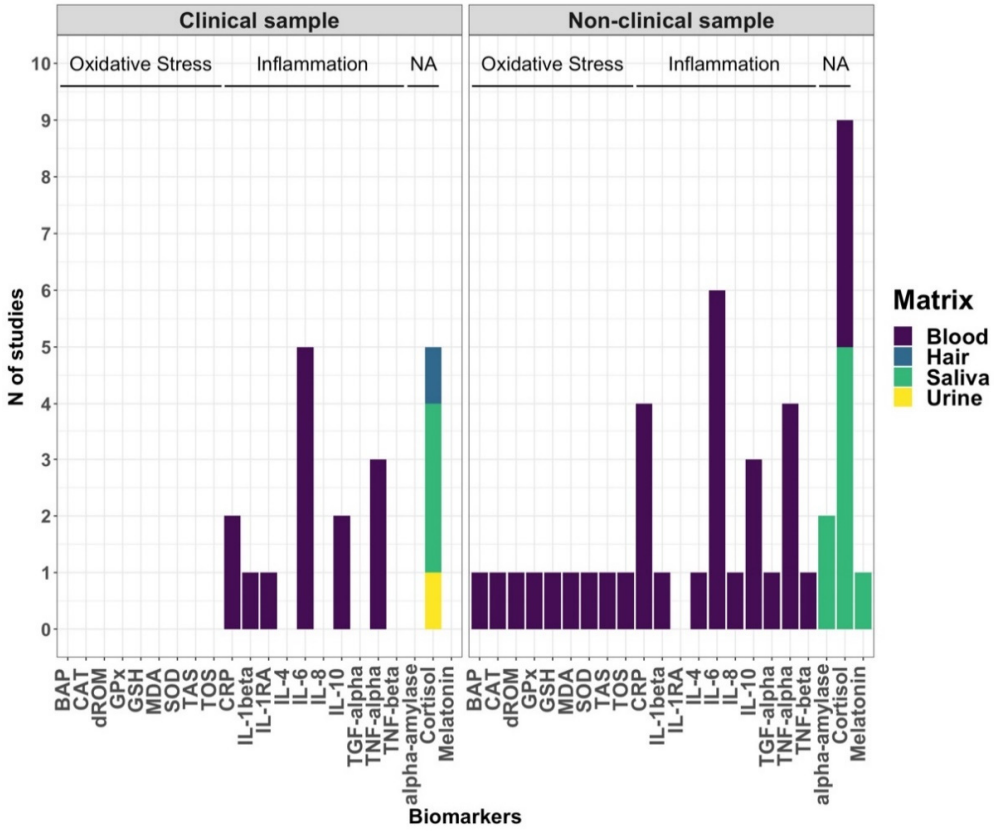

Figure 2. Biomarkers assessed and their frequency in the studies included in the review. BAP = Biological Antioxidant Potential; CAT = Catalase; dROM = diacrons reactive oxygen metabolic; GPx = Glutathione Peroxidases; GSH = Reduced Glutathione; MDA = Malondialdehyde; SOD = Superoxide Reductase; TOS = Total Oxidant Status; TAS = Total Antioxidant Status; CRP = C-Reactive Protein; IL- = Interleukin; NA = Neuroendocrine Activation.

3.4. QOL Assessment Method Selection

As can be seen in Figure 3, six different methods have been employed to assess the QOL of the enrolled subjects in the included articles.

3.5. Clinical Population

3.5.1. Inflammatory Biomarkers

In a study on TBI aftermath in military personnel, Devoto et al. found higher blood levels of IL-6 and TNF-α in the TBI group than in controls ($p = 0.007$ and $p = 0.003$, respectively), while no difference was reported in IL-10 levels. Comparing the SF-36 questionnaire domain scores, the TBI group reported lower levels for emotional well-being ($p = 0.001$), energy/fatigue ($p = 0.007$), health perceptions ($p = 0.001$), emotional role limitations ($p = 0.035$), physical role limitations ($p = 0.018$), and social functioning ($p = 0.003$). No differences were instead found for bodily pain (p = ns) and physical functioning (p = ns). The exploratory factor analysis performed in the TBI group to describe the latent relationship between emotional and physical health variables and the inflammatory profile revealed the high association between high inflammation (TNF-α, IL-6, IL-6/IL-10 ratio) and poor mental health (PTSD and depression). A high association was also found between low PTSD, depression, TNF-α, and QOL scores (SF-36 domains—bodily pain, high emotional functioning, emotional wellbeing, emotional role functioning, social functioning, vitality, and physical role functioning) [27].

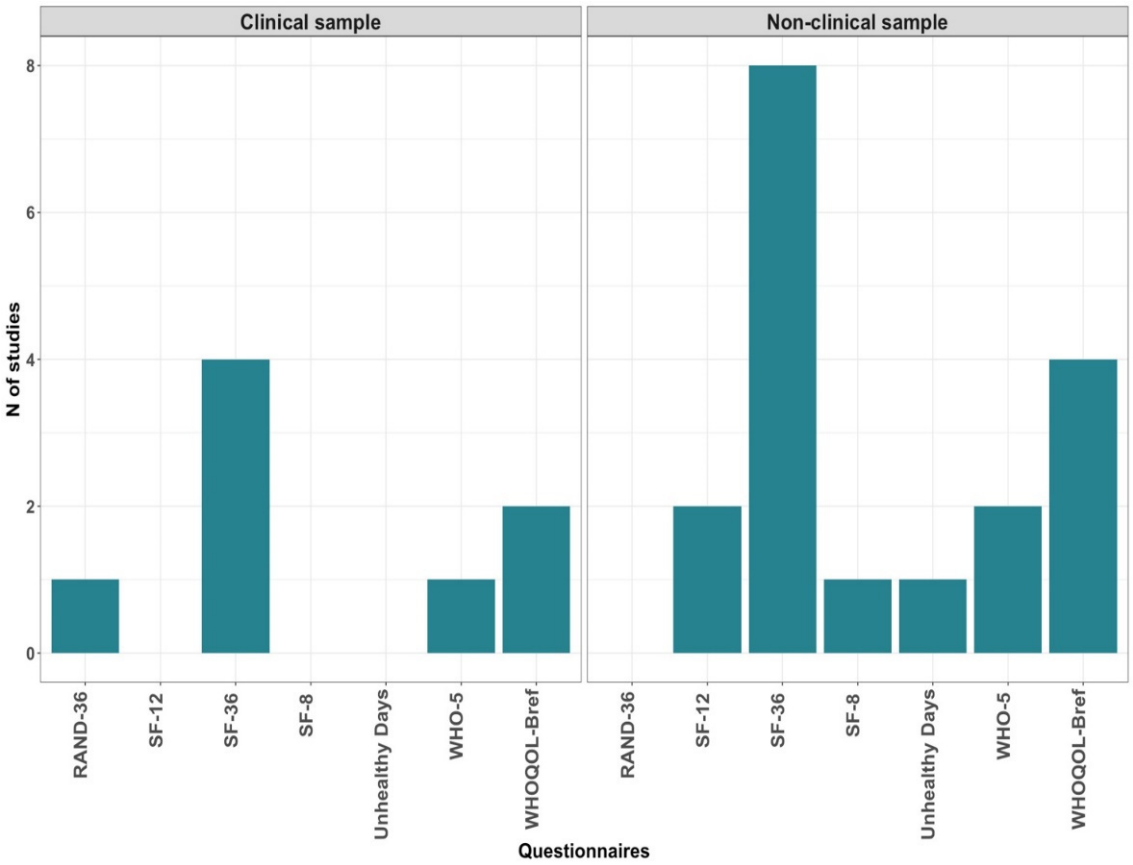

Figure 3. QOL questionnaires employed and their frequency in the studies included in the review.

Gill et al., in a population of active-duty military personnel recently returned from operations in Iraq and Afghanistan, reported significantly higher values of IL-6 and CRP levels in the high comorbid group (2–3 service-related disorders among PTSD, depression, and TBI) than in the low comorbid group (0–1 service-related disorders) ($p < 0.01$ and $p < 0.05$, respectively). The relationship remains significant only for IL-6 after correction for sleep disorders ($p < 0.05$). The QOL assessment revealed lower scores in both the total SF-36 and in all the domain scores ($p < 0.01$). The further comparison between the groups with service-related disorders (TBI alone, PTSD and depression, and PTSD, depression, and TBI) and the no co-occurring group revealed an analogue difference ($p < 0.01$), except for the TBI alone group (p = ns). The IL-6 concentration was found to be significantly related to HRQOL, even after controlling for age, medications, and BMI. This relationship was found to be mediated by depression (22.3%, $p < 0.01$) and PTSD (19.1%, $p < 0.05$). On the contrary, no significant relationship was found between CRP and HRQOL [28].

Similarly, comparing military personnel with a history of TBI who experienced or did not have a concurrent Loss of Consciousness (LOC) and a control group, Kanefsky et al. reported a significant difference ($p < 0.001$) in plasma IL-6 levels, even after controlling for Combat Experiences Scale and insomnia status, with the highest levels found in the LOC group ($p < 0.001$). Specifically, insomnia was associated with a 0.37 pg/mL increase in IL-6 levels. No differences had been found instead for IL-10 and TNF-α levels. The QOL (SF-36) was lower in the TBI groups in all eight domains ($p < 0.05$). No association has been found between cytokine levels and self-reported QOL [30].

In a similar population with all volunteers affected by insomnia, Heinzelmann et al. found a significant reduction in CRP plasma levels in those subjects following a standard-of-care intervention therapy (cognitive behavioural therapy, pharmacological agents, and/or auto-adjusting positive airway pressure treatment) ($p < 0.01$), while no effect was detected in IL-6 levels. As well, they reported an increase and a significant interaction effect between

sleep groups and time in the subjects' QOL perception (RAND-36), specifically in the physical functioning (p = 0.04), the social functioning (p = 0.03), emotional well-being (p = 0.03), and energy/fatigue ($p < 0.001$) domains. For the last two domains, there was also a significant effect for time (p = 0.05 and p = 0.03, respectively) [29].

In a study on workers previously diagnosed with work-related exhaustion, Sandstrom et al. (2011) found significantly higher values of IL-1β (p = 0.015) than in a control group. As well, they reported lower levels in the Environment and Psychological domains of the WHOQOL-bref questionnaire (p = 0.036 and $p < 0.001$, respectively) [33].

3.5.2. Stress Biomarkers—Hypothalamic-Pituitary-Adrenocortical Activity (Cortisol)

Knuth et al. (2016) reported higher cortisol levels in community health agents with less than 1 year of service compared to their colleagues with a longer career (p = 0.026) and a significant negative association between salivary cortisol levels and the WHOQOL-bref environmental domain score (r = −0.214; p = 0.017). No association was found with the other domains (physical, psychological, and social). The physical domain of QOL was significantly lower in those suffering accidents at work (p = 0.007) and in those perceiving health changes due to work (p = 0.001). Those having suffered accidents at work also reported lower scores in the environmental domain (p = 0.008) [31].

In comparing women with stress-related exhaustion with healthy controls, Sandstrom et al. did not report significant differences in urinary and diurnal salivary cortisol concentrations [33].

A trial involving workers affected by work-related stress by Nieuwenhuijsen et al. revealed that light plus electromagnetic therapy combined with coaching is not sufficient to induce a significant improvement in QOL (SF-36) and hair cortisol levels [32].

In a similar population, Schaffler et al. evaluated the potential role of Eleutherococcus senticosus (ES) administration in workers affected by stress-related fatigue, impaired work, or concentration, revealing a general trend supporting a possible superiority of treatments involving the combination of ES with classical Stress Management Therapy (SMT) in improving QOL (WHO-5, p = 0.051). The cortisol awakening response (i.e., the increase within 30 min after awakening) significantly changed during the time without group differences (p = 0.047) [34].

3.6. Non-Clinical Population

3.6.1. Oxidative Stress Biomarkers

In a study aiming to find potential objective biomarkers of fatigue in working women, Ebata et al. analysed serum concentrations of diacrons reactive oxygen metabolic (d-ROMs) and biological antioxidant potential (BAP). The authors highlighted significantly higher BAP levels in shift-workers compared with daytime workers. The relationship remained significant even after adjusting for age, BMI, commuting time, sleep, drinking/smoking, and VDT ($p < 0.001$). In shift-workers, the BAP level was even associated with the Visual Analysis Scale for "sensation of fatigue". No significant differences were reported in QOL (SF-8), on both mental and physical scales [35].

Pandaran Sudheeran et al. developed a trial to evaluate the potential role of curcumin-based products in handling occupational stress among workers in responsible positions. After a 31-day supplementation with curcumagalactomannoside (CGM), the authors reported a significant increase in plasmatic levels of glutathione and antioxidants enzymes such as catalase, superoxide dismutase, and glutathione peroxidase ($p < 0.01$) and a decrease in MDA ($p < 0.001$). The supplementation with standard curcumin was reported to have a similar effect, but with lower efficacy ($p < 0.05$). As expected, no difference in these biomarker levels was found in the placebo group (p = ns). In the two intervention groups, a significant increase in QOL (SF-36) (CGM $p < 0.01$ and standard curcumin $p < 0.05$, respectively) can be observed, with the higher levels reached in the CGM group. As for the biomolecular profile, no significant variation in QOL perception was found in the placebo group [44].

3.6.2. Inflammatory Biomarkers

In a study on law enforcement officers, Everding et al. grouped participants according to their sleep quality. No significant differences among the three analysed sleep quality groups (good, borderline, poor) were found in cytokine levels (IL-1β, IL-4, IL-6, IL-8, IL-10, TGF-α, TNF-α, and TNF-β). In contrast, the QOL (unhealthy days) was reported to be significantly different among the three sleep groups ($p < 0.001$), with the subject reporting poor sleep experiencing a higher number of unhealthy days when compared with the other two groups ($p < 0.05$). As well, the poor sleepers were reported to have a higher OR for worsened mental health and impaired HRQOL ($p < 0.001$) [36].

Rector et al. attempted to evaluate the association between psychological stress and CMV antibody levels in an occupational sample. Systemic inflammation measured by CRP was not reported to be associated with infection status or CMV-Ig levels. In contrast, the authors found an association between lower QOL (SF-12) scores and increased CMV-Ig levels in CMV+ subjects ($p < 0.05$), even though any association was found with CMV infection [46].

Sadowska et al. did not find any difference in blood concentration of systemic inflammatory biomarkers in professional caregivers compared to healthy controls. As well, no significant difference was found in QOL scores (WHOQOL-Bref) [48].

Jordakeva et al., in an attempt to evaluate the role of shift-work in health care professionals, did not find any difference in both QOL scores (WHOQOL-Bref) and inflammatory biomarkers (IL-6 and CRP) comparing day workers vs rotating night shift workers [40].

The results of Kasemy et al., comparing health care workers vs white collars employed in the same facilities, revealed, instead, that health care professionals reported a significantly lower QOL scores (WHOQOL-Bref, $p < 0.001$), while the results of the comparison of the two groups according to the inflammatory biomarker concentration (IL-6 and TNF-α) were not reported [41].

3.6.3. Stress Biomarkers—Hypothalamic-Pituitary-Adrenocortical Activity (Cortisol)

In a study aiming to evaluate the role of a 7-week web-based happiness training in improving workers' psychological well-being, Feicht et al. did not find a significant variation in salivary cortisol due to the intervention. The comparison of QOL scores (WHO-5) revealed a significant increase in the intervention group after the training ($p < 0.001$), which resulted in significantly higher levels when compared to the control group ($p < 0.001$) [37].

On the other hand, in a study on nursing staff, Harris et al. reported a positive correlation between daily cortisol in saliva and QOL (SF-36) domains. Specifically, they reported a positive correlation between cortisol decline and physical functioning, general health, and vitality ($p < 0.05$). This last was also negatively correlated with cortisol level at 10:00 p.m. ($p < 0.05$). Some working conditions were found to be correlated with cortisol. A positive association was found between awakening levels and both the decision latitude and decision authority, which was revealed to also be positively associated with cortisol decline during the day (both $p < 0.05$) and negatively correlated with awakening cortisol response ($p < 0.05$) and evening cortisol levels ($p < 0.01$). Effort/reward imbalance and self-reported job stress did not seem to have a significant influence on this biomarker. A regression analysis revealed that vitality and decision authority, together with coffee consumption and coping strategies, accounted for 22.2% of the variance in evening cortisol levels [39].

In a trial aiming to evaluate the potential effectiveness of behavioural/psychoeducational training on chronic occupational stress, Nickel et al. found that the training resulted in lowering cortisol levels, comparing post-intervention results with both the baseline ($p < 0.001$ upon awakening and 15, 30, and 60 min after awakening) and the control group. The intervention also resulted in a significant improvement of QOL scores (SF-36—$p < 0.05$), with the only exception of the physical functioning domain [42].

Instead, in a group of professional jockeys, Poon et al. did not report any difference in blood cortisol levels and QOL scores (WHOQOL-bref) in comparison with a control group of healthy students [45].

Rector et al. grouped the professionally active epidemiological sample according to the prevalence of CMV infection. Neither cortisol levels, either considered as daily cortisol output (AUC) or cortisol awakening response (CAR), nor CRP were reported to be associated with CMV infection or reactivation (CMV-IgG) [46].

In a study involving hotel housekeepers, Rosemberg et al. reported relatively poor physical and mental health (SF-12) scores, with 38% and 39% of participants scoring below the US population, respectively. Six participants (12.2%) had cortisol levels higher than the clinical cut-off point (>23 ug/dL). The Allostatic Load Index (CRP, High-Density Lipoprotein (HDL), waist/hip ratio (WHR), Body Mass Index (BMI), Hemoglobin A1c (HbA1c), cortisol, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), and Heart Rate (HR)) resulted in being associated with high job strain ($p = 0.011$), while no correlation has been found with physical and mental health (SF-12) [47].

On the contrary, Sadowska et al. did not find any difference in cortisol levels between caregivers and the control group [48].

An N-to-1 study involving a patrol police officer followed for 3 weeks, revealed a typical daily salivary cortisol pattern, characterised by overall high levels and a flattened cortisol awakening response. The QOL scores (SF-36), measured at the beginning of the study, were on average, with the lower score associated with vitality [38].

3.6.4. Stress Biomarkers—Autonomic Nervous System Activity (α -Amylase)

Contrary to what was reported for cortisol, the trial reported by Feicht et al. using the web-based happiness training revealed a significant reduction in the α-amylase morning activity at the end of the study ($p = 0.002$) [37].

According to the results on salivary cortisol, Giessing et al. reported a daytime salivary concentration of α-amylase higher than those found in the literature for high-stress populations [38].

3.6.5. Circadian Cycle—Melatonin

Vlahoyiannis et al. [49] investigated the role of work schedule in a sample of nurses, comparing those with a fixed morning shift (07:00 AM–03:00 PM) with those working rotating shifts. Nurses in this last group reported QOL scores (SF-36) significantly lower than their colleagues with a fixed morning shift ($p = 0.010$), specifically in the physical functioning and general health domains ($p = 0.006$ and $p = 0.010$, respectively). No differences were found in the salivary melatonin concentration, either in morning or evening sampling.

4. Discussion

The way work is conceived and its characteristics has evolved over time, particularly in the last few decades. Indeed, in the recent past, we have assisted in the creation of several new jobs and in huge modifications to most of those already existing, even though their organisation and management often convey an old-fashioned approach [50]. Consequently, the interest in promoting the health of workers has become more and more crucial, with particular attention to the well-being and QOL of workers.

In this scenario, workers employed in healthcare and emergency departments, police officers, and military personnel have distinctive working conditions and characteristic duties, making them at a higher risk of occupational stress, physical injuries, and psychological outcomes. Emergency workers, for example, were reported to have a significant risk to experience major depression and post-traumatic stress disorder, which can, in turn, be associated with an increased risk of poor physical health [51]. Studies on trauma-exposed subjects, particularly on World Trade Center responders, highlighted the relevance of prevention, screening, and treatment strategies dedicated to high-risk disaster responders [52]. At the same time, routine interventions aiming to mitigate the onset of such negative out-

comes might have a reduced efficacy not focusing on critical mental health predictors and, above all, being usually offered after the exposure to traumatic events [53]. Not surprisingly, fourteen of the twenty-three papers included in our review investigate the conditions of active-duty military personnel and veterans [27–30], community health agents [31], sworn officers and patrol police officers [36,38], health care professionals [35,39–41,43,49] and caregivers [48]. A further critical issue involving these professionals is the presence of shift work, which has a significant impact on workers' health, QOL, and well-being [49]. Indeed, working asocial hours can result in a misalignment in the circadian system and in the sleep-wake cycle, with a consequent increase in the risk for chronic health conditions [40].

Eventual alterations in biological processes that could be ascribable to chronic stress can provide valuable insights into a person's health and well-being, in a different but complementary way to self-reported evaluations [54].

Unexpectedly, the assessment of both the QOL perception and the bio-molecular profile in working settings turned out to be a relatively uncommon practice and the accurate statistical analysis of their mutual relationship was even rarer. This represents a real loss, given the potential great value of these results from a health promotion perspective. Indeed, even in the absence of symptoms, alterations in biomarkers associated with the onset of clinical outcomes might be helpful in the early identification of workers at higher risk of health impairment in the future [35]. Since self-rated health has been proposed as an early predictor of mortality [55], it would be interesting to investigate the relationship between QOL and the bio-molecular profile, especially in populations including young and healthy subjects not experiencing the most common morbidity risk factors [28]. This approach might be critical in evaluating the role of ageing in modulating these alterations [40]. Furthermore, some professionals are trained to deal with high-stress situations, introducing an additional element in shaping the eventual relationship between these two domains, and highlighting the importance of both biological and psychological assessment [38].

In our search, we also observed a huge heterogeneity in both QOL and bio-molecular profile assessment methods. The employment of questionnaires and biomarkers providing outcomes that are not completely superimposable represents an issue in comparing data, making it difficult to identify a "golden standard" assessment protocol. Notably, the vast majority of the included studies relied on biomarker assessment in blood specimens, despite the current tendency to prefer matrices involving non-invasive sampling. Moreover, in most articles, the complete description of the working context and work-related factors is missing, preventing the abstraction of results valid for the general, professionally active population.

In our review, we grouped the epidemiological samples into "clinical" and "non-clinical" populations according to the presence of a clinical diagnosis of psychological disorders. These conditions, indeed, can have a relationship with both the QOL and the bio-molecular profile, especially in terms of oxidative stress and inflammation [56–58]. Psychological and social aspects of work [59–61] can also have a role in the aetiology of mental health disorders, resulting in possible targets for intervention in the workplace. High levels of job strain (i.e., low decision latitude and high demands), low levels of social support at work, job insecurity, discrimination, and perceived imbalances between job efforts and rewards are linked to common mental disorders like depression and anxiety and, more in general, with lower psychological well-being [62–65]. Conversely, higher levels of job control, social support, and job security are associated with being free of disorders and flourishing mental health [66]. In our review, four of the eight articles describing clinical populations [27–30] investigated the alteration in inflammatory status and QOL in active military duty personnel and veterans suffering from depression, PTSD, and TBI. Even if the alteration in biomarker levels might be more likely related to the peculiar physical and psychiatric conditions, these last could be a consequence of the distinctive working conditions and requirements these subjects have been exposed to. Indeed, veterans, being a population with a broad range of mental, physical, and social needs, with some members facing health issues related to their service experience [67], represent a group needing particular attention in terms of QOL and well-being promotion,

and in which the onset of chronic inflammation is a common outcome [28]. Focusing on risk factors for this condition in a young cohort not experiencing inflammatory-related comorbidities might return valuable knowledge for the mitigation of long-term morbidity and mortality risks associated with chronic inflammation [27]. This preventive approach can be extended to all the working population, trying to figure out and eliminate or, at least, attenuate all those factors triggering the later onset of health issues. Special attention should be paid to understanding how biological pathways could be affected by work-related factors in a window of opportunity where subclinical hallmarks of chronic inflammation may still be reversible. Having a valid array of biological indicators sensitive to both derangements from physiological conditions and stress reduction would be useful to investigate the effectiveness of interventions attempting to promote workers' health and safety and, eventually, to address occupational health disparities [47]. The approach is in line with the Total Worker Health Program of the National Institute for Occupational Safety and Health (NIOSH), supporting policies, programs, and practises aiming to promote the protection of workers' health and safety and the prevention of injury and illness in order to advance workers' well-being [22].

We considered the alteration in three main biological processes: neuroendocrine activation, oxidative stress, and inflammation.

The stress response is a complex process characterised by the activation of several interacting mechanisms, including behavioural, autonomic, endocrine, and immune systems, occurring whenever there is a discrepancy between expectation and reality [39]. Although this process leads to an adaptive response, the sustained activation of these pathways can trigger physiological and behavioural alterations which, in the long run, may result detrimental to survival and well-being [68]. Among these, the adoption of unhealthy lifestyles like poor dietary choices proves to be a common effect [6]. The analyses of psychobiological responses to daily-life stressors in order to understand the mechanisms leading to psychological, physical and behavioural disorders is currently a field requiring more research [38]. The harmful array of physical and emotional responses occurring when the job requirements do not match workers' capabilities, resources, or needs, known as work-related stress, can as well result in the sustained activation of these pathways [39]. Stress can trigger the activation of both the sympathetic-adrenal-medullary (SAM), resulting in autonomic nervous system regulation (e.g., heart rate), and the hypothalamus-pituitary-adrenal (HPA) axes, leading to the release of glucocorticoids such as cortisol [6]. Salivary α-amylase has been proposed as a biomarker of the SAM activation and short-term stress, being positively correlated with norepinephrine and (nor)adrenaline levels [37]. The abnormal activation of the SAM axis, as in the case of sleep deprivation, could lead to increased heart rate and blood pressure, activation of the renin-angiotensin system, and trigger oxidative stress and inflammation [69]. Simultaneously, the sustained and repeated HPA axis activation can lead to excessive production of cortisol and, in turn, to physiological and psycho-neuro-endocrinological alterations and health issues such as hypertension, insulin resistance, hyperglycaemia, inflammation, visceral fat accumulation, and metabolic syndrome [6]. The different patterns of HPA axis activation have been also related to neuropsychiatric disorders, such as, for example, an increase in cortisol production in subjects affected by major depression, often associated with cognitive impairment [33]. Cortisol has a particular circadian rhythm, characterised by a peak just before awakening followed by a gradual decline during the day. Hyper- and hypo-activation of this system have been associated with several health outcomes; for example, a high awakening cortisol response has been related to depressive symptoms, while an attenuated response was reported in subjects affected by burnout [39,70]. Interestingly, Knuth et al. reported higher cortisol levels in community health agents with less than one year of service and a negative correlation between the blood concentration of this biomarker and QOL, hypothesising the dominant role of experiencing new situations with the related redistribution of energy to cope with the new needs [31]. Sandstrom et al., instead, revealed a general trend of an increased cortisol/ACTH response after the administration of corticotropin-releasing hormone associated

with work-related stress, similarly to patients affected by major depression. Notably, in non-clinical samples, behavioural training seems to be effective in improving health-related QOL, with measurable modifications in the bio-molecular profile [33]. Feicht et al. reported a significant improvement in QOL scores as well as a decrease in morning α-amylase activity after the administration of a web-based training aiming to improve workers' well-being. According to the authors, these results might be a tendency of workers to start their day in a less "stressed" way, probably due to better recovery in the evening or during the night, highlighting the eventual connection between self-perception and bio-molecular profile [37]. Similarly, Nickel et al. reported that treatment with behavioural/psychoeducational training could reduce limitations due to bodily pain and physical health, improving personal perceptions of factors related to health and emotional domains able to interfere with work and daily activities [42]. The key message is thus the uttermost importance of early identification of subjects needing support even beyond conventional care and encouraging the adoption of healthier lifestyles, including the regular practise of physical activity and a proper nutrition regimen [42,44].

Oxidative stress and inflammation are interdependent mechanisms able to trigger each other [71] and can represent another molecular pathway through which chronic stress can lead to health worsening. Chronic and sub-chronic psychological stress has been associated with lipid peroxidation, oxidative DNA damage, hydrogen peroxide, and superoxide dismutase (SOD) [72,73]. Moreover, oxidative stress biomarkers had been proposed as a potential biomarker for fatigue [35]. Chronic inflammation, instead, can occur in either an asymptomatic or symptomatic way. A chronic inflammatory state is the hallmark of several metabolic conditions and plays a key role in the pathophysiology and progression of several disorders, such as metabolic syndrome, type 2 diabetes, stroke, and cardiovascular disease, altered neuronal functions, increased risk of mood and cognitive decline, neurodegenerative processes during ageing, neuronal health impairment and neuronal loss [27]. The maintenance of high circulating inflammatory cytokine levels and/or the sustained activation of the stress system can result in immune and metabolic disturbances leading to an increase in morbidity and all-cause mortality [74]. Specifically, concerning the relationship with HRQOL, IL-6 was found to be related to lower HRQOL scores in PTSD patients [75] and associated with depression, fatigue, disturbed sleep, sleep restriction, and cognitive impairment [29,58]. In our review, inflammation was reported to be associated with HRQOL in active-duty military personnel in a relationship mediated by PTSD and depression, revealing a possible path for preventive intervention aiming to reduce morbidity risks in ageing veterans through the treatment of PTSD and depression [28]. Indeed, Gill et al. reported an elevated IL-6 blood concentration in young military personnel, suggesting that elevated levels of this cytokine might be predictive of morbidity and mortality risk factors' development in later years [28]. Moreover, in a similar population, insomnia was reported to significantly increase IL-6 plasma levels [30]. Sleep restoration thus seems effective in reducing inflammation and increasing health and well-being, representing a useful intervention to avoid the subsequent onset of other inflammatory-related risk factors, especially in young populations [29]. Moreover, proinflammatory cytokines play a role in modulating the HPA axis activity in a complex mechanism providing the basis for a neuroendocrine-immune response to homeostasis derangements due to stress, inflammation, and infections [76]. Many studies have analysed the role of natural or synthetic antioxidant supplementation in counterbalancing oxidative stress and lowering the onset risk of oxidative stress-mediated disorders, even with contrasting results [77]. This approach has also been proposed to manage physical and mental stress due to occupational stress. Indeed, the lipid-rich constitution makes the brain particularly vulnerable to oxidative stress and lipid peroxidation, leading to a decrease in membrane fluidity and damage to membrane proteins that results, in turn, in nervous system impairment such as anxiety, major depressive disorders, and neurological diseases [57]. Pandaran Sudheeran et al. reported significant effects of curcumin-based supplementation in boosting the endogenous antioxidant profile in healthy workers experiencing significant occupational

stress, highlighting a simultaneous improvement in QOL scores [44]. In order to evaluate the impact of psychological stress on the immune system, Rector et al. also analysed its role in driving the subclinical reactivation of CMV infection, assuming the increase in CMV-IgG as a signal of weakened immune control of the latent virus, which is able to replicate anew. The study reported an association between psychological stress and CMV-IgG levels in an employee CMV+ sample, with indicators such as low mental health associated with an increase in CMV-IgG and not with being infected per se. Interestingly, the association was found to be stronger in low socio-economic status (SES) employees (job status and education), while virtually absent among high-SES workers. The authors proposed this result as an outcome of the exposure to stressors whose influence cannot be counterbalanced by coping resources, leading, from a biological point of view, to an allostatic load condition. Unexpectedly, researchers did not find any association between serum CRP and salivary cortisol, seeming not to be mediators in the association [46].

In this scenario, a better understanding of the role of lifestyle habits such as sleep quality and nutrition in modulating the inflammatory profile is crucial [36].

5. Conclusions

In conclusion, besides some critical issues in addressing the research on this topic, the review highlights the importance of investigating the possible relationship between QoL and bio-molecular domains in order to promote workers' health and safety. The development of a valid array of biological indicators sensitive to both derangements from physiological conditions and stress reduction measurable in non-invasive matrices could be particularly useful, especially to identify those groups at higher risk of health outcomes and, eventually, promote workers' wellbeing.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/su14138100/s1, Table S1: Summary of studies, epidemiological sample characteristics, and results as originally reported in the articles included in the systematic review in the "*Clinical population group*". Table S2: Summary of studies, epidemiological sample characteristics, and results as originally reported in the articles included in the systematic review in the "*Non-clinical population group*".

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Appendix A

Search strings employed in the article query.

PubMed

#1 "Oxidative Stress"[Mesh]

#2 oxidative[tiab] OR oxidation[tiab] OR oxidant[tiab] OR anti-oxidant[tiab] OR antioxidant[tiab] OR antioxidative[tiab] OR anti-oxidative[tiab]

#3 "Inflammation"[Mesh]

#4 inflammat*[tiab] OR pro-inflammat*[tiab] OR anti-inflammat*[tiab] OR antiinflammat*[tiab] OR antinflammat*[tiab]

#5 "Hydrocortisone"[Mesh]

#6 cortisol*[tiab] OR hydrocortison*[tiab]

#7 "Malondialdehyde"[Mesh]

#8 malondialdehyde[tiab] OR malonylaldehyde[tiab] OR malonaldehyde[tiab] OR malonyldialdehyde[tiab] OR MDA[tiab]

#9 "8-Hydroxy-2′-Deoxyguanosine"[Mesh]

#10 8-hydroxy-2′-deoxyguanosine[tiab] OR 8-hydroxy-deoxyguanosine[tiab] OR 8-hydroxydeoxyguanosine[tiab] OR 8-hydroxyguanine[tiab] OR 8-hydroxy-guanine[tiab] OR 8-Oxo-2′-Deoxyguanosine[tiab] OR 8-Oxo-Deoxyguanosine[tiab] OR 8-oxo-dGuo[tiab] OR 8-Ohdg[tiab] OR 8OHdG[tiab] OR 8-OH-dG[tiab] OR 8-ohg[tiab] OR 8-hydroxy-g[tiab] OR 8-hydroxy-dg[tiab] OR 8-oxodG[tiab] OR 8-oxodGuo[tiab] OR 8-oxo-dG[tiab] OR 8-OH-2dG*[tiab] OR 8-isoprostane*[tiab]

#11 "F2-Isoprostanes"[Mesh]

#12 IsoP[tiab] OR F2-isoprostane*[tiab]

#13 "Dinoprost"[Mesh]

#14 dinoprost[tiab] OR 15-f2t-isop[tiab] OR 8-iso-PGF2a[tiab] OR 8-isoprostaglandin-f2[tiab] OR 8-iso-prostaglandin-f2[tiab] OR 8-iso-PGF2a[tiab] OR 8-epi-prostaglandin-F2alpha[tiab] OR 8-epi-prostaglandin-f2alpha[tiab] OR 8-epiprostaglandin-f2alpha[tiab] OR 8-epi-PGF2alpha[tiab]

#15 "C-Reactive Protein"[Mesh]

#16 C-reactive-protein[tiab] OR CRP[tiab]

#17 "Interleukin-6"[Mesh]

#18 interleukin-6[tiab] OR IL6[tiab] OR IL-6[tiab]

#19 "Interleukin-8"[Mesh]

#20 interleukin-8[tiab] OR IL-8[tiab] OR IL8[tiab]

#21 "Interleukin-1"[Mesh]

#22 interleukin-1[tiab] OR IL1[tiab] OR IL-1[tiab]

#23 "Tumor Necrosis Factor-alpha"[Mesh]

#24 Tumor-Necrosis-Factor-alpha[tiab] OR Tumor-Necrosis-Factor-a[tiab] OR TNF-alpha[tiab] OR TNFalpha[tiab] OR TNF-a[tiab] OR TNFa[tiab] OR cachectin[tiab] OR cachexin[tiab]

#25 "Melatonin"[Mesh]

#26 melatonin*[tiab]

#27 "6-sulfatoxymelatonin"[Supplementary Concept]

#28 6-sulfatoxymelatonin*[tiab] OR 6-sulfatoxy-melatonin*[tiab] OR 6-sulphatoxymelatonin*[tiab] OR 6-sulphatoxy-melatonin*[tiab] OR 6-hydroxymelatonin*[tiab] OR 6-hydroxy-melatonin*[tiab]

#29 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28

#30 "Quality of Life"[Mesh]

#31 quality-of-life[tiab] OR life-quality[tiab] OR QoL[tiab] OR HRQoL[tiab] OR HR-QoL[tiab] OR WHOQOL-bref*[tiab] OR World-Health-Organization-Quality-of-Life[tiab]

#33 "healthy days"[tiab]

#34 #30 OR #31 OR #32

#35 "Work"[Mesh]

#36 "Employment"[Mesh]

#37 "Occupations"[Mesh]

#38 "Occupational Groups"[Mesh]

#38 "Job Satisfaction"[Mesh]

#39 "Occupational Stress"[Mesh]

#40 "Occupational Health"[Mesh]

#41 "Occupational Exposure"[Mesh]

#42 work*[tiab] OR job[tiab] OR jobs[tiab] OR occupation*[tiab] OR profession*[tiab] OR shift[tiab] OR shifts[tiab] OR employe*[tiab] OR personnel[tiab] OR staff*[tiab] OR manager*[tiab]

#43 workaholi*[tiab] OR work-addict*[tiab] OR burn-out[tiab] OR burnout[tiab] OR burned-out[tiab]

#44 #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43

#45 #29 AND #34 AND #44

Embase

#1 'oxidative stress'/exp

#2 oxidative:ti,ab,kw OR oxidation:ti,ab,kw OR oxidant:ti,ab,kw OR 'anti oxidant':ti,ab,kw OR antioxidant:ti,ab,kw OR antioxidative:ti,ab,kw OR 'anti oxidative':ti,ab,kw

#3 'inflammation'/de

#4 inflammat*:ti,ab,kw OR 'pro inflammat*':ti,ab,kw OR 'anti inflammat*':ti,ab,kw OR antiinflammat*:ti,ab,kw OR antinflammat*:ti,ab,kw

#5 'hydrocortisone'/exp

#6 cortisol*:ti,ab,kw OR hydrocortison*:ti,ab,kw

#7 'malonaldehyde'/exp

#8 malondialdehyde:ti,ab,kw OR malonylaldehyde:ti,ab,kw OR malonaldehyde:ti,ab,kw OR malonyldialdehyde:ti,ab,kw OR mda:ti,ab,kw

#9 '8 hydroxydeoxyguanosine'/exp

#10 '8 hydroxy 2 deoxyguanosine':ti,ab,kw OR '8 hydroxy deoxyguanosine':ti,ab,kw OR '8 hydroxydeoxyguanosine':ti,ab,kw OR '8 hydroxyguanine':ti,ab,kw OR '8 hydroxy guanine':ti,ab,kw OR '8 oxo 2 deoxyguanosine':ti,ab,kw OR '8 oxo deoxyguanosine':ti,ab,kw OR '8 oxo dguo':ti,ab,kw OR '8 ohdg':ti,ab,kw OR 8ohdg:ti,ab,kw OR '8 oh dg':ti,ab,kw OR '8 ohg':ti,ab,kw OR '8 hydroxy g':ti,ab,kw OR '8 hydroxy dg':ti,ab,kw OR '8 oxodg':ti,ab,kw OR '8 oxodguo':ti,ab,kw OR '8 oxo dg':ti,ab,kw OR '8 oh 2dg*':ti,ab,kw OR '8 isoprostane*':ti,ab,kw

#11 'isoprostane derivative'/exp

#12 isop:ti,ab,kw OR 'f2 isoprostane*':ti,ab,kw

#13 'prostaglandin F2 alpha'/exp

#14 dinoprost:ti,ab,kw OR '15 f2t isop':ti,ab,kw OR '8 isoprostaglandin f2':ti,ab,kw OR '8 iso prostaglandin f2':ti,ab,kw OR '8 iso pgf2a':ti,ab,kw OR '8 epi prostaglandin f2alpha':ti,ab,kw OR '8 epiprostaglandin f2alpha':ti,ab,kw OR '8 epi pgf2alpha':ti,ab,kw

#15 'c reactive protein'/exp

#16 'c reactive protein':ti,ab,kw OR crp:ti,ab,kw

#17 'interleukin 6'/exp

#18 'interleukin 6':ti,ab,kw OR il6:ti,ab,kw OR 'il 6':ti,ab,kw

#19 'interleukin 8'/exp

#20 'interleukin 8':ti,ab,kw OR 'il 8':ti,ab,kw OR il8:ti,ab,kw

#21 'interleukin 1'/exp

#22 'interleukin 1alpha'/exp

#23 'interleukin 1beta'/exp

#24 'interleukin 1':ti,ab,kw OR il1:ti,ab,kw OR 'il 1':ti,ab,kw

#25 'tumor necrosis factor'/exp

#26 'tumor necrosis factor-alpha':ti,ab,kw OR 'tumor necrosis factor-a':ti,ab,kw OR 'tnf-alpha':ti,ab,kw OR tnfalpha:ti,ab,kw OR 'tnf-a':ti,ab,kw OR tnfa:ti,ab,kw OR cachectin:ti,ab,kw OR cachexin:ti,ab,kw

#27 'melatonin'/exp

#28 melatonin*:ti,ab,kw

#29 '6 hydroxymelatonin o sulfate'/exp

#30 '6 sulfatoxymelatonin*':ti,ab,kw OR '6 sulfatoxy melatonin*':ti,ab,kw OR '6 sulphatoxymelatonin*':ti,ab,kw OR '6 sulphatoxy melatonin*':ti,ab,kw OR '6 hydroxymelatonin*':ti,ab,kw OR '6 hydroxy melatonin*':ti,ab,kw

#31 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30

#32 'quality of life'/exp

#33 'quality of life':ti,ab,kw OR 'life quality':ti,ab,kw OR QoL:ti,ab,kw OR hrQoL:ti,ab,kw OR 'hr-QoL':ti,ab,kw OR 'whoQoL bref*':ti,ab,kw OR 'world health organization quality of life':ti,ab,kw

#34 'healthy days':ti,ab,kw

#35 #32 OR #33 OR #34

#36 'work'/exp

#37 'occupation'/exp

#38 'named groups by occupation'/exp

#39 'occupational health'/exp

#40 work*:ti,ab,kw OR job:ti,ab,kw OR jobs:ti,ab,kw OR occupation*:ti,ab,kw OR profession*:ti,ab,kw OR shift:ti,ab,kw OR shifts:ti,ab,kw OR employe*:ti,ab,kw OR personnel:ti,ab,kw OR staff*:ti,ab,kw OR manager*:ti,ab,kw

#41 workaholi*:ti,ab,kw OR 'work addict*':ti,ab,kw OR 'burn out':ti,ab,kw OR burnout:ti,ab,kw OR 'burned out':ti,ab,kw

#42 #36 OR #37 OR #38 OR #39 OR #40 OR #41

#43 #31 AND #35 AND #42

Cochrane CENTRAL

#1 MeSH descriptor: [Oxidative Stress] explode all trees

#2 (oxidative OR oxidation OR oxidant OR anti-oxidant OR antioxidant OR antioxidative OR anti- oxidative):ti,ab,kw

#3 MeSH descriptor: [Inflammation] explode all trees

#4 (inflammat* OR pro-inflammat* OR anti-inflammat* OR antiinflammat* OR antinflammat*):ti,ab,kw

#5 MeSH descriptor: [Hydrocortisone] explode all trees

#6 (cortisol* OR hydrocortison*):ti,ab,kw

#7 MeSH descriptor: [Malondialdehyde] explode all trees

#8 (malondialdehyde OR malonylaldehyde OR malonaldehyde OR malonyldialdehyde OR MDA):ti,ab,kw

#9 MeSH descriptor: [8-Hydroxy-2'-Deoxyguanosine] explode all trees

#10 ("8-hydroxy-2'-deoxyguanosine" OR "8-hydroxy-deoxyguanosine" OR "8-hydroxydeoxyguanosine" OR "8-hydroxyguanine" OR "8-hydroxy-guanine" OR "8-Oxo-2'-Deoxyguanosine"):ti,ab,kw

#11 ("8-Oxo-Deoxyguanosine" OR "8-oxo-dGuo" OR "8-Ohdg" OR 8OHdG OR "8-OH-dG" OR "8-ohg" OR "8-hydroxy-g" OR "8-hydroxy-dg" OR "8-oxodG" OR "8-oxodGuo" OR "8-oxo-dG" OR "8-OH-2dG" OR "8-isoprostane"):ti,ab,kw

#12 MeSH descriptor: [F2-Isoprostanes] explode all trees

#13 (IsoP OR "F2-isoprostane"):ti,ab,kw

#14 MeSH descriptor: [Dinoprost] explode all trees

#15 (dinoprost OR "15-f2t-isop" OR "8-iso-PGF2a" OR "8-isoprostaglandin-f2" OR "8-iso-prostaglandin- f2" OR "8-iso-PGF2a" OR "8-epi-prostaglandin-F2alpha" OR "8-epi-prostaglandin-f2alpha" OR "8- epiprostaglandin-f2alpha" OR "8-epi-PGF2alpha"):ti,ab,kw

#16 MeSH descriptor: [C-Reactive Protein] explode all trees

#17 ("C-reactive protein" OR CRP):ti,ab,kw

#18 MeSH descriptor: [Interleukin-6] explode all trees

#19 (interleukin-6 OR IL6 OR IL-6):ti,ab,kw

#20 MeSH descriptor: [Interleukin-8] explode all trees

#21 (interleukin-8 OR IL-8 OR IL8):ti,ab,kw

#22 MeSH descriptor: [Interleukin-1] explode all trees

#23 (interleukin-1 OR IL1 OR IL-1):ti,ab,kw

#24 MeSH descriptor: [Tumor Necrosis Factor-alpha] explode all trees

#25 ("Tumor Necrosis Factor-alpha" OR "Tumor Necrosis Factor-a" OR TNF-alpha OR TNFalpha OR TNF-a OR TNFa OR cachectin OR cachexin):ti,ab,kw
#26 MeSH descriptor: [Melatonin] explode all trees
#27 (melatonin*):ti,ab,kw
#28 ("6-sulfatoxymelatonin" OR "6-sulfatoxy-melatonin" OR "6-sulphatoxymelatonin" OR "6- sulphatoxy-melatonin" OR "6-hydroxymelatonin" OR "6-hydroxy-melatonin"):ti,ab,kw
#29 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28
#30 MeSH descriptor: [Quality of Life] explode all trees
#31 ("quality of life" OR "life quality" OR QoL OR HRQoL OR HR-QoL OR WHOQOL-bref OR "World Health Organization Quality of Life" OR "healthy days"):ti,ab,kw
#32 #30 OR #31
#33 MeSH descriptor: [Work] explode all trees
#34 MeSH descriptor: [Employment] explode all trees
#35 MeSH descriptor: [Occupations] explode all trees
#36 MeSH descriptor: [Occupational Groups] explode all trees
#37 MeSH descriptor: [Job Satisfaction] explode all trees
#38 MeSH descriptor: [Occupational Stress] explode all trees
#39 MeSH descriptor: [Occupational Health] explode all trees
#40 MeSH descriptor: [Occupational Exposure] explode all trees
#41 (work* OR job OR jobs OR occupation* OR profession* OR shift OR shifts OR employe* OR personnel OR staff* OR manager* OR workaholi* OR work-addict* OR burn-out OR burnout OR burned-out):ti,ab,kw
#42 #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41
#43 #29 AND #32 AND #42

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