**Abstract**

Extensive literature demonstrates associations between occupational stress and adverse health outcomes. This review addresses occupational stress’s effects on specific physiological biomarkers among teachers, a workforce with high occupational stress, and the potential for broad social impacts when stress compromises teacher health. A systematic PRISMA search identified 38 papers evaluating occupational stress and biomarkers in teachers (early childhood education (ECE) and K-12). Findings indicate that occupational stress (burnout, perceived acute stress, job strain, effort-reward imbalance) negatively relates to teacher health. Most endocrine (CV) studies (n = 20 of 29) found negative associations between higher chronic stress (burnout) and muted hypothalamic-pituitary-adrenal axis (HPA) responses, and/or positive associations between acute stress (e.g., job strain) and increased HPA response. Cardiovascular (CV) studies (n = 10) showed inconsistent relations between stress and CV measures. Immunologic studies (n = 6) found that chronic work stress was associated with increased pro-inflammatory and less effective anti-inflammatory activity. We provide recommendations for future research topics and policy implications.

**Keywords**

teacher; educators; occupational stress; stress biomarkers; psychoneuroimmunology; cardiovascular; immune; endocrine; stress physiology

**1. Introduction**

Teacher stress presents unique challenges as teaching is a dynamic combination of individual characteristics and school and classroom environments, setting the stage for learning. National data suggests that teaching can be a highly stressful profession [1,2], and this chronic stress relates to adverse health outcomes such as physical exhaustion, and worse self-reported physical health [3, 4]. Previously identified sources of stress for teachers include high workload, a lack of professional support or development, lack of autonomy, student behavior problems, low compensation, and poor working conditions [2,5,6]. These working conditions and stress sources considerably influence teacher and child well-being [1,4,7,8]. In addition, teachers are broadly underfunded and undertrained, and teachers experience higher burnout, exhaustion, and turnover compared to other professions [1,5,9].

Job-related stressors and negative emotional states impact performance [3] and lead to worse mental and physical health [2]. These stressors relate to adverse outcomes for teachers and their students, such as poor health and burnout, lower-quality instruction, and teacher absenteeism and turnover [1,10,11]. Researchers often characterize occupational stress as burnout, effort-reward imbalance (ERI), and overcommitment. Burnout is a chronic negative state resulting from chronic workplace stress characterized by exhaustion, negative attitudes toward work, and reduced professional efficacy [7,12, 13]. This “burnout cascade” leads to poor teaching, burnout, teacher attrition, and negative impacts on teachers’ physical and mental health [7,12,13,14,15]. ERI focuses on the imbalance created when rewards (money, esteem, job security or benefits) are inadequate for high effort [11,16]. Overcommitment is another facet of the ERI model, further adding to occupation strain imbalance [16]. These facets of occupational stress affect child and teacher outcomes and general classroom and school quality.

Teacher stress also has implications for both teaching and learning environment quality. When teachers are highly stressed or experiencing job-related emotional exhaustion, they may interpret children’s behavior as more negative, ultimately influencing student interactions [3,4, 5,17]. Higher work stress can result in more conflicts with children in their classroom, and highly stressed teachers show lower professional commitment and more negative responsiveness to students [17]. Additionally, teacher turnover predicts poorer student achievement outcomes, especially for teachers who leave in the middle of the school year [18]. Further, occupational stress in this population predicts increased sick leave due to increased physical complaints and mental health problems [6,17,19,20]. The recent COVID-19 pandemic has dramatically increased demands and accelerated these negative associations while simultaneously shedding light on the negative impacts of stressed educational environments.

Distance learning and limited social support intensified teachers’ stress during the pandemic, further undermining a
critical buffer for those experiencing stress [21,22,23,24]. COVID-19-specific issues include increased role ambiguity and blurring of professional and private lives, increased exhaustion and isolation, lack of appropriate training for distance learning, and increased workload [21,22,23,24]. Various studies across the globe found that teachers experienced increased levels of stress and psychopathology, such as anxiety and depression, and teacher’s health and well-being suffered as a consequence [21,22,23,24,25].

A better understanding of physiological stress experienced by educators may help school districts, non-profit organizations, and healthcare providers mitigate adverse health outcomes and ultimately improve education quality. In particular, biological indicators give objective, reliable, noninvasive markers of how psychosocial stress “gets under the skin,” making them valuable in psychoneuroimmunology (PNI) and clinical research [26,27,28]. The links between psychosocial stress and physiological health are well established—when we experience stress, our bodies initiate physiological responses that, when chronically activated, negatively impact our health over time [29, 30,31]. Chronic stress, specifically that experienced by teachers as outlined above in the form of occupational stress, contributes to these systems’ dysregulation, leading to an increased risk of adverse long-term health outcomes [4, 11,31].

The sympathetic nervous system is responsible for up- and down-regulating many homeostatic mechanisms in mediating the neuronal and hormonal stress response, commonly known as fight-or-flight, in response to danger or stressful situations. In these situations, the sympathetic nervous system activates to speed up heart rate, and deliver more blood to areas of the body that need more oxygen or other responses to help escape danger or stress. Chronic stress can strain the sympathetic nervous system [31]. Prior research in other populations details associations between psychological stress and aberrant health biomarkers associated with sympathetic activity, including the neuroendocrine system, cardiovascular system, and immune and inflammatory responses [11,31]. The biological capacity for flexible and adaptive stress responses also weakens with continued exposure to chronic stress, shown by less optimal endocrine, cardiovascular, and immune functioning [30,32]. Stress has widespread impact on these systems. For instance, both stress and person characteristics (such as timing and chronicity, or individual emotion regulation; [15,31]) contribute to HPA axis variability, and neuroendocrine markers such as salivary α-amylase (sAA) and cortisol are implicated in responses to stressful events [28,33]. Additionally, catecholamines, made by nerve cells and used to send signals to other cells, act as modulators for the stress response. Increased catecholamine levels impact the fight-or-flight response through other physical systems like the cardiovascular and immune systems, resulting in increased HR, BP, and general reactions in the sympathetic nervous system [30,31]. Within the cardiovascular system, compromised cardiovascular function, such as decreased heart rate variability (HRV), increased HR, and increased blood pressure (BP), are associated with psychological stress [30,34,35]. Finally, psychological stressors are associated with poor or weakened immune functioning [16, 36,37], such as inhibiting the production of white blood cells central to the immune response (lymphocytes; [36]), as well as increased inflammation which in the short term is helpful for fighting against pathogens and physical insults. Over time, however, chronic systemic inflammation impacts the body’s ability to repair and respond to damage or illness. These systems are interrelated, and this multisystemic “wear and tear,” known as allostatic load, contributes to chronic adverse health outcomes [30,32]. However, as teaching is a career associated with increased burnout, poor work support and training, and greater attrition and mental health problems for teachers, the physical impacts of occupational stress among teachers also impact long-term child and teacher outcomes. The specific relations between chronic occupational stress and teacher physical functioning remain inconsistent for teachers. Prior reviews [11,16] specific to ERI found inconsistent significant relations across HRV and altered immune function, but did not conduct a broader systematic review of occupational stress and stress-related biomarkers. They also did not include a more robust list of physiological biomarkers nor intervention science that may show additional benefits for teachers. A further systematic review is warranted as the burden of teachers’ physical function and illness has downstream consequences for teachers and the children in their care.

Physiologic stress markers can provide an important pre-clinical indicator of wear and tear and serve both to better understand mechanisms linking occupational stress and later disease, serve as objective warning signs, and guide potential intervention efforts to improve teacher physical and mental health. A comprehensive understanding of current knowledge about associations between occupational stress and physiological stress indicators in teachers is needed to identify research gaps and ultimately improve job satisfaction, retention, and health outcomes in teachers and the quality of students’ educational environments. This paper aims to review and organize the existing literature on the associations between teachers’ occupational stress and stress biomarkers.

2. Methods
Using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, we systematically reviewed articles from the earliest available records to April 2022 using four electronic databases related to
education, psychology, and medicine: PsychINFO, PubMed, ERIC, and Web of Science. We specified eligibility criteria and the process for reviewing publications in advance. As the endocrine, cardiovascular, and immune systems are implicated in stress regulation and are particularly sensitive to the impact of stress on the body, we have chosen to focus on studies examining these systems. Specifically, studies had to include a sample of teachers, a measure of stress, a biological measure from teachers related to the HPA-axis, cardiovascular health, or immune processes, and be published in English in a peer-reviewed journal. Physiological measures provide promising reliable, noninvasive markers of psychosocial stress [28]. In contrast, subjective reports of stress and health are based on individual awareness or experience and may be influenced by interpretation or bias [27,28,38]. While subjective health indicators are important and powerful tools, we focused on measured physiological functioning and excluded self-report. We entered a broad range of search terms relating to teacher roles, biomarkers, and stress. These search terms included terms relating to various teaching positions such as educator, caregiver, teacher, or instructor, with respect to teachers providing different levels of schooling, such as primary or secondary, kindergarten, or elementary; as well as various terms related to biomarkers across PNI systems (see the appendix for full search terms). This study was registered with PROSPERO (registration#: CRD42020186556).

2.1. Study selection
The search generated 3,290 articles and 425 duplicates were removed, leaving a total of 2,865 articles. Of these, 2,744 publications did not meet eligibility criteria after screening and were excluded. Articles were excluded if they did not include teachers, if biomarkers were not drawn from the endocrine, cardiovascular, or immune systems, if biomarkers were only assessed through self-report or if no biomarkers were measured, if the studies were not empirical, if no occupational stress measure was included in the study design, or if biomarkers data was only available for students. The remaining 121 articles were selected for full-text review. The first author (ABM) screened all titles, abstracts, and full texts. The second author (SS) dually coded 20% of these ($k = .603$). The two authors discussed and reconciled any disagreements. The first two authors also scanned each included article’s reference list to identify other potentially eligible references. The final sample of papers yielded 38 papers (see Figure 1 for PRISMA chart). We extracted sample size, biomarkers, stress measures, sample age, years of experience teaching, and study design (Table 1). Due to a large number of single studies, the
The current review does not apply a unified quality assessment. Rather, we provide a descriptive synthesis of the main findings for each biomarker. The results and discussion sections are organized by class of biomarkers: (1) HPA axis; (2) cardiovascular system; and (3) immune system.

### 2.2. Risk of bias

We evaluated study quality on measurement reliability and validity for the biomarker outcome measurement and measures of self-reported stress included as independent variables (for ratings see Table 2). For independent stress variables, “strong” ratings were assigned to studies using formally validated instruments assessing stress and multiple measures of stress; “fair” ratings were assigned to studies using established but not formally validated measures (such as one- or two-item measures or studies utilizing indirect measurements of stress such as emotional labor or coping styles); and “poor” ratings were assigned to studies using measures that did not have validity established. For example, papers utilizing the Maslach Burnout Inventory, a

<table>
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<th>Female (%)</th>
<th>Sample type</th>
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<td>100%</td>
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<td>30.8 ± 8.5</td>
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<td>100%</td>
<td>100%</td>
<td>Nursery and primary school teachers</td>
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<td>28 ± 6</td>
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<tr>
<td>43</td>
<td>28 ± 6</td>
<td>5 ± 4</td>
<td>100%</td>
<td>77%</td>
<td>Kindergarten teachers</td>
<td>China</td>
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</tr>
<tr>
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<td>43.6 ± 9.5</td>
<td>N/A</td>
<td>N/A</td>
<td>63.65%</td>
<td>School teachers</td>
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<td>[56]</td>
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<td>14.9 ± 8.5</td>
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<td>USA, Canada</td>
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<tr>
<td>58</td>
<td>43.21 ± 11.44</td>
<td>17.15 ± 12.95</td>
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</tr>
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<td>N/A</td>
<td>80%</td>
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<td>Germany</td>
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<td>50.2 ± 8.37</td>
<td>22.49 ± 10.9</td>
<td>N/A</td>
<td>63%</td>
<td>School teachers</td>
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<td>[70]</td>
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<td>55</td>
<td>50 ± 8.47</td>
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<td>Germany; Luxembourg</td>
<td>[71]</td>
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<td>Germany; Luxembourg</td>
<td>[74]</td>
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<table>
<thead>
<tr>
<th>Total N</th>
<th>Mean age (weighted)</th>
<th>Mean work experience (y) weighted</th>
<th>Mean female (%)</th>
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<td>Sample type</td>
<td>Study design</td>
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<td>Hair rating (biomarker &amp; measurement)</td>
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<td>-------------</td>
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<td>--------------------------------------</td>
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<tr>
<td>School teachers</td>
<td>Cross-sectional</td>
<td>Salivary cortisol, ACTH, plasma</td>
<td>Strong Occupational stress, ERI &amp; OC scales</td>
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<tr>
<td>School teachers</td>
<td>Cross-sectional</td>
<td>Salivary cortisol</td>
<td>Strong</td>
</tr>
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<td>Cross-sectional</td>
<td>Salivary cortisol</td>
<td>Strong</td>
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<tr>
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<td>Cross-sectional</td>
<td>Salivary cortisol</td>
<td>Strong</td>
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<td>School teachers</td>
<td>Cross-sectional</td>
<td>Salivary cortisol</td>
<td>Strong</td>
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<td>Cross-sectional</td>
<td>Salivary cortisol</td>
<td>Strong</td>
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<td>Longitudinal</td>
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<td>Cross-sectional</td>
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<td>Teachers</td>
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<td>Salivary cortisol; MBI</td>
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<td>Salivary cortisol; ERI</td>
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<td>Hair cortisol</td>
<td>Strong</td>
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<td>Teachers</td>
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<td>Primary school teachers</td>
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<td>Salivary cortisol; aAA, HRV</td>
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### Cardiovascular system

<table>
<thead>
<tr>
<th>Sample type</th>
<th>Study design</th>
<th>Biomarkers</th>
<th>Stress construct &amp; measures</th>
<th>Stress rating (stress construct &amp; measurement)</th>
<th>Results</th>
<th>Reference</th>
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<td>Occupational stress; RCQ</td>
<td>Fair</td>
<td>Teachers had lower BP &amp; lower sensory extinction than teachers; occupational stress not related to biomarkers.</td>
</tr>
<tr>
<td>Elementary school teachers</td>
<td>Experimental</td>
<td>BP</td>
<td>Fair</td>
<td>Anxiety</td>
<td>Fair</td>
<td>Fair total scores of students with higher BP related to cortisol.</td>
</tr>
<tr>
<td>Primary school teachers</td>
<td>Cross-sectional</td>
<td>BP</td>
<td>Poor</td>
<td>Quality of life</td>
<td>Poor</td>
<td>A combination of chronic health conditions (obesity, hypertension) negatively impacts health among rural teachers.</td>
</tr>
<tr>
<td>Elementary school teachers</td>
<td>Experimental</td>
<td>BP, HRV</td>
<td>Fair</td>
<td>Workload; anxiety, BAI; objective number of classes taught each day</td>
<td>Fair</td>
<td>Older teachers benefit more from aromatherapy than younger teachers.</td>
</tr>
<tr>
<td>Preschool &amp; primary school teachers</td>
<td>Cross-sectional</td>
<td>HRV</td>
<td>Poor</td>
<td>Work place location</td>
<td>Poor</td>
<td>Rural teachers had higher BP than city teachers.</td>
</tr>
<tr>
<td>Teachers</td>
<td>Cross-sectional</td>
<td>BP</td>
<td>Strong</td>
<td>Stress perceptions; perceived stress, stress perceptions questionnaire, CAR, stress short-sleep</td>
<td>Strong</td>
<td>Stronger associations with psychological variables; lower quality teamwork, the lower morning cortisol values.</td>
</tr>
</tbody>
</table>

### Immune system

<table>
<thead>
<tr>
<th>Sample type</th>
<th>Study design</th>
<th>Biomarkers</th>
<th>Stress construct &amp; measures</th>
<th>Stress rating (stress construct &amp; measurement)</th>
<th>Results</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>School teachers</td>
<td>Experimental</td>
<td>Immune assays, IL-6</td>
<td>Strong</td>
<td>ERI, OC</td>
<td>Strong</td>
<td>Less effective anti-inflammatory regulation by IL-6 in teachers utilizing from chronic work stress.</td>
</tr>
<tr>
<td>School teachers</td>
<td>Cross-sectional</td>
<td>Immune assays, saliva cortisol</td>
<td>Strong</td>
<td>ERI, vital exhaustion, anxiety, depression</td>
<td>Strong</td>
<td>Increased pro-inflammatory activity in teachers high on ERI &amp; OC.</td>
</tr>
<tr>
<td>Teachers</td>
<td>Cross-sectional</td>
<td>Immune assays, ACTH, blood cortisol, HR, BP</td>
<td>Strong</td>
<td>Daily hassles</td>
<td>Strong</td>
<td>No stress effect on inflammatory variables; increases in IRR &amp; BP blood pressure, with similar effects on cortisol.</td>
</tr>
<tr>
<td>Primary school teachers</td>
<td>Cross-sectional</td>
<td>Salivary cortisol</td>
<td>Strong</td>
<td>Number of classes taught each day</td>
<td>Strong</td>
<td>Differences in NE &amp; V; cortisol slopes in free &amp; high stress groups.</td>
</tr>
<tr>
<td>Primary school teachers</td>
<td>Cross-sectional</td>
<td>Salivary cortisol</td>
<td>Strong</td>
<td>Stress perceptions; perceived stress, stress perceptions questionnaire, BP, stress short-sleep</td>
<td>Strong</td>
<td>Stronger associations with psychological variables; lower quality teamwork, the lower morning cortisol values.</td>
</tr>
</tbody>
</table>

Note: ACTH = adrenocorticotropic hormone; ASS = anxiety and stress scales; BAI = back anxiety inventory; BMI = body mass index; BP = blood pressure; CAR = cortisol awakening response; CRT = cognitive behavioral therapy; DHEA = dehydroepiandrosterone; ERI = effort-reward imbalance; FAD = fast addison; G.I.A.M. = immunoglobulin M; IL-6 = interleukin 6; IRR = job content questionnaire; IL-6 = job stress rating scale; MBI-ES = Medtech burnout inventory-educators survey; NFR = need for recovery; OC = overcommitment; OSH = occupational stress indicator; PANAS = positive and negative affect schedule; PSS = perceived stress scale; TICS = stress inventory of chronic stress; TNF = tumor necrosis factor; TICS = teacher self-efficacy scale; TSE = teacher stress inventory.
measure validated across cultures and samples (see [9,12]), received a “strong” rating for independent stress variables. Suppose that a paper utilized a self-report rating of stress levels not validated in any other study or created by the authors for this specific study without reliability or validity information; this paper might receive a “poor” rating on that measure. For the biomarker outcome variable, “strong” ratings were assigned to studies that measured biomarkers using gold standard specimen type for their study question and established biological protocols; “fair” if biomarker measurement used established variables that were not the gold standard; and a study would receive a “poor” rating on biomarker measurement if the specimen type was not well-established for measuring stress’ influence on physiology (e.g., body mass index and blood pressure but no other physiological measures). For example, if a study collected salivary cortisol for five samples across three days to more accurately model diurnal cortisol, they received a “strong” rating for biomarker measurement. Suppose that a study measured HRV with no controls for respiration and data cleaning approaches were unclear. In that case, this paper may receive a “poor” rating for that measure. The first two authors independently coded each included article on these dimensions and reconciled differences ($k = .561$).

3. Results

After removing duplicates and screening articles, we identified 38 studies that met inclusion criteria. The lack of an objective physiological measure was the most common study exclusion reason (see PRISMA diagram for all exclusion reasons, Figure 1).

Descriptives and averages were calculated using the variables in question multiplied by the number of participants and divided by the sum. The 38 publications included 2,968 participants, with a weighted average of 78.11 ± 57.77 participants per study, ranging from 8 to 302 participants. A weighted 79.82% of participants were reported as female. One study did not report participant sex [50]. Study participants were primarily teachers in primary/elementary schools and kindergarten/nursery schools (Table 1). The weighted average age of participants was 39.68 ± 8.13 years, and the weighted mean years of teaching experience was 7.84 ± 3.79. The majority of studies were conducted in Europe (55%). We report sample characteristics, including sex, race/ethnicity, age, years of work experience, covariates, and other characteristics or designs that could account for variability in findings in Figure 1 and Table 1. Information extracted from each study included study design, sample characteristics, biomarkers measured, stress constructs assessed, measures, and results as described (see Table 2). Of the included papers, 26 used a cross-sectional design, nine used an experimental design, and three used a longitudinal design.

We first organized studies by biomarker category to facilitate the synthesis of findings. Of the included studies, 28 studies examined endocrine biomarkers (salivary cortisol, hair cortisol, urinary catecholamine samples), 10 studies measured cardiovascular biomarkers (HR, HRV, blood pressure), and six studies assessed immunological indices (immune assays, explained further in the immune system section of the results). Seven of these studies examined biomarkers from more than one physiological system. The seven studies that included biomarkers from more than one system will be discussed in all relevant sections to synthesize their biomarkers. We further organized studies by design within each biomarker category, including cross-sectional, longitudinal, and experimental studies and present each finding with the predictor (stress) followed by the outcome variable (biomarker).

3.1. Endocrine system

Both saliva and hair extraction provide ecologically valid options for studying the HPA axis [75]. Ten included studies out of 28 found no associations between self-reported stress and HPA axis correlates. Across several studies, there was no association between job strain or daily hassles [47,50,52,72], ERI or overcommitment [39,51], or burnout and job satisfaction [40,48,50] and salivary cortisol. The remaining significant results are reported below by cortisol source (salivary or hair cortisol).

3.1.1. Salivary cortisol and sAA

Prior research has established that both cortisol and sAA are measured effectively in salivary samples [28,76,77]. Both cortisol and sAA have basal and stress-reactive functions. Typical diurnal patterns follow a circadian rhythm with higher values immediately following wake, followed by a steady decline across the day with a low point or nadir near midnight [32,78]. Research suggests elevated or blunted cortisol levels are often associated with chronic stress, and sAA is more responsive to acute social stress responses [28,77]. Generally, included studies indicated that self-perceived stress in teachers was associated with dysregulated cortisol across the day. Specifically, across studies, poor perception by teachers about their training [32], high job demands [39], burnout [46,56], and depersonalization and ambition [46] were associated with a blunted cortisol awakening response (CAR). In a sample of middle school teachers, perceived stress was associated with a lower sAA awakening response [46]. More acute stress and higher self-perceived stress were associated with a higher CAR [59] and greater cortisol increase following wake [63] but not associated with differences across the course of the day [59]. Within the included studies, acute stress and day-to-day perceived stress were related to greater and steeper cortisol reactivity to stressors and dysregulated
diurnal cortisol patterns compared to other samples with lower stress [40,44,46,50,56,59,63].

Across multiple studies, teachers exhibited more typical diurnal cortisol on free days vs. workdays [40,44,46,50,63]. Specifically, a sample of Swedish teachers showed a more typical diurnal curve on non-workdays and higher cortisol on workdays [50]. Likewise, Dutch childcare workers showed more typical cortisol decreases across non-workdays and remained elevated on workdays [44], and Swiss teachers demonstrated elevated morning cortisol levels on workdays [63]. In a sample of German teachers, participants had higher cortisol across workdays than non-workdays [40]. In several studies, above and beyond other predictors, lower-quality caregiving behavior related to higher cortisol, particularly at the beginning of the day [41,44,63].

Similarly, variations in education and experience (training quality; self-efficacy and pedagogical preparation [the act of teaching]; years spent teaching) impacted HPA axis functioning for teachers across settings and samples [32,49,58,59]. Higher teamwork and education among Finnish [49] and Swedish [59] ECE workers related to lower morning cortisol values. Using a person-centered approach, von Suchodoletz and colleagues [32] found that teachers with more experience, but lower education, had blunted cortisol and a flatter diurnal slope than highly trained mid-career teachers. Finally, compared to teachers with low self-efficacy, teachers with high self-efficacy showed attenuated cortisol responses across the day [58].

3.1.2. Hair cortisol

Three studies from the same sample measured hair cortisol [53,54,55]. All three demonstrated a significant positive relationship between effort-reward imbalance (ERI) and hair cortisol [53]. In this sample of Chinese teachers, the need for recovery (which may lead to chronic fatigue) was negatively correlated with hair cortisol concentration [54,55]. Additionally, greater emotional labor was related to increased HPA axis activity (e.g., higher hair cortisol; [55]).

3.1.3. Longitudinal research

Three studies examining HPA axis activity used longitudinal designs. Travers and Cooper (1994) found that increased stress across the school year related to blood cortisol and enzymes described in the study as “alcohol indicators” (gamma GTP, alanine and aspartate transaminase), and a blunted cortisol response later in the school year [61]. In a separate study in the United States, burnout was associated with a blunted diurnal cortisol pattern a year later, whereas job strain/work stress was associated with elevated salivary cortisol levels across the day [60]. Similarly, Katz and colleagues (2018) found blunted CAR among teachers in the spring compared to the fall start of the school year, an effect that authors report as lessened by the summer break. Effective emotion regulation buffered this effect, but self-reported perceived stress was unrelated to biomarker outcomes [14].

3.1.4. Experimental designs

Five studies used experimental designs to examine HPA axis markers among teachers. Findings in the present literature are mixed for interventions improving HPA functioning among teachers. For example, a cognitive behavior therapy (CBT) intervention for Spanish primary school teachers is designed to identify work sources of stress and identify the physiological, behavioral, cognitive, and emotional consequences of stress reduced psychosomatic complaints and significantly increased cortisol levels post-intervention [42]. Other mindfulness RCTs found reduced burnout and occupational stress [43,57] and depression and anxiety [57] among teachers. However, findings in these studies were mixed on the impact of mindfulness on HPA biomarkers. One study found increases in morning cortisol values three weeks later [43], and the other found no changes in cortisol three months post-intervention [57].

A stress management intervention demonstrated short-term reductions in depression, anxiety, and stress; however, both the intervention and control groups showed salivary cortisol decreases, suggesting that stress management was not uniquely associated with salivary cortisol [62]. Similarly, a multimodal secondary-level intervention (including relaxation, mindfulness, and reflective supervision) showed salivary cortisol levels (waking and resting) and CAR decreases from baseline to week 6 [45]. In that study, immediate pre- and post-session salivary cortisol levels indicated an immediate decrease following intervention participation in cortisol for weeks 4 to 6 [45].

Several studies used a dexamethasone suppression test, which measures cortisol levels in timed samples after administering a synthetic glucocorticoid [40,56,60,70]. Dexamethasone suppresses ACTH production and should decrease cortisol production more if the source of excess cortisol is stress [40,56,60,70]. Indeed, four studies found associations between increased acute and chronic stress measures among teachers and cortisol suppression [40,56,60]. After dexamethasone administration, higher burnout, vital exhaustion, and lower reward related to stronger cortisol suppression in German and Luxembourghish teachers [40], and in a separate sample of U.S. teachers [56]. These findings further demonstrate that chronic and acute stress negatively impacts teacher HPA axis function through the strengths of experimental designs.

3.2. Cardiovascular system

Cardiovascular activity (HRV, BP, HR, respiratory rate) is associated with emotion regulation, social connection, and the fear response, among a host of basal and regulatory
functions [34,35,79]. Like the endocrine system, the cardiovascular system responds to social and emotional factors [30,34,35]. This system often indexes challenge and threat [34,79], and its dysregulation contributes to vulnerabilities in physical and mental health [34]. Ten papers included at least one biomarker from this system, with seven utilizing cross-sectional designs and three using longitudinal or experimental designs. Findings for associations between stress and BP were mixed. Job strain was not related to BP among US teachers [64]. However, higher occupational stress (greater workplace stress and less preparation) moderated the relation between mood (measures of emotional and mental states) and high BP (hypertension) where worse mood and mental health related to higher BP in German and Chilean teachers [66,69]. Similarly, higher HRV is a physiological indicator of better response to challenge and better emotion regulation with a curvilinear relation to stress such that greater variation in HRV is thought to indicate a healthier pattern of response, but too great may have detrimental effects on health [34,35,79]. On days without job stress, teachers had higher HRV (e.g., better autonomic control) and lower HRV on workdays [63]. Another study found that HRV differed by geographic region: rural teachers demonstrated higher HRV than urban teachers [63,68].

3.2.1. Longitudinal research

Only one study used a longitudinal design to examine the cardiovascular correlates of teaching-related stress. Similar to the patterns they observed in cortisol as discussed above, Travers and Cooper (1994) found no significant differences in blood pressure across one school year; however, in multiple regression analyses using stress indicators (higher stress and higher role ambiguity), greater stress related to higher individual blood chemistry components including globulin, alanine transaminase, and gamma GTP levels at time 2. According to the authors, these associations suggest that teachers with higher job stress and pressures potentially drank more alcohol as a coping mechanism [61].

3.2.2. Experimental designs

Two studies from the same sample of Taiwanese teachers examined aromatherapy’s impact on cardiovascular stress indicators. Among the experimental group of stressed teachers, both studies found improved HRV and decreased HR, BP, and anxiety [65,67]. Other physical factors impacted this relation: BMI moderated the impact of aromatherapy on teacher anxiety and stress [67], such that aromatherapy did not impact teacher stress or anxiety if teachers had an underweight or overweight BMI [67]. In a study measuring multiple biomarkers (also reported among the HPA axis results), a mindfulness intervention decreased depression, burnout, anxiety, and occupational stress but no significant changes in HRV three months later [57]. Similarly, daily hassles had a similar effect on both high and low stress groups, where more daily hassles were associated with higher BP and resting HR [72].

3.3. Immune system

The immune system works in conjunction with other physiological systems in both innate fast and slow adaptive processes in response to pathogens or stressors that adapt and update over time [31]. The assays used in these studies varied based on which immune system functions are under investigation, as both innate and adaptive processes involve multiple cell types and components [30,80]. For example, assays can investigate humoral versus cell-mediated processes, cell populations (e.g., leukocyte counts), antibody levels, inflammatory signaling, or the speed and effectiveness of dynamic cellular responses (e.g., stimulated cytokine production), which together offer snapshots of different immune processes [16,30,31,37,80]. Growing evidence demonstrates the impacts of psychological stress on immune function [16,37]. Among the current collection of papers, six studies included markers of immune processes. Imunoglobulin (Ig)M and IgG antibodies are produced during an initial infection or antigen exposure, providing short-term protection [16,47,73,81]. IgA protects against infection in mucosal areas of the body, including respiratory and gastrointestinal tracts (sinus and lungs, stomach and intestines), and is often the first line of defense for irritants or pathogens, as well as providing support to anti-inflammatory functions [16,47,73]. Prior work has demonstrated differential relations between psychosocial stress and immunoglobulin levels, which also vary depending on contextual factors and the types of stress present [16,81]. In the current review, age and occupational stress were associated with higher IgA, IgG, and IgM concentrations [73]. Furthermore, special education teachers had higher antibody activity than general education classroom teachers for the same immunoglobulin markers [47], suggesting unique stress associated with teaching roles.

A separate study demonstrated that higher burnout predicted lower anti-inflammatory IL-4 levels [74] and found that a higher level of total burnout symptoms predicted higher tumor necrosis factor (TNF) levels and a higher TNF/IL-4 ratio [74]. Briefly, TNF acts as a signal for inflammation, with IL-4 modulating this reaction; therefore, higher burnout appears to be associated with a higher ratio of TNF to IL-4, which may result in greater inflammation [70,71,74].

3.3.1. Longitudinal research

No studies examining immune system biomarkers included in this systematic review utilized a longitudinal design.
3.3.2. Experimental designs

One sample with findings in two studies used the Trier Social Stress Test (TSST) with a low dose of dexamethasone to suppress IL-6 production in vitro throughout an experimental design [70, 71] in teachers. Lymphocyte change in TNF-α, interferon (IFN)-c, IL-2, -4, -6, and -10 were measured before and after the TSST to provide a robust immune assay of both innate and adaptive immune responses. Teachers suffering from chronic work stress (operationalized as ERI) demonstrated higher IL-6 levels after acute stress [70]. High levels of ERI and overcommitment were associated with greater pro-inflammatory activity and lower natural killer (NK) cell numbers after challenge [70, 71]. This is similar to earlier findings in an experimental manipulation with Dutch teachers where higher daily hassles were associated with a less pronounced NK cell response following a mild stressor compared to those with lower daily hassles [72]. In the same study, the low hassles group had a greater increase in T-helper cells than the high group [72]. In contrast, high overcommitment was related to a smaller than expected increase in T-helper cells after stress [70, 71]. Furthermore, subjects with higher ERI showed higher overall pro-inflammatory activity, with higher TNF production at both time points and elevated pre-stress IL-6 production [70, 71]. IL-10 (an anti-inflammatory cytokine) production decreased with higher ERI after acute stress [70, 71].

Facing repeated stressors at the workplace, such as burnout or ERI, may cause an imbalance between pro- and anti-inflammatory activity where anti-inflammatory activity cannot compensate for overstimulation of inflammatory agonists [70, 71, 74] but from current research, the direction and consistency of effects are unclear. Such pathways could be responsible for increased vulnerability to stress-related diseases following chronic work stress [71]. The complex interactions of multiple immune processes require more research to clarify the direction of effects and the long-term impacts on health and disease outcomes.

3.4. Moderators and potential protective factors

Various studies demonstrate that workplace contextual factors and individual resources may buffer or moderate the negative impact of occupational stress on stress physiology. Moderators have important implications for informing strategies to improve teacher physiological health and occupational supports; 13 studies in this systematic review measured some moderator or potential protective factor. Factors identified as moderators include considering the job “worthwhile” or “fulfilling”; a strong sense of teacher identity and role clarity; ongoing professional development; teacher self-efficacy; and external resources such as enhanced access to teaching equipment or support from specialist support personnel [2, 7, 13, 32, 58, 82, 83].

Below, these findings are reported by physiological system.

3.4.1. HPA axis

In one study, higher teamwork quality in pedagogical work was associated with lower morning cortisol values [49]. In another study, high-stress teachers did more pedagogical planning than low-stress teachers, and salivary cortisol did not differ between groups, suggesting that preparation may be protective [59]. Among Japanese nursery teachers, researchers found negative associations between social support and DHEA; this may indicate that cortisol and DHEA serve opposing functions, with DHEA mitigating the effects of cortisol [51, 52]. In addition, while overcommitment and ERI were consistently negatively related to teacher cortisol, appropriate job commitment and professional ambition may protect teacher health over time [46].

3.4.2. Cardiovascular function

Self-efficacy, an individual’s belief in their capability to meet challenging demands, was another moderator that may operate as a resource preventing negative consequences of occupational stress in several studies [7, 13, 21, 24, 58]. In the present review, high self-efficacy related to lower burnout, improved HRV, and attenuated morning cortisol levels compared to teachers with low self-efficacy [58].

3.4.3. Immune function

No studies examining immune system biomarkers examined specific protective factors concerning teacher health.

4. Discussion

This systematic review synthesizes research findings on associations between teacher stress and various stress response biomarkers. These collective findings suggest that high acute and chronic stress among teachers, and specifically occupational stress (such as burnout, perceived stress, and job strain), negatively impact teacher health across all three systems evaluated in this systematic review. The HPA axis or endocrine system is the most studied system, with 26 studies examining HPA axis biomarkers (i.e., salivary cortisol, hair cortisol); 10 studies measured cardiovascular biomarkers (i.e., HR, BP) and six studies assessed immunological indices (immune assays including functional assays). Most papers were cross-sectional, with a small subset of longitudinal or experimental designs. Specific relations within and across biomarkers depended on the study’s methodology and occupational stress construct under investigation. Most papers operationalized stress as chronic sources of stress, namely constructs and processes such as burnout, exhaustion, overcommitment, and effort-reward imbalance. Although relatively subtle and small, stress responses may manifest as deviations from normal levels or patterns (increase or decrease; altered secretion pattern, delayed recovery rate). While short-term physiologic activation is generally considered
adaptive, recurrent chronic activation may alter stress system functions and trigger changes to other organs and systems, resulting in structural changes and overt disease across time [31]. Below we discuss the findings by type of stressor (acute and chronic) and then by type of study, including findings from all three types of stress biomarkers in each section where relevant. Then, we discuss intervention and experimental findings before discussing limitations and implications.

4.1. Acute

In the reviewed papers, acute stressors such as daily work demands and perceived occupational stress were negatively associated with teacher biomarkers via multiple pathways. While a significant portion of studies exploring acute stress among teachers found no significant associations or no difference between groups [40, 44, 47, 48, 50, 51, 52, 62], 10 out of 15 studies did find associations. For studies using the endocrine system, there were positive associations between acute stress (job strain, perceived stress) and increased HPA axis activation (higher CAR, higher salivary cortisol; [14, 46, 56, 59, 60, 63]). For cardiovascular studies, acute occupational stress significantly impacted cardiovascular function, with teachers with greater occupational stress demonstrating higher BP [72], higher HR [57, 72], and lower HRV (indicating lower autonomic regulation; [63, 68]). No studies assessing immune function examined acute stress, although some utilized cross-sectional designs to examine chronic stress.

4.2. Chronic

Physiological stress-related systems have both short-term adaptations that are protective and long-term effects that can be damaging in both primary and secondary effects (negative alterations in response to primary effects) and tertiary outcomes across physiological symptoms (disease; [30, 31]). Across studies, findings for the impact of chronic occupational stress on physiology depended on the type of biomarker being measured.

The research linking chronic stress and HPA function are contradictory depending on the construct under investigation: some studies report increased activation, and others report the opposite [15]. Different aspects of occupational stress may have unique relations with salivary cortisol, hair cortisol, and sAA; specifically for burnout, perceived stress, and job strain. For the HPA-axis/endocrine system, longer-term stress sources, such as burnout and overcommitment, relate to a blunted cortisol response in teachers, mirroring findings in studies of other sources of chronic stress [14, 15, 31, 32, 45]. A third of studies examining the HPA axis found no association between stress and physiological alterations. The remaining HPA axis studies found associations between higher chronic stress (burnout) and blunted HPA responses or hypo-reactivity. These relations depend on the studies’ methodology regarding how stress was measured, and the number of samples collected. For adults, a healthy circadian rhythm shows a sharp awakening response increase, followed by a steep decline and then a more gradual decline across the day—reaching its nadir (low point) near midnight [15, 26, 76]. Since cortisol secretes in a circadian pattern, it is imperative to consider the time of day and the number of samples across the day for accurate measurement when collecting samples for consistency across subjects [15, 26]. There was significant variability across studies in protocols and reported HPA axis parameters. The number of salivary cortisol samples gathered in studies ranged from one time point on one day [47] to eight samples over a single day [60], with an average of four samples across an average of two days. In general, research recommends a minimum of four to five saliva samples across multiple days to obtain a typical diurnal pattern (wake, an hour after wake, noon, mid-afternoon, and before bed; [26, 76, 78, 84]). Similarly, some studies measured AUC for the total cortisol secretion throughout the day, while others used CAR, which captures the increase from wake to the peak level of the awakening response. Rhythm parameters such as these are needed to properly assess diurnal cortisol [78]. Using these different salivary cortisol output indices can yield differential results and may account for inconsistencies across studies. In contrast, hair cortisol is an excellent biomarker for analyzing chronic cortisol exposure because as an average across 1–3 months, it is less sensitive to specific stressors or minor fluctuations than is salivary cortisol [53, 54, 55, 85].

The cardiovascular system historically is known to be adaptable to changes over time; however, chronic stress negatively accumulates and results in changes such as cardiovascular disease and increased chance of cardiac events, i.e., heart attacks or hypertension, among others [30, 31, 34, 35, 86]. Most cardiovascular findings were cross-sectional such as studies measuring BP but as hypertension relates to a range of long-term health problems, these suggest associations in long-term biomarker alterations related to stress [86]. One study examined chronic stress (burnout) and cardiovascular biomarkers but found no significant differences between groups in a mindfulness intervention [57]. Prior work more broadly on chronic stress and cardiovascular health found that the effects of chronic stress were more pronounced on cardiovascular recovery than reactivity in a nonlinear fashion [86]. In prior work, moderate stress was associated with greater RSA recovery from a stressor than individuals reporting high or low chronic stress [86].

All six studies that included immune assays found significant results for the relations between chronic occupational stress and immune functioning. Notably, all studies assessing alterations in physiological response
related to the immune system focus on long-term alterations due to chronic stress [47,70,71,72,73,74]. In studies assessing immune function, chronic work stress was associated with increased pro-inflammatory (three studies; [47,71,73]) and less effective anti-inflammatory activity (two of the six studies; [70,72]). Further, the sixth and final immune study found mixed associations between burnout and pro-inflammatory markers [74].

The above findings are exclusive of experimental and longitudinal findings, explored further below. Data from each physiological system provides unique insights into the association between psychological stress and stress physiology in this group. In particular, both acute and chronic teacher stress may lead to downstream physiological impacts that over time may have a more far-reaching impact on teacher health than previously thought. Notably, the endocrine system/HPA axis was the most studied across biomarkers, whereas the immune system and immune function were least studied. This may reflect methodological challenges such as funding and difficulties and invasiveness of techniques, or how relevant the current field of stress physiology finds these systems to their research.

4.3. Experimental and longitudinal designs

From this data synthesis, only a quarter (26.32%) of studies utilized experimental or longitudinal designs, with the majority being cross-sectional. While cross-sectional data is valuable and adds important knowledge on how teacher stress may be associated with teacher health, experimental or longitudinal designs can help inform potential mechanisms or protective factors.

Logically, experimental manipulations or interventions may differentially affect different parameters, with particular nuance arising because physiological responses to chronic and acute stress may function via different pathways [78]. Only six studies used experimental or intervention designs with control groups to understand the relations between chronic sources of stress (perceived stress, burnout, overcommitment; [42,43,45,57,70,72]). In addition, intervention work might effectively reduce acute or short-term stressors or processes, such as acute job stress and daily hassles, that negatively impact immediate well-being and physical health and may also contribute to chronic stress (such as mindfulness, [43,57]; multi-step stress management programs, [45]; CBT, [42]; and others, [62,65,67]). Findings are inconsistent on whether these interventions impact the physiological mechanisms of how stress “gets under the skin”. For example, three of these studies found no intervention or experimental effects for endocrine or cardiovascular indices of stress [57,62,72]). The paucity of consistent impacts points to the need for improved precision in physiological measurement and diversification of intervention approaches [78].

Overall, these findings suggest several potential mechanisms that may help reduce teacher stress and improve teacher health. Support for teacher pedagogy from administration and professional development can improve both teacher and child outcomes [10,17,24,82,87]. Further, improved classroom management and higher social support at work may indirectly enhance teacher and student outcomes across domains [82,83]. Creating a sense of empowerment can help educators manage the psychological stress associated with providing services directly to historically underserved or traumatized populations [88]. Sources of support might include instructional, technology, or emotional support from school administrators or districts [23,83]. Time spent in reflective supervision provided by school psychologists, mental health consultants, or social workers may protect teachers against stressors’ adverse effects [89,90,91]. These characteristics or benefits may help reduce teacher stress and also potentially improve teacher physiological health. Further research should explore the physiological impacts of these potential moderators. In addition, interventions with proven benefits for physical health and biomarker function should be implemented more widely, such as mindfulness or reflective supervision [21,90,92,93,94].

4.4. Limitations

4.4.1. Methodology

Methodological limitations may interfere with data interpretation for both experiments and cross-sectional designs, and we note areas for improvement in methodology across designs in this research area. Experiments may have poor internal and external controls, such as lacking appropriate covariates or an appropriate comparison group. Cross-sectional and observational designs also demonstrate methodological limitations, as they may fail to assess important factors (in addition to inherent limitations regarding causality). Research with teachers must consider the complex relationships among biological systems, the experimental task under consideration, the influence of other health factors and aging, the appropriateness of biological system measurements and analysis, and specific guidelines for data editing [34,65,67,79]. Longitudinal designs may address some of these concerns, but as occupational stress, other life stressors, individual factors, and interactions among biological systems are all important considerations, a broader perspective is needed. For example, other independent variables influence the impact of interventions for teacher stress, such as chronic health conditions like obesity or hypertension [66,67], pointing to the import of a working understanding of the dynamics among biological systems when conducting psychological research to improve teacher health.
A limitation of the current review is the variation in the methodologies present. Although a great deal of consensus emerged, variability in cortisol sampling procedures makes it difficult to integrate these findings fully [78]. Researchers must establish an appropriate baseline and monitor respiration when gathering cardiovascular data [34, 79]. Some studies assessing cardiac function did not control for respiration (see Table 2 for risk of bias ratings). Only two studies, both experimental designs, controlled for respiration as related to cardiovascular data ([65,67], see Table 2); more broadly, researchers may limit the utility of findings by not including controls for other potential explanatory variables such as respiration. Future studies in teacher immune function should measure both anti-inflammatory and pro-inflammatory markers to assess these influences’ balance and interaction [71]. These studies also suggest that individual characteristics or contextual factors interact with occupational stress concerning physiology, which may influence intervention efforts’ effectiveness. The majority of studies used well-established occupational stress or general stress measures (Table 2). However, some studies used proxies for stress such as psychopathology (anxiety; conceiving urban settings as more stressful than rural settings; quality of life as measured by the Short-Form 36 Health Survey; [65, 66,68]). Studies operationalizing “stress” should use gold-standard validated measures of stress in order to clarify the direction of effects and to add reliable data to stress research. Future studies should jointly assess chronic and acute stress to ascertain their influence on health outcomes.

4.4.2. Demographic limitations

Among the current papers, most participants were female (83%). While reflecting the sex composition of the workforce, this may obfuscate health and stress differences by sex and may limit the generalizability of findings [33]. Few studies reported race or ethnicity among the demographics of participants. Due to systemic racism and other factors, ethnic/racial groups may experience different occupational stresses and may respond differentially to psychosocial and pharmacological interventions [95,96]. Since 1993, the United States National Institutes of Health have policies ensuring that minority groups are reported in study samples unless there is a compelling reason not to do so [95,96,97]. In studies from Europe and other included regions, reporting rates vary by research discipline and country [95,96,97]. To make progress on knowledge and intervention, research must reflect populations’ identities and address whether similar findings or important differences emerge.

4.4.3. General limitations

Publication bias may compromise any generalization of these findings. Although several negative findings were present in this research, and there was no strong evidence for publication bias, significant results are more likely to be submitted than non-significant ones. A second unresolved issue concerns the temporal sequence of reported associations. The majority of papers under investigation were cross-sectional and observational; thus, we cannot infer causality. As most papers utilized a single time point, disentangling chronic and acute stress is challenging in the present synthesis. These relations depend on the studies’ methodology regarding how stress was measured, and the number of samples collected; however, fully disentangling acute and chronic effects would require a longitudinal approach. Future studies should use gold-standard collection procedures for any biomarker under investigation to provide solid evidence for their findings.

4.5. Implications for policy and practice

While the collected findings present challenges and difficulties, this systematic review is the first to synthesize specific physiological impacts of occupational stress among educators and caregivers. More research will clarify the unique associations between facets of occupational stress (burnout, exhaustion, effort-reward imbalance, acute stress) and stress physiology. Most findings in our present collection are cross-sectional, making it challenging to describe causal relations or directions of effects between physiology and occupational stress. Researchers should utilize longitudinal or experimental study designs and directly assess chronic and acute stress to map the impact of stress on teacher health accurately. Just as research must parse out acute and chronic stress interactions, more research is needed to assess the unique relations between occupational stress (burnout, overcommitment, ERI) and teacher biomarkers. Further, the vast majority of studies utilize HPA axis-related biomarkers with relatively fewer studies assessing cardiovascular or immune biomarkers, further limiting our standing knowledge of how occupational stress impacts these systems. Further work should integrate biomarkers into intervention studies and examine relations with protective factors that may buffer teacher health from stress.

Occupational stress among teachers has consequences for both the quality of education and support stressed teachers provide, as retention and engagement among teachers is at a critical pressure point. This review identifies how this stress contributes to physical health consequences. Teachers need qualified, integrated behavioral health care with physicians’ involvement to effectively treat stress-related illness [6,94]. Policymakers across levels should improve teacher support policies and programs, including ongoing professional development, increased pay and benefits, and more informal practices such as increased social support in schools. These are all factors found to protect teacher physiological functioning in this review. Policymakers and school districts should consider policies that support and hold schools accountable for occupational
climate and policies related to identifying and intervening for teachers experiencing burnout [13,23,83]. Districts can provide telehealth options for teachers to have an outlet to address stress that teachers may have during the school year and in areas where access may be challenging. Districts may also provide teachers mental health days to support the greater degree of self-care needed during these stressful times. Administrators can also provide a supportive environment by talking to teachers about their needs, resources, and expectations. These supports are especially critical at present, with increased recruitment and retention concerns in education across the globe.

Unique facets of occupational stress and self-perceived stress generally exhibit differential associations with individual biological stress-regulated systems. This comprehensive synthesis found evidence that various biomarkers are involved in exposure to stress, resulting in alterations in teacher health physiology. If further confirmed, these findings can instruct targeted preventive measures for identifying and diminishing stress sources at work in research, practice, and policy. Researchers should conduct ongoing iterative assessments on the impact of intervention and prevention efforts among teachers to improve teacher health.

Appendix

The following list of search terms was applied: ((teacher* OR lecturer* OR school teacher* OR educator* OR instructor* OR caregiver* OR early childcare worker*) and (primary OR secondary OR nursery OR pre-primary OR head start OR kindergarten OR preschool OR pre-k OR elementary OR early childhood OR early child)) AND stress* AND (psychophysiology OR biochemistry OR psychophysiology* OR "HRV" OR "heart rate variability" OR "respiratory sinus arrhythmia" OR "RSA" OR "cortisol" OR physio* OR "HPA axis" OR hypothalamus pituitary adrenal axis OR alpha amylase OR immun* OR immune function OR cytokine* OR vaccine n2 response OR expression n2 gene OR "cell culture" OR cytokine* OR susceptibility n2 cold OR immune n2 dampening OR titers OR "immune gene*" OR "viral response" OR "virus response" OR "bacteria" response OR immunoreactivity OR c-reactive protein OR epstein-barr OR flu OR proinflamm* OR "anti-inflamm*" OR antiinflammatory OR vaccine n2 uptake OR "impaired immune response" OR "serum response" OR immunogenicity OR "serological response" OR "viral disorder*" OR antigen OR macrophage* OR inflammasones OR "immune-endocrine*" OR immunoendoctrine OR "C reactive protein" OR titer*).

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