



## REVIEW ARTICLE

# The potential of using hair cortisol to measure chronic stress in occupational healthcare; a scoping review

Frederieke G. Schaafsma<sup>1</sup>  | Gerben Hulsegge<sup>1</sup>  | Merel A. de Jong<sup>2</sup> |  
Joyce Overvliet<sup>1</sup> | Elisabeth F. C. van Rossum<sup>3</sup>  | Karen Nieuwenhuijsen<sup>2</sup> 

<sup>1</sup>Department of Public and Occupational Health, Amsterdam Public Health research institute, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands

<sup>2</sup>Department of Public and Occupational Health, Coronel Institute of Occupational Health, Amsterdam Public Health research institute, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands

<sup>3</sup>Adult Division, Erasmus MC, Rotterdam, The Netherlands

## Correspondence

Karen Nieuwenhuijsen, Department of Public and Occupational Health, Coronel Institute of Occupational Health, Amsterdam Public Health Research Institute, Amsterdam UMC, University of Amsterdam, Meibergdreef 9, P.O. Box 22700, 1100 DE Amsterdam, The Netherlands.  
Email: k.nieuwenhuijsen@amsterdamumc.nl

## Present address

Gerben Hulsegge, Sustainable Productivity and Employability, The Netherlands Organization for Applied Scientific Research, TNO, Leiden, 2316 ZL, The Netherlands  
Merel A. de Jong, Reinier van Arkel, Den Bosch, The Netherlands

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## Abstract

**Objectives:** Workplace-based selective prevention of mental health problems currently relies on subjective evaluation of stress complaints. Hair cortisol captures chronic stress responses and could be a promising biomarker for the early identification of mental health problems. The objective was to provide an overview of the state-of-the-art knowledge on the practical value of hair cortisol in the occupational setting.

**Methods:** We performed a scoping review of cross-sectional and longitudinal studies in PubMed, Embase, and PsycINFO up to November 2019 assessing the relations of hair cortisol with work-related stressors, perceived stress, and mental health outcomes in healthy workers.

**Results:** We found five longitudinal studies, of which two observed an increase in work-related stressors to be associated with higher hair cortisol, one found a relation with lower hair cortisol and one did not find a relationship. Findings of cross-sectional studies were also mixed. The one available longitudinal study regarding mental health showed that hair cortisol was not related to depressive symptoms.

**Conclusions:** Hair cortisol measurement within occupational health research is still in its early stage and more longitudinal studies are urgently needed to clarify its relationship with work-related stressors and perceived stress before hair cortisol can be used to identify workers at risk for mental health problems.

## KEYWORDS

disease prevention, glucocorticoids, mental stress, work related

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## 1 | INTRODUCTION

Chronic stress has adverse effects on many aspects of human development and health, among which the developing human brain,<sup>1</sup> cardiovascular,<sup>2</sup> and mental health.<sup>3,4</sup> Chronic stress is also a threat to the mental health and well-being of the working population.<sup>5,6</sup> Various mental and physical stressors can cause chronic stress in workers, these can be either work-related, related to the private or personal life of the worker, or both. Workplaces are not only a potential source of stress, they also provide a vital context in which to both protect and promote the health of workers. The workplace has been identified as a platform to reach the population with preventive programs.<sup>7</sup> Workers constitute a large proportion of the population and they can be reached through the facilities already in place at the workplace, such as occupational health services and Employee Assistance Programs. Preventive strategies for chronic stress at workplaces can target workers at three levels, all workers (universal prevention), workers at high risk of developing a mental health problems (selective prevention), and workers with a current mental health problem (indicated prevention). Various interventions are available directed at either improving the psychosocial aspects of work in a universal prevention strategy,<sup>8</sup> reducing the negative impact of stress as part of selective prevention,<sup>9-11</sup> or improving work outcomes in workers with mental health problems, constituting an indicated prevention strategy.<sup>12-14</sup>

Identification of workers who have a high risk of experiencing chronic stress with the associated (mental) health consequences, is a key part of workplace-based selective prevention. Current prevention programs rely on the subjective evaluation of work or other stressors and stress complaints by workers with most of the studies using self-report instruments. These instruments are not equipped to measure unconscious exposure to stressors or the effects of mental stress to the body. Moreover, exposure to stressors is measured at one point in time,<sup>15-17</sup> whereas sustained exposure is likely most harmful to the (mental) health of workers.<sup>4</sup> Epidemiological studies looking at the health effects of cumulative exposure to work stressors are still rare.<sup>15-17</sup>

In search for biomarkers of stress, cortisol has been at the focus of attention of researchers, including those in the field of occupational health. In response to a mental or physical stressor, cortisol is involved in energy mobilization by stimulating the production of glucose and the mobilization and brake-down of fatty acids. Cortisol is also involved in the suppression of the immune-system via the inhibition of pro-inflammatory cytokines.<sup>18,19</sup> This bodily response of cortisol release in response to stressors is within seconds but not as quick as the response via the autonomous nervous system. The hypothesis is that when the stressor remains or is repeatedly present and the body develops a chronic response to stressors, these responses can become harmful to long-term

health.<sup>20</sup> Studies in occupational health have most often used cortisol in saliva, blood, and urine to examine the link between work stressors and stress reactions.<sup>21</sup> However, these studies either focused on exposure to working conditions that disrupt the biorhythm of workers, such as shift work.<sup>22</sup> Or they were only able to capture short-term stress responses in reaction to work stressors, as saliva and blood samples represent cortisol concentrations from 20 minutes to several hours before the samples were taken.<sup>23</sup>

Advances in the field of stress biomarkers now allow for hair cortisol concentrations (HCC) to provide an easily obtainable index of cortisol levels over a period of several months using the predictable growth rate of hair.<sup>24-33</sup> The test-retest reliability of HCC within individuals is considered good,<sup>24,34</sup> although the more distant parts of the hair seem less reliable. HCC can be determined using various techniques, such as immunoassay ELISA or LC-MC/MS methods<sup>35,36</sup> with both type of analytical methods being well correlated.<sup>37</sup> Although cut off values for HCC have not yet been determined, reference values in healthy people using different analysis techniques have been established.<sup>37,38</sup> Promising results have been found, showing a relationship between exposure to stressors and an increase in hair cortisol,<sup>20</sup> and also linking hair cortisol to cardiovascular disease.<sup>39-41</sup> Early identification of increased cortisol could become an important starting point for occupational health selective prevention programs. Nevertheless, several unanswered questions currently preclude the use of hair cortisol in workplace-based prevention. Evidence for the reliability and feasibility of HCC measurements have now been established albeit not yet particularly within an occupational health setting. Evidence of associations between HCC measurements and work-related mental stress is now developing.

Scoping reviews are a way of mapping the key concepts that underpin a research area, and they can be particularly useful for bringing together literature in disciplines with emerging evidence.<sup>42,43</sup> As the research on cortisol and the relation with biological and psychological stress is still in its early stages and comes from various research fields, the current scoping review aims to deepen the understanding of the potential of measuring HCC to identify high-risk workers for preventive interventions. In this review, the state-of-the-art knowledge on the value of HCC for occupational healthcare is explored and the types of available evidence are identified for three situations relevant in occupational healthcare:

What evidence is available on the potential use of HCC as:

1. an indicator of exposure to unfavorable working conditions, that is, what is known on the association between measurement of HCCs and work-related stressors?
2. an indicator of current stress reactions in workers, that is, what is known on the association between measurement of HCCs and perceived (work-related) stress?

3. a predictor of future common stress-related health problems, that is, what is known on the predictive value of measuring HCC for depression, anxiety, and cardiovascular disorders?

## 2 | METHODS

For the design of our scoping review, we followed the guidelines as suggested by Peters et al<sup>43</sup> and Arksey et al<sup>44</sup> and we followed the PRISMA-ScR standard for our reporting.<sup>45</sup> We provide an overview of the existing literature to explore the state-of-the-art with regard to HCC and its potential for use in an occupational health setting. We did not register the protocol of our scoping review.

### 2.1 | Search strategy

Two authors (JO, MdJ) independently searched the literature in PubMed, Embase, and PsycINFO up to November 2019. Thereafter, we used a snowball for other potentially relevant studies. As the amount of literature on hair cortisol is still rather limited we decided to use a broad search strategy to answer our questions. We used the following search terms (including synonyms and closely related words) as index terms or free-text words: (a) cortisol, (b) hair, and (c) stress, depression, anxiety, well-being, burn-out, demand, cardiovascular disease, or mortality (see Appendix S1 for details).

### 2.2 | Inclusion criteria

Three authors (FS, GH, and KN) examined the full-text articles independently to check if the study met the inclusion criteria. Any disagreements that arose were resolved via discussion. Inclusion criteria for all three research questions were as follows: studies reporting on hair cortisol in a working population, written in English or Dutch. For research question one, the association with work-related stressor was an inclusion criterion. For research question two, an inclusion criterion was the association with stress complaints. For research question three, an inclusion criterion was that the study reported on either depressive, anxiety, or cardiovascular disorders. For the first two research questions, we included both cross-sectional and longitudinal studies, for the third research question we only included longitudinal studies. Exclusion criteria for all three research questions were a non-healthy or pregnant population (at baseline), and studies dealing with non-working populations such as students or informal caregiving.

### 2.3 | Charting and summarizing the results

Information of studies on the potential association between HCC and work-related stressors or perceived stress were charted according to key study characteristics, that is, study design, population, gender, ethnicity, age, sample size, hair analysis technique, and adjustment procedures. In addition, the results of the studies were synthesized according to a positive, negative or no association.

## 3 | RESULTS

Figure 1 presents the details of the number of studies identified at each stage of the searching process that were used to answer the questions for this scoping review. We found 22 individual studies, reported on in 25 publications, that investigated the association between hair cortisol and work-related stressors or perceived stress. There were five longitudinal cohort studies and 17 cross-sectional studies. We found only one study that investigated the association between hair cortisol and future health problems in the working population.

### 3.1 | Hair cortisol and work-related stressors

Hair cortisol concentration in relation to effort-reward imbalance has been studied in four longitudinal<sup>46-49</sup> and two cross-sectional studies<sup>23,50</sup> (Tables 1 and 2). Demand-decision latitude has been studied in five cross-sectional studies.<sup>50-54</sup> One study among 132 UK employees in the public sector observed no association between effort-reward imbalance and HCC after 3 months follow-up.<sup>46</sup> Herr et al published two longitudinal studies among men of a metal manufacturing plant and observed in one study among 40 employees with relatively low levels of effort-reward imbalance that an increase in effort-reward imbalance was associated with an increase in HCC over a 1-year follow-up period.<sup>48</sup> Effort-reward imbalance was not associated with HCC after 3-year follow-up among 66 employees in the Herr et al study.<sup>47</sup> In contrast, another longitudinal study,<sup>49</sup> found an increase in effort-reward imbalance over 2 years to be associated with a decrease in HCC over time in a sample of 150 workers from various workplaces.

Both cross-sectional studies observed that higher HCC were significantly associated with higher effort-reward imbalance.<sup>23,50</sup> HCC were not associated with factors from the demand-decision latitude model in four available cross-sectional studies,<sup>50-53</sup> but HCC were positively associated with iso-strain (high demand, low control, and low social support) in a cross-sectional study.<sup>54</sup>

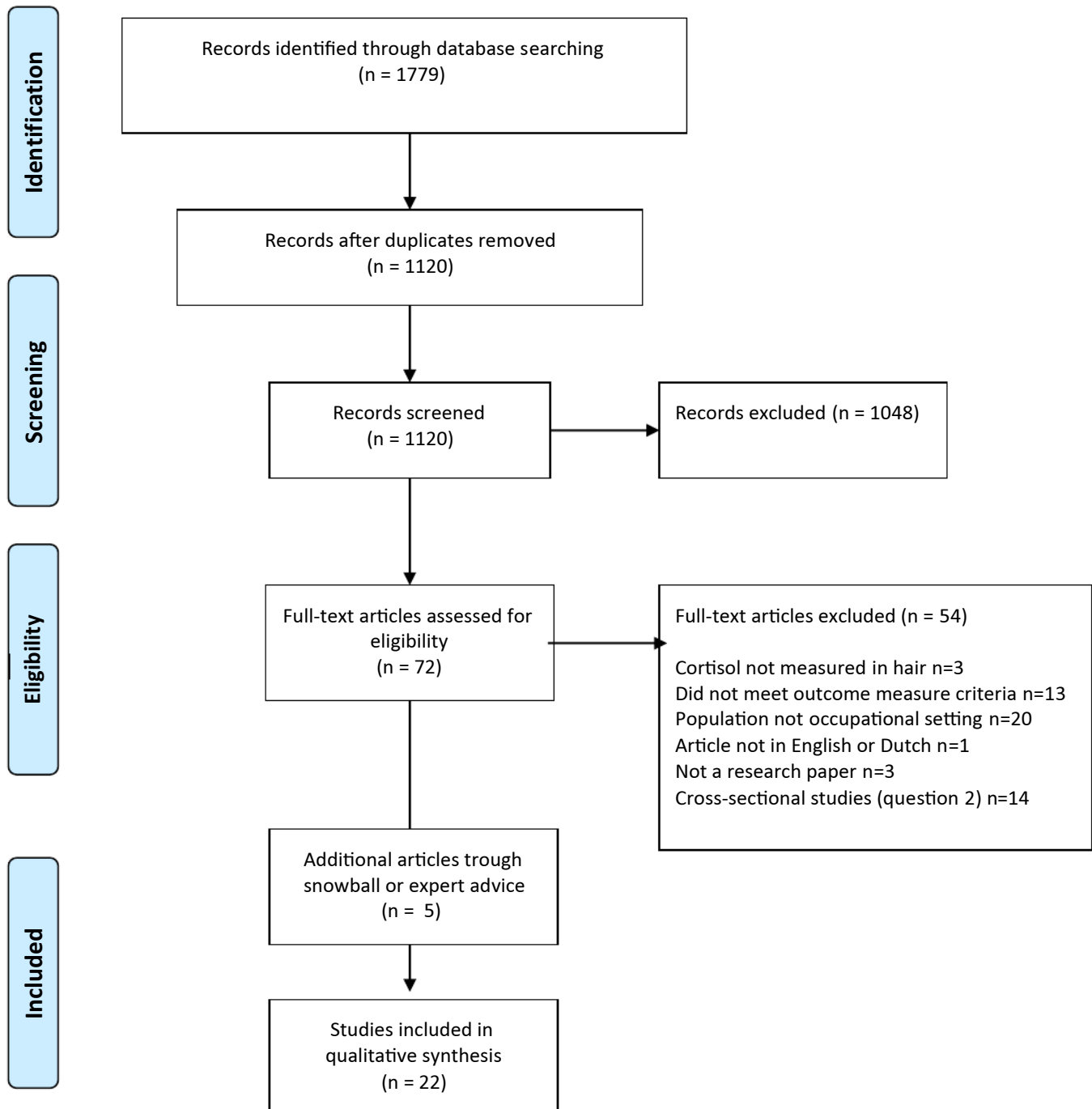


FIGURE 1 PRISMA flow diagram

Hair cortisol concentration have been studied in relation to various work stressors in one longitudinal study<sup>55</sup> and five cross-sectional studies<sup>53,56-59</sup> (Tables 1 and 2). A longitudinal study<sup>55</sup> showed that Swiss youth residential caregivers (N = 121) who experienced verbal or verbal and physical aggression had a 1.6 times higher risk of high HCC after 13-14 months of follow-up compared to those who experienced no aggression. A Dutch study observed that compared to day workers, shift workers aged <40 years had higher HCC,<sup>56</sup> whereas a Belgium study observed lower HCC levels in shift workers,<sup>53</sup> although the latter study did not correct for

the common use of (local) corticosteroids, known to decrease HCC. A small cross-sectional German study comparing employed and unemployed individuals found that the latter had higher HCC.<sup>57</sup> In addition, in a German cross-sectional study, instrumental leadership (focused on results, not on relationships) was negatively associated with HCC but transformational leadership (focused on change in tandem with committed members of a group) was not.<sup>58</sup>

Finally, high surface acting (ie, modifying affective displays by suppressing their felt emotions) was correlated with high HCC among kindergarten teachers in China.<sup>59</sup>

Overall, evidence for an association between HCC and work-related stressors from longitudinal studies is inconsistent as three studies found a positive association<sup>48,55,60</sup> and two did not<sup>46,47</sup> (Tables 1 and 2). Cross-sectional studies also show inconsistent results for effort-reward imbalance and demand-decision latitude, whereas HCC were positively associated with shift work, aggression, type of leadership, and type of emotional labor in single studies.

### 3.2 | Hair cortisol and perceived work-related stress

Two longitudinal<sup>46,60</sup> and seven cross-sectional studies<sup>51,61-66</sup> investigated the associations between HCC and burnout or perceived stress (Tables 1 and 2). Among 74 medical interns an increase in HCC was significantly correlated with an increase in perceived stress over 1-year period.<sup>60</sup> In contrast, another longitudinal study observed no significant association between HCC and perceived stress among UK employees in the public sector over a 3-month follow-up period.<sup>46</sup> The cross-sectional studies also showed mixed results, with some studies finding a positive association between HCC and burn-out<sup>61,66</sup> and HCC and perceived stress,<sup>62,64,65</sup> and other studies finding no association with burn-out<sup>51</sup> or perceived stress.<sup>63</sup> Two cross-sectional studies looked at the association between Need for Recovery and HCC, with one study finding no significant association<sup>63</sup> and one finding a significant correlation of HCC with a favorable outcome, a lower Need for Recovery.<sup>52</sup> Finally, one cross-sectional looked at the stress symptom “cognitive disorganization,” but found no significant relation with HCC.<sup>67</sup>

### 3.3 | Predictive value of HCC

There is a lack of longitudinal studies on the relationship between HCC and health outcomes (Tables 1 and 2). The only available longitudinal study<sup>68</sup> showed an increase in HCC and depressive symptoms in medical interns, but the increase in HCC and depressive symptoms were not related to each other.

## 4 | DISCUSSION

### 4.1 | Main results

With this scoping review, we sought for state-of-the-art knowledge on the practical value of HCC within the occupational health context. We found that only a limited number of longitudinal studies were conducted on the relationship between HCC and work-related stress or stressors. The findings

across studies were inconsistent. Most striking was the inconsistency in findings of longitudinal studies of the work stressor Effort-Reward Imbalance and HCC; The Herr 2018 study found a statistical significant relation of higher HCC related to more imbalance, whereas the Penz 2019 study found a statistical significant relation of higher HCC and less imbalance. And the Herr 2017 and Gidlow 2017 studies both found no statistical significant relation between Effort-Reward Imbalance and HCC. The inconsistent findings may be partly attributed to the sample sizes and selection bias; both Herr studies had less than 70 participants, primarily men and all from one workplace who had participated in a stress reduction program. While the Gidlow 2017 and the Penz 2019 studies both had larger sample sizes ( $n = 153$  and  $n = 150$ , respectively), the Penz 2019 included heterogeneous sample, but the Gidlow 2017 only included workers from two workplaces.

They further used different longitudinal designs. The Gidlow study measured Effort-Reward Imbalance at baseline and HCC 3 months later, whereas the Penz study measured both Effort-Reward Imbalance and HCC at baseline, after one and after 2 years of follow-up. In sum, the status of HCC as an indicator of unfavorable working conditions and of subsequent stress reactions has not been clarified in the currently available literature. We further only found one longitudinal study investigating the relationship between HCC and mental health. This study showed that an increase in HCC was not related to an increase in depressive symptoms. Therefore, the available evidence on HCC as a predictor of future health problems is also limited.

### 4.2 | Comparison with the literature

Occupational healthcare has been focusing more and more on preventing work-related mental stress.<sup>69</sup> Not only is too much exposure to work stressors related to mental health issues,<sup>70,71</sup> there is also a substantial amount of literature linking work stressors, such as job strain and long working hours, to an elevated risk of incident coronary heart disease and stroke.<sup>72</sup> In the majority of studies perceived work stress is measured with questionnaires based on different stress models, such as job demands and control or effort-rewards imbalance. The prevention of work-related stress and its consequences could be enhanced by insights on the interplay of work stressors, psychological, and biological processes. However, our findings show that the body of evidence linking HCC to work stressors and stress responses is not sufficient to unravel the combined psychological and biological pathway of work stressors leading to health outcomes. Besides the potential association between mental stress and HCC, the recent interest of occupational healthcare research in linking HCC with other occupational risk factors, such as shift work, highlights

**TABLE 1** Study characteristics of included studies on the associations between hair cortisol and work-related stressors and perceived stress

Reference	Design	Duration follow-up	Focus Work stressors	Focus Perceived stress	Focus Health outcomes	Population (workplace, country)	Gender (% women)	Age (mean nr yr) and SD	Sample size	Hair analysis technique	Age, gender, ethnicity corrected
Boschi et al 2017 <sup>67</sup>	CS	NA		The Calgary Symptoms of Stress Inventory		US England, Norway, Switzerland Private sector organizations	64%	41 (9)	100	1-6 cm strands from posterior vertex. Methanol extracts using a radioimmunoassay	No
Dettenborn et al 2010 <sup>57</sup>	CS	NA		Trier Inventory for the Assessment of Chronic Stress		Germany Employed versus unemployed	Employed (57%); unemployed (97%)	Employed: 33 (9); unemployed: 37 (11)	59	3 cm strands from posterior vertex. Immunoassay with chemiluminescence detection	No
Faresjö et al 2014 <sup>62</sup>	CS	NA		Perceived Stress Scale (PSS)		Sweden Nurses and librarians	100%	46 (12)	112	3 cm strands from posterior vertex. Methanol extracts using a radioimmunoassay	Yes (not ethnicity)
Gidlow et al 2016 <sup>46</sup>	LCS	3 mo	Effort-Reward Imbalance (ERI)	PSS		UK Employees of large public sector employers	81%	41 (11)	132	At least 3 cm strands from posterior vertex. Methanol extracts using ELISA	Yes (not ethnicity)
Hall et al 2018 <sup>54</sup>	CS	NA	Job Content Questionnaire (JCQ)			US	96%	43	106	3 cm strands from posterior vertex. Sensitivity enzyme immunoassay kit	No Correlation
<sup>a</sup> Herr et al 2018 <sup>48</sup>	LCS	1 yr	ERI			Germany Metal manufacturing plant	0%	48 (6)	40	3 cm strands from posterior vertex. Online solid phase extraction. Liquid chromatography-tandem mass spectrometry method	Yes (not ethnicity)
<sup>a</sup> Herr et al 2017 <sup>47</sup>	LCS	3 yr	ERI			Germany Metal manufacturing plant	0%	41 (7)	66	3 cm strands from posterior vertex. Online solid phase extraction. Liquid chromatography-tandem mass spectrometry method	Yes (not ethnicity)
Janssens et al 2017 <sup>53</sup>	CS	NA	JCQ + Copenhagen Psychosocial Questionnaire			Belgium Production companies	41%	43 (10)	102	2-3 cm strand at vertex posterior. Methanol extracted samples analysed with liquid chromatography tandem mass spectrometry	No
Kind et al 2018 <sup>55</sup>	LCS	11 mo	Survey about personal boundary violations at the workplace			Switzerland Caregivers youth residential care	62%	23-61	121	1.5 cm strands from posterior vertex region. High-sensitivity cortisol enzyme immunoassay kit	Yes (not ethnicity)
Manenschijn et al 2011 <sup>56</sup>	CS	NA	Shift work			Netherlands Textile company	0%	Shift workers: 41; day workers: 33	122	3 cm strand from posterior cortex. ELISA cortisol kit	Yes (not ethnicity)

(Continues)

**TABLE 1** (Continued)

Reference	Design	Duration follow-up	Focus Work stressors	Focus Perceived stress	Focus Health outcomes	Population (workplace, country)	Gender (% women)	Age (mean nr yr) and SD	Sample size	Hair analysis technique	Age, gender, ethnicity corrected
Mayer et al 2018 <sup>60,68</sup>	LCS	13-14 mo		PSS	Patient Health Questionnaire (PHQ-9)	US Medical Interns	56%	25-33	74	2 cm strands from posterior vertex. Immunoassay with chemiluminescent detection	No Within-person analysis
Mellemen et al 2016 <sup>51</sup>	CS	NA		Maslach Burnout Inventory (MBI)	SF Health Questionnaire	Germany Nurses geriatric care institutions	90%	42 (11)	246	3 mm diameter strands near posterior cortex of 3 cm. Immunoassay with chemiluminescence detection kit	No Bivariate correlation
O'Brien et al 2013 <sup>64</sup>	CS	NA		PSS		US University staff	65%	30 (13)	135	100 strands (3 cm) from the posterior vertex of the head. Enzyme immunoassay	No
Penz et al 2018 <sup>61</sup>	CS	NA		MBI		Germany/Sweden Workers	84%	42 (11)	314	3 cm strands from posterior vertex. Liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS)	Yes (not ethnicity)
Penz et al 2019 <sup>49</sup>	LCS	2 yr	ERI			Germany Workers	65%	42 (11)	150	3 cm strands from posterior vertex. LC-MS/MS	Yes (not ethnicity)
<sup>a</sup> Qi et al 2014 <sup>23</sup>	CS	NA	ERI			China Kindergarten teachers	100%	Median 27, (IQR 24-30)	39	1 mm diameter hairstrands near posterior cortex of 3 cm. methanol extracted sample analyzed with 3200 QTRAP liquid chromatography tandem mass spectrometer	No
<sup>a</sup> Qi et al 2015 <sup>52</sup>	CS	NA	JCQ	Need for Recovery (NFR)		China Kindergarten teachers	100%	28 (6)	43	1 mm diameter hairstrands near posterior cortex of 3 cm. Methanol extracted sample analyzed with 3200 QTRAP liquid chromatography tandem mass spectrometer	No
<sup>a</sup> Qi et al 2017 <sup>59</sup>	CS	NA	Emotional Labor Scale Stressful Life Events Scale			China Kindergarten teachers	100%	28 (6)	43	1 mm diameter hairstrands near posterior cortex of 3 cm. methanol extracted sample analyzed with 3200 QTRAP liquid chromatography tandem mass spectrometer	No
Rowold et al 2017 <sup>58</sup>	CS	NA	Transformational Leadership Inventory			Germany	50%	33 (12)	131	3 cm strand from posterior cortex	No
Van der Meij et al 2018 <sup>60</sup>	CS	NA	JCQ ERI Questionnaire			Netherlands	66%	39 (12)	172	3 cm strand from to posterior cortex. LC-MS/MS	Yes (not ethnicity)

(Continues)

TABLE 1 (Continued)

Reference	Design	Duration follow-up	Focus Work stressors	Focus Perceived stress	Focus Health outcomes	Population (workplace, country)	Gender (% women)	Age (mean nr yr) and SD	Sample size	Hair analysis technique	Age, gender, ethnicity corrected (correlation)
Van Holland et al 2012 <sup>63</sup>	CS	NA		Stress Screener NFR		Netherlands Meat-processing industry	19%	46 (10)	29	3 cm strand from to posterior cortex	No
Wang et al 2019 <sup>66</sup>	CS	NA		MBI		China Hospitals	100%	< 30: n = 22 30-35: n = 20 >35 n = 26	68	3 cm strand from occipital position	Yes (not ethnicity)
Wells et al 2014 <sup>65</sup>	CS	NA		PSS		Canada sample with over-representation of persons who have mental health, substance use/addiction and violence problems.	72%	42 (16)	324	3 cm strand from to posterior cortex. Analyzed on a salivary ELISA kit manufactured by Alpco Diagnostics for quantification	Yes (not ethnicity)

Note: Abbreviations: CS, cross-sectional; LCS, longitudinal cohort study; SD, standard deviation.

<sup>a</sup>The Q1 publications from 2014, 2015, and 2017 are from the same study, as are the Herr 2017 and 2018 publications.

the need for more longitudinal studies on HCC within the occupational setting.<sup>28</sup> For now, the practical value of HCC measurements in occupational health is limited. Compared to a meta-analysis of HCC associations with a wide range of outcomes conducted 3 years earlier than this review,<sup>20</sup> the state of knowledge relevant to occupational health has not substantially increased. In that analysis, only ongoing stress was found to be related to HCC, but no further associations with future stress-related symptoms or mental disorders were investigated.

In other medical domains, however, the more biological pathway of stressors such a hormonal imbalance due to Cushing Syndrome leading to abdominal obesity and many other health problems, or the relation between stressful life-events, HCC and psychiatric illness has already been an important topic for researchers.<sup>39,73</sup> There indeed seems to be a relationship between hormonal changes or imbalance and disease, but to what extent these hormonal changes can also predict long-term disease still needs further study.<sup>74</sup> The question remains whether psychological stressors, such as high work load and unperceived stress,<sup>73</sup> can be measured with HCC, and to what extent this measurement is predictive for future disease and related sick leave. We found many small cross-sectional studies for the assessment of work stressors and perceived work stress. As perceived work stress is not yet standardized with one clear cut-off level using one particular model integrated into one questionnaire accepted by all, correlating perceived work stress with HCC will remain challenging for future research. Furthermore, the temporal relationship between work stressors and HCC may not be linear, with the possibility of differential effects on cortisol secretion related to short term versus chronic stressors.<sup>75</sup>

We suggest a large longitudinal study design using various types of workers and combining both biological and psychological measurements for more understanding of the potential added value of HCC in an occupational context. The first step should be assessing acceptability for workers to have HCC routinely measured as a marker for both perceived as unperceived stress, although large-scale studies in both population-based cohorts as well as pediatric or patient cohorts show the feasibility of hair analysis.<sup>30</sup> The next step should be to establish cut-off scores for those with prolonged high work stress based on accepted standardized measurements for perceived work stress. The last step should then be to assess whether prolonged high HCC is related to an increased risk of disease in the future.

### 4.3 | Methodological considerations

This scoping review used the methodological framework as suggested<sup>43,44</sup> to achieve in-depth and broad results to explore the value of HCC for occupational healthcare. The mapping of



**TABLE 2** Synthesis of studies investigating the associations between hair cortisol and work-related stressors and perceived stress

	<b>+</b> <b>Higher HCC related to poorer stressor/stress outcome</b>	<b>0</b> <b>No significant effect</b>	<b>-</b> <b>Higher HCC related to better stressor/stress outcome</b>
<b>Work-related stressors</b>			
Effort-reward imbalance	<b>Herr et al 2018<sup>48</sup></b> ; Qi et al 2014 <sup>23</sup> ; Van der Meij et al 2018 <sup>50</sup>	<b>Gidlow et al 2016<sup>46</sup></b> ; <b>Herr et al 2017<sup>47</sup></b>	<b>Penz et al 2019<sup>49</sup></b>
Demand-decision latitude	Hall et al 2018 <sup>54</sup>	McLennan et al 2016 <sup>51</sup> ; Van der Meij et al 2018 <sup>50</sup> ; Qi 2015 <sup>52</sup> ; Janssens et al 2017 <sup>53</sup>	
Shift work	Manenschijn et al 2011 <sup>56</sup> (<40 yr)	Manenschijn et al 2011 <sup>56</sup> (≥40 yr)	Janssens et al 2017 <sup>53</sup>
Unemployment	Dettenborn et al 2010 <sup>57</sup>		
Verbal and physical aggression	<b>Kind et al 2018<sup>55</sup></b>		
Surface learning	Qi et al 2017 <sup>59</sup>		
Deep learning		Qi et al 2017 <sup>59</sup>	
Transformational leadership		Rowold et al 2017 <sup>58</sup>	
Instrumental leadership	Rowold et al 2017 <sup>58</sup>		
<b>Perceived stress</b>			
Burn-out	Penz et al 2018 <sup>61</sup> (dichotomous outcome); Wang et al 2019 <sup>66</sup> (exhaustion & depersonalization)	McLennan et al 2016 <sup>51</sup> (exhaustion & depersonalization); Penz et al 2018 <sup>61</sup> (continuous outcome); Wang et al 2019 <sup>66</sup> (personal accomplishment)	McLennan et al 2016 <sup>51</sup> (personal accomplishment)
Perceived stress	Faresjö et al 2014 <sup>62</sup> ; Mayer et al 2018 <sup>60</sup> ; O'Brien et al 2013 <sup>64</sup> ; Wells et al 2014 <sup>65</sup>	Gidlow et al 2016 <sup>46</sup> ; Van Holland et al 2012 <sup>63</sup>	
Need for recovery		Van Holland et al 2012 <sup>63</sup>	Qi et al 2015 <sup>52</sup>
Cognitive disorganization		Boschi et al 2017 <sup>67</sup>	
<b>Health outcomes</b>			
Depression		<b>Mayer et al 2018<sup>68</sup></b>	

Note: Longitudinal studies are highlighted in bold.

the data within this scoping review had the focus of assessing the value of HCC for occupational healthcare. Using this methodology was helpful to identify the available evidence of HCC from the perspective of the use of HCC in occupational health. However, the choice to conduct a scoping review entails that we did not generate a critically appraised and synthesized answer to a strictly defined research question. As we identified 25 papers, one might argue that a systematic review would have been more appropriate. However, these 25 papers covered three separate relationships of HCC, with stressors, stress responses, and health outcomes. And we identified no more than five longitudinal studies. Given the current state of the art, systematic reviews on HCC as an indicator of exposure to stressors and current stress reactions, and as a predictor of future stress-related health problems should be performed after longitudinal primary studies in large, heterogeneous sample sizes have been conducted with repeated measures of both HCC and the predictor of interest over a longer period of time.

#### 4.4 | Conclusion and implications

After having reviewed the literature relevant to the application of hair cortisol measurement in an occupational health setting, we conclude that several prerequisites to such application in practice have not yet been met. Prospective studies in working populations are needed to first show which (duration of) high HCC levels are related to mental and physical health problems. Moreover, to guide preventive efforts in the occupational health setting, the relationship between HCC levels and exposure to perceived work stressors needs to be more clear.

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**DISCLOSURES**

Approval of the research protocol: N/A. Informed consent: N/A. Registry and the registration no. of the study: N/A. Animal studies: N/A. Conflict of interest: None declared.


**AUTHOR CONTRIBUTIONS**

All authors made substantial contributions to this article. FS and KN designed the study, analyzed and interpreted the data, and wrote the manuscript. GH helped with fine-tuning the design of the study, analyzed and interpreted the data, and contributed to the writing of the manuscript. MJ and JO searched the literature and screened for relevant articles and contributed to writing of the manuscript. EvR advised on the interpretation of the validity of HCC measurements and contributed to the writing of the manuscript. Additionally, all authors approve this version to be published.

**ORCID**

Frederieke G. Schaafsma  <https://orcid.org/0000-0001-5827-7000>

Gerben Hulsegge  <https://orcid.org/0000-0003-4649-9436>

Elisabeth F. C. van Rossum  <https://orcid.org/0000-0003-0120-4913>

Karen Nieuwenhuijsen  <https://orcid.org/0000-0003-1218-775X>

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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## Appendix 1: Literature search strategies

Three literature databases were searched: PubMed, EMBASE and PsycINFO.

Listed below are the different literature and search strategies used for each of the different databases and review questions.

Table.S1 PubMed search strategy Search time: November 19<sup>th</sup> 2019

**Review question 1:** Is hair cortisol measurement a reliable and feasible instrument to measure psychological stress?

**Review question 2:** How good is the association between hair cortisol measurement and work related (mental) stress?

((((("Hydrocortisone"[Mesh] OR cortisol[tiab] OR hydrocortisone[tiab])) AND ((hair[tiab] OR hairs[tiab]) OR "Hair"[Mesh]))) AND ("Stress, Psychological"[Mesh] OR stress[tiab] OR depression[tiab] OR anxiety[tiab] OR well-being[tiab] OR burn-out*[tiab] OR burnout*[tiab] OR psychosocial*[tiab] OR psycho-social*[tiab] OR distress[tiab] OR demand[tiab]))))	<u>601</u>
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**Review question 3:** What is the predictive value of hair cortisol measurement for depression, anxiety, myocardial disorders?

("Hydrocortisone"[Mesh] OR cortisol[tiab] OR hydrocortisone[tiab] AND (hair[tiab] OR hairs[tiab] OR "Hair"[Mesh]) AND ("cardiovascular diseases"[mesh] OR death[tiab] OR mortality[tiab] OR coronary[tiab] OR cardiac[tiab] OR heart[tiab] OR cardiovascular[tiab] OR "myocardial infarction"[tiab]))	<u>111</u>
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**Review question 1:** Is hair cortisol measurement a reliable and feasible instrument to measure psychological stress?

**Review question 2:** How good is the association between hair cortisol measurement and work related (mental) stress?

('hair analysis'/exp OR hair:ti,ab,kw OR hairs:ti,ab,kw) AND ('hydrocortisone'/exp OR cortisol:ti,ab,kw OR hydrocortisone:ti,ab,kw) NOT ([animals]/lim NOT [humans]/lim)	1550
'mental stress'/exp OR stress:ti,ab,kw OR depression:ti,ab,kw OR anxiety:ti,ab,kw OR 'well being':ti,ab,kw OR 'burn out':ti,ab,kw OR burnouts:ti,ab,kw OR psychosocial:ti,ab,kw OR 'psycho social':ti,ab,kw OR distress:ti,ab,kw OR demand:ti,ab,kw	1845063
#1 AND #2	715

**Review question 3:** What is the predictive value of hair cortisol measurement for depression, anxiety, myocardial disorders?

('hair analysis'/exp OR hair:ti,ab,kw OR hairs:ti,ab,kw) AND ('hydrocortisone'/exp OR cortisol:ti,ab,kw OR hydrocortisone:ti,ab,kw) NOT ([animals]/lim NOT [humans]/lim)	1550
'cardiovascular disease'/exp OR death:ti,ab,kw OR mortality:ti,ab,kw OR coronary:ti,ab,kw OR cardiac:ti,ab,kw OR heart:ti,ab,kw OR cardiovascular:ti,ab,kw OR 'myocardial disease':ti,ab,kw OR 'myocardial infarction':ti,ab,kw	6113809
#1 AND #2	302

Table.S3 PsycINFO search strategy Search time: November 13<sup>th</sup> 2019

**Review question 1:** Is hair cortisol measurement a reliable and feasible instrument to measure psychological stress?

**Review question 2:** How good is the association between hair cortisol measurement and work related (mental) stress?

(DE "Hydrocortisone" OR TI hydrocortisone AB hydrocortisone OR TI cortisol OR AB cortisol) AND (DE "Hair" OR TI hair OR AB hair OR TI hairs OR AB hairs) AND (DE "Stress" OR DE "Chronic Stress" OR DE "Environmental Stress" OR DE "Occupational Stress" OR DE "Physiological Stress" OR DE "Psychological Stress" OR DE "Social Stress" OR DE "Stress Reactions" OR DE "Anxiety" OR DE "Distress" OR DE Depression)	155
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**Review question 3:** What is the predictive value of hair cortisol measurement for depression, anxiety, myocardial disorders?

(DE "Hydrocortisone" OR TI hydrocortisone AB hydrocortisone OR TI cortisol OR AB cortisol) AND (DE "Hair" OR TI hair OR AB hair OR TI hairs OR AB hairs) AND (DE "cardiovascular diseases" OR TI death OR AB death OR TI mortality OR AB mortality OR TI coronary AB coronary OR TI cardiac AB cardiac OR TI heart AB heart OR TI cardiovascular AB cardiovascular OR TI myocardial infarction OR AB myocardial infarction)	8
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Table.S4 Search strategy all databases Search time: November 13<sup>th</sup> 2019

PubMed (search question 2 and 3)	712
Embase (search question 2 and 3)	1017
PsycINFO (search question 2 and 3)	163
Total	1779
Duplicates	643
Total	1136