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Direktor: Univ.-Prof. Dr. med. Peter Angerer

Acute and chronic stress among medical students and healthcare professionals in Germany

Dissertation

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Meike Heming
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Zusammenfassung

Der Arbeits- und Universitätskontext bei Krankenhausmitarbeitenden und Medizinstudierenden ist durch hohe Stressbelastungen gekennzeichnet. Daher weisen diese ein erhöhtes Risiko für stressbedingte Erkrankungen, z.B. für Depressionen auf. Das übergeordnete Ziel dieser Arbeit ist es, ein besseres Verständnis der Ursachen und Folgen von psychosozialem Stress bei medizinischen Fachkräften zu erlangen. Hierzu wird der psychologische und epidemiologische Stressansatz mithilfe von Selbstberichten mit dem Modell der beruflichen Gratifikationskrisen (ERI), einem etablierten Arbeitsstresskonzept, betrachtet. Außerdem wird der biologische Ansatz mit physiologischen Indikatoren berücksichtigt.

Bei Krankenhausmitarbeitenden wurden Assoziationen zwischen dem ERI Modell und Wohlbefinden im Querschnitt untersucht (Studie 1). Führungskräfte berichteten wie sie ERI bei Mitarbeitenden wahrnehmen. Bei Medizinstudierenden wurden Assoziationen zwischen psychosozialen Stressoren und Haarkortisolkonzentrationen (HCC) untersucht (Studie 2). HCC soll als physiologischer Marker die Aktivität der Hypothalamus-Hypophysen-Nebennieren-Achse über einen längeren Zeitraum zeigen. Nachfolgend wurde experimentell untersucht, ob unterschiedliche HCC zu unterschiedlich starken Ausprägungen akuter Stressreaktionen beitragen (Studie 3).

Es wurde gezeigt, dass alle Komponenten des ERI Modells mit dem Wohlbefinden von Krankenhausmitarbeitenden assoziiert sind. Die deskriptiven Ergebnisse zeigten, dass Führungskräfte die Anstrengungen von Mitarbeitenden ähnlich einschätzen wie Mitarbeitende selbst. Führungskräfte gaben an, dass sie glauben Mitarbeitende stärker zu belohnen als Mitarbeitende dies selbst berichteten. Somit gaben Führungskräfte insgesamt an, dass Mitarbeitende ein geringeres Ungleichgewicht zwischen Aufwand und Belohnung hatten, als Mitarbeitende dies selbst wahrnahmen. Bei Medizinstudierenden waren Anforderungen, Anstrengungen und das Anstrengungs-Belohnungs-Verhältnis positiv mit HCC assoziiert. Andere psychosoziale Stressoren wiesen keine Assoziationen zu HCC auf. Bei Medizinstudierenden, die ein höheres Maß an HCC aufwiesen, zeigten sich während des Trier Social Stresstests geringere akute Stressreaktionen in Form von geringerem Blutdruckanstieg. Andere physiologische Indikatoren waren nicht mit HCC assoziiert.

Die Ergebnisse bei Krankenhausmitarbeitenden zeigten, dass die wahrgenommenen Diskrepanzen zwischen Führungskräften und Mitarbeitenden für die Stressprävention in Krankenhäusern relevant werden könnten, wenn künftige Forschungen die Ergebnisse bestätigen. Die Ergebnisse bei Medizinstudierenden könnten zu einem besseren Verständnis der Zusammenhänge zwischen psychosozialen Stressoren und physiologischen Stressindikatoren beitragen, wenn diese ebenfalls durch Studien repliziert werden, die eine Kausalität bestätigen. Die letzten Ergebnisse dieser Dissertation deuten darauf hin, dass Medizinstudierende mit erhöhten HCC möglicherweise unzureichende Stressreaktionen aufweisen.

Abstract

The work and study environment of healthcare professionals and of medical students is characterized by high stress levels. Those groups consequently show increased risks for stress-related diseases, especially for depression. The overall aim of this thesis is to gain a better understanding of causes and consequences of psychosocial stress among healthcare professionals. Therefore, causes and effects of stress among healthcare professionals and medical students are investigated with various methodological approaches. This dissertation considers the psychological and epidemiological stress approach via self-report with the effort-reward imbalance (ERI) model, which is an established work stress concept. It also considers the combination with the biological approach with physiological indicators.

Among hospital employees, associations between ERI and well-being were investigated in a cross-sectional design (study 1). Manager's perceptions of ERI for employees were investigated. Among medical students, associations between psychosocial stressors, such as in the ERI model, and hair cortisol concentration (HCC) were investigated (study 2). As a physiological marker, HCC is considered to reflect the hypothalamus–pituitary–adrenal axis activity over a prolonged period of time. Subsequently, it was experimentally investigated whether different levels of HCC contribute to different magnitudes of acute stress reactions (study 3).

It was shown that all parts of the ERI model were associated with well-being among hospital employees. Descriptive results showed that managers rated effort of employees similar to the employees themselves. However, managers reported higher rewards for their employees, compared to rewards reported by employees themselves. Thus, managers overall reported that employees had a lower effort-reward ratio than what employees perceived themselves. Among medical students, demands, effort and effort-reward ratio were positively associated with HCC. Other psychosocial stressors were not associated with HCC. Among medical students reporting higher levels of HCC, lower acute stress reactions in terms of lower increase in blood pressure were shown during the Trier Social Stress Test. Other physiological indicators were not associated with HCC.

The results among hospital staff showed that, if future research would support the findings, the perceived discrepancies between managers and employees may become relevant for stress prevention in hospitals. The results among medical students may help to better understand the links between psychosocial stressors and physiological stress indicators, also if replicated by studies that can confirm causality. The last results of this dissertation suggested potentially inadequate stress responses of the sympathetic nervous system for medical students having higher HCC levels.

List of abbreviations

ACTH	Adrenocorticotropic hormone
ANS	Autonomic nervous system
BMI	Body mass index
CFA	Confirmatory factor analyses
CRH	Corticotropin-releasing hormone
DBP	Diastolic blood pressure
ER-ratio	Effort-reward-ratio
ERI	Effort-reward imbalance
GFI	Goodness-of-fit index
JCQ	Job content questionnaire
JDCS	Job demand control support
HCC	Hair cortisol concentration
HPA axis	Hypothalamus–pituitary–adrenal axis
HR	Heart rate
HRV	Heart rate variability
LC-MS/MS	Liquid Chromatography-Mass Spectrometry
mmHg	Millimeter of mercury
RMSSD	Root mean square of successive differences
sAA	Salivary alpha-amylase
SAM	Sympathetic-adreno-medullar
SBP	Systolic blood pressure
SNS	Sympathetic nervous system
TSST	Trier Social Stress Test
PNS	Parasympathetic nervous system
PSS	Perceived stress scale
PTSD	Post-traumatic stress disorder
VR	Virtual reality

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1. Introduction

It is widely acknowledged that certain forms of work stress are associated with increased risks of diseases such as cardiovascular diseases or depression (Cohen et al., 2007; Epel et al., 2018). In order to develop prevention approaches to promote well-being and reduce risks of stress-related diseases, it is crucial to understand the complexity of stress and its impact on individuals working in demanding or high-pressure environments, such as the healthcare sector. This dissertation aims to describe and present valuable insights into the ways stress may be caused and which reactions (strain) it elicits in individuals working or planning to work in the healthcare sector, helping to gain a more detailed understanding of the interplay between stressors (i.e., occupational demands), stress indicators and health outcomes.

Preparing to work and working in the healthcare sector, especially working in the hospital and studying in medical school, goes along with increased stress levels and an increased risk of subsequent diseases. Medical students report performance pressure, lack of support or high workload during their medical education as well as high levels of perceived stress (Erschens et al., 2018b; Heinen et al., 2017; M. R. Hill et al., 2018). Numerous studies have already shown, that medical students show increased risks for depression, anxiety or burnout in comparison to young adults of the general population (Dyrbye et al., 2014; Rotenstein et al., 2016; Tian-Ci Quek et al., 2019). Similar stressors are observed in healthcare professionals: High demands, such as high workload or high emotional demands, are reported as well as long working hours (Körber et al., 2018; Parent-Thirion et al., 2016; Rosta & Aasland, 2011; Stiawa et al., 2022). Similar to medical students, higher levels of depression or burnout are also prevalent among employees in the healthcare sector compared to other working populations (Shanafelt et al., 2012; Wieclaw et al., 2006).

Early on, stress was defined as "the nonspecific response of the body to any demand made upon it" (Selye, 1973, p. 692). Since then, various definitions have emerged (Cooper & Quick, 2017), depending on the research discipline, considering different stages or approaches of the stress process: stressors, stress, acute stress reaction, strain and sequelae of stress. These causes and effects of stress are mainly studied by three research disciplines: 1) epidemiology, 2) psychology and 3) biology.

(1) Stressors are viewed as causes of stress and are mainly investigated by the epidemiological or environmental approach (Kopp et al., 2010). Stressors are negative stimuli (e.g., chronic work stressors such as high demands), which can trigger reactions. They can refer to one-time events that are thought to create harm or can be of chronic nature (Cohen et al., 2016). Psychosocial stressors, such as work stressors are also included by this environmental approach (Kopp et al., 2010; Vanaelst et al., 2012). Originally, (objective) environmental life events or stimuli were assessed by this approach (Holmes & Rahe, 1967).

(2) Stress is considered as the reaction to these stimuli depending on whether a stressor is evaluated as a threat or a challenge (Lazarus, 1984) and can be assessed on a psychological level (e.g., perceived stress) or on a physiological level (e.g., acute stress reaction in form of an increased heart rate, for example). Within the psychological approach it is investigated how an individual evaluates their own resources to cope with environmental stressors (i.e., transactional model of stress) (Folkman et al., 1986; Kopp et al., 2010; Lazarus, 1984). At first, there is the cognitive appraisal, where individuals assess if a situation is considered a threat and at second, there is the evaluation of available resources to cope with the situation (Lazarus, 1984). Coping strategies help to deal with problems (i.e., stressful situation) and help to regulate emotions (Folkman et al., 1986). Thus, the psychological approach considers measurements that can reflect coping strategies, personality traits or stress experiences, such as the perceived stress scale (PSS) (Cohen et al., 1983; Kopp et al., 2010).

If stress is evaluated as a threat, if no available resources are identified and if this situation is present with over a prolonged period of time (or cumulative), this can result in strain (i.e., feeling exhausted). In the context of work, job strain can arise for example, when demands are high and decision latitude is low (Karasek et al., 1998). Experiencing strain over time, it can ultimately result in sequelae of stress (i.e., diseases such as depression). Thus, there are numerous findings available linking stressors (such as high job demands) with stress, strain and ultimately increased risks for diseases (Dragano et al., 2017; Karasek, 1979; Niedhammer et al., 2021; Sanne et al., 2005).

(3) As mentioned, a stress reaction can also be assessed on a physiological level, which is mainly done so by the biological approach (Kopp et al., 2010). When being exposed to an acute stressor, the allostatic system is activated by first responding and then terminating the response once the stressor is over to achieve homeostasis again (McEwen, 1998). This process is helpful in general and protects the individual from damage (McEwen, 1998). Within this adaptive process, the sympathetic nervous system (SNS) and hypothalamus–pituitary–adrenal (HPA) axis are the most common stress response systems that are involved and assessed by physiological measures (McEwen, 1998).

As different definitions and assessments are used in research, it is not surprising that measures of stress are not consistently related to each other and are also not consistently associated with health outcomes (Epel et al., 2018). Varying time frames and the duration of measurements can contribute to these findings: there are acute and chronic stress reactions observable, short- and long-term exposure to stressors and to perceptions of stressful situations that need to be considered in research (Kopp et al., 2010). Beside these, varying sample characteristics (i.e., healthy vs. non-healthy samples), the individual's context and the observed health outcome itself can contribute to different associations between stress and health (Epel et al., 2018).

All of these differences need to be considered and understood for the development of intervention strategies aimed at promoting health and well-being. Therefore, it is relevant to get a differentiated

picture of the causes and consequences of psychosocial stress and the mechanisms towards adverse health outcomes in the long-term. This thesis will thus investigate acute and chronic causes and effects of stress among healthcare professionals and medical students, i.e., two populations known to be exposed to and affected by stress.

The following pages of this introduction are structured into three overarching parts, where at first the relevance of psychosocial stressors is described within healthcare professionals and medical students. Hereby a focus is shed not only on relevant work/study stress models but also on the importance of workplace managers for successful stress prevention in the workplace. In the second part of the introduction, physiological acute stress reactions and their assessment in research and its relevance for health effects are explained. The third part describes chronic stress and related assessments, i.e., hair cortisol concentration (HCC) as a promising physiological marker of long-term HPA axis activity. Investigating healthcare professionals in their working environment may help to find new starting points for interventions for stress reduction, while the closer look at medical students and their physiological stress reactions will provide more evidence for physiological pathways which are needed to understand the long-term links between stress and disease.

1.1 Assessment of psychosocial work stressors

Sources of stress in daily life can be of psychosocial nature, i.e., a combination of social and psychological factors (Upton, 2013). Psychosocial stressors or events can relate to the psychological state of an individual itself and to the environment, such as the work environment or social interactions (Long & Cumming, 2013; Upton, 2013). Thus, many instruments try to assess exposure to psychosocial stress (i.e., stressors) and its effects on individuals. Psychosocial stressors can occur only once, frequently or be of prolonged nature (Vanaelst et al., 2012). However, there is often no sharp differentiation between acute and chronic stressors, which makes assessment difficult (Liu & Doan, 2019). Usually, the assessment of psychosocial stressors is carried out via self-reported questionnaires (Kopp et al., 2010).

Psychosocial work stressors are usually understood as factors in the working environment that can cause stress and show associations towards well-being and health of employees and therefore represent challenges for occupational health and safety (Leka & Jain, 2010; Mark & Smith, 2008). For example, burnout is suggested to be a possible consequence of exposure to poor psychosocial working environments and the subsequent experience of work-related stress (Leka & Jain, 2010). Currently, numerous theoretical models and questionnaires try to describe and assess psychosocial work stressors and their impact on health. Two prominent models used in epidemiology are the job demand control support (JDCS) model and the effort-reward imbalance (ERI) model (Karasek, 1979; Siegrist, 1996).

The job demand control model was first conceptualized in 1979 by Karasek (1979). It describes that a so-called job strain can occur when high job demands and low decision latitude (i.e., control) is experienced (Karasek, 1979). Decision latitude thereby contains the two factors decision authority, meaning to have control over the work situation, and skill discretion, meaning to learn and use new skills (Karasek, 1979). In 1988, social support was also included in the model as a potential buffer for negative effects of high demands (Johnson & Hall, 1988; Mark & Smith, 2008). Lack of social support on the other hand, can also compound effects of job strain. Researchers can use the job content questionnaire (JCQ) in order to assess these psychosocial work conditions (Karasek et al., 1998).

The ERI model was introduced in 1996 by Siegrist (1996). The model suggests that spending high efforts at work and receiving low reward at the same time contributes to work stress (Siegrist, 1996). Thus, the key concept of the model relies on reciprocity and subjective perceptions of the working environment (Mark & Smith, 2008; Siegrist, 1996). Efforts can be understood as perceiving time pressure or high demands, for example (Mark & Smith, 2008; Siegrist, 1996). Reward can be defined as receiving an adequate monetary compensation or being offered better career opportunities, for example (Siegrist, 1996). The model allows the calculation of an effort-reward (ER-) ratio with its cut-off value of one, which can help to determine whether an imbalance between effort and reward is experienced (Siegrist, 1996). The model was also expanded by a scale for over-commitment, as individuals characterized by an excessive work-commitment may be at an increased risk for perceiving work stress (Siegrist et al., 2004). Researchers can use questionnaires of different lengths and for various population groups when applying the ERI model.

As the JDCS and ERI models are widely established, their application over the years has shown associations with strain and health consequences in numerous employees of different occupational groups. A great amount of research shows that the application of these models can predict increased risks for coronary heart disease (Dragano et al., 2017; Kuper et al., 2002; Niedhammer et al., 2021), depressive symptoms (Leineweber et al., 2010; Niedhammer et al., 2021; Sanne et al., 2005), anxiety (Sanne et al., 2005) or psychological well-being (Lange et al., 2003), for example.

1.2 Psychosocial work stressors and health in healthcare professionals

1.2.1 Medical students

As the future workforce in the healthcare sector, medical students should not be overlooked when conducting in depth stress-related research among healthcare professionals. Medical students experience and report high levels of stress throughout the years of their medical education (Dyrbye et al., 2005; Heinen et al., 2017) and also show elevated risks of mental health disorders: For example, a meta-analysis reported a global prevalence rate of anxiety in medical students of 33.8%, which was

higher compared to a general population (Tian-Ci Quek et al., 2019). Also in Germany, higher levels of anxiety were found in medical students compared to reference samples (Heinen et al., 2017). Another meta-analysis showed a prevalence rate of depression of 27.2% in medical students, also being higher compared to a similarly aged general population (Rotenstein et al., 2016). A study among newly enrolled medical students in 2012 or 2013 of one German university showed a prevalence rate of 4.7% indicating a major depression and a prevalence rate of 5.8% for depressive symptoms (both assessed with different cut-offs of Patient-Health-Questionnaire-9) (Wege et al., 2016). Over the course of one semester, another study showed an increase of mild depressive symptoms from 16.3% to 21.4% in first semester medical students (Pelzer et al., 2022). Burnout, which was originally assessed in the working population, is also being evaluated more frequently in students and it was shown that study demands can contribute to perceived exhaustion (Schaufeli et al., 2002). A meta-analysis estimated the prevalence of burnout among medical students to be 44.2% (Frajerman et al., 2019). A study among medical students in Germany showed an average burnout rate of 35% (Erschens et al., 2018a). Compared to college graduates, medical students showed a higher prevalence of burnout (Dyrbye et al., 2014).

Factors contributing to this high risk of disorders may include exposure to poor study conditions resulting in feeling stressed during medical school. For example, feeling stressed during medical school may increase the risk of burnout later on in working life (Ishak et al., 2009). Perceived stress levels among medical students are higher than in a general population in Germany (Heinen et al., 2017). Perceived stress levels exist throughout the study course and can either increase over time or show their highest values at different stages in medical school (Erschens et al., 2018b; Ludwig et al., 2015). When medical students begin their education, perceived stress levels show greater correlations with private-related stressors than with educational stressors (Erschens et al., 2018b). Especially at the beginning of medical school, students need to adapt to a new environment and are often separated from family or friends (Dyrbye et al., 2005). Perceived stress levels of students being halfway through the educational program show the strongest correlation with educational stressors, compared to private-related stressors (Erschens et al., 2018b). Lack of support, performance pressure and time management are some of the most frequently reported stressors related to the medical education program (Erschens et al., 2018b). Other frequently mentioned psychosocial stressors, in quantitative and qualitative research, are the high workload, work-life balance difficulties and health concerns or financial stressors (M. R. Hill et al., 2018). Medical students of one German university reported in a qualitative study mostly organizational stressors, such as lack of flexibility, or stressors related to exams, such as unfair grading procedures or lack of options to repeat exams (Weber et al., 2019).

The above-discussed work stress models JDCS and ERI were also adapted for and validated for students in university settings (Schmidt et al., 2019; Wege et al., 2017). Applying validated and established measures to students, which are based on theoretical models and thus focus on key

constructs, can help to better understand the associations between stress and health in an academic setting (Hilger-Kolb et al., 2018).

Based on the JCQ, a questionnaire on structural study conditions was developed and validated in university students in Germany (Schmidt et al., 2019). Demands within an academic setting can refer to the workload during the studies or can refer to perceptions of time pressure (Schmidt et al., 2015). Similar to the work setting, students can have restricted decision latitude, which can be indicated by fixed or mandatory schedules or courses (Schmidt et al., 2015). High demands were associated with perceived stress and high demands and low decision latitude were associated with decreased satisfaction among students in Germany (Sieverding et al., 2013).

The ERI model can also be applied to a student environment to investigate study stressors or conditions and their association to stress and health. Similar to demands, effort can be understood as a high study load (Portoghese et al., 2019). Rewards within an academic setting can refer to receiving respect from lecturers and professors (Portoghese et al., 2019). An increased effort-reward-ratio (ER-ratio) was associated with adverse self-rated health, depressive symptoms (Hilger-Kolb et al., 2018) or burnout (Hodge et al., 2020) among students.

1.2.2 Hospital staff

The tendencies of high stress levels among medical students can also be observed in their future professions, namely in the healthcare sector in general, where work intensity is the highest compared to several other occupational sectors (Parent-Thirion et al., 2016). In terms of demands, staff in the healthcare sector is often interrupted during work tasks and has to deal with high emotional demands, such as handling angry or frustrated patients, for example (Parent-Thirion et al., 2016). Physicians and hospital staff in Germany report high workloads (Körber et al., 2018; Stiawa et al., 2022), lack of opportunities for sufficient breaks (Stiawa et al., 2022) and longer work hours, compared to physicians in Norway (Rosta & Aasland, 2011).

Taking a closer look at healthcare professionals and hospitals in particular, it has been shown that physicians more often report an imbalance between effort and reward when compared to a general German working population (Knesebeck et al., 2010) A meta-analysis on the ERI model also suggested that physicians may have higher ER-ratios than other health professionals, taking into account several countries worldwide (Le Huu et al., 2022). However, the prevalence rate of ERI showed a broad range from 3.5 to 96.9% (Le Huu et al., 2022). In terms of individual consequences for the physicians themselves, it has been shown that imbalance between effort and reward is associated with increased depressive symptoms in physicians in training (Li et al., 2013). Especially in younger physicians higher ER-rates are observed (Arnold et al., 2017; Raspe et al., 2016). Achieving a better position during medical career (i.e., higher salary) may contribute to lower ER-rates (Knesebeck et al., 2010). The consequences of poor psychosocial work conditions do not only

entail health risks for employees themselves but can also impact patient care (Angerer & Weigl, 2015), as for example high ER-ratios among physicians have been shown to be associated with reduced quality of patient care (Loerbroks et al., 2016), which highlights the need for improvement and reduction of stress in this occupational group.

Among health workers in general also broad ERI ranges are found from 3.5 to 80.7% (Nguyen Van et al., 2018). Health effects of exposure to psychosocial work stressors do occur in the same way for nurses: Higher imbalance of effort and reward is associated with depression (Kikuchi et al., 2010), well-being (Nguyen Van et al., 2018; van Vegchel et al., 2001; Weyers et al., 2006) and days of sickness absence (Schreuder et al., 2010). Nurses who report better working environments report less often poor quality of care (Aiken et al., 2012). Another consequence that is often prevalent in healthcare professionals is burnout: Nurses and physicians report a high prevalence of burnout (Aiken et al., 2012; Klein et al., 2010) and also general healthcare staff shows increased symptoms of depression or burnout (Dyrbye et al., 2017). Also in comparison to a general working population, physicians are more likely to report symptoms of burnout (Shanafelt et al., 2012). Male nurses show elevated risks for affective disorders in comparison to other human service occupations (Wieclaw et al., 2006). Thus, it is plausible that depression and burnout among physicians and nurses have been shown to be associated with reporting major medical errors (Shanafelt et al., 2010) reduced job satisfaction (López-López et al., 2019; Shanafelt et al., 2009) and decreased quality of care (Klein et al., 2010). When considering leaders and employees without leadership responsibility in hospitals, it has been shown that a greater well-being is reported by leaders (Erschens et al., 2022). It has been suggested that the lacking ability in control and autonomy may contribute to these findings (Erschens et al., 2022).

1.2.3 Importance of workplace managers

Increased psychosocial work stressors are not only harmful for the employees' health themselves or their patients, but can also impact the company via higher turnover rates, higher sickness absence days or lower productivity (Mark & Smith, 2008). Promoting health at work is not solely the responsibility of employees, as they often lack the authority to change a challenging work environment. Company managers are instrumental in both identifying these challenges and implementing solutions to enhance working conditions (Jiménez et al., 2017; Montano et al., 2017; Shanafelt & Noseworthy, 2017; Tuckey et al., 2012). Also, leadership style is associated with well-being in healthcare professionals (Erschens et al., 2022), with job satisfaction in nurses (McCay et al., 2018) and with physicians' burnout and satisfaction levels (Shanafelt et al., 2015). Physicians also reported to perceive less stress if their interests were in alignment with leadership interests (Williams et al., 2007). Further, a leadership focus on mental health may contribute to good teamwork among healthcare professionals by reducing interpersonal conflicts at work (Paganin et

al., 2023). Of course, leadership behavior can also be a stressor for employees if managers have deficits in conflict management or leadership behavior in general (Gregersen et al., 2011).

To enhance working conditions and reduce stressors effectively, managers must first develop an awareness of the workplace conditions and demonstrate a genuine understanding of employees' potential sources of strain (Franke et al., 2014; Worringer et al., 2020b). Two qualitative studies assessed how managers in hospitals perceive the stressors and strain of their staff (Worringer et al., 2020a; Worringer et al., 2020b). It has been shown that hospital managers do report relevant stressors accordingly to JDCS and ERI model and that they were able to recognize strain such as fatigue or sick leave as a consequence of psychosomatic complaints by their staff (Worringer et al., 2020a). However, it is not known whether these perceptions of managers would align with self-reports from staff. Assessing if there are discrepancies between managers and employees' perceptions of work stressors may be relevant to recognize if managers are prepared to support their staff's concerns accordingly.

1.3 Physiological acute stress reactions and recovery

1.3.1 Assessment of acute stress reactions after stress exposure

There are different mechanisms that describe how, for example, psychosocial work stressors are linked to adverse health outcomes when they are physiologically manifested as strain. When an individual has evaluated a stressor as harmful or threatening, a stress reaction occurs that can be assessed with physiological indicators. Within the physiological response, metabolic, immune, autonomic, and neuroendocrine systems are activated and all of these are involved in changes of the pathophysiology (Lupien et al., 2009). For example, exposure to stressful experiences can reduce various immune functions or enhance them (i.e., related to inflammation) and both the autonomic nervous system (ANS) and the HPA axis can alter or suppress immune functions (Kemeny, 2003). The responses most researched are the SNS of the ANS and the HPA axis (King & Hegadoren, 2002; Lupien et al., 2009).

Already a few seconds after stressor exposure, the SNS is activated (known for the fight or flight reaction) and releases adrenaline and noradrenaline via neuronal pathways as well as salivary alpha-amylase (sAA) (Ali et al., 2020; King & Hegadoren, 2002). Through its activation (and the prior withdrawal of the parasympathetic nervous system; PNS) (van Dammen et al., 2022), the cardiovascular system is responding at first by an increase of blood pressure and heart rate (HR). Diastolic blood pressure (DBP) increases due to withdrawal of the PNS hampering the blood vessels' ability to relax (van Dammen et al., 2022). Systolic blood pressure (SBP) increases due to the SNS influence (van Dammen et al., 2022). To assess the PNS withdrawal, as the first start of the stress response, researchers also often measure heart rate variability (HRV) (van Dammen et al., 2022). For

example, the root mean square of successive differences (RMSSD), one of several HRV measures, indicates the parasympathetic activity (L. K. Hill et al., 2009). RMSSD serves as a time-domain metric and takes into account temporal fluctuations between consecutive peaks in the electrocardiograph waveform within a specified timeframe (van Dammen et al., 2022). Once the stressor is over, the parasympathetic nervous system is activated to achieve homeostasis again.

The HPA axis response occurs much slower than the SNS response, as its activation begins with secretion of corticotropin-releasing hormones (CRH) from the hypothalamus (King & Hegadoren, 2002). After that release of adrenocorticotropic hormone (ACTH) is triggered and secreted into the circular system and leads further to secretion of cortisol into the blood stream (King & Hegadoren, 2002; Lupien et al., 2009). The glucocorticoids partly regulate ACTH and CRH by binding to receptors (Lupien et al., 2009). If the stressor is terminated, feedback loops occur which help to achieve homeostasis by deactivating the HPA axis (Lupien et al., 2009). The activity of the HPA axis is usually assessed via measuring cortisol. Therefore, saliva samples, or even blood samples can be used. The measurements can reflect different time periods of cortisol and thus reflect either short-term or long-term HPA axis activity (Vanaelst et al., 2012). For example, saliva samples can reflect the activity of the past ten minutes up to one hour (Miller et al., 2007). When assessing cortisol, it is important to consider its diurnal rhythm. Cortisol increases to its highest point in the morning and decreases to its lowest point in the evening (Miller et al., 2007). Therefore, timing is very important for the assessment of cortisol. Several different approaches exist, where cortisol is either collected in the morning, evening or throughout the day with several measurements or with calculations to create the diurnal rhythm of a day (Miller et al., 2007).

In term of measures, researchers can use experimental study designs, which can induce acute stress reactions in individuals by exposing them to stressors. Depending on the nature of the stressor, a suitable stress test can be chosen. Numerous tests available and validated expose individuals to psychosocial or physical stressors such as temperatures or prolonged exercises that can be used to reflect physical stressors (Dickerson & Kemeny, 2004). A well-known measurement to expose individuals to psychosocial stress and to induce acute stress reactions is the Trier Social Stress Test (TSST) (Kirschbaum et al., 1993).

It is characterized by uncontrollability, social-evaluative threat and unpredictability and is thus a reliable task to activate the HPA axis and the ANS to induce stress responses (Campbell & Ehlert, 2012; Dickerson & Kemeny, 2004; Kudielka et al., 2009). Individuals arrive in a preparation room, get a rest period to establish baseline values and prepare a speech explaining why they are suitable for their dream job. After being guided to the test room, they perform the speech in front of an audience for five minutes (Kirschbaum et al., 1993). Directly afterwards they have to solve mental arithmetic exercises (Kirschbaum et al., 1993). After the math task, the participants are guided back

to the preparation room to have a recovery period. Thus, several measurements are taken before and after the stressor, with the exact time frame depending on the measures chosen (Allen et al., 2014).

The reliability of the TSST was investigated and supported by several studies so that it is recognized as the gold standard for inducing psychosocial stress in laboratory settings. The TSST shows the largest and most reliable associations with salivary cortisol (Dickerson & Kemeny, 2004), but is also associated with other acute stress indicators, such as blood pressure or HR (Allen et al., 2014; Man et al., 2023). Moderators that can alter reactions and should be considered in research are age, body mass index (BMI) and baseline physiological values (Herhaus & Petrowski, 2018; Zänkert et al., 2019).

Since the introduction of the TSST in the early nineties, several adaptations have been developed. In order to save personnel resources, costs and to increase standardization of the process, a relatively new approach uses virtual reality (VR) to conduct the TSST (Helminen et al., 2019; van Dammen et al., 2022). Often immersive VR environments are created by head-mounted displays such as VR-glasses (van Dammen et al., 2022). Thus, within a VR-TSST participants go through the same procedure, but experience the environment and stress test via VR.

A systematic review and a meta-analytic comparison showed that VR-TSST can also reliable induce stress responses with similar effect sizes for cortisol, HR and self-report measures compared to traditional TSST (Helminen et al., 2019, 2021). Another review and meta-analysis on various VR stress tasks showed that significant changes were observed for markers such as HR, SBP, DBP, sAA but not for RMSSD in healthy populations (van Dammen et al., 2022). The smallest effect sizes were shown for PNS markers (i.e., RMSSD), the largest effects sizes for SNS markers (i.e., blood pressure) and medium effect sizes for HPA axis markers (i.e., cortisol) (van Dammen et al., 2022).

1.3.2 Health effects of acute stress reactions after stress exposure and recovery

Assessing acute physiological responses is an approach that can help to gain more knowledge about involved pathways of stress and disease. In the present state of discussion, both exaggerated and blunted reactions to stressors are suggested to be potentially harmful for cardiovascular health (Turner et al., 2020). More than 40 years ago, researchers almost only investigated the reactivity hypothesis, which suggested that exaggerated or prolonged reactions to psychological stressors are harmful for cardiovascular health (Obrist, 1981; Phillips et al., 2013). For example, stronger blood pressure responses to psychological stressors were longitudinally associated with increased odds of increased blood pressure or the development of hypertension (Gasperin et al., 2009). Still today, most of the prospective evidence on maladaptive responses and their impact on health can be found for cardiovascular responses and cardiovascular diseases (Epel et al., 2018). However, newer research also investigates blunted reactions (also including HPA axis) or simply altered responses and broadens disease outcomes towards mental health, for example (Epel et al., 2018; O' Riordan et al.,

2023; Turner et al., 2020). Exaggerated cardiovascular responses (SBP, DBP, HR) to acute stress are still prospectively associated with increased risk of heightened resting blood pressure or increased mortality risks (due to any cause) and coronary death (Turner et al., 2020). Exaggerated blood pressure responses are also associated with greater risk of hypertension or an earlier onset of hypertension (Turner et al., 2020). For HPA axis response indicators (salivary cortisol), exaggerated reactions are predictive of higher risks of hypertension as well as coronary artery calcification (Turner et al., 2020). For blunted reactions, increased risks of being obese (for HR), poorer self-reported health (for HR and DBP) and also more symptoms of depression (for HR) and increased anxiety symptoms (for SBP) are shown (Turner et al., 2020). Blunted HPA axis reactions in terms of salivary cortisol are predictive of more symptoms of post-traumatic stress disorder (PTSD) (Turner et al., 2020). A recent systematic review tried to formulate suggestions to clinicians and researchers on how to recognize individuals at risk for developing cardiovascular diseases by presenting cardiovascular threshold levels for blunted reactions (O' Riordan et al., 2023).

As the physiological response to stress does not only entail activating the allostatic response, but also terminating it when the stressor is gone, researchers also assess physiological reactions of the recovery (Chida & Hamer, 2008) with different methodological assessment (Panaite et al., 2015). Usually, recovery is defined as the amount of time that is observed until values return to baseline levels (Chida & Hamer, 2008; Panaite et al., 2015), but can also be defined as observing sustained higher values than baseline values in a predetermined recovery period (post stressor) (Chida & Steptoe, 2010) or as rate of decrease from a peak value. There are also differences between active recovery (i.e., standing) or passive recovery (i.e., seating) (Panaite et al., 2015). Not many researchers investigate stress recovery separately or at all, although capturing the duration of an activation may be more suitable than only the extent of activation (Panaite et al., 2015). The stress recovery can be inefficient if hormones are overexpressed, potentially resulting in adverse health consequences, such as hypertension or carotid atherosclerosis (Chida & Hamer, 2008; Heponiemi et al., 2007; Hocking Schuler & O'Brien, 1997). Inadequate recovery is associated with poorer cardiovascular outcomes, such as increased risk for cardiovascular diseases or mortality (Panaite et al., 2015). Poor recovery of HR and SBP has been shown to be associated with future cardiovascular risk status (Chida & Steptoe, 2010). Age is an important moderator for stress recovery and health outcomes: Stronger associations are shown between recovery and cardiovascular outcomes for higher ages (above 45 years) compared to lower ages (below 45 years) (Panaite et al., 2015).

1.4 Chronic stress

1.4.1 Chronic stress exposure and its pathways towards adverse health consequences

As mentioned above, investigating causes and consequences of stress is difficult due to different definitions and (time dependent) assessments. Investigating acute stress responses and recovery

becomes even more complex when additional stress-related factors are considered which could contribute to disease risks or adverse health outcomes: Exposure to chronic stress is assumed to be associated with increased disease risks due to its potential permanent changes in physiological responses (Cohen et al., 2007; McEwen, 1998). While acute stress responses are essential in the acute moment and are protective, prolonged stress reactions can result in dysregulation of the biological stress systems and can increase risks or vulnerabilities for diseases (McEwen, 1998). These dysregulations are suggested to occur in four different forms, contributing to allostatic load, i.e., "the wear and tear" of the body (McEwen, 1998, p. 171). The first pathway describes how frequent stressors can induce repeated acute stress reactions, the second describes how similar stressors that occur frequently can contribute to lack of adaptation during the stress response, thus resulting in prolonged exposure to stress hormones (McEwen, 1998). The third pathway illustrates how the stress response is not terminated, although the stressor itself is not present any more (McEwen, 1998). The fourth type describes how limited, decreased responses in one stress system can lead to the activation of another stress system, indicating a compensatory mechanism (McEwen, 1998).

Another potential pathway was also described very early on by Dienstbier (1989) and his model of physiological toughness. The model tries to explain that when individuals are exposed to moderate stressors, this can result in an increased but also adaptive acute stress reaction (Chatkoff et al., 2010). It was proposed that moderate stressors can help to "toughen" individuals in a way that these are prepared for future stressors via adaptive responses (Dienstbier, 1989; Miller et al., 2007). Toughened individuals would have lower baseline values, a stronger and faster response and then also a faster recovery than non-toughened individuals (Blascovich & Mendes, 2010; Dienstbier, 1989). Dienstbier proposed his ideas for both the sympathetic-adreno-medullar (SAM) and HPA axis and suggested that a non-healthy stress response of the SNS system would be reflected by higher baseline levels, a not so steep increase but longer response and also a not so steep decrease during recovery (Blascovich & Mendes, 2010; Dienstbier, 1989). The HPA axis response would result in high baseline levels of cortisol, greater increases in cortisol during the acute response and then a not so steep decrease during recovery (Blascovich & Mendes, 2010; Dienstbier, 1989). However, it has been pointed out that the explanations are likely not true for every study population (i.e., healthy or non-healthy samples) (Miller et al., 2007).

When measuring cortisol under acute stressful situations in laboratories, it is assumed that increased levels indicate a stress response. This assumption becomes more complex when investigating chronic stress exposure and acute HPA axis responses: For chronic stress both hypo- and hypercortisolism have been shown (Miller et al., 2007; Vanaelst et al., 2012). Therefore, Miller et al. suggested with their meta-analysis that HPA axis activity may be different depending on how much time has passed since the stressor onset, suggesting that a lower HPA axis activity relates to a long-term chronic stress experience, while higher HPA axis activity relates to a more recent onset of stress (Miller et al., 2007;

Rohleder, 2016). Thus, hypo- and hypercortisolism may not be contradictory, but may reflect different time periods within a stress process (Miller et al., 2007).

1.4.2 Hair cortisol concentration (HCC)

In order to investigate chronic stress assessing HCC may be a helpful approach. Raul et al. (2004) were the first to report and determine HCC in humans. HCC reflects cumulative cortisol secretion retrospectively, which was validated in animals (Davenport et al., 2006) and humans (Kirschbaum et al., 2009; Manenschijn et al., 2011). HCC is thus an indicator for long-term HPA axis activity (Stalder et al., 2012b) and is discussed as an indicator of chronic stress (Russell et al., 2012). Cortisol is incorporated into the hair through various potential mechanisms that still have to be fully understood (Gow et al., 2010; Stalder et al., 2012b). Despite this, it is assumed that hair grows on average one centimeter per month, indicating that one centimeter of hair closest to the scalp reflects cortisol secretion of the previous month (Russell et al., 2012; Wennig, 2000). This assessment of cumulative cortisol secretion over a longer period of time is seen as a great advantage to existing measures, such as urine or saliva samples of cortisol which can only reflect shorter time periods (Stalder et al., 2012b). Another benefit for research is the non-invasive method of collecting HCC which also reduces the risk that the data collection itself can alter cortisol secretion (Russell et al., 2012). Additionally, HCC is not affected by the daily fluctuations of cortisol (Russell et al., 2012). Other advantages for research are the rather simple collection of HCC and the easy storage at room temperature (Gow et al., 2010). HCC is also suggested to be relatively stable within individuals, which supports its use in research as an indicator of long-term cortisol secretion and is thus a benefit over the use of blood or saliva samples (Stalder & Kirschbaum, 2012).

When investigating HCC there are some potential correlates that should be considered: Age and sex are frequently associated with HCC, suggesting higher HCC for males and higher age (Stalder et al., 2017). In addition, positive associations between BMI, high alcohol intake, vigorous physical activity and HCC are reported (Wosu et al., 2013). There are also some indications of negative correlations between HCC and the frequency of hair washing or hair treatment such as hair dye (Stalder et al., 2017), but other findings showed no evidence for these correlations (Stalder & Kirschbaum, 2012; Wosu et al., 2013).

In addition, there are different methodological approaches in hair cortisol determination, which can lead to mixed results in studies assessing HCC or make comparability between studies more difficult (Herane Vives et al., 2015). Most often, researchers use either different immunoassays or liquid chromatography-mass spectrometry (LC-MS/MS) to determine HCC (Herane Vives et al., 2015). One study reported that different laboratories, which determined a common batch of hair by different immunoassays, were able to show high inter-correlations (Russell et al., 2015). The authors suggested to either use correction factors for immunoassay approaches or to change to LC-MS/MS

method to determine HCC (Russell et al., 2015). This is an important finding that could contribute to further research to find potential clinical benchmarks for HCC (Russell et al., 2015).

1.4.3 Associations between stressors, perceived stress and HCC

Researchers have investigated whether the measurement of HCC can reflect psychosocial stress and its causes. Several studies were conducted on HCC and its association with exposure to stress (life events, psychosocial stressors, individual or demographic characteristics) and with perceived stress. For example, exposure to stress was assessed with either stressful contexts (e.g., environmental factors) or individuals being in stress-related conditions (e.g., subjective experiences): Dettenborn et al. (2010) showed higher HCC in a chronic stressor, namely in individuals being long-term unemployed compared to a healthy control group. However, HCC was not associated with any perceived stress measures (Dettenborn et al., 2010). One study showed, that participants reporting serious life events such as death of a relative, had increased HCC compared to participants not reporting these events (Karlén et al., 2011). Another review could show that a subsample of chronically stressed individuals had a 22% more increased median HCC (Stalder et al., 2017). When dividing this sample into ongoing and past stress, it was shown that ongoing stress resulted in a 43% increase of HCC (Stalder et al., 2017). It is suggested that HCC is associated with ongoing stress (Herane Vives et al., 2015; Liu & Doan, 2019). Staufenbiel et al. (2013) presented a review that structured research on HCC in terms of its association towards chronic stressors and mental health. In this review, medium to large effect sizes were found for the six studies that investigated exposure to long-term stress and elevated HCC (Staufenbiel et al., 2013). Van Uum et al. (2008) showed higher HCC in chronic pain patients, which is a known physical and psychological stressor. In addition they could also show higher perceived stress levels in the chronic pain patients, compared to healthy controls (van Uum et al., 2008).

However, when HCC is investigated with perceived stress assessed via self-report, findings report more often no associations (Stalder et al. 2017). Two studies on healthy students and undergraduate students have shown weak negative associations between perceived stress (assessed with PSS) and HCC (Gerber et al., 2013; Karlén et al., 2011). In contrast to this, in a sample of healthy pregnant women, the PSS was positively correlated with HCC (Kalra et al., 2007) but not associated with HCC in endurance athletes (Skoluda et al., 2012). Another study has not found linear associations between HCC and perceived stress of the past month (assessed with PSS) or between HCC and current chronic stress in pooled data from several samples (Wells et al., 2014). Instead, a curvilinear association was found: It was found that HCC increased with perceived stress levels, but decreased when perceived stress levels were highest (Wells et al., 2014). Similar evidence of this potential hypocortisolism is also found in earlier studies of individuals suffering from PTSD, burnout, chronic fatigue syndrome or other conditions of chronic stress (Heim et al., 2000). A more recent study could

also show that lower HCC were associated with subsequent increased PTSD symptoms in soldiers reporting new traumatic events (Steudte-Schmiedgen et al., 2015). Stalder et al. supported this in their meta-analysis by showing lower HCC in individuals with anxiety disorders (including PTSD) (Stalder et al., 2017).

However, is it difficult to distinguish if associations are due to the context of having underlying conditions of chronic stress (for example chronic pain patients) or due to effects of psychological stress (Stalder et al., 2014). Therefore, it can be helpful to conduct research in samples, where psychosocial stress is easier to define without a potential of underlying medical conditions (Stalder et al., 2014). Investigating HCC and work stress and thus the working population can be helpful to minimize this risk of more severe underlying medical conditions as being actively in employment would be more difficult. Cross-sectional studies so far have shown no associations between HCC and JDSC (Janssens et al., 2017; Qi et al., 2015; van der Meij et al., 2018). Cross-sectional studies investigating ERI have shown positive correlations and associations with HCC (Qi et al., 2014; van der Meij et al., 2018). Longitudinal studies reported either positive associations between ERI and HCC (Herr et al., 2018) or negative associations between ERI and HCC indicating that elevated work stress levels were associated with subsequent decreased HCC (Penz et al., 2019).

HCC was also investigated among university students, with both exposure to stress and perceived stress. Results showed no associations between HCC and perceived stress (Karlén et al., 2011; Mayer et al., 2018; Stalder et al., 2012a; Stetler & Guinn, 2020) but showed positive associations between exposure to stress (assessed with serious or stressful life events) and HCC (Karlén et al., 2011; Stetler & Guinn, 2020). Thus, it seems that HCC is more often associated with either stressful conditions or life events than with perceived stress. Researchers often explain the inconsistent findings of associations between cortisol concentrations and perceived stress with the 'lack of psychoendocrine covariance' (Gerber et al., 2013; Schlotz et al., 2008; Staufenbiel et al., 2013). This concept tries to explain that different on- and offsets of the stress response systems (i.e., lag effects where psychological responses precede endocrine responses) could contribute to the null findings (Schlotz et al., 2008). Next to this reasoning, differences in study sample characteristics and different measurements of perceived stress are also possible explanations (Staufenbiel et al., 2013).

The presented inconsistent findings show the complexity of associations between HCC and stress (and its causes) and further show that the classification of HCC as an indicator of chronic stress may not be readily accepted (Liu & Doan, 2019).

1.4.4 Associations between chronic stress and physiological acute stress reactions and recovery

There are not many studies to date investigating associations between HCC and physiological stress reactions by applying the TSST. There are however more studies investigating other concepts of

stress with acute physiological reactions in laboratory stress tests, but comparisons between these different conceptualizations need to be carefully made. Studies on increased subjective chronic stress or work stress have presented lower blood pressure or HR responses (Cavanagh & Obasi, 2021; Hamer et al., 2006; Matthews et al., 2001; Pruessner et al., 2013; Siegrist & Klein, 1990). In contrast, higher role uncertainty at work was not associated with blood pressure (Wirtz et al., 2013). A high number of adverse childhood events was associated with a blunted salivary cortisol response in TSST, but not with HR or blood pressure responses (Elzinga et al., 2008).

For the few studies that already investigated HCC within TSST and healthy study samples, the following results occurred: HCC was negatively associated with salivary cortisol, HR and HRV responses (Sandner et al., 2020; Wekenborg et al., 2019). However, in one of the two studies participants showed different levels of burnout symptomatic (Wekenborg et al., 2019). In patients at risk for psychosis, no associations between HCC and HR or salivary cortisol have been found, but for skin conductance level in TSST (Söder et al., 2020).

There are even less studies to date particularly investigating chronic stress and acute (cardiovascular) recovery from psychosocial stressors such as the TSST in healthy samples. One study assessing mainly acute stress recovery in terms of salivary cortisol did not show associations between HCC and salivary cortisol recovery in healthy adults (Degering et al., 2023). In patients at risk for psychosis it has been shown that HCC predicted a less pronounced recovery (Söder et al., 2020). Self-reported chronic stress (combining perceived stress, job and relationship satisfaction) was not associated with blood pressure or HR recovery (Matthews et al., 2001), but general life stress (distinctive of job stress) has been shown to be associated with poorer cardiovascular recovery in meta-analytical results (Chida & Hamer, 2008).

Due to the mixed findings in the literature, applying a physiological measure as an indicator of HPA-axis activity may thus be of help when investigating potential links between chronic stress and acute stress reactions or long-term health consequences. It may be especially helpful if differences occur because of differing conceptualizations when investigating the concept of stress (Zänkert et al., 2019).

1.5 Aims of this dissertation

This thesis aims to investigate acute and chronic causes and effects of stress among future (i.e., medical students) and current healthcare professionals as they show increased risks for stress-related adverse health consequences. It has been shown that the current state of scientific evidence on the complex associations between stressors, (work) stress and biological stress reactions (acute and chronic) is very mixed and therefore two overarching aims are investigated: First, psychosocial stressors among hospital staff are investigated by analyzing associations with well-being but also by

applying newer approaches (i.e., external rating of ERI) which consider managers as important levers for well-being and stress reduction in hospitals. Second, psychosocial stressors and acute stress reactions are further investigated in more detail with a promising physiological marker (i.e., HCC) among medical students. A contribution to fill knowledge gaps in this field may enhance understanding of the mechanisms that lead from stress to disease in this high risk professional group and to design effective interventions. Table 1 presents an overview of the study papers of this dissertation and their measurements.

The first part of this dissertation investigates the criterion validity of the ERI model in a sample of hospital employees in Germany. It also compares mean values of the ERI model, provided by hospital employees and mean values of an adapted ERI model, where managers reported how they perceived employees' efforts and rewards. The research questions are as follows:

1. Is there an association between effort, reward, or ER-ratio and subjective well-being in hospital employees?
2. Do managers who are asked to report effort, reward and ER-ratio values about employees report similar values to those reported by the employees themselves?

The second part of this dissertation investigates whether psychosocial study conditions, assessed with ERI model and JDCS model, are associated with HCC in medical students in Germany. The research questions are as follows:

3. Is there an association between reported demands, decision latitude, social support (from professors/lecturers or social support from students) and HCC in medical students?
4. Is there an association between reported efforts, rewards or ER-ratio and HCC in medical students?

The third part of this dissertation investigates whether HCC is associated with acute stress reactions in medical students. In particular, the research questions are as follows:

5. Is HCC associated with the magnitude of acute blood pressure responses in VR-TSST?
6. Is HCC associated with the magnitude of acute HRV responses in VR-TSST?
7. Is HCC associated with the magnitude of acute blood pressure recovery in VR-TSST?
8. Is HCC associated with the magnitude of acute HRV recovery in VR-TSST?

Table 1. Overview of dissertation papers and study variables.

	Study 1	**Study 2**	**Study 3**
Reference	Heming et al., 2023b	Heming et al., 2023a	Heming et al., 2024
Study design	Cross-sectional	Cross-sectional	Cross-sectional, experimental
Study sample	Hospital staff	Medical students	Medical students
Chapter	2.1	2.2	2.3
Stress approach	Environmental /epidemiological	Environmental /epidemiological	Biological
Independent variables	ERI model	ERI model, JDCS model	HCC
Dependent variables	Well-being	HCC	Blood pressure, HRV

ERI: Effort-reward imbalance. JDCS: Job demand control support. HCC: Hair cortisol concentration. HRV: Heart rate variability.

1.6 Ethics vote

The following ethic committees approved the first study: Ulm University (No. 501/18), Heidelberg University (No. S-602/2019) and Heinrich-Heine University Düsseldorf (No. 6193R). The ethics committee of the medical faculty of the Heinrich-Heine-University of Düsseldorf approved the two following studies (2019-714).

2. Publications

2.1 Heming, M., Siegrist, J., Erschens, R., Genrich, M., Hander, N. R., Junne, F., Küllenberg, J. K., Müller, A., Worringer, B., & Angerer, P. (2023). Managers perception of hospital employees' effort-reward imbalance. Journal of Occupational Medicine and Toxicology (London, England), 18(1), 8. https://doi.org/10.1186/s12995-023-00376-4

2.2 Heming, M., Angerer, P., Apolinário-Hagen, J., Nater, U. M., Skoluda, N., & Weber, J. (2023). The association between study conditions and hair cortisol in medical students in Germany - a cross-sectional study. Journal of Occupational Medicine and Toxicology (London, England), 18(1), 7. https://doi.org/10.1186/s12995-023-00373-7.

2.3 Heming, M., Angerer, P., Apolinário-Hagen, J., Liszio, S., Nater, U. M., Skoluda, N., & Weber, J. (2024). Hair cortisol concentration and its association with acute stress responses and recovery in a sample of medical students in Germany. Psychoneuroendocrinology, 163, 106986. https://doi.org/10.1016/j.psyneuen.2024.106986

3. Discussion

The reduction of high stress levels among healthcare professionals as well as medical students is an important public health aim which can be beneficial for the individuals themselves, for treated patients and the healthcare system. Psychosocial stress and its social, psychological and biological consequences require various methodological approaches to investigate its causes and effects. The three studies at hand can show a selection of some well-established approaches combined with newer measures, resulting in different implications for research and practice. Revealing discrepancies between the perception of managers and employees concerning the level of stress may offer an opportunity to improve leadership and thereby working conditions (Heming et al., 2023b). Taking a step back and observing medical students in more detail, as the future workforce in the healthcare sector, revealed that specific psychosocial stressors were associated with long-term HPA-axis activity (Heming et al., 2023a). This stressed group of students may entail higher risks for future diseases if their acute stress responses maintain impaired (Heming et al., 2024).
Within the following chapters, summaries of the three studies will follow as well as interpretation of results in light of the existing scientific literature. Strengths and limitations will be discussed and implications both for research and practice will be given.

3.1 Summary of results

3.1.1 Summary of results for psychosocial stressors in hospital staff

The first study and research question aimed to investigate the criterion validity of the ERI questionnaire by investigating associations between effort, reward, ER-ratio and subjective well-being in hospital employees in Germany. Results on this research aim showed that all components, namely effort, reward and the ER-ratio were associated with well-being in hospital employees, while adjusted for age, sex, marital status, employment status, occupational position and the respective components of the ERI model (Heming et al., 2023b).

To investigate the second research question ‘Do managers who are asked to report effort, reward and ER-ratio values about their employees report similar values to those reported by the employees themselves?’, descriptive statistics were shown for the ERI questionnaire assessed by managers and the ERI questionnaire self-reported by employees. It was shown that there are some discrepancies between managers and employee’s perceptions of ERI. Mean values for effort were reported relatively similarly by managers and employees (Heming et al., 2023b). In contrast, managers reported higher mean values of rewards for their employees than employees reported reward mean values themselves. These findings resulted in a lower, more favorable ER-ratio, representing a lower level of stress, reported by managers compared to employees (Heming et al., 2023b).

3.1.2 Summary of results for the association between psychosocial stressors and HCC among medical students

For the second study, results have shown that out of the JDCS model only demands were positively associated with HCC among medical students while adjusted for sex and age (third research aim). Accordingly, decision latitude, social support from professors/lecturers or social support from students were not associated with HCC among medical students (Heming et al., 2023a).

Regarding, the fourth research aim it has been shown that of the ERI model, effort and ER-ratio were positively associated with HCC among medical students, when adjusted for sex and age (Heming et al., 2023a). When regression analyses included all components of the two questionnaires together (except ER-ratio), only the association between demands and HCC remained significant (Heming et al., 2023a).

3.1.3 Summary of results for the association between HCC and physiological acute stress reactions among medical students

To investigate the research aims five to eight in the third study, piecewise linear growth analyses have been conducted. Results have shown an effect of HCC on acute blood pressure responses in VR-TSST among medical students (research aim five). Participants who reported higher HCC levels (>75th percentile) showed lower SBP and DBP responses compared to medium HCC levels (25th – 75th percentile). There was no effect observable of HCC on acute HRV responses or acute HRV recovery (research aim six and eight). There was also no effect of HCC observable on blood pressure recovery (research aim seven). Including HCC as a continuous variable into the piecewise linear growth analyses, showed no significant results, but similar directions of associations to the observed significant interaction effect of HCC on acute blood pressure reactions.

3.2 Psychosocial work stressors in hospital staff and managers' perspective

Before multiple linear regression analyses investigated the associations between ERI components and subjective well-being among hospital employees, confirmatory factor analyses (CFA) were performed to investigate factorial validity of ERI questionnaires for employees and managers. Results showed that, overall, both models did not achieve acceptable model fits according to indices such as the goodness-of-fit index (GFI), adjusted-goodness-of-fit index, root mean square error of approximation or comparative fit index (Heming et al., 2023b). However, excluding a further reward item ("The job promotion prospects for my employees are poor") from the ERI questionnaire for managers from the CFA improved the indices substantially (GFI for example increased to 0.937) (Heming et al., 2023b). As the study sample was relatively small to conduct CFA, and as two items have been excluded from the original version, this may explain the not acceptable model fit indices, as with this approach the underlying theoretical model (i.e., a second order model for distinct reward

components) could not be fully investigated but only a first order model. Due to inadequate item characteristics, one item asking about receiving respect from a superior was excluded as well as one item asking about job security as this aspect is of no relevance in the German hospital sector (Heming et al., 2023b). Further, internal consistency assessed with Cronbach's alpha was acceptable for both questionnaires. In comparison to previous studies, Cronbach's alpha values were slightly lower compared to studies using the short questionnaire version (Leineweber et al., 2010; Siegrist et al., 2009), but were more comparable to studies among healthcare staff, using the long version of the questionnaire (Msaouel et al., 2012; Weyers et al., 2006).

The results of multiple linear regression analyses of associations between ERI and well-being were in the direction expected and support findings of previous research. It was shown that efforts and ER-ratio were negatively associated with well-being and reward was positively associated with well-being among hospital employees (Heming et al., 2023b). The results go in hand with the literature mentioned in chapter 1.2.2 that shows poorer well-being for adverse psychosocial work stressors (Nguyen Van et al., 2018; van Vegchel et al., 2001; Weyers et al., 2006). For example, among Chinese physicians, job strain as well as ERI were associated with poorer health functioning (Li et al., 2006). ERI however, better explained health functioning, compared to job strain (Li et al., 2006). The authors suggested that ERI may have more explanative power in regard of service occupations due to the frequent occurrence of personal interactions in the job (Li et al., 2006).

The results of the second research question carefully suggested that the participating managers might be able to assess their employee's effort in an accurate way (Heming et al., 2023b). With this, the term *accurately* can only refer to the subjective rating that was given by the employees themselves. As the ERI model is validated and established in numerous countries and shows links between working conditions and work stress (and health), it seems unlikely that the employees would fail to correctly report their own perception of effort and reward (Heming et al., 2023b). In addition, self-report is the standard environmental approach used to study psychosocial stressors.

Considering the reward component, managers may have overestimated the amount and quality of rewards they or the organization provide to employees (Heming et al., 2023b). Rewards can refer to salary, esteem and also career opportunities such as job security (Siegrist, 2012). Managers may, over time, internalize the contractual or established conditions that are common in hospitals, making it easier for them to adjust their perceptions to these conditions (Heming et al., 2023b). This could contribute to weakened skills of self-awareness and to become less aware of workers' perceptions of a lack of fairness or recognition in these areas of work. In favor of this line of thought may be research that divided managers (according to their self-ratings and assessments of their employees) into being overestimators, underestimators or those being in-agreement regarding transformational leadership style: Results showed that employees reported to be more satisfied with their job and supervision, if

their managers were underestimators or in-agreement, compared to being overestimators (Moshavi et al., 2003). Other research, using 360 degree feedback approach (where managers are rated by multiple sources), showed also that overestimators, when confronted with their inaccurate ratings, assume that their subordinates ratings are less accurate and also show more negative reactions (Brett & Atwater, 2001). Thus, it could be possible that the managers who overestimate their given rewards, are less aware or emphatic towards their employees' rewards (Moshavi et al., 2003). However, in regard of successful stress prevention, leaders have to be aware of their role of providing recognition, esteem and feedback to their employees (Siegrist, 2012).

Transformational leaders are for example known to provide esteem in terms of being attentive towards needs or appreciation for good work (Weiß & Süß, 2016). It was shown that a perceived transformational leadership is negatively associated with ERI among employees of different occupational sectors in Germany (Weiß & Süß, 2016). Being an attentive leader may correspond to the reward component of the ERI model (Weiß & Süß, 2016). Thus, to carefully suggest, training transformational leadership skills including self-awareness may result in increased satisfaction of rewards reported among hospital staff in Germany and potential work stress reduction for employees. In regard of this, another longitudinal study conducted in Germany showed that leadership quality moderated the association between ERI and physical self-rated health reported by nurses (Kuchenbaur & Peter, 2023). Among employees reporting a better leadership quality, the negative association between ERI and self-rated health was stronger (Kuchenbaur & Peter, 2023). However, among employees reporting a worsening of leadership quality, the impact of ERI on self-rated health became non-significant. These findings may also suggest that components of leadership quality are also covered by components, such as support and esteem, present in the ERI model (Formazin et al., 2014). This could also show that the ability to adequately assess employee's efforts and rewards is helpful in being an attentive and supportive leader. Thereby, the components of the ERI model may be even more relevant for health than the sole influence of good leadership quality (Kuchenbaur & Peter, 2023). Investigating leadership behavior remains important, as it was shown, for example, that leadership behavior and social relations are important work-related factors, since they are reported by healthcare professionals as relevant in the development of mental disorders (Junne et al., 2018). In terms of prevention approaches for reducing work stress in hospitals, leadership behavior should be considered as an important opportunity (Erschens et al., 2022).

As it was shown, assessing ERI to measure workload is not only valid for employees, but may offer a newer approach in terms of health promotion by assessing manager's perceptions of their employees' effort and reward, if further researched.

3.3 Psychosocial stressors in hospital staff and medical students

In order to reflect on psychosocial stressors for hospital employees and for medical students, it is reasonable to have a closer look at the reported ER-ratios, assessed in both study one and two. These comparisons are not based on any statistical tests, but are rather just descriptive as also the ERI questionnaires used differed for the study groups as well as their score calculations. In general, reported ER-ratios of hospital employees are considerably higher compared to ER-ratios of medical students. However, as the questionnaires were used in different settings and across different study populations, the components reflect different stressors. While effort can for example refer to effort at work spent for hospital employees, this does rather reflect effort spent for studies and exams in case of medical students. While the reward component among working populations can consider for example satisfaction with salary, among a student population reward considers different aspects relevant for the university setting, such as an evaluation of whether the study program can be completed successfully. Thus, it does seem reasonable that implications for hospital staff and medical students need to be different in order to target the relevant psychosocial stressors. In addition, different ER-ratios can also be due to different age distributions, gender or other characteristics of the samples. For example, higher ER-ratios are found among men, compared to women (Siegrist et al., 2009).

3.4 HCC and its association to psychosocial stressors

Some of the results of research aims three and four stand in contrast to the previous literature mentioned in chapter 1.4.3. Previous studies conducted in working populations showed no associations between HCC and JDCS (Janssens et al., 2017; Qi et al., 2015; van der Meij et al., 2018). As also mentioned in chapter 1.4.3, this can have different reasons, which need explanation. In one study it was argued that the number of workers who experienced high work demands could have simply been too low (Janssens et al., 2017). Other authors suggested that demands could have been experienced only for a short amount of time, not resulting in important HPA-axis activity changes (Qi et al., 2015). This would also be supportive of previous research suggesting that stress must be ongoing for HPA-axis activity changes to occur (Herane Vives et al., 2015; Liu & Doan, 2019). One recent study has found indications for a potential hypocortisolism in new and young hospital employees in Germany: as one of the first prospective studies they have shown that technostress was associated with subsequent reduced HCC (Kaltenegger et al., 2024). Technostressors referred to multitasking at work, work interruptions and overload of information (Kaltenegger et al., 2024). Thus, as a consequence of experienced technostress at work, this could have resulted in blunted HPA-axis activity (Kaltenegger et al., 2024). A similar study showed also a negative association between work stress and HCC (Penz et al., 2019). However, different stressors are known to elicit different stress responses, which could also indicate that the technostressors were evaluated by the participants

as a challenging situation that could be coped with (Dickerson & Kemeny, 2004; Kaltenegger et al., 2024). In favor of this last explanation, the authors have shown for example a non-significant positive relationship between a demand-control ratio and HCC, indicating that technostressors and their appraisal may differ from work stressors (Kaltenegger et al., 2024). As for the study population at hand, in medical studies the workload experienced is constant and an important stressor reported by medical students (Dyrbye et al., 2005; M. R. Hill et al., 2018). Thus, this may show that the association between demands and HCC reflects this high workload in terms of increased physiological reactions and thus increased HPA-axis activity (Heming et al., 2023a).

Other null findings of the second study go in hand with previous literature. For example, no associations have been found between other components of the JDCS model and HCC. Also, other research among students has not found significant results for associations between control and perceived stress (Schmidt et al., 2015; Sieverding et al., 2013). Further, the existing workplace studies have not found associations between control and HCC (Janssens et al., 2017; Qi et al., 2015; van der Meij et al., 2018). According to the JDCS model, a high level of control is helpful for a healthy working environment. However, there may be individuals with lower self-efficacy, which may not aim to have high control at their jobs as they perceive high control potentially as negative stressors because they feel overwhelmed by the responsibility of being able and having to make their own decisions (Mark & Smith, 2008). In that way, increased decision latitude could be perceived as a greater stressor (O'Donnell et al., 2015) resulting in a compensation effect, where positive and negative perceptions of increased control could have balanced each other out.

While the JDCS has received some critique as the assessed job characteristics are limited and cannot explain intra-individual differences due to the focus on mainly environmental conditions (Mark & Smith, 2008), it is also helpful to consider the ERI model. In the second study among medical students, associations between effort and HCC and between ER-ratio and HCC were shown (Heming et al., 2023a). This goes in line with previous literature, as also other studies among working populations have found associations between ERI and HCC (Qi et al., 2014; van der Meij et al., 2018). As the effort and demand components are rather similar (Li et al., 2006), this may also strengthen the result that a high workload during studies may increase HPA-axis activity among medical students. However, also the ER-ratio showed a significant association with HCC, which shows that also rewards, i.e., receiving appreciation from lecturers/ professors or fellow students or feeling treated fairly at university, may be relevant for HPA-axis activity among students. Received rewards can for example either balance out high efforts or in case of low rewards, they could increase physiological stress reactions (Heming et al., 2023a).

There were some non-significant indications within the analyses of the JDCS model that support from fellow students may be more relevant for the study participants' HCC levels than support from

lecturers or professors (Heming et al., 2023a). There may be more comprehensive coping opportunities that can be supportive from fellow students as they are more closely connected in the study environment and share the same experiences and may feel more empathy from them compared to lecturers, for example. With this for example, fellow students may be relevant for reduction of mental health symptoms (Cotton et al., 2002).

To sum up, the findings in this part of the dissertation could expand previous research findings among working populations, precisely by showing that for students, demands may be the strongest factor associated with HCC (Heming et al., 2023a). Applying the work stress theories among a group of students helped to shed a light on some different magnitudes of stressors for medical students and their potential relevance for long-term HPA-axis activity.

3.5 HCC and its relevance for the association of physiological acute stress responses

Using HCC as a marker reflecting prolonged HPA-axis activity, it was aimed to investigate in more detail how acute physiological stress responses occur for different HCC levels among this group of students in the third study. Thus, considering not only self-reported study conditions, but applying the biological approach, is helpful as physiological reactions of the body itself can be observed and investigated. Thereby, applying the TSST, as an established tool to induce psychosocial stress, can be helpful for more detailed assessment of physiological stress reactions and their associations with HCC.

A blunted blood pressure response was shown among medical students having higher HCC (Heming et al., 2024). One explanation, for the blunted blood pressure response may offer the allostatic load model, introduced in chapter 1.4.1 (McEwen, 1998). Within this mechanism, one of four pathways describes that inadequate acute stress responses can occur due to chronic stress exposure: reduced (or inadequate) stress responses of one stress response system can lead to the activation of another stress system (McEwen, 1998). In case of the study findings, this could indicate that reduced responses of the SNS system (i.e., lower blood pressure responses) occurred due to the increased activation of the HPA-axis activity (i.e., higher levels of HCC) (Heming et al., 2024).

In the literature there are also findings that indicate and support the findings of blunted stress responses for higher HCC: Wekenborg et al. have shown that higher HCC were associated with lower HR and heightened HRV responses (2019). As an important difference to the study results at hand, the study population needs to be described in more detail. While the medical students were screened for several potential (mental) health disorders and were younger, the study by Wekenborg et al. was especially conducted among male employees that showed various levels of burnout symptoms (2019). Thus, one could suggest that their sample was less healthy and was more likely to already

suffer from stress-related health consequences. The only other study conducted at the time using the TSST and HCC among a healthy sample, found that higher HCC were associated with reduced salivary cortisol reactions (Sandner et al., 2020). Although these findings may be in line with the study results at hand (Heming et al., 2024), their research was investigating the same underlying stress response system, namely the HPA-axis, which cannot fully support the fourth pathway of the allostatic load model where different stress response systems are involved. As studies among HCC and acute stress reactions are still scarce, more research may be helpful in interpreting the observed results shown in Heming et al. (2024). For example, among working populations, self-reported chronic (work) stress has been shown to be associated with reduced cardiovascular responses in acute stress situations (Hamer et al., 2006; Matthews et al., 2001). Also, among primarily female students, it has been shown that chronic stress exposure before undergoing TSST, was associated with lower HR reactions (Cavanagh & Obasi, 2021).

Next to the allostatic load model, the model of "toughness" by Dienstbier was introduced in chapter 1.4.1. This model may offer additional explanation for the research findings at hand, as it describes both the SNS and HPA-axis during acute stress and offers pathways for both stress response systems (Dienstbier, 1989). As it was shown in the previous study that study demands were associated with HCC in medical students (Heming et al., 2023a), it may be that students have been toughened due to experienced past stressors and thus react with increased SNS reactions, i.e., higher blood pressure reactions for medium HCC levels. Thus, for these students, HCC may show experienced study stress of the past two months. This was indicated in the second study, as next to the multiple regression results, also mean values for the psychosocial stressors in the study setting and HCC mean values for each study year were reported (Heming et al., 2023a). Study demands and HCC were either on average both higher or both lower, indicating that study stress may be reflected in increased HCC levels. However, the model of toughness further proposes that moderate stress levels would go in hand with a faster recovery once the stressor is terminated, which was not supported by our data (Dienstbier, 1989; Heming et al., 2024). Furthermore, next to this adaptive response, Dienstbier also suggested how a maladaptive response of SNS would look like, i.e., the increase during acute stress would not be very steep (Blascovich & Mendes, 2010; Dienstbier, 1989). In our case, this may reflect the response of the medical students with higher HCC levels as they showed lower blood pressure responses compared to the students with medium HCC levels.

Unfortunately, there are no available reference values for a VR-TSST indicating which magnitudes of blood pressure reactions are appropriate (Helminen et al., 2019), but there is one study that tried to find out which values of different indicators could result in subsequent diseases, examined within various laboratory stress tests (O' Riordan et al., 2023). The authors have estimated thresholds for blood pressure being predictive of diseases such as depression or obesity: For example, the threshold for DBP was estimated between -2.4 to -5.00 mmHg (O' Riordan et al., 2023). Applying this

threshold level to the study results at hand, the group of medical students with higher HCC would belong to the risk group (Heming et al., 2024).

Next to these potentially important findings, other indicators investigated showed no significant results in the study (Heming et al., 2024). It was aimed to investigate HRV (in terms of RMSSD) as well as the recovery period of the TSST as a separate time period. Previous research has shown that parasympathetic markers such as RMSSD showed the smallest effect sizes when compared to SNS markers, which showed larger effect sizes and when compared to HPA markers which showed medium effect sizes (Dickerson & Kemeny, 2004; van Dammen et al., 2022). This could give an indication why there were no significant results for RMSSD, as the study sample was potentially too small to detect these smaller effect sizes. Other significant research findings were observed for only male participants (Wekenborg et al., 2019), which may also show that gender differences may contribute to differing results. Observing larger effect sizes for SNS markers (van Dammen et al., 2022) can also support the idea to introduce more studies and research on blood pressure as an important cardiovascular health indicator, next to well-established measures such as HR.

However, also the null findings of Heming et al. (2024) on recovery after VR-TSST should not discourage researchers to further reflect separately on recovery and reaction. For example, the allostatic load model describes that sustained arousal may be harmful for health, in the long-term (McEwen, 1998). Thus, it is a possibility that the study sample was potentially too young for adverse consequences of long-term experienced stress (Heming et al., 2024). Age has been shown to be a relevant moderator for the association between stress recovery and health outcomes (Panaite et al., 2015). Differing findings of various studies around this topic can show that it is important which conceptualization of stress is assessed. For example, when self-report is used, it has been shown that general life stress was related to blunted recovery (Chida & Hamer, 2008). However, different stressors or perceived stress are not necessarily contributing to the same results, which is why researcher should cautiously choose their study population according to the specific stress concept which is examined. However, combining the use of psychological and physiological indicators in research may help to achieve even more details for the interplay of the processes from stress reactions towards health consequences (Geurts & Sonnentag, 2006). Thus, using HCC as a somewhat newer addition to the physiological approach seems to be promising in view of the research results shown so far.

3.6 Strengths and limitations

3.6.1 Strengths

The first study among hospital employees and managers is unique in that self-reports of employees were contrasted with self-reports of managers about their employees. Precisely by using the well-

established ERI model, we were among the first to present how managers perceive their employees' efforts and also rewards given to them. Our contributions can further support criterion validity for the use of the ERI model in healthcare (Heming et al., 2023b).

A second strength of this dissertation was the use of the established work stress models and applying their validated version for students. It can also be considered a strength that this project aimed to combine and compare self-report with physiological indicators, i.e., HCC. In this way, the links between the different stress approaches, i.e., environmental and physiological approach, may be better understood and new insights are gained.

Furthermore, the studies of this dissertation entail the strength of applying relatively new tools in research, namely HCC in combination with blood pressure and the use of the externally rated ERI questionnaire. These measures are compared with well-established measures, such as the ERI model or investigated in a setting with an established knowledge base, i.e., TSST, which can help to make better interpretations of results. This can also contribute to gaining a better comparability towards existing studies. Nevertheless, it is important to acknowledge the differences in statistical methods, for example in score calculations, different questionnaire versions or different methods for extracting physiological measurements, for example.

Another strength for the two studies among medical students is the strict procedure to achieve a healthy sample, yet under high stress. In stress research in general, it can help to either exclude or carefully take underlying medical conditions into account, as they could bias the results.

3.6.2 Limitations

It is important to consider and discuss the limitations of the studies. All three presented studies are of cross-sectional design. This makes it impossible to draw causal conclusions. Within cross-sectional research design, there is always the risk of reverse causation or third variables influencing the associations investigated.

Some of the assessed measures were collected by self-report. This gives rise to the common method variance bias, especially in the first presented study (Podsakoff et al., 2003). Also, along with self-reported data goes the risk of receiving answers that are viewed as socially desirable by the participants.

All three studies entail risk of selection bias due to the recruitment approaches (i.e., convenience sampling). There is the risk that either especially stressed individuals wanted to participate within the studies, or especially not-stressed individuals wanted to participate as they feel to have more time to be part in a study. This can either under or overestimate the results at hand.

In regard of the first two research questions among hospital employees, the following limitations have to be addressed. Conducting CFA usually requires relatively big sample sizes, therefore the sample size at hand may be too small, which could have resulted in the restricted model fit. Further, due to the data structure there was no possibility to match the data of managers directly with the employees. Thus, interpretations of these results need to be considered carefully. It was tried to minimize this methodological limitation by presenting results on hospital department levels (Heming et al., 2023b).

The two studies among medical students had relatively small sample sizes. Thus, there is a possibility that smaller effects could not be observed. However, it was tried to minimize this risk by conducting a power analysis beforehand (Heming et al., 2023a) and considering previous literature in the field, which stated that medium effect sizes are observable for chronic stressors and HCC (Staufenbiel et al., 2013). Also in the third study, it has to be acknowledged that the sample size was somewhat small. However, for conducting a VR-TSST, the sample size is comparable to other studies in the field (Sandner et al., 2020; Wekenborg et al., 2019) and even greater than an average of 25 participants reported by a meta-analysis (van Dammen et al., 2022). In that meta-study, larger sample sizes did not lead to larger effect sizes in the VR studies reviewed (van Dammen et al., 2022).

Further, the two studies among medical students were conducted at one medical school in Germany, which limits generalizability of results (Heming et al., 2024; Heming et al., 2023a). However, high stress levels exist also in other medical schools and countries (Dyrbye et al., 2005). Thus, it may be reasonable to think that similar results of associations between study stressors and HCC may be found in medical students studying in other countries. For both studies and their underlying research questions it is in important to keep in mind, that medical students are a population group which normally represent young and relatively healthy individuals showing higher perception of stress than the average population of similar age (Heinen et al., 2017).

In order to reflect non-linear associations between different HCC levels and acute stress reactions, a categorization of the HCC variable was applied in the third study. This goes in hand with loss of information, which is a limitation worth mentioning. This was tried to be balanced out by including sensitivity analyses using a continuous HCC variable, for which results can be found in the published study as well (Heming et al., 2024).

3.7 Implications

3.7.1 Implications for research

Some methodological implications can be named for the three studies of this dissertation. Regarding the used measurements of this project, the first study assessed ERI by managers for employees (Heming et al., 2023b). Showing discrepancies between self-report and manager's reporting's in a

descriptive manner can highlight the need for future research to shed more light on managers and their perceptions for improvement and awareness of working conditions in hospitals. In line with this, future studies should aim for data that would enable matching of managers and their employees to conduct more comprehensive analyses considering a nested data structure.

Further in the second study, it was shown that HCC as a physiological marker may be used to reflect prolonged HPA axis activity in medical students (Heming et al., 2023a). Therefore, future research should aim to further investigate and apply HCC in similar study populations. If doing so, future studies would also benefit from applying longitudinal studies which can investigate causality and future health consequences of elevated HCC. It may be of help to maintain this longitudinal research in (medical) students, as they are considered a relatively healthy and young group of individuals where underlying diseases may be more easily manageable or not yet observable. If results can be replicated and strengthened, future studies should be conducted in diverse study populations to test the generalizability of findings. Conducting research with multiple measurement points of HCC and psychosocial stressors may help to understand the observed HCC fluctuations over time (Heming et al., 2023a).

Regarding theoretical implications, showing an association between study conditions and HCC (Heming et al., 2023a) as well as associations between acute stress reactions and HCC (Heming et al., 2024) can strengthen the understanding of physiological stress reactions in medical students. It can help to better understand the interplay of acute and chronic stress as well as of self-reported stressors and physiological markers. Considering and focusing on the perceptions of managers, as done in study one (Heming et al., 2023b), may give new insights on how individuals with leadership responsibilities perceive their employees work stress or rewards. This can expand the scientific evidence and suggests that besides a personal awareness of own work stressors among managers, the awareness of employees' work stressors may be relevant as well for promotion of working conditions in hospitals.

3.7.2 Practical implications

All practical implications of this dissertation are tentative suggestions what may be beneficial, when having the results in mind. It is important to mention that findings based on longitudinal studies are warranted in order to develop targeted practical implications.

Interventions on leadership behavior are rarely implemented in the healthcare sector (Stuber et al., 2021). Therefore, future approaches would benefit from including a leadership component, such as providing relational competencies, into their health promoting prevention programs. Trying to keep the results of the potentially overestimated rewards in mind, leader who consistently perceive their behavior towards their employees as better, as employees themselves, may benefit from

interventions, especially targeted to this group (Moshavi et al., 2003). This could be tried by self-awareness training, for example (Moshavi et al., 2003). This line of thought is also supported by Siegrist who suggested that promoting leadership skills may be one measure to reduce work stress for employees in companies on a personal level (Siegrist, 2012). In support of our research and findings, it is aimed to include trainings for managers on reflection of their leadership role as well as establishing appreciative relationships (Küllenberg et al., 2022). Generally, it may be helpful to look at the components of the ERI model in order to improve working conditions in hospitals, especially in order to find ways on how to increase reward perceptions of employees.

Due to the high stress levels among medical students, but also among healthcare professionals in general, it is important to start early on to prevent stress-related diseases to occur in the future. Therefore, as it was tried to do by the first study among medical students, it is important to already investigate the causes of stress in students. Applying models which are established and based on theoretical constructs and have been shown to predict an increased risk of certain diseases (Niedhammer et al., 2021), may be promising to establish factors which are potentially harmful for health. In terms of interventions for psychosocial stress reduction in students, it has already been suggested that measures should take place on an organizational level (Kötter et al., 2015). This can for example entail more flexible arrangements for attendance or exams (Dederichs et al., 2020; Kötter et al., 2015). On an individual level, time management courses may be helpful to better deal with high demands during the studies (Häfner et al., 2014). However, as certain stressors (i.e., high demands) may already result in increased HPA axis activity (Heming et al., 2023a), it should be prioritized by universities to reduce chronic stress already early on in the medical program.

4. Conclusions

This dissertation aimed to gain a better overall understanding of causes and consequences of psychosocial stress among (future) healthcare professionals. This dissertation wants to highlight the need for research that can help to build foundations for advances in stress research and ultimately stress prevention by applying novel as well as established measurements in stress research.

Within the first study of this dissertation, it has been shown, that ERI remains a valid tool to assess work stressors via self-report of hospital staff. The ERI model was associated with general well-being in hospital staff, within a cross-sectional design. Descriptive comparisons showed, that using the ERI model for external ratings may offer some insights on discrepancies between managers and employees in hospitals in regard of rewards. This could become relevant in stress prevention at the workplace if future research applies more sound methods to further test and support the results. However, stress prevention in hospitals should aim to reduce poor working conditions, such as perceptions of a lack of rewards received.

Previous assessments of the ERI model have already shown that an adapted version for university setting is valid to use in medical students, just like the JDCS model. Within a cross-sectional design, demands, efforts and ER-ratio, were associated with HCC, indicating increased HPA-axis activity of the past two months. If these results would also hold true for longitudinal studies and thus confirm causality, prevention approaches should aim to reduce study demands in medical students by prevention measures on an organizational level.

After showing the potential of HCC for reflecting prolonged HPA-axis activity among medical students, the last study of this dissertation further investigated acute and chronic stress among these individuals. Medical students took part in a VR-TSST and their stress reactions were analyzed for different HCC levels. Medical students reporting higher HCC levels showed lower blood pressure reactions when compared to medium HCC levels. These findings may provide information on potential inadequate stress responses of medical students with increased HCC levels.

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