Received: 31 July 2017 | Revised: 21 December 2017 | Accepted: 23 January 2018

DOI: 10.1002/mpr.1613

ORIGINAL ARTICLE

WILEY

The Dresden Burnout Study: Protocol of a prospective cohort study for the bio-psychological investigation of burnout

Marlene Penz[1†] | Magdalena K. Wekenborg[1†] | Lars Pieper[2] | Katja Beesdo-Baum[2] | Andreas Walther[1] | Robert Miller[1] | Tobias Stalder[1,3] | Clemens Kirschbaum[1]

[1] Institute of Biological Psychology, Technische Universität Dresden, Dresden, Germany

[2] Institute of Clinical Psychology and Psychotherapy, Behavioral Epidemiology, Center for Clinical Epidemiology and Longitudinal Studies, Technische Universität Dresden, Dresden, Germany

[3] Clinical Psychology, University of Siegen, Siegen, Germany

Correspondence
Marlene Penz, Institute of Biological Psychology, Technische Universität Dresden, Zellescher Weg 19, D-01069 Dresden, Germany.
Email: marlene.penz@tu-dresden.de

Funding information
"The Synergetic University" - Excellence Initiative, Grant/Award Number: F-003661-553-61B-1040100

Abstract

Objectives: The Dresden Burnout Study (DBS) is a 12-year longitudinal cohort study that aims to provide a description of the burnout syndrome on the basis of time and symptom criteria with a special focus on the search for biomarkers. Biological and psychosocial approaches are applied to examine the long-term course and consequences of burnout within a population-based German-speaking sample aged 18 to 68 years.

Methods: Demographics and psychosocial data are generated by online assessments, including demographics and questionnaires on burnout, burnout-related constructs, work-environment, and health-related factors. The lab-based biomarker assessment includes endocrine, physiological, immunological, and epigenetic markers obtained from blood and hair samples. In addition, heart rate variability is also measured repeatedly. Within the first 2 years, the DBS collected psychosocial data from over 7,600 participants with biological data obtained from more than 800 individuals. During the following 10 years, detailed assessments of biomarkers and psychosocial factors will be collected in annual study waves.

Results: Results will be generated during the following decade.

Conclusion: The findings of the DBS are expected to pave the road for an in-depth biopsychosocial characterization of burnout and to give insight into the long-term course and potential mental and physical health consequences of the burnout syndrome.

KEYWORDS

biomarker, biopsychosocial assessment, burnout, chronic work stress, prospective cohort study

1 | INTRODUCTION

According to the World Health Organization, work-related stress forms a growing health risk for western societies (Leka & Jain, 2010), pointing to the serious threat for both, the individual and the society. Up to 20% of the German population is affected by moderate to very high chronic stress. A variety of work-related parameters have been identified as main contributors to this high societal stress level (Kocalevent, Klapp, Albani, & Brähler, 2013). A crucial condition in this context is burnout—a syndrome defined by (a) emotional and physical exhaustion, (b) negative attitudes toward work, and (c) negative evaluation of ones work performance (Maslach, Schaufeli, & Leiter, 2001; Shirom & Melamed, 2006). Studies on the epidemiology of burnout are scarce and restricted by the fact, that burnout can be masked by other diagnoses, like depression or chronic fatigue syndrome. Despite these conceptual challenges, there is consensus that burnout is associated with immense economic costs, for example, due to an increase in sick leave (Korczak, Huber, & Kister, 2010). Burnout syndrome is considered a major risk factor for mental disorders (Ahola et al., 2005; Hakanen & Schaufeli, 2012) and physical disease (Toker, Melamed,

[†] These authors contributed equally to the work.

Berliner, Zeltser, & Shapira, 2012; Toppinen-Tanner, Ahola, Koskinen, & Väänänen, 2009), multiplying the burden for the individual and for the public health care system. Considering these consequences, surprisingly, little is known about aetiology, course, and pathophysiology of burnout. Relatedly, research is hampered by the lack of an accepted syndrome definition or standardized diagnostic instruments (Korczak, Kister, & Huber, 2008). Only exhaustion is considered as a sound psychological and physiological syndrome component (Kaschka, Korczak, & Broich, 2011).

Given the above described situation, the Dresden Burnout Study (DBS) was initiated to advance the development of more effective screening methods, which form the basis for future development of standardized prevention and treatment programs. Launched in January 2015, the DBS is designed as a prospective cohort study to assess burnout on a psychological, social, clinical, and biological level. The DBS is scheduled to run for 12 years with annual monitoring of up to 10,000 participants for psychometric and biological parameters. The present paper presents the study protocol and aims of the DBS and gives a brief overview of the first two assessment years.

1.1 | Aims of DBS

The following paragraph will highlight the main aims of the DBS and gives a brief overview of current shortcomings of the burnout concept.

Aim 1. Understanding the development of symptoms and transition into burnout

So far, the burnout syndrome has primarily been described on the basis of cross-sectional studies, which does not allow for solid temporal and/or causal inferences about aetiological factors of symptom development. The few available longitudinal studies show restricted generalizability of results by focusing on specific populations, for example, middle-aged working women or employees from a single company (Evolahti, Hultell, & Collins, 2013; Leiter et al., 2013) or particular factors that were expected to cause burnout (Borritz et al., 2010; Lindwall, Gerber, Jonsdottir, Börjesson, & Ahlborg Jr, 2014). In addition, cross-sectional designs show large symptom overlap of burnout with related disorders, primarily depression (Ahola et al., 2005; Bianchi, Boffy, Hingray, Truchot, & Laurent, 2013; Bianchi, Schonfeld, & Laurent, 2015; Hakanen & Schaufeli, 2012; Schonfeld & Bianchi, 2015). Based on these findings, burnout is widely believed to be not a syndrome by itself but rather a less stigmatizing label for depression. We hypothesize that symptom development within the burnout syndrome could be distinct to other disorders, even if cross-sectional symptomatology may show considerable overlap. In order to overcome shortcomings of previous studies, longitudinal data from a larger sample are needed to understand a potential syndrome-specific progression of symptoms from work stress to adverse health conditions.

Aim 2. Identifying biomarkers of burnout

Repeated assessments of potential burnout biomarkers may help to significantly advance the (differential) diagnosis of the syndrome and the individual trajectories of burnout from preclinical symptoms into clinical disease manifestation. According to a current meta-analysis (Danhof-Pont, van Veen, & Zitman, 2011; see also Grossi, Perski, Osika, & Savic, 2015), no reliable biomarker of burnout has been identified to date. This may be due to a rather small number of available studies and heterogenic study designs.

Due to its crucial role for the human stress response, the hypothalamic–pituitary–adrenal (HPA) axis and its regulation by glucocorticoids (GC) have been the main focus for systematic research on biomarkers in burnout so far (Mommersteeg, Heijnen, Verbraak, & van Doornen, 2006a, 2006b; Oosterholt, Maes, Van der Linden, Verbraak, & Kompier, 2015, 2016). By widespread central receptors, GC can influence cognitive processes like learning and memory (Wolf, 2009) or exert effects on mood (Miller, Chen, & Zhou, 2007). Both aspects, cognition and mood regulation, seem to be pivotal for burnout development and progression (Grossi et al., 2015; Maslach & Jackson, 1981). Furthermore, GC have potent immunomodulatory effects (Dhabhar, 2014; Hänsel, Hong, Cámara, & Von Kaenel, 2010; Rohleder, 2014), indicating a possible link between chronic stress in burnout and increased vulnerability to inflammatory or infectious diseases in burnout patients. Studies on burnout and immune parameters are scarce, but the available data consistently suggest reduced immune competence in affected individuals (Mommersteeg, Heijnen, Kavelaars, & van Doornen, 2006; von Känel, Bellingrath, & Kudielka, 2008).

Sex steroids have also been linked to burnout although studies are scarce. Positive associations between burnout symptoms and testosterone levels were found in a study with a 3-year follow-up (Grossi, Theorell, Jürisoo, & Setterlind, 1999). In contrast, a study by Grossi, Perski, Evengård, Blomkvist, and Orth-Gomér (2003), comparing two groups of women with high or low burnout symptomatology, respectively, revealed no differences between the groups for cortisol, progesterone, estradiol, or dehydroepiandrosterone-sulphate. In accordance with these results, another study reported no associations between estradiol levels and burnout severity in either men or women (Lennartsson, Billig, & Jonsdottir, 2014).

Heart rate variability (HRV) is another valid starting point for the search of biological markers of burnout, given its frequently reported association with work-related stress (Jarczok et al., 2013). HRV is operationalized as the variability of time intervals between consecutive heart beats and is one of the most extensively studied indicators of autonomic nervous system (ANS) function (Task Force, 1996). The few existing studies on burnout, however, provide a contradictory picture with studies reporting either reduced (de Vente, van Amsterdam, Olff, Kamphuis, & Emmelkamp, 2015), elevated (Zanstra, Schellekens, Schaap, & Kooistra, 2006), or no differences in HRV (Jönsson et al., 2015) between individuals with burnout compared with controls.

Finally, the search for genes contributing to burnout vulnerability is warranted due to consistent reports of twin studies on the heritability of burnout symptoms (Mather, Bergström, Blom, & Svedberg, 2014; Middeldorp, Cath, & Boomsma, 2006). Using data from the Swedish twin cohort study including 20,286 individuals, Blom, Bergström, Hallsten, Bodin, and Svedberg (2012) conclude that genetic factors explain about a third of the variance of individual differences in burnout symptoms. In addition, specific methylation patterns in candidate genes have been identified for burnout, linking epigenetic regulation with burnout vulnerability (Bakusic, Schaufeli, Claes, & Godderis,

2017). In consequence, genetic and epigenetic analyses are also incorporated into the biomarker assessment.

Taken together, the DBS aims to carefully evaluate a comprehensive set of promising biological markers for the risk, development and/or progression of burnout. Annual measurements over in total 12 years will provide longitudinal data on the trajectories of biological markers in relation to burnout symptomatology. Different physiological systems such as the endocrine system, the immune system, the ANS, and (epi)genetic markers will be examined (a detailed description of biomarkers is provided in Section 3).

Aim 3. Paving the road for an improved definition of the burnout syndrome

Following on Aim 1, considering burnout as a specific diagnosis is currently still highly problematic. The classification systems Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (American Psychiatric Association, 2013) and International Classification of Disease, 10th Revision (ICD-10; WHO, 1992) do not list burnout as a clinically relevant mental disorder. However, in the ICD-10, burnout is mentioned within the residual category Z 73—problems related to life management difficulty. Importantly, burnout is listed within this residual category unrelated to symptoms or time criteria. For the definition of a burnout diagnosis meeting classification standards, a set of mandatory burnout symptoms and certain persistence criteria are needed. Such a diagnosis should demarcate burnout from other mental disorders such as depressive disorders or chronic fatigue syndrome (Bianchi et al., 2015; Huibers et al., 2003; Leone, Wessely, Huibers, Knottnerus, & Kant, 2011). Two examples for standardized burnout diagnosis exist: The Swedish and the Dutch health systems provide standardized diagnoses that integrate burnout as a definable syndrome (Schaufeli, Leiter, & Maslach, 2009; Van Der Klink & Van Dijk, 2003). However, these approaches currently lack validation for an international transfer.

The DBS thus aims to identify a burnout-specific set of symptoms. In addition, to identify a valid syndrome-specific time criterion, changes over time indicating remission, chronification, or relapse will be observed and linked to indicators of quality of life, impairment, and disability. In parallel, we will compare the results with those of standardized measurement instruments for depressive disorder and general fatigue to explore syndrome overlaps, transition, and comorbidities with burnout. Overall, this will allow to provide a criteria set for burnout including differential diagnosis considerations.

Aim 4. Finding the commonalities between psychosocial factors associated with burnout

Over the last decades, several potentially burnout-associated psychosocial variables have been discussed, with a particular focus on risk rather than protective factors. Predominantly, these either involve (work) environment factors or individual-level factors. With reference to the former, a recently published systematic review on psychosocial work conditions by Seidler et al. (2014) found quantitative job demands and increased job strain being most predictive for the emergence of burnout. At the individual level, personality and cognition are the most frequently studied concepts. With respect to personality, neuroticism and extraversion have most consistently been associated with burnout symptomatology (Alarcon, Eschleman, & Bowling, 2009; Swider & Zimmerman, 2010). The vast majority of studies on cognition revealed impairments in memory, executive function, and attention, most consistently at severe stages of burnout symptomatology (Deligkaris, Panagopoulou, Montgomery, & Masoura, 2014).

In contrast to most of the previously conducted research, the DBS will simultaneously monitor different psychosocial variables on environmental and individual levels in a large, heterogeneous sample. With annual assessment waves, we aim to identify those protective and risk factors with the strongest predictive value for burnout development and progression.

2 | MATERIALS AND METHODS

The study was approved by the local ethics committee and conducted in accordance with the Helsinki Declaration of 1975 as revised in 2008.

2.1 | Sampling

The DBS is a prospective cohort study with a planned duration of 12 years. In annual examination waves, psychological, social, and biological data will be collected. The primary aim of the first 3 years of the DBS is to build a large-scale sample (recruitment goal: 10,000 participants) within German speaking countries, including an overlapping subsample that will be representative for the city of Dresden. To overcome a shortcoming of previous studies, which focused predominately on very specific populations, inclusion criteria for the DBS are solely based on age (18–68 years) and adequate language skills (capable of reading and filling out questionnaires in German). Therefore, participants differing with respect to burnout symptomatology and professional and socio-economic status, as well as working area, are recruited regardless of their individual work and stress antecedents. Subsequently, the sample will be stratified by demographics, burnout characteristics, and comorbidities (major depressive disorder, anxiety disorder, and general fatigue). Medical conditions of participants are assessed but will not lead to exclusion. Burnout severity is measured with the Maslach Burnout Inventory-General Survey (Büssing & Glaser, 1999), which is considered the gold standard for empirical burnout assessment.

2.2 | Recruitment procedure

Two recruitment strategies are employed in parallel, as described below.

Sample 1. Convenient sample of participants that are recruited by public media presence since January 2015. Participants' recruitment is transmitted by heterogenic medial platforms. Furthermore, the DBS receives support from various companies and associations that inform associates and staff members about the DBS.

Sample 2. To decrease selection bias in our convenient sample, a second recruitment strategy was used for Sample 2. Recruitment strategy for Sample 1 implies a very heterogenic sample

composition, which is the aim of DBS. Indeed, it can be expected that people, who already have a history with burnout and/or are currently highly stressed, might rather respond to our medial recruitment than do healthy people without any involvement with the study topic. To improve generalizability of study results, we include the supplementary Sample 2. The recruitment phase for Sample 2 was initiated in December 2016 to January 2017 via the population registry. Addresses of 10,000 private Dresden households were obtained from the Dresden City Registry by random sampling, and household members were informed about the DBS by postal invitation letters. In response to this effort, 850 participants (8.5%) have registered for study participation in the meantime. Even if we will not achieve a representative composition of Dresden residents with Sample 2, the random drawing strategy will enlarge the generalizability of result and will furthermore provide the first estimates of burnout epidemiology in the city Dresden.

2.3 | Registration and study homepage

Study participation starts after registration to the DBS on our study homepage (www.dresdner-burnout-studie.de). The homepage further informs about participation formalities and provides information about help facilities and theoretical background about the burnout syndrome. Participants provide an email address to which personalized login data are automatically sent. After the individual login and provision of their informed consent, participants are recorded as DBS participants.

2.4 | Baseline and follow-up assessments

The DBS subsumes online assessments of detailed questionnaire data and self-reported individual characteristics, lab-based sampling of biological markers, and standardized clinical interview data. Figure 1 gives an overview of the cross-sectional and longitudinal DBS study design. A brief summary of the current sample characteristics is provided in Table 2.

After registration, participants are invited to provide sociodemographic data and to complete a set of questionnaires (see Table 1) via the study homepage. After completion, an automatized individual feedback is provided and can be downloaded from the homepage. Participants will be prompted to repeat the online questionnaire assessment annually. We are aware that annual feedback about burnout and other health-related factors have to be considered as a kind of intervention. Participants who complete the questionnaires yearly will receive a regular feedback about their individual burnout and depression risk as well as about their sleep quality, behavioural work style, and health-related quality of life. Despite the consequence of a decrease in generalizability of our results, we decided for that strategy for the benefit of a respectable sample size. Receiving individual feedback like a regular risk assessment is expected to improve study involvement and compliance by working as a major motivator for short- and long-term participation.

For the purpose of an in-depth examination of burnout syndrome development and associated comorbidities, we developed a burnout section for a standardized clinical interview that was already successfully tested in a first pilot study with N = 94 participants (details will be published elsewhere). The burnout section was added to the DIA-X/CIDI (Wittchen & Pfister, 1997), which was modified for the DBS to be applied as computer-assisted telephone interview. Because the computer-assisted telephone interview is going to be applied all over Germany, stationary assessment of biological markers can only be assessed by biological samples that participants could assess on their own and send to our institute (hair samples and dried blood spots). Albeit after completing the clinical interview, participants are asked to send hair samples for analysis (following guidelines for assessing hair samples provided to them; see below). Prospectively, dried blood spots will be included to the assessment of the interviewed subsample.

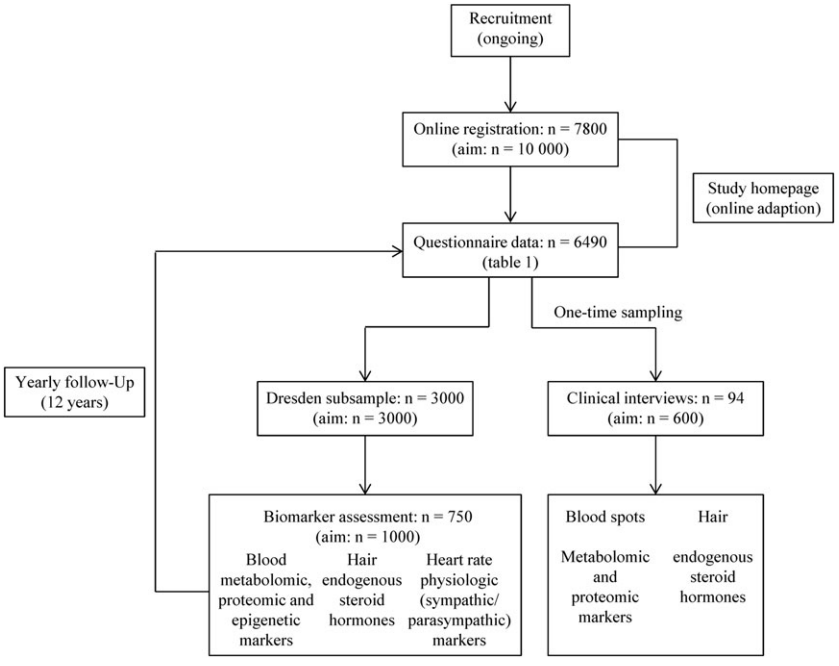

FIGURE 1 Flow chart of the prospective cohort study design of the Dresden Burnout Study

TABLE 1 Questionnaire-based measures

		Items	Scales
Burnout and related constructs			
Maslach Burnout Inventory-General Survey (Schaufeli & Leiter, 1996); German version (Büssing & Glaser, 1999)[a]	MBI-GS	16	Emotional exhaustion, cynicism, and reduced personal efficacy
Copenhagen Burnout Inventory (Kristensen, Borritz, Villadsen, & Christensen, 2005); German translation (Nübling, Stößel, Hasselhorn, Michaelis, & Hofmann, 2006)	CBI	6	Personal burnout
ICD-10 diagnose for exhaustion disorder (Söderström, Jeding, Ekstedt, Perski, & Åkerstedt, 2012)	ED	4	Exhaustion
Occupational Stress and Coping Inventory, short form (Schaarschmidt & Fischer, 1996)	AVEM	44	Four types of work-related coping behaviour: Type G (healthy ambitious), Type S (unambitious), Type A (tense), Type B (exhausted/burned out)
Work environment factors			
Copenhagen Psychosocial Questionnaire (Kristensen et al., 2005), German version (Nübling et al., 2006)	COPSOQ	44	Emotional demands, work-privacy conflict, possibilities for development, role clarity, role conflict, social support, feedback at work, social relations, sense for community, mobbing, procedural justice, and job insecurity
Effort–reward imbalance questionnaire (Siegrist et al., 2004); short form (Siegrist, Wege, Pühlhofer, & Wahrendorf, 2009)	ERI	16	Effort, reward, and overcommitment
Work–home interaction—Nijmegen (Geurts et al., 2005); German version (Nitzsche, 2011)	SWING	22	Negative work–home interaction, negative home–work interaction, positive work–home interaction, and positive home–work interaction
Individual level factors			
Big Five Inventory (John, Donahue, & Kentle, 1991); German version; short form (Rammstedt & John, 2007)	BFI-10	10	Extraversion, agreeableness, conscientiousness, neuroticism, and openness
General self-efficacy scale; German version (Schwarzer, 1993)	GSE	10	General self-efficacy
Locus of control; German short scale (Kovaleva, Beierlein, Kemper, & Rammstedt, 2012)	IE-4	4	Internal and external locus of control
Perceived Stress Questionnaire (Levenstein et al., 1993); German short version (Fliege, Rose, Arck, Levenstein, & Klapp, 2001)	PSQ	20	Worries, tension, joy, and demands
Need for cognition; German scale (Bless, Wanke, Bohner, Fellhauer, & Schwarz, 1994)	NfC	16	Need for cognition
Health-related factors and comorbidities			
Patient Health Questionnaire, German version (Kroenke, Spitzer, & Williams, 2001)[a]	PHQ-9	9	Depressive disorder and screening
Generalized Anxiety Disorder Scale (Spitzer, Kroenke, Williams, & Löwe, 2006), German version (Löwe et al., 2008)[a]	GAD-7	7	General anxiety disorder and screening
SF-36 health survey (Ware & Sherbourne, 1992), German translation (Bullinger, Kirchberger, & Ware, 1995)	SF-36	36	Physical functioning, role limitations because of physical health problems, bodily pain, social functioning, general mental health, role limitations because of emotional problems, vitality, and general health perception
Pittsburg Sleep Quality Index, German translation (Backhaus, Junghanns, Broocks, Riemann, & Hohagen, 2002)	PSQ-I	24	Subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction

[a]Questionnaire is part of the online assessment as well as of laboratory session.

For assessment of biological markers of burnout, Dresden participants were invited for a first biomarker collection of hair samples, blood samples, and heart rate measures in autumn 2015 with a second study wave in autumn 2016. Follow-ups will be repeated annually during a comparable time window, to avoid seasonal effect confounding (Foster & Roenneberg, 2008).

2.4.1 | Biomarker sampling procedure

All Dresden participants (including Samples 1 and 2) are invited via email to participate at the laboratory session for biomarker assessment. The email gives a brief process description, an estimate for duration, and information about monetary compensation. After receiving the email, participants can choose day and time for a study appointment via a calendar through the study homepage.

The laboratory session includes reception and clarification, informed consent, biomarker sampling, and completion of a set of questionnaires (see Table 2). The approximate duration of procedure is 45 min. Figure 2 provides an overview of procedure and temporal sequence during the laboratory session.

2.5 | Self-report measures

The DBS is the first prospective cohort study to assess burnout by using a variety of validated burnout questionnaires (see also Table 2). The Maslach Burnout Inventory-General Survey (Büssing & Glaser, 1999) was selected because of its importance for systematic burnout research. The 16 items score on three subscales (emotional exhaustion, cynicism, and reduced personal efficacy). The response format for each item is a 7-point Likert scale with frequency ratings, ranging from 0 (*never*) to 6 (*daily*). Next, the personal burnout scale of the Copenhagen Burnout Inventory (Kristensen et al., 2005) was added as further burnout estimate, which assesses burnout free from a concrete work context. The Copenhagen Burnout Inventory scale comprises six items scoring on a 5-point Likert scale with frequency ratings from 1 (*never/almost never*) to 5 (*always*). As a third burnout measure, with reference to the Swedish burnout diagnosis (Beser et al., 2014), ICD-10 diagnostic criteria for exhaustion disorder are assessed as part of the DBS. More precisely, syndrome specificities are prompted employing four questions, taken from Söderström et al. (2012).

Finally, for the measurement of job-related experience and associated behaviour outcomes, the 44-item short form of the Occupational Stress and Coping Inventory (Schaarschmidt & Fischer, 1996) was included. All items score on a 5-point rating scale (1 = *completely disagree*, 5 = *completely agree*). The Occupational Stress and Coping Inventory sum score allows the allocation to one of four patterns of work-related coping behaviour (Type G = healthy ambitious, Type S = unambitious, Type A = tense, Type B = exhausted/resigned), based on the maximal alignment with one's individual profile. The risk Type A in its pure manifestation describes a person who "burns" for its work, whereas the second risk Type B can be considered as "burned out" at work (Schaarschmidt, 2006).

The decision to include a variety of burnout measures in the online assessment is rooted in growing criticism about the current standard to assess burnout solely on basis of the Maslach Burnout Inventory. Critical aspects are, for example, the lack of clinical validity (Kleijweg, Verbraak, & Van Dijk, 2013), a tautological syndrome definition (Kristensen et al., 2005), and considerable overlap with other syndromes or general exhaustion (Maslach & Leiter, 2016a). By a simultaneous assessment of alternative burnout measures, we aim to extract key factors that describe the burnout syndrome on the continuum between mild and clinical burnout and demarcate it from related diseases. For an assessment of comorbidities and/or overlaps, screening questionnaires for related diseases was included as well as general health measures. Furthermore, instruments assessing the work environment and individual trait and state factors were included, based on validity and comparability considerations.

TABLE 2 Demographic, health-related, and clinical characteristics for the sample of the Dresden Burnout Study (N = 7,058; all registered participants)

	M^a	Range
Age (years)	41.0 (11.5)	18–72
Sex (% female)	63.0	
BMI (kg/m^2)	25.5 (5.1)	13.1–52.0
Underweight (%; BMI < 18.5)	2.4	
Normal (%; BMI 18.5–24.9)	51.6	
Overweight (%; BMI 25–29.9)	29.0	
Obesity (%; BMI ≥ 30)	16.1	
Married/leaving with partner (%)	43.4	
Divorced (%)	5.7	
Currently employed (%)	89.0	
Main earner (%)	54.5	
Working hours/week	40.2 (10.9)	0.0–80.0
Additional side-job (%)	17.3	
Shift work (%)	14.0	
University degree (%)	52.4	
Income >2,000 € (net, %)	46.8	
Income <1,000 € (net, %)	16.4	
Current smokers (%)	23.1	
Duration smoking (years)	17.6	0.0–50.0
Constant medication (all, %)	45.1	
Burnout diagnose (lifetime, %)[b]	17.5	
MBI	2.4 (1.1)	0.0–6.0
PHQ-9	8.6 (5.5)	0.0–27.0
GAD-7	6.9 (4.9)	0.0–21.0

Note. Standard deviations are in parentheses. BMI = body mass index; MBI = Maslach Burnout Inventory-General Survey total score; PHQ-9 = Patient Health Questionnaire sum score; GAD-7 = Generalized Anxiety Disorder 7.

[a]Means and standard deviations in parentheses for metric measures; percentages for categorical measures.

[b]Phrasing: "Did a medical doctor or psychotherapist ever made you the diagnosis 'burnout'?"

2.6 | Assessment of biological burnout markers

2.6.1 | Endocrine biomarkers

The DBS involves annual assessments of different steroid hormones, for example, cortisol, cortisone, testosterone, progesterone, dehydroepiandrosterone, and estradiol, from hair and blood serum specimens. Hair steroid analyses comprise a recently developed method that allows capturing stress-related changes in long-term patterns of hormone secretion (Stalder et al., 2017).

For hormone extraction from hair, strains are cut scalp-near at posterior vertex position. Hormones are determined from the 3-cm segment most proximal to the scalp as an index of cumulative output over the preceding 3-month period (Stalder et al., 2012) and quantified

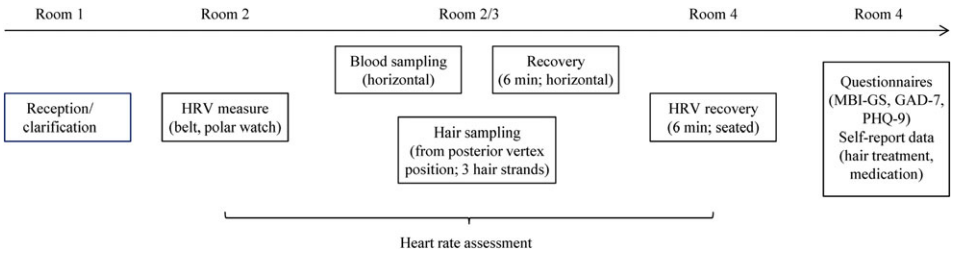

FIGURE 2 Flow chart of laboratory session for biomarker sampling. HRV = heart rate variability; MBI-GS = Maslach Burnout Inventory-General Survey; PHQ-9 = Patient Health Questionnaire; GAD-7 = Generalized Anxiety Disorder 7

using gold-standard liquid-chromatography tandem mass spectrometry approach (Gao, Kirschbaum, Grass, & Stalder, 2016; Gao et al., 2013).

2.6.2 | Immunologic biomarkers

The HPA axis regulates the availability of GCs, which in turn interact with immune parameters. As a consequence, due to the stress reactiveness of the HPA axis, immune functions can be influenced by chronic stress conditions (Dhabhar, 2014; Dhabhar & Mcewen, 1997; Glaser & Kiecolt-Glaser, 2005). This also indicates that immune parameters are likely to be sensitive to the conditions of burnout (Hänsel et al., 2010). In the DBS, immune parameters are annually collected via EDTA blood tubes. With the longitudinal assessment of immune parameters, we aim to further explore the link between burnout and disease processes, including the potential shift from immune competence to immune suppression (Dhabhar, 2014) that could accompany this condition.

2.6.3 | Physiologic biomarkers

Given that the ANS is known to be primarily involved in the regulation of stress reactivity, astonishingly, little research has been carried out investigating burnout associated alterations in autonomic function. HRV, defined as beat-to-beat variations in the timing of heart beats, is used in the DBS to examine the role of the ANS in burnout diseases. More precisely, interbeat intervals are recorded with a Polar RS800 CX system via the corresponding chest belt (Polar Electro OY, Kempele, Finland) from all participants during biomarker sampling procedures. Data are transferred to the Polar Precision Performance Software (Polar Electro OY, Kempele, Finland) and subsequently artefact-corrected according to the guidelines of the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996).

On grounds of previous findings that certain dysregulations in biological systems become evident only under specific experimental conditions (Kudielka & Wüst, 2010), HRV is analysed during different measurement occasions, namely, an emotionally arousing situation (blood sampling), a recumbent recovery period directly after blood sampling, and a seated resting condition (6 min each).

2.6.4 | Genetic and epigenetic biomarkers

Several relevant candidate genetic variations for burnout have been identified by genome wide association studies such as in the melatonin receptor 1A gene or in the intron of uronyl-2-sulfotransferase (rs13219957; Sulkava et al., 2013, 2017). These results provide promising avenues to better identify people with an increased susceptibility for burnout and corresponding allocations to prevention programs. Furthermore, epigenetic analyses will be conducted focusing on the glucocorticoid receptor gene (NR3C1) and brain-derived neurotrophic factor, which have been reported to display different methylation patterns in chronic stress and depression, whereas the serotonin transporter gene (SLC6A4) methylation was similarly affected by chronic stress, burnout, and depression (Bakusic et al., 2017). Therefore, the longitudinal prospective assessment of changes in methylation patterns of key genes in large samples is needed to clarify the role of epigenetic regulation in burnout.

2.7 | Why focusing on the assessment of biomarkers of burnout?

Even if previous studies suggest physiological alterations to be involved in burnout, a ground base for specific biomarkers is still missing. Most results are single findings and lack comparability and replication. The majority of biomarker-based burnout studies assessed endocrine alterations, mainly on level of the HPA axis, but with huge variability in study protocols. Summarizing up to date, there is no biomarker that can be considered as prime candidate in burnout research (Danhof-Pont et al., 2011). On the other hand, there is sound evidence that burnout enters the body somehow and acts as a risk factor for physical illness, for example, cardiovascular disease (Toker et al., 2012), Type 2 diabetes (Melamed, Shirom, Toker, & Shapira, 2006), vascular dementia (Andel et al., 2012), and a shortened life cycle (Ahola, Väänänen, Koskinen, Kouvonen, & Shirom, 2010). Furthermore, decades of stress research provide a solid ground for potential pathways of stress/body interactions (e.g., Dhabhar, 2014; Glaser & Kiecolt-Glaser, 2005; Kudielka, Schommer, Hellhammer, & Kirschbaum, 2004; Miller et al., 2007; Rohleder, 2012), and even if a standardized definition and diagnose for the burnout syndrome is still missing (Kaschka et al., 2011), there is no doubt that burnout sufferers experience a significant level of stress. A major challenge in the search of burnout biomarkers is the anticipated overlap with other syndromes. Together with a close self-report assessment, we aim to find patterns of psychological and biological data that are specific for burnout and distinguishable from other syndromes (e.g., depression) or general exhaustion (Maslach & Leiter, 2016a). In line with Maslach and Leiter (2016b), we expect that burnout is not just an equivalent of exhaustion and aim to evaluate potential burnout patterns with specific biological outcomes.

3 | RESULTS

The DBS started in January 2015. Since then, data are consecutively generated. Initial cross-sectional analysis of the DBS data supports the idea of burnout-associated autonomic dysfunction, indicated by reduced vagally mediated HRV in individuals with elevated burnout symptomatology (Kanthak et al., 2017). Upcoming analysis of longitudinal data will give further insight into the replicability and questions of causality regarding the observed effect. Recently published data on associations between hair cortisol concentrations (HCC) and burnout symptomatology by Penz et al. (2018) suggest alterations on level of the HPA axis. Burnout measured with a dichotomous classifier (high versus no/medial burnout symptomatology) was positively related to HCC, indicating hypercortisolism in individuals who suffer from chronic stress in burnout.

As the DBS is still in its initial stage, no longitudinal data are currently available. First cross-sectional analyses focused solely on potential burnout biomarkers, as the DBS declares its emphasis on the research of physiological consequences of burnout or work-related stress. Indeed, within the following months, baseline and follow-up questionnaire data will be available and will provide first insight in risk and health factors, overlaps, patterns, and comorbidities.

Longitudinal biomarker and online questionnaire data will provide a sound basis for understanding the burnout syndrome with specific antecedents and consequences. The collected data will help to clarify if burnout is a syndrome by its own, with syndrome specific symptomatology, and specific treatment requirements, or rather a new word for already well established diseases (e.g., depression or chronic fatigue syndrome).

4 | DISCUSSION

The DBS aims to close the empirical gap between myth, unstandardized, intuitive clinical practice and personal opinions about burnout syndrome on the one hand, and the detrimental consequences that this condition is likely to have for a number of individuals on the other hand. The aim is a longitudinal assessment of a potential burnout development on symptom and syndrome level, with a synchronous monitoring of biological markers that might precede, co-occur, or follow a burnout development. Annual assessment waves over 12 years provide a unique opportunity to investigate burnout symptom trajectories in relation to underlying neurobiological changes. This should further provide a sound basis for preventive policies and treatment of the burnout syndrome. Ensuing advancements in the prediction of burnout risk and course will further enable a more accurate handling and resource allocation in the early stages of this condition. For example, the identification of potential biological markers of burnout could complement screening options for burnout susceptibility and help to validate diagnosis. Thus, given the large sample size and the prospective-longitudinal study design, this study might pave the road for a comprehensive characterization of burnout and potential internationally accepted burnout diagnosis.

ACKNOWLEDGEMENTS

This work was supported by the TU Dresden's Institutional Strategy ("The Synergetic University"), which is funded by the Excellence Initiative of the German Federal and State Governments. Funders were not involved in design, collection, analysis, interpretation, and publication decisions of the data. We acknowledge Prof. Dr. Nina Alexander, Prof. Dr. Angelika Buske-Kirschbaum, and Prof. Dr. Jürgen Hoyer for their valuable help regarding the design and the conduction of the Dresdner Burnout Study.

CONFLICTS OF INTEREST

There are no conflicts of interest.

ORCID

Marlene Penz http://orcid.org/0000-0002-9436-7190

REFERENCES

Ahola, K., Honkonen, T., Isometsä, E., Kalimo, R., Nykyri, E., Aromaa, A., & Lönnqvist, J. (2005). The relationship between job-related burnout and depressive disorders—Results from the Finnish Health 2000 Study. *Journal of Affective Disorders*, *88*(1), 55–62. https://doi.org/10.1016/j.jad.2005.06.004

Ahola, K., Väänänen, A., Koskinen, A., Kouvonen, A., & Shirom, A. (2010). Burnout as a predictor of all-cause mortality among industrial employees: a 10-year prospective register-linkage study. *Journal of Psychosomatic Research*, *69*(1), 51–57. https://doi.org/10.1016/j.jpsychores.2010.01.002

Alarcon, G., Eschleman, K. J., & Bowling, N. A. (2009). Relationships between personality variables and burnout: A meta-analysis. *Work & Stress*, *23*(3), 244–263. https://doi.org/10.1080/02678370903282600

American Psychiatric Association (2013). *Diagnostic and statistical manual of mental disorders (DSM-5®)*. American Psychiatric Pub.

Andel, R., Crowe, M., Hahn, E. A., Mortimer, J. A., Pedersen, N. L., Fratiglioni, L., … Gatz, M. (2012). Work-related stress may increase the risk of vascular dementia. *Journal of the American Geriatrics Society*, *60*(1), 60–67. https://doi.org/10.1111/j.1532-5415.2011.03777

Backhaus, J., Junghanns, K., Broocks, A., Riemann, D., & Hohagen, F. (2002). Test–retest reliability and validity of the Pittsburgh Sleep Quality Index in primary insomnia. *Journal of Psychosomatic Research*, *53*(3), 737–740. https://doi.org/10.1016/S0022-3999(02)00330-6

Bakusic, J., Schaufeli, W., Claes, S., & Godderis, L. (2017). Stress, burnout and depression : A systematic review on DNA methylation mechanisms. *Journal of Psychosomatic Research*, *92*, 34–44. https://doi.org/10.1016/j.jpsychores.2016.11.005

Beser, A., Sorjonen, K., Wahlberg, K., Peterson, U., Nygren, A., & Asberg, M. (2014). Construction and evaluation of a self rating scale for stress-induced Exhaustion Disorder, the Karolinska Exhaustion Disorder Scale. *Scandinavian Journal of Psychology*, *55*(1), 72–82. https://doi.org/10.1111/sjop.12088

Bianchi, R., Boffy, C., Hingray, C., Truchot, D., & Laurent, E. (2013). Comparative symptomatology of burnout and depression. *Journal of Health Psychology*, *18*(6), 782–787. https://doi.org/10.1177/1359105313481079

Bianchi, R., Schonfeld, I. S., & Laurent, E. (2015). Burnout-depression overlap: A review. *Clinical Psychology Review*, *36*, 28–41. https://doi.org/10.1016/j.cpr.2015.01.004

Bless, H., Wanke, M., Bohner, G., Fellhauer, R., & Schwarz, N. (1994). Need for cognition—A scale measuring engagement and hapiness in cognitive tasks. *Zeitschrift fuer Sozialpsychologie*, *25*(2), 147–154.

Blom, V., Bergström, G., Hallsten, L., Bodin, L., & Svedberg, P. (2012). Genetic susceptibility to burnout in a Swedish twin cohort. *European*

Journal of Epidemiology, *27*, 225–231. https://doi.org/10.1007/s10654-012-9661-2

Borritz, M., Christensen, K. B., Bültmann, U., Rugulies, R., Lund, T., Andersen, I., … Kristensen, T. S. (2010). Impact of burnout and psychosocial work characteristics on future long-term sickness absence. Prospective results of the Danish PUMA Study among human service workers. *Journal of Occupational and Environmental Medicine*, *52*(10), 964–970. https://doi.org/10.1097/JOM.0b013e3181f12f95

Bullinger, M., Kirchberger, I., & Ware, J. (1995). Der deutsche SF-36 health survey. Übersetzung und psychometrische Testung eines krankheitsübergreifenden Instruments zur Erfassung der gesundheitsbezogenen Lebensqualität. *Zeitschrift für Gesundheitswissenschaften= Journal of public health*, *3*(1), 21–36.

Büssing, A., & Glaser, J. (1999). *Deutsche Fassung des Maslach Burnout Inventory—General survey (MBI-GS-D)*. München: Technische Universität, Lehrstuhl für Psychologie.

Danhof-Pont, M. B., van Veen, T., & Zitman, F. G. (2011). Biomarkers in burnout: A systematic review. *Journal of Psychosomatic Research*, *70*(6), 505–524. https://doi.org/10.1016/j.jpsychores.2010.10.012

de Vente, W., van Amsterdam, J. G., Olff, M., Kamphuis, J. H., & Emmelkamp, P. M. (2015). Burnout is associated with reduced parasympathetic activity and reduced HPA axis responsiveness, predominantly in males. *BioMed Research International*, *2015*, 1–13. https://doi.org/10.1155/2015/431725

Deligkaris, P., Panagopoulou, E., Montgomery, A. J., & Masoura, E. (2014). Job burnout and cognitive functioning: A systematic review. *Work & Stress*, *28*(2), 107–123. https://doi.org/10.1080/02678373.2014.909545

Dhabhar, F. S. (2014). Effects of stress on immune function: The good, the bad, and the beautiful. *Immunologic Research*, *58*(2–3), 193–210. https://doi.org/10.1007/s12026-014-8517-0

Dhabhar, F. S., & Mcewen, B. S. (1997). Acute stress enhances while chronic stress suppresses cell-mediated immunityin vivo: A potential role for leukocyte trafficking. *Brain, Behavior, and Immunity*, *11*(4), 286–306. https://doi.org/10.1006/brbi.1997.0508

Evolahti, A., Hultell, D., & Collins, A. (2013). Development of burnout in middle-aged working women: A longitudinal study. *Journal of Women's Health*, *22*(1), 94–103. https://doi.org/10.1089/jwh.2012.3507

Fliege, H., Rose, M., Arck, P., Levenstein, S., & Klapp, B. (2001). Validierung des "Perceived Stress Questionnaire" (PSQ) an einer deutschen Stichprobe. *Diagnostica*, *47*(3), 142–152. https://doi.org/10.23668/psycharchives.351

Foster, R. G., & Roenneberg, T. (2008). Human responses to the geophysical daily, annual and lunar cycles. *Current Biology*, *18*(17), R784–R794. https://doi.org/10.1016/j.cub.2008.07.003

Gao, W., Kirschbaum, C., Grass, J., & Stalder, T. (2016). LC–MS based analysis of endogenous steroid hormones in human hair. *The Journal of Steroid Biochemistry and Molecular Biology*, *162*, 92–99. https://doi.org/10.1016/j.jsbmb.2015.12.022

Gao, W., Stalder, T., Foley, P., Rauh, M., Deng, H., & Kirschbaum, C. (2013). Quantitative analysis of steroid hormones in human hair using a column-switching LC–APCI–MS/MS assay. *Journal of Chromatography B*, *928*, 1–8. https://doi.org/10.1016/j.jchromb.2013.03.008

Geurts, S. A., Taris, T. W., Kompier, M. A., Dikkers, J. S., Van Hooff, M. L., & Kinnunen, U. M. (2005). Work-home interaction from a work psychological perspective: Development and validation of a new questionnaire, the SWING. *Work & Stress*, *19*(4), 319–339. https://doi.org/10.1080/02678370500410208

Glaser, R., & Kiecolt-Glaser, J. K. (2005). Stress-induced immune dysfunction: Implications for health. *Nature Reviews Immunology*, *5*(3), 243–251. https://doi.org/10.1038/nri1571

Grossi, G., Perski, A., Evengård, B., Blomkvist, V., & Orth-Gomér, K. (2003). Physiological correlates of burnout among women. *Journal of Psychosomatic Research*, *55*(4), 309–316. https://doi.org/10.1016/S0022-3999(02)00633-5

Grossi, G., Perski, A., Osika, W., & Savic, I. (2015). Stress-related exhaustion disorder—Clinical manifestation of burnout? A review of assessment methods, sleep impairments, cognitive disturbances, and neuro-biological and physiological changes in clinical burnout. *Scandinavian Journal of Psychology*, *56*(6), 626–636. https://doi.org/10.1111/sjop.12251

Grossi, G., Theorell, T., Jürisoo, M., & Setterlind, S. (1999). Psychophysiological correlates of organizational change and threat of unemployment among police inspectors. *Integrative Physiological and Behavioral Science*, *34*(1), 30–42. https://doi.org/10.1007/BF02688708

Hakanen, J. J., & Schaufeli, W. B. (2012). Do burnout and work engagement predict depressive symptoms and life satisfaction? A three-wave seven-year prospective study. *Journal of Affective Disorders*, *141*(2), 415–424. https://doi.org/10.1016/j.jad.2012.02.043

Hänsel, A., Hong, S., Cámara, R. J., & Von Kaenel, R. (2010). Inflammation as a psychophysiological biomarker in chronic psychosocial stress. *Neuroscience & Biobehavioral Reviews*, *35*(1), 115–121. https://doi.org/10.1016/j.neubiorev.2009.12.012

Huibers, M., Beurskens, A., Prins, J., Kant, I., Bazelmans, E., Van Schayck, C., … Bleijenberg, G. (2003). Fatigue, burnout, and chronic fatigue syndrome among employees on sick leave: Do attributions make the difference? *Occupational and Environmental Medicine*, *60*(suppl 1), i26–i31. https://doi.org/10.1136/oem.60.suppl_1.i26

Jarczok, M. N., Jarczok, M., Mauss, D., Koenig, J., Li, J., Herr, R. M., & Thayer, J. F. (2013). Autonomic nervous system activity and workplace stressors—A systematic review. *Neuroscience & Biobehavioral Reviews*, *37*(8), 1810–1823. https://doi.org/10.1016/j.neubiorev.2013.07.004

John, O. P., Donahue, E. M., & Kentle, R. L. (1991). *The big five inventory—Versions 4a and 54*. Berkeley, CA: University of California, Berkeley, Institute of Personality and Social Research.

Jönsson, P., Österberg, K., Wallergård, M., Hansen, Å. M., Garde, A. H., Johansson, G., & Karlson, B. (2015). Exhaustion-related changes in cardiovascular and cortisol reactivity to acute psychosocial stress. *Physiology & Behavior*, *151*, 327–337. https://doi.org/10.1016/j.physbeh.2015.07.020

Kanthak, M. K., Stalder, T., Hill, L., Thayer, J. F., Penz, M., & Kirschbaum, C. (2017). Autonomic dysregulation in burnout and depression: Evidence for the central role of exhaustion. *Scandinavian Journal of Work, Environment & Health*, in press. DOI: https://doi.org/10.5271/sjweh.3647, *43*, 475–484.

Kaschka, W. P., Korczak, D., & Broich, K. (2011). Burnout: A fashionable diagnosis. *Deutsches Ärzteblatt International*, *108*(46), 781–787. https://doi.org/10.3238/arztebl.2011.0781

Kleijweg, J. H. M., Verbraak, M. J. P. M., & Van Dijk, M. K. (2013). The clinical utility of the Maslach Burnout Inventory in a clinical population. *Psychological Assessment*, *25*, 435–441. https://doi.org/10.1037/a0031334

Kocalevent, R. D., Klapp, B. F., Albani, C., & Brähler, E. (2013). Zusammenhänge von Ressourcen, chronisch aktiviertem Distress und Erschöpfung in der deutschen Allgemeinbevölkerung. *PPmP-Psychotherapie· Psychosomatik· Medizinische Psychologie*, *63*(03/04), 115–121. https://doi.org/10.1055/s-0032-1327705

Korczak, D., Huber, B., & Kister, C. (2010). Differential diagnostic of the burnout syndrome. *GMS Health Technology Assessment*, *6*. https://doi.org/10.3205/hta000087

Korczak, D., Kister, C., & Huber, B. (2008). *Differentialdiagnostik des Burnout-Syndroms*. Köln: Deutsches Institut für Medizinische Dokumentation und Information.

Kovaleva, A., Beierlein, C., Kemper, C., & Rammstedt, B. (2012). *Eine Kurzskala zur Messung von Kontrollüberzeugung: Die Skala Internale-Externale-Kontrollüberzeugung-4 (IE-4)*. Mannheim: GESIS-Leipniz Institut für Sozialwissenschaften. Retrieved: http://nbn-resolving.de/urn:nbn:de:0168-ssoar-312096

Kristensen, T. S., Borritz, M., Villadsen, E., & Christensen, K. B. (2005). The Copenhagen Burnout Inventory: A new tool for the assessment of

burnout. *Work & Stress*, *19*(3), 192–207. https://doi.org/10.1080/02678370500297720

Kroenke, K., Spitzer, R. L., & Williams, J. B. (2001). The Phq-9. *Journal of General Internal Medicine*, *16*(9), 606–613. https://doi.org/10.1046/j.1525-1497.2001.016009606.x

Kudielka, B. M., Schommer, N. C., Hellhammer, D. H., & Kirschbaum, C. (2004). Acute HPA axis responses, heart rate, and mood changes to psychosocial stress (TSST) in humans at different times of day. *Psychoneuroendocrinology*, *29*(8), 983–992. https://doi.org/10.1016/j.psyneuen.2003.08.009

Kudielka, B. M., & Wüst, S. (2010). Human models in acute and chronic stress: Assessing determinants of individual hypothalamus–pituitary–adrenal axis activity and reactivity. *Stress*, *13*, 1–14. https://doi.org/10.3109/10253890902874913

Leiter, M. P., Hakanen, J. J., Ahola, K., Toppinen-Tanner, S., Koskinen, A., & Väänänen, A. (2013). Organizational predictors and health consequences of changes in burnout: A 12-year cohort study. *Journal of Organizational Behavior*, *34*(7), 959–973. https://doi.org/10.1002/job.1830

Leka, S., & Jain, A. (2010). *Health impact of psychosocial hazards at work: An overview*. Geneva: World Helath Organisation. Retrieved from http://apps.who.int/iris/bitstream/10665/44428/1/9789241500272_eng.pdf

Lennartsson, A.-K., Billig, H., & Jonsdottir, I. H. (2014). Burnout is associated with elevated prolactin levels in men but not in women. *Journal of Psychosomatic Research*, *76*(5), 380–383. https://doi.org/10.1016/j.jpsychores.2014.03.007

Leone, S. S., Wessely, S., Huibers, M. J., Knottnerus, J. A., & Kant, I. (2011). Two sides of the same coin? On the history and phenomenology of chronic fatigue and burnout. *Psychology and Health*, *26*(4), 449–464. https://doi.org/10.1080/08870440903494191

Levenstein, S., Prantera, C., Varvo, V., Scribano, M. L., Berto, E., Luzi, C., & Andreoli, A. (1993). Development of the Perceived Stress Questionnaire: A new tool for psychosomatic research. *Journal of Psychosomatic Research*, *37*(1), 19–32. https://doi.org/10.1016/0022-3999(93)90120-5

Lindwall, M., Gerber, M., Jonsdottir, I. H., Börjesson, M., & Ahlborg, G. Jr. (2014). The relationships of change in physical activity with change in depression, anxiety, and burnout: A longitudinal study of Swedish healthcare workers. *Health Psychology*, *33*(11), 1309–1318. https://doi.org/10.1037/a0034402

Löwe, B., Decker, O., Müller, S., Brähler, E., Schellberg, D., Herzog, W., & Herzberg, P. Y. (2008). Validation and standardization of the Generalized Anxiety Disorder Screener (GAD-7) in the general population. *Medical Care*, *46*(3), 266–274. https://doi.org/10.1097/MLR.0b013e318160d093

Maslach, C., & Jackson, S. E. (1981). The measurement of experienced burnout. *Journal of Occupational Behaviour*, *2*(2), 99–113. https://doi.org/10.1002/job.4030020205

Maslach, C., & Leiter, M. (2016a). Latent burnout profiles: A new approach to understanding the burnout experience. *Burnout Research*, *3*(4), 89–100. https://doi.org/10.1016/j.burn.2016.09.001

Maslach, C., Schaufeli, W. B., & Leiter, M. P. (2001). Job burnout. *Annual Review of Psychology*, *52*(1), 397–422. https://doi.org/10.1146/annurev.psych.52.1.397

Maslach, C., & Leiter, M. (2016b). Understanding the burnout experience: Recent research and its implication for psychiatry. *World Psychiatry*, *15*(2), 103–111. https://doi.org/10.1002/wps.20311

Mather, L., Bergström, G., Blom, V., & Svedberg, P. (2014). The covariation between burnout and sick leave due to mental disorders is explained by a shared genetic liability: A prospective Swedish Twin Study with a five-year follow-up. *Twin Research and Human Genetics*, *17*(6), 535–544. https://doi.org/10.1017/thg.2014.46

Melamed, S., Shirom, A., Toker, S., & Shapira, I. (2006). Burnout and risk of type 2 diabetes: A prospective study of apparently healthy employed persons. *Psychosomatic Medicine*, *68*(6), 863–869. https://doi.org/10.1097/01.psy.0000242860.24009.f0

Middeldorp, C. M., Cath, D. C., & Boomsma, D. I. (2006). A twin-family study of the association between employment, burnout and anxious depression. *Journal of Affective Disorders*, *90*(2), 163–169. https://doi.org/10.1016/j.jad.2005.11.004

Miller, G. E., Chen, E., & Zhou, E. S. (2007). If it goes up, must it come down? Chronic stress and the hypothalamic-pituitary-adrenocortical axis in humans. *Psychological Bulletin*, *133*(1), 25–45. https://doi.org/10.1037/0033-2909.133.1.25

Mommersteeg, P. M., Heijnen, C. J., Kavelaars, A., & van Doornen, L. J. (2006). Immune and endocrine function in burnout syndrome. *Psychosomatic Medicine*, *68*(6), 879–886. https://doi.org/10.1097/01.psy.0000239247.47581.0c

Mommersteeg, P. M., Heijnen, C. J., Verbraak, M. J., & van Doornen, L. J. (2006a). Clinical burnout is not reflected in the cortisol awakening response, the day-curve or the response to a low-dose dexamethasone suppression test. *Psychoneuroendocrinology*, *31*(2), 216–225. https://doi.org/10.1016/j.psyneuen.2005.07.003

Mommersteeg, P. M., Heijnen, C. J., Verbraak, M. J., & van Doornen, L. J. (2006b). A longitudinal study on cortisol and complaint reduction in burnout. *Psychoneuroendocrinology*, *31*(7), 793–804. https://doi.org/10.1016/j.psyneuen.2006.03.003

Nitzsche, A. (2011). *German translation of the SWING-scale*. Köln: IMVR der Universität zu Köln.

Nübling, M., Stößel, U., Hasselhorn, H.-M., Michaelis, M., & Hofmann, F. (2006). Measuring psychological stress and strain at work: Evaluation of the COPSOQ Questionnaire in Germany. *GMS Psycho-Social Medicine*, *3*. Retrieved: http://www.egms.de/en/journals/psm/2006-3/psm000025.shtml

Oosterholt, B. G., Maes, J. H., Van der Linden, D., Verbraak, M. J., & Kompier, M. A. (2015). Burnout and cortisol: Evidence for a lower cortisol awakening response in both clinical and non-clinical burnout. *Journal of Psychosomatic Research*, *78*(5), 445–451. https://doi.org/10.1016/j.jpsychores.2014.11.003

Oosterholt, B. G., Maes, J. H., Van der Linden, D., Verbraak, M. J., & Kompier, M. A. (2016). Getting better, but not well: A 1.5 year follow-up of cognitive performance and cortisol levels in clinical and non-Clinical burnout. *Biological Psychology*, *117*, 89–99. https://doi.org/10.1016/j.biopsycho.2016.02.009

Penz, M., Stalder, T., Miller, R., Ludwig, V. M., Kanthak, M. K., & Kirschbaum, C. (2018). Hair cortisol as a biological marker for burnout symptomatology. *Psychoneuroendocrinology*, *87*, 218–221. https://doi.org/10.1016/j.psyneuen.2017.07.485

Rammstedt, B., & John, O. P. (2007). Measuring personality in one minute or less: A 10-item short version of the Big Five Inventory in English and German. *Journal of Research in Personality*, *41*(1), 203–212. https://doi.org/10.1016/j.jrp.2006.02.001

Rohleder, N. (2012). Acute and chronic stress induced changes in sensitivity of peripheral inflammatory pathways to the signals of multiple stress systems—2011 Curt Richter Award Winner. *Psychoneuroendocrinology*, *37*(3), 307–316. https://doi.org/10.1016/j.psyneuen.2011.12.015

Rohleder, N. (2014). Stimulation of systemic low-grade inflammation by psychosocial stress. *Psychosomatic Medicine*, *76*(3), 181–189. https://doi.org/10.1097/PSY.0000000000000049

Schaarschmidt, U. (2006). AVEM: Ein Instrument zur interventionsbezogenen Diagnostik beruflichen Bewältigungsverhaltens. In Arbeitskreis Klinische Psychologie in der Rehabilitation BDP (Hrsg.). In *Psychologische Diagnostik-Weichenstellung für den Reha-Verlauf* (pp. 59–82). Bonn: Deutscher Psychologen Verlag GmbH.

Schaarschmidt, U., & Fischer, A. (1996). *Arbeitsbezogenes Verhaltens-und Erlebensmuster*. Swets Test Services: Frankfurt a. M.

Schaufeli, W. B., & Leiter, M. P. (1996). Maslach burnout inventory-general survey. *The Maslach burnout inventory-test manual*, *1*, 19–26.

Schaufeli, W. B., Leiter, M. P., & Maslach, C. (2009). Burnout: 35 years of research and practice. *Career Development International*, *14*(3), 204–220. https://doi.org/10.1108/13620430910966406

Schonfeld, I. S., & Bianchi, R. (2015). Burnout and depression: Two entities or one? *Journal of Clinical Psychology*, *36*, 28–41. https://doi.org/10.1002/jclp.22229

Schwarzer, R. (1993). *Measurement of perceived self-efficacy: Psychometric scales for cross-cultural research*. Berlin, Germany: Freie Universität Berlin.

Seidler, A., Thinschmidt, M., Deckert, S., Then, F., Hegewald, J., Nieuwenhuijsen, K., & Riedel-Heller, S. G. (2014). The role of psychosocial working conditions on burnout and its core component emotional exhaustion-a systematic review. *Journal of Occupational Medicine and Toxicology*, *9*(1), 10. https://doi.org/10.1186/1745-6673-9-10

Shirom, A., & Melamed, S. (2006). A comparison of the construct validity of two burnout measures in two groups of professionals. *International Journal of Stress Management*, *13*(2), 176–200. https://doi.org/10.1037/1072-5245.13.2.176

Siegrist, J., Starke, D., Chandola, T., Godin, I., Marmot, M., Niedhammer, I., & Peter, R. (2004). The measurement of effort–reward imbalance at work: European comparisons. *Social Science & Medicine*, *58*(8), 1483–1499. https://doi.org/10.1016/S0277-9536(03)00351-4

Siegrist, J., Wege, N., Pühlhofer, F., & Wahrendorf, M. (2009). A short generic measure of work stress in the era of globalization: Effort–reward imbalance. *International Archives of Occupational and Environmental Health*, *82*(8), 1005–1013. https://doi.org/10.1007/s00420-008-0384-3

Söderström, M., Jeding, K., Ekstedt, M., Perski, A., & Åkerstedt, T. (2012). Insufficient sleep predicts clinical burnout. *Journal of Occupational Health Psychology*, *17*(2), 175–183. https://doi.org/10.1037/a0027518

Spitzer, R. L., Kroenke, K., Williams, J. B., & Löwe, B. (2006). A brief measure for assessing generalized anxiety disorder: The GAD-7. *Archives of Internal Medicine*, *166*(10), 1092–1097. https://doi.org/10.1001/archinte.166.10.1092

Stalder, T., Steudte, S., Miller, R., Skoluda, N., Dettenborn, L., & Kirschbaum, C. (2012). Intraindividual stability of hair cortisol concentrations. *Psychoneuroendocrinology*, *37*(5), 602–610. https://doi.org/10.1016/j.psyneuen.2011.08.007

Stalder, T., Steudte-Schmiedgen, S., Alexander, N., Klucken, T., Vater, A., Wichmann, S., … Miller, R. (2017). Stress-related and basic determinants of hair cortisol in humans: A meta-analysis. *Psychoneuroendocrinology*, *77*, 261–274. https://doi.org/10.1016/j.psyneuen.2016.12.017

Sulkava, S., Ollila, H. M., Ahola, K., Partonen, T., Viitasalo, K., Vahtera, J., et al. (2013). Genome-wide scan of job-related exhaustion with three replication studies implicate a susceptibility variant at the UST gene locus. *Human Molecular Genetics*, *22*(16), 3363–3372. https://doi.org/10.1093/hmg/ddt185

Sulkava, S., Ollila, H. M., Alasaari, J., Puttonen, S., Härmä, M., & Viitasalo, K. (2017). Common genetic variation near melatonin receptor 1A gene linked to job-related exhaustion in shift workers. *Sleep*, *40*(1), 1–10. https://doi.org/10.1093/sleep/zsw011

Swider, B. W., & Zimmerman, R. D. (2010). Born to burnout: A meta-analytic path model of personality, job burnout, and work outcomes. *Journal of Vocational Behavior*, *76*(3), 487–506. https://doi.org/10.1016/j.jvb.2010.01.003

Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996). Heart rate variability: Standards of measurement, physiological interpretation and clinical use. *Circulation*, *93*, 1043–1065.

Toker, S., Melamed, S., Berliner, S., Zeltser, D., & Shapira, I. (2012). Burnout and risk of coronary heart disease: A prospective study of 8838 employees. *Psychosomatic Medicine*, *74*(8), 840–847. https://doi.org/10.1097/PSY.0b013e31826c3174

Toppinen-Tanner, S., Ahola, K., Koskinen, A., & Väänänen, A. (2009). Burnout predicts hospitalization for mental and cardiovascular disorders: 10-year prospective results from industrial sector. *Stress and Health*, *25*(4), 287–296. https://doi.org/10.1002/smi.1282

Van Der Klink, J. J., & Van Dijk, F. J. (2003). Dutch practice guidelines for managing adjustment disorders in occupational and primary health care. *Scandinavian Journal of Work, Environment & Health*, *29*(6), 478–487.

von Känel, R., Bellingrath, S., & Kudielka, B. M. (2008). Association between burnout and circulating levels of pro-and anti-inflammatory cytokines in schoolteachers. *Journal of Psychosomatic Research*, *65*(1), 51–59. https://doi.org/10.1016/j.jpsychores.2008.02.007

Ware, J. E. Jr., & Sherbourne, C. D. (1992). The MOS 36-item short-form health survey (SF-36): I. Conceptual framework and item selection. *Medical Care*, *30*, 473–483.

Wittchen, H. U., & Pfister, H. (1997). *DIA-X interview*. Swet Test Services: Frankfurt a.M.

Wolf, O. T. (2009). Stress and memory in humans: Twelve years of progress? *Brain Research*, *1293*, 142–154. https://doi.org/10.1016/j.brainres.2009.04.013

World Health Organization (1992). *International statistical classification of diseases and related health problems: 10th revision*. Geneva: WHO.

Zanstra, Y. J., Schellekens, J. M., Schaap, C., & Kooistra, L. (2006). Vagal and sympathetic activity in burnouts during a mentally demanding workday. *Psychosomatic Medicine*, *68*(4), 583–590. https://doi.org/10.1097/01.psy.0000228012.38884.49

How to cite this article: Penz M, Wekenborg MK, Pieper L, et al. The Dresden Burnout Study: Protocol of a prospective cohort study for the bio-psychological investigation of burnout. *Int J Methods Psychiatr Res*. 2018;27:e1613. https://doi.org/10.1002/mpr.1613