Physiological differences between burnout patients and healthy controls: blood pressure, heart rate, and cortisol responses

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Objectives: To investigate differences between burnout patients and healthy controls regarding basal physiological values and physiological stress responses. Measures of the sympathetic-adrennergic-medullary (SAM) axis and the hypothalamic-pituitary-adrenal (HPA) axis were examined.

Methods: SAM axis and HPA axis activity was compared between 22 burnout patients and 23 healthy controls. SAM axis activity was measured by means of heart rate (HR) and blood pressure (BP). HPA axis activity was investigated by means of salivary cortisol levels. Resting levels of HR, BP, and cortisol were determined as well as reactivity and recovery of these measures during a laboratory session involving mental arithmetic and speech tasks. In addition, morning levels of cortisol were determined.

Results: Burnout patients showed higher resting HR than healthy controls. BP resting values did not differ between burnout patients and healthy controls, nor did cardiovascular reactivity and recovery measurements during the laboratory session. Basal cortisol levels and cortisol reactivity and recovery measures were similar for burnout patients and healthy controls. However, burnout patients showed elevated cortisol levels during the first hour after awakening in comparison to healthy controls.

Conclusions: The findings provided limited proof that SAM axis and HPA axis are disturbed among burnout patients. Elevated HR and elevated early morning cortisol levels may be indicative of sustained activation.

Although originally exclusively related to social professions, burnout is nowadays commonly accepted as a health problem characterised by symptoms such as mental exhaustion and physical fatigue, detachment from work, diminished competence, loss of energy, increased irritability and sleep, and concentration problems which can occur irrespective of the type of profession. The symptoms of burnout are also known as subjective health complaints, as up until now, no objective signs of illness have been found for these complaints. Comparable symptom clusters, with exclusion of the work related complaints, are also characteristic of chronic fatigue syndrome (CFS) and post traumatic stress disorder (PTSD).

Concerning the relation between stress and health complaints, attention is paid within psychobiological research to the association between failure to effectively cope with stressors and physiological responses. Two physiological stress systems are commonly distinguished: the sympathetic-adrennergic-medullary (SAM) axis and the hypothalamic-pituitary-adrenal (HPA) axis. Simply stated, the SAM axis concerns immediate sympathetic activation preparing an individual to deal with a stressor, resulting in for example increased heart rate (HR) and blood pressure (BP) and release of catecholamines such as epinephrine and norepinephrine. SAM activation occurs within seconds as a result of a stressor and permits adaptive responding to a stressor. The HPA axis is a slower response system involving release of corticosteroids such as corticotropin releasing hormone, adrenocorticotropic hormone, and cortisol, resulting in immune suppression. HPA activation is associated with inability to cope, helplessness, affective distress, and perceived uncontrollability. Generally, low SAM and HPA activation is seen in persons with high levels of effective coping and control.

According to the “sustained activation theory”, sustained or frequently repeated activation of the stress systems without the possibility to rest resulting in chronic allostatic load, may develop in illness. Sustained activation can be a result of prolonged or repeated exposure to stressors, with which a person cannot adequately cope. Consequently, the SAM axis and HPA axis stay persistently activated, recovery does not occur, and the systems do not return to homeostasis. Lasting changes in the neuroendocrine system are thought to be particularly health threatening.

Elevated BP or hypertension may be considered a sign of dysregulation of the SAM axis while hypersecretion or hyposcretion of cortisol is indicative of dysregulation of the HPA axis. Associations between SAM and HPA functioning on the one hand, and workload, job strain, and chronic stress on the other, have been repeatedly observed. Elevations in BP and HR during the workday were shown in various populations and professions. In addition, positive associations were found between job strain and BP and between cortisol and cardiovascular parameters. Furthermore, relations were observed between cortisol and workload or job strain.

Since burnout symptoms highly resemble symptoms that are characteristic of CFS, Frankenhaeuser suggested that burnout patients as CFS patients might show lower basal cortisol activity resulting for example in hyposcretion of cortisol. Basal hyposcretion of cortisol has also been observed in individuals who developed PTSD after an extreme stressor compared to normal subjects and other psychiatric patients. However, studies concerning chronic stress due to high job strain, work overload, and/or vital exhaustion show both decreases and increases in cortisol levels. The findings from the study of Melamed et al. suggested that within a
sample of employees, a longer history of burnout complaints implying chronicity was associated with higher cortisol levels. With respect to the relationship between stress and health, it appears relevant to investigate reactivity to stressors, rather than looking at basal values of SAM activation and HPA activation alone. Different reactivity might occur concerning the magnitude and/or the duration of the response. Likewise, recovery may not come about to the same extent and/or within the same time frame. McEwen has stated that delayed recovery following a stressor is indicative of sustained activation. Kristenson et al found that elevated cortisol levels among persons reporting job strain and vital exhaustion were associated with attenuated cortisol reactivity to stress inducing tasks. Roy et al found that among healthy fire fighters reporting a higher density of recent life events, high social support was associated with stronger HR reactivity to stress inducing tasks. Roy et al swifter recovery despite increased reactivity may be seen as adequate adaptation.

It should be noted that above mentioned studies were carried out among participants who could still carry out their daily activities. Thus, although participants reported chronic stress or even burnout symptoms, these conditions were not impairing their daily functioning to a large extent. To our knowledge, studies concerning SAM axis and HPA axis functioning among burnout patients who are unable to work are absent.

The objective of the present study is to investigate differences between burnout patients and healthy controls concerning SAM axis and HPA axis functioning as indicated by both basal values and reactivity and recovery measures. Therefore, burnout patients and healthy controls visited the laboratory to perform mental arithmetic and speech tasks. In addition, participants collected morning saliva to obtain information about the cortisol response to awakening, which, according to Pruessner shows good intra-individual stability over time and can serve as an indicator for HPA axis activity. We expected to find dysregulation of SAM axis and HPA axis functioning in burnout patients.

METHODS

Participants

Forty-five participants took part in the present study, consisting of 22 burnout patients and 23 healthy persons. Group characteristics such as gender distribution, average age, education level, and type of occupation are presented in table 1. Healthy controls were younger than burnout patients (t(43) = 4.0, p < 0.001).

Burnout patients were included in the study if (1) they reported stress complaints such as emotional and physical fatigue, loss of energy, increased irritability, and sleep and concentration problems; (2) the complaints were considered to be predominantly work related; and (3) participants reported burnout related (partial) sick leave, which has lasted between two weeks to three months full time, or six months part time. A semi-structured diagnostic interview was administered by a clinical psychologist. Primary Axis I disorders were excluded by a short version of the Composite International Diagnostic Interview (CIDI), a structured interview covering depression, social phobia, panic disorder, somatoform disorder, post-traumatic stress disorder, obsessive-compulsive disorder, hypomania, and psychotic disorders. Additionally, the Beck depression inventory (BDI) was used to exclude severe depression. Since depressive symptoms such as difficulty concentrating and loss of energy are also characteristic of burnout, the cut off score was set at a conservative 25.

Healthy individuals were screened by a telephone interview. Participants in good physical health and working for at least eight hours a week were included in the study. Exclusion criteria were: having experienced a traumatic event in the past six months, psychiatric illness, pregnancy, currently taking sick leave and scoring both within the clinical range of the mental exhaustion scale of the Maslach burnout inventory (>2.60) and within the clinical range of the total fatigue score of checklist individual strength (>76).

Participants reporting a history of immune, diabetic, or other medical disease that could possibly explain fatigue were excluded from the study. Two burnout patients were using anti-hypertensive medication in the form of beta-blockers. No healthy controls were using medication, except for three women who were on oral contraceptives.

Burnout patients were recruited through occupational health practitioners and general practitioners. Healthy subjects were recruited by flyers in libraries and other public places, and among part time working psychology students. Healthy subjects were paid €20 after attending the laboratory session, completion of the questionnaires, and delivering the morning saliva samples. Burnout patients received refund of their travel expenses. Burnout patients and healthy controls received a printed report of their baseline BP and HR. All participants in the study gave written informed consent.

Procedure

Participants collected morning saliva, visited the laboratory in order to perform mental arithmetic and speech tasks, and filled out questionnaires concerning biographic characteristics, burnout, and fatigue. On the day of morning saliva collection and on the day of stress test performance, participants filled out a state questionnaire pertaining to mood, physical activity, and smoking. Participants were asked to refrain from smoking and coffee consumption for at least 60 minutes before the start of the laboratory session. The stress test was held in the afternoon, starting at 13.30, in order to reliably differentiate the experimentally induced cortisol from the strong early morning elevation, which is inherent to the circadian rhythm of the morning cortisol secretion.

To prevent effects of anticipatory stress for the laboratory session on morning cortisol levels, morning saliva was collected on another day than the laboratory session. With the exception of five participants, all burnout patients collected the morning saliva on the day before they visited the laboratory. The control group collected the morning saliva

| Table 1 Characteristics of burnout patients and healthy controls* |
|-----------------|-----------------|-----------------|
|                  | Burnout patients | Healthy controls |
| Gender           |                 |                 |
| Men | 14 (64%) | 10 (43%) |
| Women | 8 (36%) | 13 (57%) |
| Age (in years)  | 42 (10.2) | 31 (7.6) |
| Cigarette smokers | 9 (41%) | 7 (30%) |
| Burnout (UBOS)  |                 |                 |
| Mental exhaustion | 2.5 (1) | 1.3 (0.8) |
| Distance         | 3.1 (1.2) | 1.4 (0.9) |
| Competence       | 4.1 (1.0) | 4.3 (1.0) |
| Fatigue (CIS total score) | 105.4 (19.7) | 47.8 (22.8) |
| Type of occupation† |   |   |
| Non-social       | 11 (48%) | 15 (62%) |
| Social           | 12 (52%) | 9 (38%) |
| Duration of complaints |   |   |
| <3 months        | 1 (4%) | - |
| >3 and <6 months | 3 (14%) | - |
| >6 and <12 months | 10 (46%) | - |
| >12 months       | 8 (36%) | - |

*Values are counts (percentages) and means (SD)
†Social occupation includes human service occupations, teachers, and managers.
‡Difference with patient group is significant at alpha < 0.05.
participants were instructed not to have breakfast or brush their teeth within 15 minutes before a sample was collected. Additionally, participants were instructed to store all samples in the fridge until next day's visit to the laboratory (burnout patients) or postage/delivery (healthy controls). All samples were centrifuged at (5000 g, 5 mins) and stored at −20°C until analysis. The amount of free cortisol was determined by enzyme immunoassay (DSL, Veghel, The Netherlands). Sensitivity of assay was 1 ng/ml.

Psychological variables
The Dutch version of the Maslach Burnout Inventory-General Survey (MBI-GS) was used to measure burnout (Utrechtse Burnout Schaal: UBOS).

The UBOs consists of 15 items regarding mental exhaustion, distance, and competence, which are scored on a seven point Likert scale ranging from 1 (never) to 7 (always/daily).

General fatigue was measured with the Checklist Individual Strength (CIS). The CIS consists of 20 items referring to four dimensions of fatigue: (a) subjective feeling of fatigue and physical fitness, (b) activity level, (c) motivation, and (d) concentration, which are scored on a seven point Likert scale ranging from 1 (false) to 7 (true). A total fatigue score is calculated by adding all item scores and can thus range from 20 to 140.

The subjective response during the laboratory session was measured by means of the Vigor and Tension subscales of the Profile Of Mood Scale (POMS), consisting of five and six items respectively. Items are scored on a five point scale ranging from 0 (not at all) to 4 (very much). The Vigor subscale is indicative of psychological activation and the Tension subscale contains items referring to tension and anxiety. These mood dimensions have been previously used to measure subjective response during stress inducing tasks. The mood questionnaires were completed five times during the laboratory session, while saliva was collected.

Occupation and education
Type of occupation was categorised according to the social character of the profession. Two categories were distinguished: (1) human service occupations, teachers and managers; (2) less/non-social occupations—for example, writer, truck driver, administrative employee. Average education level has been assessed as the highest completed education on a six point scale ranging from 1 (primary school) to 6 (university grade).

Statistical analyses
Proportion of smokers, type of profession, mental exhaustion, and fatigue were compared between the patient group and the healthy controls using χ² tests and t-tests. Group differences in resting values of cardiovascular measures during the adaptation phase and the second resting phase of the laboratory session were analysed by means of analysis of variance (ANOVA), using one between-subjects (group) design. Basal cortisol levels measured on midday (fourth sample of the morning saliva samples) and at 15.00 (final sample of the laboratory session) were analysed in the same manner (ANOVA, using group as one between-subjects factor).

Reactivity and recovery during the laboratory session were analysed by means of ANOVA for repeated measures, using a one within- (time), one between-subjects (group) design for the cardiovascular measures, the cortisol outcomes, and the subjective responses separately. Early morning cortisol response was analysed likewise. If the assumption of sphericity was violated, corrected results according to Greenhouse-Geisser method were presented. Post hoc contrasts were
employed to reveal group differences concerning changes between subsequent measurements. Analyses were performed with and without relevant covariates. Both age and gender have consistently been associated with cardiovascular measures and cortisol levels, and were therefore added as covariates, despite the fact that the difference of gender distribution was not statistically significant between the burnout patients and healthy controls.

Some data were missing due to equipment problems (e.g., unrecorded data) or to lost saliva samples. Analysis of blood pressure and heart rate was based on 22 burnout patients and 22 healthy controls, with the exception of baseline values during the adaptation period, which was based on 23 healthy controls. In addition, analysis of cortisol during the laboratory session was based on 21 burnout patients and 23 healthy controls, as was comparison of baseline values at 15:00 hours. Furthermore, analysis of morning cortisol was carried out for 20 burnout patients and 23 healthy controls, with exception of baseline comparison at 12:00 hours, which was based on 21 burnout patients and 23 healthy controls.

RESULTS
As expected, burnout patients scored significantly higher than healthy controls on the mental exhaustion subscale and the distance subscale of the UBOS (t(43) = 11.0, p < 0.001; t(43) = 5.3, p < 0.001) and on the CIS (t(43) = 9.1, p < 0.001) (see Table 1). Within the group of burnout patients, the majority (82%) reported chronic burnout complaints, that is, complaints of more than six months duration.

Cardiovascular measures
Burnout patients had higher resting HR than healthy controls as measured during the adaptation and the second recovery phase of the laboratory session (F(1,43) = 7.17, p < 0.05; F(1,42) = 5.93, p < 0.05). A trend in the same direction was found for systolic BP during the second recovery phase (F(1,42) = 3.14, p < 0.10), indicating higher resting systolic BP for burnout patients compared to healthy controls. After correction for age and gender, the difference for HR during the adaptation phase remained statistically significant (F(1,41) = 4.21, p < 0.05), the difference during the second recovery phase became marginally significant (F(1,40) = 3.75, p < 0.10) and the difference of systolic BP was no longer significant (F(1,41) = 0.81, p > 0.05).

Systolic BP, diastolic BP, and HR were different during the six laboratory session phases indicating a development over time (within-subjects effect of time: F(5,210) = 35.72, p < 0.001; F(5,210) = 58.09, p < 0.001; F(5,210) = 46.23, p < 0.001, respectively). Burnout patients had higher HR during the entire laboratory session (between-subjects effect: F(1,42) = 6.66, p < 0.05). No between-group differences were observed with respect to development over time for any of the cardiovascular measures during the laboratory session (time-group interaction: systolic BP: F(5,210) = 1.99, p > 0.05; diastolic BP: F(5,210) = 1.04, p > 0.05; HR: F(5,210) = 0.25, p > 0.05). Post hoc analyses revealed that overall (irrespective of group) differences between subsequent phases of the laboratory session were all statistically significant, with exception of diastolic BP between the adaptation and preparation phase and HR between the first and second recovery phase. After correction for age and gender, the within-subjects time effect remained statistically significant for systolic and diastolic BP (F(5,200) = 4.29, p < 0.01; F(5,200) = 4.34, p < 0.01), and became marginally significant for HR (F(5,200) = 2.30, p < 0.10). The between-subjects group effect remained statistically significant for HR (F(1,40) = 4.12, p < 0.05). Again, no time group interaction effects were found. Figures 1 to 3 show average systolic and diastolic BP and HR values during the different phases of the laboratory session.

Cortisol
Basal values of cortisol measured at 12:00 hours and at 15:00 hours revealed no differences between burnout patients and healthy controls (F(1,42) = 0.24, p > 0.05; F(1,42) = 0.18, p > 0.05). Correction for age and gender did not change the results. During the laboratory session, cortisol changed over the different phases (within-subjects time effect: F(4,168) = 17.80, p < 0.001). No overall group differences emerged (between-subjects group effect: F(1,42) = 2.27, p > 0.05). Burnout patients showed a different development of cortisol levels during the laboratory session in comparison to healthy controls.
controls (time-group interaction effect: F(4,168) = 4.16, p < 0.05). Post hoc analyses of the overall within-subjects time effect revealed that differences between subsequent phases of the laboratory session were all statistically significant, with exception of the differences between the preparation and the speech task samples. The time group interaction effect could not be attributed to a particular phase, but is probably a result of the overall steeper decrease in cortisol of burnout patients than healthy controls during the laboratory session. After correction for age and gender the within-subjects time effect became marginally significant (F(4,160) = 2.57, p < 0.10), the difference between burnout patients and healthy controls during the laboratory session (t = 1.50, p > 0.05; t = 1.49, p > 0.05). No overall difference between the groups was found (F(1,43) = 1.60, p > 0.05), nor was there any evidence for a different development of psychological activation during the laboratory session between burnout patients and healthy controls (time-group interaction effect: F(4,172) = 1.34, p > 0.05). Post hoc analyses showed significant differences between the preparation measurement and the measurement after the speech task and between the measurement after the speech task and the first recovery measurement (irrespective of group). After correction for age and gender the time effect remained significant (F(4,164) = 2.64, p < 0.05), the difference between groups became marginally significant (F(1,41) = 3.63, p < 0.10) and the time group interaction was unaffected. The results show a tendency towards higher Vigor scores for the patient group compared to the control group and a decrease of Vigor after the stress inducing tasks for both groups.

Subjective responses during the laboratory session

Psychological activation (Vigor subscale of the POMS) changed over time during the laboratory session (within-subjects time effect: F(4,172) = 18.2, p < 0.001). Furthermore, burnout patients had overall higher tension scores than healthy controls (between-subjects group effect: F(1,43) = 26.23, p < 0.001) and burnout patients and healthy controls showed a different development of tension during the laboratory session (time-group interaction effect: F(4,172) = 5.25, p < 0.01). Post hoc analyses showed significant differences between the measurement after the speech task and the first recovery measurement and between the two recovery measurements, which could be ascribed to the patient group only. After correction for age and gender the time effect remained significant (F(4,164) = 2.87, p < 0.05), as did the group effect (F(1,41) = 14.36, p < 0.001) and the time-group interaction effect (F(4,164) = 4.26, p < 0.05). These results indicate that the tension scores of the healthy group were relatively low and did not change during the laboratory session, while the tension scores of the patient group were considerably higher, showing a decrease after the stress inducing tasks.

DISCUSSION

The aim of the present study was to investigate differences between burnout patients and healthy controls regarding basal physiological values and physiological stress responses by examining measures of the SAM axis (HR and BP) and the HPA axis (cortisol).

![Figure 4](http://www.occenvmed.com/images/figure4.png)

**Figure 4** Mean concentration of salivary free cortisol (SEM) in burnout patients and healthy controls during the laboratory session (t = -4.00, baseline; t = 5.00, post preparation sample; t = 19.00, post speech sample; t = 33.00, resting phase sample; t = 47.00, recovery sample).

![Figure 5](http://www.occenvmed.com/images/figure5.png)

**Figure 5** Mean concentration of salivary free cortisol (SEM) in burnout patients and healthy controls during the first hour after awakening and at 12.00 hrs (t = 1, awakening; t = 30, half an hour after awakening; t = 60, one hour after awakening; t = 240, 12.00 hours). Statistically significant group difference (cross-sectionally) of cortisol values at awakening is indicated by enlargement of group indicators.
With respect to basal values of cardiovascular measures, burnout patients showed higher HR than healthy controls. These results are in line with low tension levels reported during the tasks. However, we did not find elevated BP levels as found by others.\(^2\) The conclusion may be that hyperactivity of the SAM axis was limited in our burnout patients. On the other hand, the lack of finding substantial differences in basal BP may also indicate that hyperactivity of the SAM axis has already recovered, as a result of the rest obtained during sick leave. This recovery could have occurred since burnout patients were tested several weeks after the chronic stressor (such as work load or job strain) had disappeared or had been reduced, and again post hoc analysis excluding these patients did not change any of the results. Our results are consistent with findings of Benschop et al\(^3\) who found no association between cardiovascular reactivity and chronic stress, despite the fact that they obtained both elevated basal BP and HR among persons reporting chronic stress in comparison to those without complaints. This recovery could have occurred since burnout patients showed elevated early morning cortisol levels in comparison to healthy controls. These findings are partly in accordance with other findings. Steptoe et al\(^4\) did not find any differences during the day between high and low job strain groups. Melamed et al\(^5\), however, obtained higher cortisol levels at 16:00 hours in a chronic burnout group compared to a non-chronic burnout group and a group without burnout complaints. The absence of a difference in the present study could not be ascribed to relatively large inter-individual differences in measurements at 15:00 hours, as suggested by Schmidt-Reinwald et al\(^6\). With respect to cortisol reactivity and recovery, no differences emerged between burnout patients and healthy controls. The outcomes are in accordance with results published by Roy et al\(^7\), addressing life events and cortisol reactivity and recovery. Other studies, however, reported associations between daily stressors or life situations and cortisol reactivity.\(^8\) An explanation for these inconsistent results may be that general stress inducing tasks might remain unnoticed. A flat physiological response may, though, be considered a response, which might have shown a steeper slope without exposure to the stress test as is suggested by Roy et al\(^8\).

Burnout patients showed elevated early morning cortisol levels in comparison with healthy controls. Our findings are consistent with the studies of Melamed et al\(^5\), Schmidt-Reinwald et al\(^6\) and Steptoe et al\(^7\) concerning people with high job strain, high workload or burnout symptoms and with the results of Kristenson et al\(^9\) concerning people reporting vital exhaustion. These findings suggest a dysregulation of the HPA axis among burnout patients. The fact that the difference seems most pronounced at the moment of awakening, burnout patients might not have recovered fully during the night, which may be a sign of “sustained activation”, as is the elevated basal HR. Other authors also reported sustained activation after a working day, as indicated by elevated BP\(^10\) and adrenaline.\(^11\) It is remarkable that although burnout patients reported severe mental exhaustion, scored in the clinical range and comparable to CFS patients on general fatigue\(^12\) and reported chronic burnout complaints, they did not have blunted cortisol levels as have been found among CFS patients\(^13\) and PTSD patients.\(^14\) On the contrary, their morning cortisol levels appeared elevated, as was found among persons reporting high job strain or high workload\(^15\) or vital exhaustion\(^14\) and no indication of flattening of circadian rhythm was found. In addition, the severity of mental exhaustion was positively associated with maximal early morning cortisol level. These outcomes suggest that the burnout syndrome is essentially different from CFS and PTSD. Another explanation may be that the neuroendocrine changes develop over time and thus can only be found in patients who suffer from burnout complaints for a certain long lasting period—for example, more than one year. Unfortunately, the size and distribution of the current sample did not allow us to do subgroup analysis to investigate differences in cortisol response between more and less chronic burnout patients.

The present study has several limitations. Firstly, a neuroendocrine representative of the SAM axis such as for example epinephrine was not measured. Second, the sample size was relatively small in comparison to similar studies using physiological measures, resulting in limited statistical power. Consequently, small effect sizes could not be detected. Thirdly, two patients used antihypertensive drugs, which may have blunted average cardiovascular activity in the patient group somewhat. Finally, the stress inducing tasks might not have caused enough distress to result in substantial HPA axis activation, thus possibly thwarting the discovery of different reactivity and recovery patterns between burnout patients and healthy controls.

In conclusion, the results of this study suggest that there is some dysregulation of the SAM axis with respect to basal cardiovascular values, indicated by elevated HR among burnout patients. Dysregulation of the SAM axis with respect to...
to reactivity and recovery values of cardiovascular measures in burnout patients was not found. In addition, deviations in HPA axis reactivity and recovery during and after stress inducing tasks were absent in burnout patients, indicating no adaption failure. The results of current study, however, are supportive of dysregulation of the HPA axis in burnout patients as indicated by elevated early morning cortisol levels. Both elevated morning cortisol and elevated HR may be indicative of sustained activation. The outcomes of burnout patients are more similar to the results observed in persons suffering from post-traumatic stress. The specific underlying mechanisms and exact meaning of these findings, however, remain to be clarified.

ACKNOWLEDGEMENTS
This study was part of the Dutch Concerted Research Action “Fatigue at work” of NWO. The Dutch Organisation of Scientific Research (NWO) and Care Research The Netherlands (ZON) funded this study. This study could not be performed without the contribution of the occupational health services AGW (Hoorn, The Netherlands) and AMD-UvA (Amsterdam, The Netherlands) and various general practitioners in and around Amsterdam. Additionally, I Geraets and F Wildschut have been of great aid during the data collection phase. The authors thank P K Beekhof for biochemical analyses and W Vleeming for advice.

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*Occup Environ Med* 2003 60: i54-i61
doi: 10.1136/oem.60.suppl_1.i54

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