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Vital exhaustion and risk of alcohol use disorders: a prospective cohort study

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Abstract

Objective

Vital exhaustion is an emotional state characterized by fatigue and depressive symptoms. We examined the prospective association between vital exhaustion and risk of alcohol use disorders (AUD). Furthermore, we investigated whether cohabitation status modifies the effect of this potential association.

Methods

Vital exhaustion was assessed by a condensed, 17 item, version of the Maastricht Questionnaire as part of the Copenhagen City Heart Study in 1991-93. The study population consisted of 8,956 individuals aged 21-93 years, who were followed for a first-time diagnosis of AUD in national registers until 2016. The mean length of follow-up was 16.6 years.

Results

During follow-up, AUD was diagnosed in 146 men and 103 women. For both sexes, the risk of AUD increased dose-dependently with increasing vital exhaustion. Individuals who reported high vital exhaustion had a 2- to 3-fold higher risk of AUD in both men (HR=2.46, 95% CI: 1.40-4.29) and women (HR=3.34, 95% CI: 1.62-6.85). A potential modifying effect of cohabitation status on the relation between vital exhaustion and AUD was found for men.

Conclusion

The results showed that vital exhaustion is significantly associated with a higher risk of AUD in both men and women and that living with a cohabitee may have a protective effect among men.
1. Introduction

Alcohol use disorders (AUD), comprising alcohol dependence and harmful use of alcohol, are among the commonest psychiatric disorders, affecting about 4.3% of the adult population worldwide (men: 7.2 %, women: 1.3 %) [1]. AUD is associated with severe health and social problems [1,2] and increases the risk of early mortality [3,4]. The onset of AUD is believed to peak during early adulthood [5], but substantial individual differences in the course of AUD exist and late-developing AUD has lately received growing recognition [6,7]. Consequently, it is highly relevant to identify factors contributing to AUD across the lifespan.

Exposure to stress during the lifespan may influence later development of AUD. Thus, early life stress and adverse events in adult life such as divorce and serious economic problems have been proposed as risk factors for AUD [8,9]. Likewise, occupational stressors [10,11] and burnout (a condition related to prolonged occupational stress) [12,13] have been associated with alcohol-related problems. In addition, evidence supports a relation between stress and higher risk of depression [14,15], and depression is closely linked with AUD as the two disorders often co-exist [16].

Vital exhaustion was introduced by Appels et al. in 1987 and is as an emotional state consisting of feelings of fatigue, irritability and demoralization [17,18]. Vital exhaustion is often understood as coinciding with longer periods of psychological stress or being the response to prolonged stress [18,19]. The Maastricht Questionnaire (MQ) was developed to assess vital exhaustion and in general, women score higher on vital exhaustion than men [20,21]. The construct was originally developed in the context of risk factors for cardiovascular disease, and higher vital exhaustion scores have, for example, been associated with higher risk of unhealthy lifestyles [22], adverse cardiac events [20,23,24], and early mortality [23]. Although related constructs such as stress,
depression and burnout have been associated with AUD, the relationship between vital exhaustion and risk of developing AUD is unexplored. We anticipate that high vital exhaustion may lead to an increase in alcohol intake and the risk of developing AUD, because increased alcohol intake could be a form of coping to reduce stress and feelings of exhaustion among individuals who have less adaptive coping skills.

In addition to studies on stress and AUD, studies have focused on the possible protecting effects of social support in the development of AUD. Thus, living alone has been associated with higher risk of alcohol dependence in both men and women [25] and positive associations have been found between being unmarried and AUD [5,26]. Evidence of a stress-buffering effect of social support has been suggested [27]; an example of this is a prospective cohort study that found financial stress to be associated with alcohol problems among people reporting low social support, whereas no association was found among people reporting high social support [28]. Similarly, it is plausible that social support modifies the possible influence of vital exhaustion upon risk of AUD.

The aims of the present study were to prospectively examine the association between vital exhaustion and risk of AUD and to assess whether the potential effect of vital exhaustion on AUD is modified by social support as reflected by cohabitation status.
2. Methods

2.1. Study population

This is a prospective cohort study with baseline examination in 1991-93 and linkage to national registers to obtain information on AUD during 24 years of follow-up. The study population was defined using data from the Copenhagen City Heart Study. This study was initiated in 1976-78 when a random sample of 14,223 of men and women above 20 years of age completed a self-administered questionnaire. Detailed descriptions of the original study and follow-ups in 1981-83, 1991-93, and 2001-03 have been published elsewhere [29,30]. A measure of vital exhaustion was introduced in the 1991-93 follow-up, which included 10,135 participants. Participants with a diagnosis of AUD (n=366) before baseline in 1991-93 or with missing data on any of the covariates (n=587) were excluded from the statistical analysis. In addition, individuals with a score of 6 or above on the brief Michigan Alcoholism Screening Test (n=226) at baseline were excluded, as this cut-off score has been used as a proxy for AUD [31]. Thus, the final study population consisted of 8,956 participants. The mean age of participants was 58 years at baseline in 1991-93–16% were 21-40 years, 43% were 40-65 years, and 41% were 65-93 years.

2.2. Alcohol use disorders

Information about AUD was obtained through linkage to three Danish registers: The Danish National Patient Register contains diagnoses of all hospital admissions since 1977 [32], the Danish Psychiatric Central Register comprises diagnoses of all individuals admitted to a Danish psychiatric hospital since 1969 [33], and the Copenhagen Alcohol Cohort contains registrations of all individuals treated for AUD in outpatient clinics in Copenhagen since 1954 [34]. The diagnoses from the Danish registers were classified according to International Classification of Diseases (ICD), using the ICD-8 revision until 1994, and the ICD-10 revision from 1994 and onwards. In this
study, AUD comprised the following diagnoses: ICD-8 (303: alcoholism), ICD-10 (F10.1: harmful use, F10.2: dependence syndrome). AUD was defined by an alcohol-related hospital admission diagnosis or by first-time registration in the Copenhagen Alcohol Cohort. At the hospitals, diagnoses were based on all available evidence including patient interviews, and for the Copenhagen Alcohol Cohort, diagnoses were primarily based on clinical interviews. Participants were followed from the date of the 1991-93 follow-up until the date of the first registration of AUD (n=249), death (n=4,692), emigration from Denmark (n=101) or end of follow-up on March 27, 2016 (n=3,914), whichever came first. The mean follow-up time was 16.6 years and 1.1% of the participants were lost to follow-up. Information about death and emigration was derived from the Danish Civil Registration System [35].

2.3. Vital exhaustion and cohabitation status

Vital exhaustion was assessed by a modified Danish version of the Maastricht Questionnaire developed by Appels et al. [17]. This version has been applied in other settings [36,37] and consists of 17 items, which are summed into a total score with a possible range from 0 to 17 (Table 1). Based on the total score, the participants were divided into 3 categories: 0, 1-7, and 8-17 (low, moderate and high vital exhaustion score, respectively) corresponding to a categorization used in a previous study based on this cohort [38]. The included items refer to symptoms of depressive feelings (8 items, e.g. ‘Do you feel that you want to give up?’), fatigue (7 items, e.g. ‘Do you sometimes feel your body is like a battery running out?’) or irritability (2 items, e.g. ‘Do little things irritate you more than they used to?’). Cohabitation status, as an indicator of social support, was assessed on the basis of whether participants were living alone or living with a spouse/cohabitee.

2.4. Covariates

We included the following baseline covariates: age, education (<8, 8-10, >10 years), household income (monthly income in 1991-93: <25,000, 25,000-50,000, >50,000 USD), physical activity
(inactive, low, moderate/high level of leisure-time physical activity), smoking (never smoker, former smoker, current smoker), alcohol consumption (men: 0, ≤21, >21 drinks/week, women: 0, ≤14, >14 drinks/week) and psychiatric disorders (yes, no). Psychiatric disorders were defined as first admission with a psychiatric diagnosis, other than AUD, comprising the following diagnostic categories: ICD-8 (290-302, 304-315), ICD-10 (F11-F99). Information about psychiatric disorders was derived from the Danish National Patient Register and the Danish Psychiatric Central Register. Descriptive information on covariates according to the vital exhaustion score is shown in Table 2.

2.5. Statistical analyses
Data were analyzed by means of Cox proportional hazards model and by including age as the underlying time scale, the estimates were adjusted for confounding by age. Since the participants entered the study population at different ages, delayed entry was implemented. Preliminary analyses showed no significant interaction between vital exhaustion and sex with respect to risk of AUD; however, due to notably sex differences in the incidence of AUD (Table 2) and in the level of vital exhaustion (women scored higher on vital exhaustion than men), all analyses will be presented separately for men and women. Initially, hazard ratios (HRs) for AUD were computed for vital exhaustion adjusted for I) age and II) age, educational level, household income, cohabitation status and psychiatric disorders (Table 3). Based on consideration of the potential role of social support, it was decided a priori to test whether the association between vital exhaustion and AUD was modified by cohabitation status. Although, the interaction was not statistically significant in the model for either men ($P = 0.06$) or women ($P = 0.87$), we decided to stratify by cohabitation status to assess a possible variation in association for the two sub-samples (those living alone and those living with cohabitee/spouse) (Table 4).

The robustness of the results was assessed in various sensitivity analyses and compared to the results in Table 3. First, to address reverse causation bias in which AUD contributes to vital
exhaustion, we repeated all analyses with a 3-year time lag. Hence, in these sensitivity analyses, the follow-up period started three years later (1994-96) and individuals who died or developed AUD from 1991-93 to 1994-96 were therefore not included (N=8,435; AUD was diagnosed in 130 men and 94 women). Second, a model further adjusted for lifestyle factors (physical activity, smoking and alcohol consumption) in addition to variables in the multiple adjusted model was fitted. Third, to evaluate whether some items from the vital exhaustion scale are more predictive of AUD than others, we examined associations between two subscales (depressive feelings and fatigue) and AUD. The assumption of proportional hazards was evaluated graphically by plotting log-log survival curves for all variables against age at exclusion from the study, but no violations were detected. All analyses were performed in SAS version 9.4.
3. Results

3.1. Baseline characteristics
The mean age of participants was 58 years and ranged from 21 to 93 years. About 11% of the men and 21% of the women reported a high degree of vital exhaustion (8-17 points). Baseline characteristics according to the vital exhaustion score in men and women are presented in Table 2. Generally, high vital exhaustion score was significantly associated with lower education and income, living alone, being physically inactive, being a current smoker, and drinking alcohol above sensible drinking limits at baseline. The prevalence of psychiatric disorders other than AUD was higher among participants with high vital exhaustion compared with participants with a low score. Regarding AUD, a slight increase in the proportion of cases was seen from the low through high category of vital exhaustion, and the marginal association between vital exhaustion and AUD was significant in both men \((P = 0.01)\) and women \((P = 0.003)\).

3.2. Vital exhaustion and alcohol use disorders
During follow-up, 146 men and 103 women were diagnosed with AUD. Vital exhaustion was associated with a higher risk of being diagnosed with AUD among both men and women (Table 3). In the age adjusted model, men in the high category of vital exhaustion were more than twice as likely to develop AUD as those with the low score \((HR = 2.73, 95\% \text{ CI: } 1.58-4.70)\). Adjusting additionally for potential confounders, the risk estimate diminished slightly but remained statistically significant \((HR = 2.46, 95\% \text{ CI: } 1.40-4.29)\). In accordance with the findings for men, a dose-response relationship between increasing vital exhaustion and increasing risk of AUD was observed among women \((P\text{-trend} < 0.001)\). The age adjusted HR for AUD among women in the high category of vital exhaustion was 3.43 \((95\% \text{ CI: } 1.69-6.97)\) compared with women with the low score. When adjusting for potential confounders, the HR for AUD in the high category of vital exhaustion decreased slightly to 3.34 \((95\% \text{ CI: } 1.62-6.85)\).
The results from the stratified analysis suggested a modifying effect of cohabitation status on the relation between vital exhaustion and AUD in men, but not women (P-value for interaction term was 0.06 for men and 0.87 for women) (Table 4). Among men living with a spouse or cohabitee, no evidence of an association between vital exhaustion and AUD was found. In contrast, a dose-response relationship between increasing vital exhaustion and increasing risk of AUD was observed among men living alone (P-trend < 0.001) and the multiple adjusted HR for those reporting high vital exhaustion was substantially increased compared with those with the lowest score (HR = 5.69, 95% CI: 2.06-15.73). The tendencies for women regarding the association between vital exhaustion and AUD did not differ between those living alone and those with a spouse/cohabitee. Thus, for both groups indications of a dose-response relationship between increasing vital exhaustion and risk of AUD was found.

Inserting a time lag of 3 years to minimize risk of reverse causation did not change the estimates notably for either men or women. Adjusting additionally for lifestyle factors attenuated the risk estimates slightly for both sexes, but a clear dose-response relationship between vital exhaustion and risk of AUD was still observed. The sensitivity analysis investigating associations between subscales of fatigue and depressive feelings and AUD showed similar effects for the two subscales, indicating that none of the item subgroups is a particularly strong predictor for AUD (data not shown).
4. Discussion

In this prospective cohort study, we found a dose-response relationship between vital exhaustion and risk of alcohol use disorders (AUD). Compared with those with a low vital exhaustion score, individuals who reported a high vital exhaustion score had a 2- to 3-fold higher risk of AUD in both men and women. In addition, a potential modifying effect of cohabitation status on the relation between vital exhaustion and AUD was found for men.

The prospective association between vital exhaustion and risk of AUD has not previously been investigated in a large population-based study. However, depression and vital exhaustion have common symptoms such as depressed mood and feelings of hopelessness and in recent decades, a large number of prospective studies have addressed the association between depression and AUD [16,39–41]. In accordance with the results of the present study, several of these studies have demonstrated a 2- to 4-fold increased risk of AUD given the presence of depression. Further, the present finding of a dose-response relationship between vital exhaustion and risk of AUD to some extent corroborate the longitudinal study by Gilman and Abraham [39], in which the odds of developing alcohol dependence increased dose-dependently according to the number of baseline depressive symptoms.

Several mechanisms may explain the observed positive association between vital exhaustion and AUD. I) A direct causal relationship in which vital exhaustion contributes to the development of AUD may underlie our findings. Psychological theories have attempted to explain associations between depression and AUD, such as using alcohol for ‘self-medicating’ depressive symptoms or general tension reduction [42,43]. Likewise, it could be hypothesized that individuals who are vitally exhausted are more likely to use alcohol as a coping response to reduce stress or feelings of exhaustion. In our analysis, the association attenuated after adjustment for physical activity,
smoking and alcohol consumption, indicating that some of the effect of vital exhaustion is mediated through these lifestyle factors. II) Another hypothesis is that personality traits such as neuroticism may influence both vital exhaustion and risk of developing AUD [44]. High neuroticism is associated with a tendency to react with distress when exposed to everyday stressors [45]. Thus, a possible interpretation of our results is that the scores on vital exhaustion reflect a person's level of neuroticism and consequently vital exhaustion appears to be related to later development of AUD. III) Lastly, reverse causation may be an issue because of possible undiagnosed AUD at baseline. Hence, although this issue was addressed using two strategies (excluding participants with a high brief Michigan Alcoholism Screening Test and introducing a time lag of 3 years), the possibility of reverse causation cannot be ruled out.

The results from the stratified analysis suggest a potential modifying effect of cohabitation status on the association between vital exhaustion and AUD in men, but not women. Hence, for men, living with a spouse may have a stress-buffering effect as vital exhaustion was not associated with risk of AUD, whereas, for women, living with a spouse does not seem to be protective as vital exhaustion was associated with a higher risk of AUD irrespective of cohabitation status. This indicates that social support from a spouse may decrease the risk of AUD in men otherwise associated with vital exhaustion and is in agreement with theories suggesting that marriage is more beneficial in terms of e.g. providing emotional support to men than to women [46]. Although cohabitation status is widely used as an indicator of social support [47], it is obviously not a precise measure of social support at the individual level since a cohabitant does not necessarily provide social support, which may often be obtained from social relations who do not share the same address.

4.1. Methodological issues
The main advantages of the present study are the prospective design as well as register information on AUD since 1954 in addition to self-reported brief Michigan Alcoholism Screening Test scores at
baseline. Due to the linkage to national registers, we assured detection of first-time admissions of AUD and a long-term follow-up for up to 24 years (on average 17 years). The brief Michigan Alcoholism Screening Test measured at baseline enabled us to screen for AUD and exclude those with current AUD, minimizing findings of reverse causation.

The validity of self-reported measures of vital exhaustion has been investigated in previous studies. Conceptually, there is a considerable overlap between vital exhaustion and depression. Like common depression scales, vital exhaustion includes items related to ‘somatic’ depressive symptoms (e.g. fatigue, sleep disturbances and appetite changes) and ‘cognitive-affective’ depressive symptoms (e.g. guilt, feelings of worthlessness and suicidal thoughts) [48,49]. Yet, fatigue and exhaustion are core characteristics of vital exhaustion and are primary components in psychometric scales for vital exhaustion which is not necessarily the case for commonly used depression scales. Current debate concerns whether vital exhaustion and depression measure distinct constructs or are entirely overlapping [48,50–53]. However, studies investigating the overlap between the two constructs are within the field of cardiovascular disease (e.g. among patients with myocardial infarction) [50,54]. As it is not possible to directly transfer results from cardiovascular studies, it would be preferable to analyze the relative importance of vital exhaustion and depression as risk factors for AUD. However, although we had access to register-based information on depression diagnoses, only few participants were registered with a clinical diagnosis making it impossible to obtain enough power to conduct analyses of depression as a predictor. Moreover, as vital exhaustion was self-reported, it would be even more optimal to compare the construct with a self-reported measure of depressive symptoms, but such a measure was unfortunately not included in the Copenhagen City Heart Study. Following the ongoing debate on the similarities between vital exhaustion and depression and because depression is associated with increased risk of AUD [16], it could be anticipated that the ‘depressive feelings’ dimension
(cognitive-affective symptoms) of vital exhaustion would perform better in the prediction of AUD than the ‘fatigue’ dimension (somatic symptoms). However, our sensitivity analyses seem to indicate otherwise as both subscales performed equally well as predictors for AUD.

Several limitations of the present study should be noted. The use of national registers enabled identification of individuals diagnosed with AUD at Danish hospitals during the follow-up period or identification of individuals treated for AUD in outpatient clinics in Copenhagen. Nonetheless, misclassification of AUD status is still likely to have occurred as the registers only included AUD diagnosed at hospital admissions or at visits to certain outpatient clinics. Although Danish citizens have equal access to hospitals, some individuals living with an AUD may never end up with a registered diagnosis or seek treatment. Thus, the incidence of AUD is likely to be underestimated. Our results suggest that vital exhaustion is associated with increased risk of AUD, even after adjustment for psychiatric disorders and other potentially important confounders. However, residual confounding due to insufficient information may be of concern. Specifically, central covariates (e.g. personality traits, prolonged life stress, and early life environment), which may influence both vital exhaustion and AUD, were not included in the present study. Also, we were unable to differentiate between subcategories of psychiatric disorders in our analyses due to few registrations. Lastly, our results could be obscured by fluctuations in vital exhaustion over time. However, we observed a correlation of 0.54 between vital exhaustion scores at baseline and scores after 10 years of follow-up in 2001-2003, indicating that vital exhaustion tends to be relatively stable over time.

4.2. Conclusion

In this large prospective cohort study, we found a 2- to 3-fold higher risk of developing AUD among individuals with high scores on vital exhaustion in both men and women. Our findings also indicated that social support from a spouse or cohabitee decreases the risk of AUD in men otherwise associated with vital exhaustion. So far, relatively few prospective studies have
investigated associations of emotional states such as vital exhaustion and fatigue with risk of AUD. A better grasp of the influence of such factors may be of considerable importance in our understanding of risk factors for development of AUD. We recommend that future studies aim at differentiating the relative importance of vital exhaustion and depression in predicting AUD in addition to investigating the mechanisms linking vital exhaustion and related emotional states to AUD.

Declaration of interests

None.

Acknowledgments

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References


Table 1. The vital exhaustion score

1. Do you often feel tired
2. Do you feel altogether weak
3. Do you feel you have not accomplished much recently
4. Do you at the moment feel that you do not have what it takes
5. Do you believe you have come to a dead end
6. Do you lately feel listless
7. Do you feel dejected
8. Do you lately have difficulties in concentrating
9. Do little things irritate you more than they used to
10. Do you feel that you want to give up
11. I feel fine*
12. Do you sometimes feel your body is like a battery running out
13. Do you sometimes wish you were dead
14. Are you feeling ‘not worth a scrap’ at present
15. Do you have feelings of hopelessness recently
16. Do you sometimes just feel like crying
17. Do you ever wake up with a feeling of exhaustion

*This question was coded in reverse

Table 2. Baseline characteristics of participants in the Copenhagen City Heart Study by vital exhaustion score, 1991-93

<table>
<thead>
<tr>
<th></th>
<th>Total population (n=8,956)</th>
<th>Men</th>
<th>Vital exhaustion score</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUD cases, n (%)</td>
<td>249 (2.8)</td>
<td>28 (2.6)</td>
<td>94 (4.1)</td>
<td>24 (5.6)</td>
</tr>
<tr>
<td>Age at baseline, mean (SD)</td>
<td>58 (16)</td>
<td>58 (15)</td>
<td>56 (16)</td>
<td>60 (15)</td>
</tr>
<tr>
<td>Education &lt;8 years, n (%)</td>
<td>3,058 (34)</td>
<td>336</td>
<td>739</td>
<td>190</td>
</tr>
<tr>
<td>Low income, n (%)</td>
<td>3,383 (38)</td>
<td>307</td>
<td>683</td>
<td>206</td>
</tr>
<tr>
<td>Living alone, n (%)</td>
<td>3,308 (37)</td>
<td>247</td>
<td>626</td>
<td>167</td>
</tr>
<tr>
<td>Psychiatric disorders, n (%)</td>
<td>465 (5.2)</td>
<td>16 (1.5)</td>
<td>83 (3.6)</td>
<td>41 (9.6)</td>
</tr>
<tr>
<td>Physically inactive, n (%)</td>
<td>1,107 (12)</td>
<td>93 (9)</td>
<td>262</td>
<td>111</td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>4,217 (47)</td>
<td>510</td>
<td>1,166</td>
<td>244</td>
</tr>
<tr>
<td>Alcohol above sensible drinking limits**, n (%)</td>
<td>1,259 (14)</td>
<td>189 (17)</td>
<td>477 (21)</td>
<td>90 (21)</td>
</tr>
</tbody>
</table>

Abbreviations: AUD, alcohol use disorders; n, number; SD, standard deviation

*P-value for chi-square tests or ANOVA

**The Danish sensible drinking limits were 21 drinks/week for men and 14 drinks/week for women
Table 3. Risk of alcohol use disorders according to vital exhaustion score among men and women

<table>
<thead>
<tr>
<th>Vital exhaustion score</th>
<th>Age adjusted</th>
<th>Multiple adjusted*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td><strong>Men (n=3,823; cases=146)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>1-7</td>
<td>1.67 (1.09-2.54)</td>
<td>1.61 (1.05-2.46)</td>
</tr>
<tr>
<td>8-17</td>
<td>2.73 (1.58-4.70)</td>
<td>2.46 (1.40-4.29)</td>
</tr>
<tr>
<td>P-trend</td>
<td>&lt;0.001</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Women (n=5,133; cases=103)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>1-7</td>
<td>2.05 (1.05-4.01)</td>
<td>1.96 (1.00-3.84)</td>
</tr>
<tr>
<td>8-17</td>
<td>3.43 (1.69-6.97)</td>
<td>3.34 (1.62-6.85)</td>
</tr>
<tr>
<td>P-trend</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Abbreviations: HR, hazard ratio; CI, confidence interval; n, number
*Adjusted for age, educational level, household income, cohabitation status and psychiatric disorders
Table 4: Risk of alcohol use disorders according to vital exhaustion score among men and women, stratified by cohabitation status*

<table>
<thead>
<tr>
<th>Vital exhaustion score</th>
<th>Age adjusted</th>
<th>Multiple adjusted**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td>Men</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Living with spouse (n=2,783; cases=91)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>1-7</td>
<td>1.37 (0.85-2.22)</td>
<td>1.37 (0.84-2.22)</td>
</tr>
<tr>
<td>8-17</td>
<td>1.33 (0.60-2.98)</td>
<td>1.40 (0.62-3.18)</td>
</tr>
<tr>
<td>P-trend</td>
<td>0.27</td>
<td>0.23</td>
</tr>
<tr>
<td>Living alone (n=1,040; cases=55)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>1-7</td>
<td>2.80 (1.09-7.16)</td>
<td>2.77 (1.08-7.12)</td>
</tr>
<tr>
<td>8-17</td>
<td>6.14 (2.25-16.78)</td>
<td>5.69 (2.06-15.73)</td>
</tr>
<tr>
<td>P-trend</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Living with spouse (n=2,865; cases=67)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>1-7</td>
<td>2.34 (0.99-5.51)</td>
<td>2.29 (0.97-5.41)</td>
</tr>
<tr>
<td>8-17</td>
<td>3.69 (1.48-9.20)</td>
<td>3.77 (1.50-9.50)</td>
</tr>
<tr>
<td>P-trend</td>
<td>0.003</td>
<td>0.003</td>
</tr>
<tr>
<td>Living alone (n=2,268; cases=36)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>1-7</td>
<td>1.65 (0.56-4.86)</td>
<td>1.51 (0.51-4.49)</td>
</tr>
<tr>
<td>8-17</td>
<td>3.09 (1.00-9.53)</td>
<td>2.85 (0.90-9.03)</td>
</tr>
<tr>
<td>P-trend</td>
<td>0.03</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Abbreviations: HR, hazard ratio; CI, confidence interval; n, number

*The interaction between vital exhaustion and cohabitation status was not statistically significant (men: P = 0.06, women: P = 0.87)

**Adjusted for age, educational level, household income and psychiatric disorders
Highlights

- About 11% of the men and 21% of the women reported a high degree of vital exhaustion
- This is the first prospective cohort study investigating the association between vital exhaustion and risk of alcohol use disorders
- Vital exhaustion is significantly associated with a 2- to 3-fold higher risk of alcohol use disorders in both men and women
- Cohabitation status may modify the effect of vital exhaustion upon risk of alcohol use disorders in men, but not women