Social economic factors and the risk of multiple chemical sensitivity in a Danish population-based cross-sectional study: Danish Study of Functional Disorders (DanFunD)

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ABSTRACT

Objectives Multiple chemical sensitivity (MCS) is a rare multisystem and poly-symptomatic disease characterised by a report of various somatic symptoms attributed to inhalation of volatile chemicals in usually harmless doses. The aim was to explore four selected social factors and the risk of MCS in the general Danish population.

Design A cross-sectional general population-based study.

Setting The Danish Study of Functional Disorders was conducted from 2011 to 2015 which included 9656 participants.

Participants A total of 8800 participants were included in analyses after observations with missing data on exposure and/or outcome were excluded. A total of 164 cases fulfilled the questionnaire criteria for MCS. Of the 164 MCS cases, 101 reported no comorbid functional somatic disorder (FSD) and were included in a subgroup analysis. A total of 63 MCS cases fulfilled the criteria for at least one additional FSD, this subgroup was not included in further analysis. The remaining study population without MCS or any FSD were regarded as controls.

Outcome measures We used adjusted logistic regression to calculate OR and 95% CIs of MCS and MCS without FSD comorbidities for each social variable separately including education, employment, cohabitation and subjective social status.

Results We found an increased risk of MCS among the unemployed (OR: 2.95, 95% CI: 1.75 to 4.97), and a twofold increased risk of MCS among individuals with low subjective social status (OR: 2.00, 95% CI: 1.08 to 3.70). At the same time, 4 years or more of vocational training were protective of MCS. No significant associations were observed among MCS cases with no comorbid FSD.

Conclusion Lower socioeconomic status was found to be associated with a higher risk of having MCS but not with MCS without FSD comorbidities. Due to the cross-sectional design of the study, we cannot determine whether social status is a determinant or a consequence of MCS.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study was based on a randomly invited population-based sample from the Danish Study of Functional Disorders cohort.
⇒ Multiple chemical sensitivity case status was delimited based on validated and previously applied case definitions which is still one of the most reliable tools.
⇒ Several indicators of social status were included in the analyses.
⇒ Information from national registry data on socioeconomic status rather than self-reported data would strengthen the study.
⇒ Larger sample sizes in future studies are warranted to study subgroups and to increase the possibility to study whether risk increases with number of functional somatic disorders.

INTRODUCTION

The association between socioeconomic status and health has been extensively investigated. Thus, inverse associations have been observed between socioeconomic status and diseases such as asthma, diabetes, cardiovascular diseases and functional somatic disorders (FSDs), and recently a crucial impact of socioeconomic status on the reductions in life expectancy and mortality was reported. Individuals with lower socioeconomic status are known to be more vulnerable to chronic health problems which has been demonstrated to be the results of several determinants including both behavioural, biological, material and psychosocial health. Moreover, it has been argued that environmental exposures to risk factors have an additive effect explaining the gradient between socioeconomic status and multiple health outcomes.
Multiple chemical sensitivity (MCS) (also often referred to as chemical intolerance, idiopathic environmental intolerance or toxicant-induced loss of tolerance) is a medically unexplained disease label used to describe a condition where patients report a range of recurrent non-specific symptoms after being exposed to low levels of chemicals commonly encountered during everyday life. Such exposures could be perfumes, cleaning agents, freshly printed newspapers or car exhausts. Although reported symptoms vary considerably among patients, some of the most common ones are migraine headaches, nausea, joint and muscular pain, extreme fatigue and respiratory symptoms. MCS is considered an FSD and symptoms often overlap with symptoms of other FSDs, thus there is a substantial overlap between MCS and other FSDs.

Studies of socioeconomic status and MCS report conflicting results. In recent and relatively large population-based studies (n=2032 to n=9656), MCS individuals have been characterised as being more often women, more often unemployed and with lower social status though other studies found a higher prevalence among women with higher education level. Another population-based study conducted in 1984–1995 found no association between marital status, employment, education or income and MCS whereas in cross-sectional studies, based on convenience samples and small groups of patients with MCS, MCS cases tended to have more years of education. Based on the Danish Study of Functional Disorders (DanFunD), the aim of this study was to explore four selected social factors and the risk of MCS in the general Danish population. Information from the extensive DanFunD database allows us, in a large population-based cross-sectional study, to distinguish between MCS individuals with and without other FSDs and compare with the general population.

METHODS

Study population
This study is based on data from DanFunD. Study details have been described elsewhere. In short, the DanFunD study is a longitudinal cohort study comprising a random sample of 9656 (33.7% of the invited) men and women aged 18–76 years. During the period from 2 November 2011 to 30 June 2015, all participants completed both a general health examination and an extensive questionnaire on, for example, general health, occurrence of chronic diseases, as well as social status. The participants were born in Denmark, living in 10 municipalities in the western part of greater Copenhagen and were randomly selected from the Danish Civil Registration system. Written informed consent was obtained from each participant.

Patient and public involvement
No patient was involved.

Social status assessment
Based on available information from the questionnaire completed at the health examination, four factors served as measures of social status: cohabitation, employment, education and subjective social status.

Cohabitation was based on the two questions: ‘What is your legal marital status?’ (married, unmarried, divorced/separated, widow) and ‘Have you ever cohabited?’ (yes, currently, formerly, never), which were combined and dichotomised as ‘cohabitating’ (reference) and ‘non-cohabitating’ for analyses. Participants who previously had been cohabitating, but were not currently, were classified as ‘not cohabitating’.

Employment was based on the question: ‘What is your employment status?’ (had never been employed, were formerly employed, is currently employed). For analyses, the three answers were dichotomised into ‘employed’ (reference) and ‘unemployed’, with those who had never been employed being merged with participants who were formerly employed. Weekly hours of work or the type of work was not available.

Two questions covered education: ‘Have you completed vocational training?’ and ‘If yes, what kind of vocational training?’ which were categorised into four levels: ‘skilled worker or <1 year of vocational training (eg, trainee or skilled craftsman)’ (reference), ‘<3 years of vocational training (eg, social and health assistant or technician)’, ‘3 or 4 years of vocational training (eg, teacher or nurse)’ and ‘>4 years of vocational training (eg, doctor or engineer)’.

Finally, subjective social status was defined based on participants rating of their own social status on a scale of 1–10, with 1 being the lowest and 10 being the highest in society. For analyses, subjective social status was categorised into below average (1–4), average (5), above average (6–7) and highest (8–10) (reference).

**MCS case definition**

From the full study population and based on self-reported symptoms questionnaires, we identified all participants fulfilling the criteria for MCS. MCS criteria were constructed as an adaptation of the 1999 US Consensus Criteria for MCS and the revisions suggested by Lacour and colleagues. Thus, three criteria should be fulfilled: (1) having experienced symptoms of at least 2 of 11 common volatile odours, (2) the presence of at least one symptom from the central nervous system and at least one symptom from another organ system and (3) symptoms cause significant changes in lifestyle.

Moreover, based on standardised validated questionnaires, three different FSDs were delimited and participants fulfilling criteria for chronic widespread pain, chronic fatigue and irritable bowel were identified. Two groups were created for analyses: one group including ‘MCS’ that is all individuals fulfilling the criteria for MCS and a subgroup ‘MCS without FSD comorbidities’ that is, individuals fulfilling MCS but none of the additional three FSDs screened for. MCS cases that also fulfilled criteria for at least one other FSD were not included in the subgroup analysis. The remaining study population without any FSDs were regarded as controls.
We used age-adjusted and sex-adjusted logistic regressions to calculate the risk of MCS and MCS without FSD comorbidities for each social variable separately, with cohabitation, employment, skilled workers and high score of subjective social status as reference groups, respectively. Results are presented as OR and 95% CIs for having MCS or MCS without comorbid FSD relative to the controls.

Two adjustment models were applied to evaluate potential confounding: education and employment were considered confounders of cohabitation whereas employment was adjusted for education and cohabitation, respectively. No further adjustments were applied when education and subjective social status were analysed as exposures.

When analysing the association between employment and MCS, only participants aged 30–60 years (n=5294) were included because this age group is considered participants of the labour force.

All analyses were performed using SAS version 7.15 Guide Enterprise and R Studio.

**RESULTS**

A total of 8800 participants were included in analyses after observations with missing data on exposure and/or outcome were excluded (n=856). Characteristics of study participants are presented in table 1. Of the total population, 164 individuals (1.8%) fulfilled the criteria for MCS, and of those 101 individuals (1.1% of the total population) were identified as MCS without FSD comorbidities. The majority were women in both MCS groups, and almost half were skilled workers or had less than 1 year of vocational training. A higher proportion of MCS and MCS without FSD comorbidities self-identified as average or below average in the subjective social status ranking (table 1).

No statistically significant associations were seen between any of the social status measures and the risk of MCS without FSD comorbidities (tables 2 and 3). As for MCS, we found no association between cohabitation and the risk of MCS and adjustment for education and employment did not change the association (tables 2 and 3). Compared with employed, unemployment was associated with a higher risk of MCS (table 2). Additional adjustments for education and cohabitation, respectively, did not substantially change this association (table 3). Moreover, education was inversely associated with the risk of MCS, and low self-rated social status compared with high was associated with a higher risk of MCS (table 2).

To explore generalisability, participants with missing data were compared with those included in analyses. This showed that participants with missing data were older (median age 57 years vs 54 years, p=0.0001) and that the percentage of women was larger (55.1% vs 53.8%, p=0.44).

**DISCUSSION**

We found an increased risk of MCS among unemployed and individuals with below average self-rated subjective social status whereas individuals with more than 4 years of vocational training had a decreased risk of MCS if the person also had another FSD. There was no significant indication of an association between cohabitation and MCS. We found no associations with any of the social

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**Table 1** Participant characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total population</th>
<th>MCS</th>
<th>MCS without FSD comorbidities</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>8800</td>
<td>164</td>
<td>101</td>
</tr>
<tr>
<td>Age, median (IQR)</td>
<td>54.0 (44.0–63.0)</td>
<td>56.0 (46.8–64.0)</td>
<td>58.0 (47.0–66.0)</td>
</tr>
<tr>
<td>Females, n (%)</td>
<td>4731 (53.8)</td>
<td>105 (64.0)</td>
<td>62 (61.4)</td>
</tr>
<tr>
<td>Non-cohabiting, n (%)</td>
<td>1948 (22.1)</td>
<td>42 (25.6)</td>
<td>20 (19.8)</td>
</tr>
<tr>
<td>Education, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skilled worker or &lt;1 year of vocational training</td>
<td>3815 (43.4)</td>
<td>81 (49.4)</td>
<td>47 (46.5)</td>
</tr>
<tr>
<td>&lt;3 years of vocational training</td>
<td>1720 (19.5)</td>
<td>28 (17.1)</td>
<td>17 (16.8)</td>
</tr>
<tr>
<td>3 or 4 years of vocational training</td>
<td>2244 (25.5)</td>
<td>45 (27.4)</td>
<td>30 (29.7)</td>
</tr>
<tr>
<td>&gt;4 years of vocational training</td>
<td>1021 (11.6)</td>
<td>10 (6.2)</td>
<td>7 (6.9)</td>
</tr>
<tr>
<td>Unemployed, n (%)</td>
<td>2748 (31.2)</td>
<td>73 (44.5)</td>
<td>43 (42.6)</td>
</tr>
<tr>
<td>Subjective social status, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>2578 (29.3)</td>
<td>42 (26.2)</td>
<td>29 (28.7)</td>
</tr>
<tr>
<td>Above average</td>
<td>4535 (51.5)</td>
<td>75 (45.7)</td>
<td>48 (47.5)</td>
</tr>
<tr>
<td>Average</td>
<td>1268 (14.4)</td>
<td>32 (19.5)</td>
<td>17 (16.8)</td>
</tr>
<tr>
<td>Below average</td>
<td>419 (4.8)</td>
<td>14 (8.5)</td>
<td>7 (6.9)</td>
</tr>
</tbody>
</table>

FSDs include chronic widespread pain,25 chronic fatigue26 and irritable bowel.27 FSDs, functional somatic disorders; MCS, multiple chemical sensitivity.
The increased risk of MCS in individuals with unemployment and low self-rated subjective social status could be explained by comorbid FSDs. Comorbidities are often not included in case definitions of MCS, which could be of importance taken the social inequality in other FSDs into considerations. Studies of other FSDs and socioeconomic status have found an association between lower education and income and chronic fatigue syndrome, whereas results were conflicting for irritable bowel syndrome and no associations were found for fibromyalgia. In a recent study based on DanFunD data, a higher risk of FSDs was found among those with lower level of education, unemployment and cohabitation.

An association between socioeconomic status and MCS is still not conclusive. Occupational status is often used as a proxy of socioeconomic status and similar to our findings of higher odds of MCS among the unemployed, a Japanese population-based cross-sectional cohort study including 7542 adults found unemployment and part-time employment to be significantly associated with chemical intolerance status. However, no association was observed between employment and chemical intolerance among 2044 Japanese women aged 18–47 years. Moreover, the directionality of the association is not possible

<table>
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<tr>
<th>Table 2</th>
<th>OR of MCS according to social status indicators</th>
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<tbody>
<tr>
<td></td>
<td>MCS*</td>
</tr>
<tr>
<td>n cases/total</td>
<td>OR (95% Cl)†</td>
</tr>
<tr>
<td>Cohabitating</td>
<td>122/6852</td>
</tr>
<tr>
<td>Non-cohabiting</td>
<td>42/1948</td>
</tr>
<tr>
<td>Employed</td>
<td>70/4868</td>
</tr>
<tr>
<td>Unemployed</td>
<td>19/426</td>
</tr>
<tr>
<td>Skilled worker or &lt;1 year of vocational training</td>
<td>81/3815</td>
</tr>
<tr>
<td>&lt;3 years of vocational training</td>
<td>28/1720</td>
</tr>
<tr>
<td>3–4 years of vocational training</td>
<td>45/2244</td>
</tr>
<tr>
<td>&gt;4 years of vocational training</td>
<td>10/1021</td>
</tr>
<tr>
<td>High subjective social status</td>
<td>43/2578</td>
</tr>
<tr>
<td>Above average</td>
<td>75/4535</td>
</tr>
<tr>
<td>Average</td>
<td>32/1268</td>
</tr>
<tr>
<td>Below average</td>
<td>14/419</td>
</tr>
</tbody>
</table>

Bold indicate significance level p < 0.05
*Includes MCS cases with one or more functional somatic disorders chronic widespread pain, chronic fatigue and irritable bowel.
†OR adjusted for age and sex.
‡Adjusted for age, sex and education.
§Adjusted for age, sex and employment.
FSDs, functional somatic disorders; MCS, multiple chemical sensitivity.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>OR of MCS according to cohabitation and employment with mutual adjustments</th>
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<tbody>
<tr>
<td></td>
<td>MCS*</td>
</tr>
<tr>
<td>n cases/total</td>
<td>OR (95% Cl)†</td>
</tr>
<tr>
<td>Cohabitating</td>
<td>122/6852</td>
</tr>
<tr>
<td>Non-cohabiting</td>
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<tr>
<td>Cohabitating</td>
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<td>70/4868</td>
</tr>
<tr>
<td>Unemployed</td>
<td>19/426</td>
</tr>
</tbody>
</table>

Bold indicate significance level p < 0.0001
*Includes cases with one or more functional somatic disorders chronic widespread pain, chronic fatigue and irritable bowel.
†Adjusted for age, sex and education.
‡Adjusted for age, sex and employment.
§Adjusted for age, sex and cohabitation.
FSDs, functional somatic disorders; MCS, multiple chemical sensitivity.
to establish due to the cross-sectional study design in our and other studies, and we cannot rule out that employment status can be a consequence of having MCS. From a population-based cohort in Atlanta, Georgia, USA (total n=1291), 1.8% of the individuals with self-reported chemical sensitivity (n=193) reported loss of employment due to their sensitivities.36

In contrast to our findings of lower risk of MCS with more years of education, the Canadian Health Survey from 2014 found no association between education and MCS.3 However, they did find an association with income, which could be argued to be proportionally related to education or occupation. Thus, income of MCS individuals will be affected if they become unemployed due to health problems. On the contrary, in the population-based cohort from Atlanta, Georgia, USA, similar distributions of educational and economic levels were seen both in the entire cohort (n=1291) and in respondents with self-reported chemical sensitivity (n=193).36 Importantly, socioeconomic composition of the study population, sample size and MCS case definitions not including comorbid FSD may explain some of the differences between our and other studies.

The potential consequences and negative influence of living with MCS and other FSDs may explain the observed significant negative association between subjective self-rated social status and MCS. In a recent study, this measurement was found to be associated with the risk of FSDs,4 and it has previously been associated with ill health.30 31 Studies have shown that subjective social status is determined by occupational status, household income and satisfaction with the standard of living among others.30 Accordingly, in our study population, almost half of the individuals characterised with MCS were skilled workers or had less than 1 year of vocational training, and 44% were unemployed. This points somewhat towards socioeconomic inequality in health which has been described previously.32 33 Similarly, it has been argued that socioeconomic disparities are associated with poor environmental quality and consequently higher risk of health outcomes.9 Thus, multiple pathways may be involved such that increased educational level has a compounded effect explained by better occupational level, higher income, more physical activity, healthier diet and increased self-care.5 Conversely, less educated individuals are likely to experience less optimal living conditions such as higher noise, air pollution and so on.5 Additionally, highly educated individuals are more likely to seek medical advice and treatment compared with less educated individuals who then stay undiagnosed.39

Strengths of this study include the randomly invited population-based sample and the unique data resource from the DanFunD cohort to study MCS.12 19 MCS case status was delimited based on validated and previously applied case definitions which is still one of the most reliable tools compared with the relatively poor capture of MCS in registries. However, the participation rate in the cohort may question the generalisability of our results.19 The fact that a similar Danish cohort found non-responders to be younger, more often living alone, less educated, have lower personal income as well as having both more and longer events of hospitalisations,40 we would expect, at a group level, participants being healthier than the non-participants. On the contrary, associations between social status and FSD were not biased by non-responders in the DanFunD study.4 Socioeconomic status is often based on different indicators across studies.2 41 It has been suggested that the measurement of socioeconomic status should not rely on a single factor but include information on income, education, housing characteristics and occupation as a measure of social and economic factors that influence the status of an individual within a society.39 Thus, it is a strength of this study that several indicators of social status were included in the analyses. However, it could strengthen the study to also add national registry data on socioeconomic status rather than rely on self-reported data. Finally, it should be noted that the observed risk of MCS may be underestimated since this group includes MCS without FSD comorbidities. To elucidate a risk in MCS with FSD only, more cases would be needed. As for MCS without FSD comorbidities rather few cases were available for analyses which may have reduced the chance of significant findings. Thus, larger sample sizes in future studies are warranted to study subgroups and to increase the possibility to study whether risk increases with number of FSDs.

CONCLUSION
In this cross-sectional general population-based study, we found educational level, subjective social status and employment to be associated with the risk of MCS with comorbid FSD but not MCS without FSD comorbidities. Thus, suffering from several comorbid FSDs, which results in more symptoms, potentially has comprehensive negative consequences that extend to lifestyle and social ability, including education and later workforce participation. Lack of significant associations in the MCS group without FSD comorbidities could be due to limited power. Due to the cross-sectional design of the study, we cannot determine whether social status is a determinant or a consequence of MCS. As MCS has been found to be associated with both negative health outcomes and lower socioeconomic status, it is important both clinically and epidemiologically to apply a multidisciplinary and multifactorial approach to better understand the nature of MCS.

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