Suicidal ideation in relation to disordered eating, body size and weight perception: a cross-sectional study of a Norwegian adolescent population: the HUNT Study

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ABSTRACT

Objective We conducted a population-based study on a sample of more than 7000 adolescents where we examined the associations between suicidal ideation (SI) and disordered eating (DE) and its related traits.

Design Cross-sectional.

Settings Data were derived from two Norwegian population-based cohorts, the Young-HUNT1 (1995–1997) and Young-HUNT3 (2006–2008) from the county of Nord-Trøndelag, Norway.

Participants A total of 7268 adolescents (15–19 years) who had completed self-reported questionnaires including items on SI, DE, body size and weight perception were included.

Primary outcome measures ORs for SI given DE, body size or weight perception. Analyses were performed in multivariate logistic regression models.

Results The prevalence of SI was 23.1% in total population. Both girls and boys who reported DE, evaluated their body size as not ‘about the same as others’ or were ‘unhappy about their weight’ had between twofold to fivefold increase in odds for SI; these incremental risks were observed independent of sex, age, body mass index and socioeconomic status. We observed higher odds for SI among boys.

Conclusions Our findings suggest a clear association between SI and DE and its associated traits, in both genders but especially in males. Special attention should be paid on early detection of DE traits among adolescents.

INTRODUCTION

Suicide presides above all other causes of death in individuals aged 15–39 years.1 The WHO has urged countries to invest in comprehensive suicide prevention strategies2 that identify and address the factors underlying suicidal ideation (SI), suicidal attempt and suicide. SI varies in form and degree of severity, from fleeting thoughts to detailed planning. A meta-analysis of 172 longitudinal studies3 has shown that in adults, SI strongly correlates with suicidal attempt and death by suicide that remains robust even after adjusting for severity of depression and stress-events.4

In adolescents, SI is associated with an array of psychiatric disorders, most significantly mood disorders and eating disorders (EDs)5 and also anxiety,5 6 weight and shape concerns,7 lack of regard for one’s own body,8 higher body mass index (BMI)9 10 and binge/purge symptoms.11 12 The suicide risk seems to be higher if EDs and other psychological problems coexist.8 Predictive ability of suicide risk factors has not changed much in the past 50 years, partly due to methodological problems and lack of research on a wider list of factors that can explain SI or behaviour in a way previously identified risk factors have not.13 14

Studying factors associating suicide in populations with traits of ED poses certain difficulties. Since no more than one in four individuals with EDs come to the attention of clinicians,15 results derived from clinical data are less generalisable. Moreover, studies on the associations between SI and EDs have been limited to clinical data on EDs with
primarily female participants, while for instance in Australia, one in four and in UK, one in three preadolescents who attend special ED clinics are male. In fact, contrary to what was initially believed, prevalence of certain ED diagnoses is higher among male population than their female counterparts. Sex differences in the clinical representation of the various specific EDs are also detected. Current diagnostic criteria are mainly derived from female populations and fail to identify a sizeable number of male sufferers who do not fit in the female ED profile. The importance of research in male populations with EDs cannot be emphasised more.

Another potential problem area in conducting research in populations with EDs is the heterogeneity within and across specific ED diagnoses. EDs, as classified by American Psychiatric Association, are ‘Disorders of feeding and eating’, and range from clinical forms that meet stringent diagnostic criteria of Anorexia Nervosa to forms that fluctuate in form and severity over the years and may not necessarily fall into diagnostic categories. In both clinical and research settings, using current diagnostic criteria will inevitably lead to missing a population who presents fewer numbers of ED symptoms that may nevertheless cause discomfort or a degree of dysfunction. This particular group is referred to as one presenting symptoms of disordered eating (DE), a clinically less pronounced form of ‘disorders of feeding and eating’, that seems to occur more frequently than EDs among adolescents, especially in those with higher BMI. New and large cross-gender population-based research is essential in reliably understanding SI and its associated factors among adolescents with DE traits.

With the age for SI onset reported to be as young as 10 years, the importance of research at young adolescence period when prevalence of both SI and eating disorders (EDs) increases cannot be overemphasised. Accordingly, the purpose of the current investigation was to study DE traits in relation to SI in a large sample of more than 7000 Norwegian adolescents, including large numbers of male participants. Prevalence of SI, DE traits and their characteristics were studied. Having found supporting evidence in literature on adults, authors first examined whether DE or its related traits, such as weight and shape concerns, are associated with SI among adolescents and second whether such potential associations could be accounted for by other factors such as individuals’ level of mental distress, BMI or socioeconomic status (SES). The authors hypothesised that SI is associated with DE and its related traits such as body size or weight perception that are independent of BMI, mental distress and SES.

MATERIALS AND METHODS
Study design and population
Research subjects participated in the Young-HUNT (YH) Study, which is the adolescent arm (13–19 years) of the Nord-Trøndelag Health Study (https://www.ntnu.edu/hunt). The HUNT Study was primarily designed to investigate major public health issues in residents of the county of Nord-Trøndelag, Norway. The YH Study comprises two cross-sectional surveys so far: YH1 (1995–1997) and YH3 (2006–2008). These surveys were carried out at schools (response rates between 83% and 90%). Data on DE traits, weight and shape concerns, mental distress, SES and SI were collected through self-reported questionnaires. Clinical measurements were undertaken by specially trained nurses. The Young-HUNT database includes anonymised data on 17,820 participants. Cohort profiles of both the adult HUNT Study and the Young-HUNT Study have been previously described.

Data from the YH1 and YH3 were combined and used for the present analyses. Only participants 15 years of age or older were asked about SI and were therefore eligible for our study. The total of 7268 participants (4057 individuals from YH1 and 3211 from YH3) that had both questionnaire and clinical examination data were included in our study. Age and gender distribution in the Young-HUNT1 (mean age: 17.62, female: 52.1%) and Young-HUNT3 (mean age 17.63, female: 49.0%) were similar.

Measurements
Suicidal ideation
SI was measured by a single question asking participants: ‘Have you ever had thoughts of taking your own life?’ to which they could answer ‘Yes’ or ‘No’.

Disordered eating (DE)
EAT-7, a shortened version of The EAT (Eating Attitude Test), was used to identify participants with DE (see online supplementary appendix). Individuals who were identified as having DE were then grouped into two groups: EAT-A or ‘poor appetite/undereating’ and EAT-B or ‘uncontrolled appetite/overeating’. Association analyses were performed on sex-stratified groups with EAT-A or EAT-B compared with those without DE (reference group). For more details on EAT-7 and its psychometric properties, please see online supplementary appendix.

It is important to note that terms EDs and DE are not used interchangeably in the current study. ED has been the preferred term whenever authors referred to previous research conducted in populations with defined EDs.

Body size perception
Body size perception (BSP) was measured by asking: ‘Do you consider yourself to be: ‘very fat’, ‘quite fat’, ‘about the same as others’, ‘quite thin’ or ‘very thin’. Participants who perceived their body size as ‘about the same as others’ have been used as reference group.

Intention to lose weight
Intention to lose weight was assessed by the following question: ‘Are you trying to lose weight?’ to which participants could answer: (1) ‘No, I am comfortable with my weight’, (2) ‘No, but I need to lose weight’ or (3) ‘Yes’. Participants who were comfortable with their weight (alternative 1) were used as reference group.
Mental distress
The Five-item Hopkins Symptom Checklist (SCL-5), a valid and reliable measure of mental distress, was used to identify participants with a high degree of mental distress (see online supplementary appendix). Based on previously reported cut-off points, participants were grouped into those with ‘high’ degree of mental distress (anxiety or depression) as opposed to those with ‘low’ levels of mental distress who were used as reference group.

Anthropometric measures
Standardised measurements of height and weight were carried out by trained nurses where participants wore light clothing and no shoes. Weight was measured to the nearest half kilo and height to the nearest cm. BMI was calculated as weight (kg)/height$^2$ (m$^2$). Based on standard definitions outlined by Cole and colleagues where age and gender are taken into consideration while interpreting BMI, participants were grouped into four categories: obese, overweight, normal weight and underweight.

Socioeconomic status
Occupation, financial wealth or deprivation have previously been used as measures of SES, but education level has been reported as the best measurement to identify health inequalities. In our study, maternal education level is used as a proxy for SES.

Every Norwegian citizen has a unique personal 11-digit identification number, which was used to identify participants’ mothers from the Norwegian Family Register. The data on education were then obtained from the Statistics Norway database (SSB) on 6852 mothers. The educational levels were coded according to the Norwegian Standard Classification of Education (NUS) into three: primary (0–10 years school attendance, reference category), secondary (11–14 years of school attendance) and tertiary (>14 years of school attendance).

Statistical analysis
Multivariable logistic regression models were employed in sex-stratified samples to investigate the associations between DE, BSP and intention to lose weight and SI in separate models for each exposure factors. Models were adjusted for age, BMI, mental distress and SES. Results are reported as OR with 95% CI. Overall missingness was <5% and considered missing at random. We performed a complete case analysis. Models were fitted in IBM SPSS Statistics 25.

Based on previous reports on validity and reliability of single-item question on SI, the authors concluded that statistical errors are less likely to have influenced the results in a meaningful way, first due to fairly large effect sizes observed and reduction in the chances for a Type II error and second due to a relatively large sample size that reduces the possibility of a Type I error. Collinearity between exposure variable was examined in linear regression model. The authors found no evidence of multicollinearity as assessed by tolerance values greater than 0.1. Inspection of correlation coefficient showed no evidence in support of high correlations (all values were under 0.7).

Independent-samples t-tests and $\chi^2$ tests of independence (both significant at the 0.05 level) were performed to determine whether participants from YH1 and YH3 differed in ways that would affect the validity of our results derived from pooled data. Participants were compared on all exposure variables. Wherever no statistically significant differences were observed, the association analyses were done on pooled data from YH1 and YH3 cohorts. Otherwise, association analyses were done separately in YH1 and YH3 as well as on the pooled data. Comparing the results from these separate analyses detected no meaningful difference. Results are therefore reported for pooled data only.

Ethics statement
Our study was conducted in accordance to the Helsinki Declaration and was approved by the Regional and National Committees for Medical and Health Research Ethics (2009/740-2) as well as by the Norwegian Data Inspectorate. In Norway, the legal age for consent is 16 years. Written consents were obtained from participants older than 16 and from their parents or legal guardians for younger participants.

Patient and public involvement statement
Patients and the public were not involved in the design and conception of the study. Recruitment phase was entry level for the public. There are no plans to disseminate the results to patients.

RESULTS
Population characteristics
Overall prevalence of SI in our study population was 23.6%. Prevalence of SI was similar between YH1 and YH3 (table 1). The prevalence of SI among adolescents in the poor appetite/undereating group was 44.1% and 35.0% among those in the uncontrolled appetite/overeating group, as opposed to 20.5% in participants without DE.

Uncontrolled appetite/overeating was more prevalent (11.8%) than poor appetite/undereating (4.7%) with girls more affected than boys in both groups (table 1). The prevalence of poor appetite/undereating was similar in YH1 and YH3 (4.5% and 5.0%, respectively) while the prevalence of uncontrolled appetite/overeating decreased from YH1 to YH3 (13.7% to 9.4%).

Compared with those without DE, more participants with DE perceived themselves as not ‘about the same as others’ (table 2). In the total sample, 57.2% perceived their body size as not ‘about the same as others’, whereas more girls compared with boys perceived themselves as ‘fat’ or ‘very fat’ while more boys, perceived themselves as ‘thin’ or ‘very thin’ (table 1). Irrespective of BMI, a general trend of underestimation of body size in boys and overestimation in girls was found (online supplementary table 1).
Association between suicidal ideation and disordered eating

Compared with those without DE and in both genders, the odds for SI were more than doubled in the poor appetite/undereating group and almost doubled in the uncontrolled appetite/overeating group. Adjustment for age made negligible changes in the OR for SI; however, adjustments for BMI further increased the odds in both sexes without losing statistical significance (tables 3 and 4). With further adjustments for mental distress, the odds for SI remained statistically significant in both sexes in the respective DE subgroups although the effect sizes decreased. After adjustment made for age, BMI and mental distress, boys had higher odds for SI compared with girls in both DE groups (tables 3 and 4).

Association between suicidal ideation and body size perception

In both sexes, perceiving body size as not ‘about the same as others’ (‘very fat’, ‘quite fat’, ‘quite thin’ or ‘very thin’) was associated with higher odds for SI. For instance, boys who perceived their body size as ‘very fat’ showed an OR of 4.45 (2.38–8.31) compared with boys who perceived their body size as ‘about the same as others’. The same comparison in girls yielded an OR for SI of 5.54 (3.75–8.18). Similar observations were made in boys or girls who perceived their body size as ‘quite fat’. Higher odds for SI in groups with BSP as ‘quite thin’ or ‘very thin’ were only statistically significant in boys (see tables 3 and 4). All results were robust to adjustment for age, BMI and SCL-5. In both sexes, ORs for SI were higher the farther BSP deviated from the population norm (‘about the same as others’), in either direction. With some small exceptions, adjustment for mental distress reduced the odds for SI across all BSP groups in both girls and boys (tables 3 and 4). Compared with boys, girls who considered their body size as ‘very fat’ showed slightly higher odds of SI after adjustments for age and BMI. Potential moderator effect of sex was examined in a two-way analysis of covariance model in the full dataset with interaction terms. We found no statistical evidence that sex had significant moderator effect on the association between BSP ‘very fat’ and SI (p value: 0.118).

Association between suicidal ideation and intention to lose weight

In the crude analyses, ‘intention to lose weight’, even without actively engaging in weight reduction measures, more than doubled the odds for SI in both genders (tables 3 and 4). Compared with those who ‘did not try to lose weight’, the OR for SI in those who intended to lose weight was doubled in boys and nearly tripled in girls. These findings were robust to adjustments made for age, BMI and mental distress (tables 3 and 4).

Testing for possible confounding effect of socioeconomic status (SES)

A subsample of 6852 participants with available information on highest maternal education level was used
to investigate possible confounding effect of SES on the associations between SI and DE, BSP or intention to lose weight. Adjusting for SES made very slight change to our findings (tables 3 and 4).

DISCUSSION

Principal findings of this study

Our findings point at a considerable collective increase in the odds for SI among adolescents with traits of DE, body size or weight concerns as well as with other factors such as BMI and mental distress. Adolescent boys with DE traits showed a vulnerability for having SI and require special attention in suicide risk assessment and treatment approaches.

Comparison with previous studies

In line with previous reports, we found that DE was far more prevalent than clinically diagnosed EDs, suggesting that in identification of vulnerable individuals and groups, more weight should be given to the presence of DE symptoms and traits rather than solely to presence or absence of a clinical diagnoses (EDs). A sizeable proportion of

| Table 2 | Intention to lose weight and body size perception in individuals with DE in pooled data |
|-----------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|--------------------------------------|
|                | **Uncontrolled appetite/overeating group**  | **Poor appetite/undereating group**             |
|                | **Total**  | **Boys**  | **Girls**  | **Total**  | **Boys**  | **Girls**  |
|                | **N (%)** | **N (%)** | **N (%)**  | **N (%)**  | **N (%)**  | **N (%)**  |
| Intention to lose weight |         |          |            |            |          |            |
| Yes            | 128 (15.3) | 20 (5.6) | 108 (22.7) | 166 (49.7) | 13 (18.1) | 153 (58.4) |
| No, but I need to lose weight | 89 (10.7) | 17 (4.7) | 72 (15.2) | 71 (21.3) | 13 (18.1) | 58 (22.1) |
| No, I am happy with my weight | 617 (74.0) | 322 (89.7) | 295 (62.1) | 97 (29.0) | 46 (63.8) | 51 (19.5) |
| Body size perception |          |          |            |            |          |            |
| Very fat       | 15 (1.8) | 4 (1.1) | 11 (2.3) | 27 (8.1) | 7 (9.9) | 20 (7.6) |
| Quite fat      | 118 (14.0) | 25 (6.9) | 93 (19.4) | 146 (43.6) | 19 (26.8) | 127 (48.1) |
| About the same as others | 356 (42.3) | 133 (35.7) | 223 (46.5) | 124 (37.0) | 27 (38.0) | 97 (36.7) |
| Quite thin     | 298 (35.4) | 163 (43.6) | 135 (28.1) | 33 (9.9) | 16 (22.5) | 17 (6.4) |
| Very thin      | 55 (6.5) | 37 (10.2) | 18 (3.8) | 5 (1.5) | 2 (2.8) | 3 (1.1) |

DE, disordered eating.

Table 3 ORs for SI given disordered eating, body size perception or intention to lose weight in boys

| Disordered eating | Non-adjusted | Adj. for age | Adj. for age/BMI | Adj. for age/BMI/SCL-5 | Adj. for age/BMI/SCL-5/SES |
|-------------------|--------------|--------------|------------------|------------------------|---------------------------|
| Poor appetite/   |              |              |                  |                        |                           |
| Undereating       | 2.47* 1.53 to 3.98 | 2.47* 1.53 to 3.97 | 2.87* 1.75 to 4.71 | 2.10* 1.19 to 3.73 | 2.28* 1.26 to 4.11 |
| Uncontrolled     |              |              |                  |                        |                           |
| appetite/overeating | 1.95* 1.53 to 2.47 | 1.95* 1.53 to 2.47 | 2.09* 1.61 to 2.71 | 1.77* 1.34 to 2.35 | 1.81* 1.35 to 2.42 |
| Body size perception |          |              |                  |                        |                           |
| Very fat         | 4.45* 2.38 to 8.31 | 4.44* 2.38 to 8.30 | 5.68* 2.78 to 11.61 | 4.20* 1.96 to 9.02 | 4.43* 2.02 to 9.71 |
| Quite fat        | 1.93* 1.56 to 2.39 | 1.93* 1.56 to 2.39 | 2.13* 1.63 to 2.78 | 1.74* 1.31 to 2.32 | 1.64* 1.22 to 2.21 |
| Quite thin       | 1.44** 1.17 to 1.76 | 1.44** 1.17 to 1.76 | 1.53* 1.22 to 1.92 | 1.47** 1.16 to 1.87 | 1.51** 1.18 to 1.93 |
| Very thin        | 3.15* 1.83 to 5.42 | 3.14* 1.83 to 5.41 | 3.82* 2.06 to 7.08 | 3.39* 1.75 to 6.53 | 2.99** 1.51 to 5.92 |
| Intention to lose weight |      |              |                  |                        |                           |
| Yes              | 2.04* 1.54 to 2.71 | 2.04* 1.54 to 2.71 | 2.24* 1.61 to 3.11 | 1.53** 1.06 to 2.21 | 1.47** 1.01 to 2.15 |
| No, but I need to lose weight | 2.01* 1.60 to 2.53 | 2.23* 1.69 to 2.95 | 2.95* 1.88* 1.39 to 2.55 | 1.83* 1.34 to 2.52 |

Reference category in the dependent variable: no SI. Reference categories in the predictors: Disordered eating: below cut-off for each trait. Body size perception: about the same as others. Intention to lose weight: No. Adjustment for SES from a subsample of 6552 participants. Primary level education used as reference category. *P<0.001, **p<0.05.

BMI, body mass index; SCL-5, The Five-item Hopkins Symptom Checklist; SES, socioeconomic status; SI, suicidal ideation.
high-risk individuals do not meet stringent diagnostic criteria for EDs and hence might slip through the safety net before a suitable care approach can be warranted.

There is a high comorbidity between DE and mental distress in the form of anxiety or depressive disorders, both closely linked to SI and attempted suicide. DE or subjective perception of body shape or weight is not routinely included in clinical suicide risk assessments which might lead to underestimation of vulnerability to future SI or suicidal attempts.

Although our findings were of similar calibre and direction in both sexes, we observed some sex differences concerning BMI and mental distress. Our observations were in line with previously found sex differences in clinical manifestations of EDs or 2-BSP in relation to actual BMI, with girls showing a tendency to overestimate and boys consistently underestimating their body size. In keeping with previous reports, our male participants showed less inclination than the females to lose weight, independent of their actual BMI. Unlike previous research that has accounted BMI for gender differences in ED manifestations, higher BMI could not explain higher OR for SI among our male participants with DE traits, possibly because they were not as much concerned with their BMI as they are with looking masculine and lean. In contrast, their female counterparts seem to be more concerned about their weight, which in effect renders BMI less indicative of presence or severity of DE among males. Similar to previous reports, we found higher vulnerability to mental distress among adult male sufferers of DE. Presence of psychiatric comorbidities can potentiate existing associations between DE and SI among males with DE. Furthermore, male populations seem to be more reluctant in seeking help for their symptoms which can further exacerbate the associations between DE and SI as these individuals will not be receiving help for either condition. Further research is required for understanding what constitutes this gender difference. Considering the increase in the incidence rates of EDs among men who also seem to present different set of symptoms of EDs, screening and treating men with EDs is becoming more and more a priority. Current reliance on a diagnostic framework based on thinness fails in identification of musculature-oriented pathology of EDs in male population, in clinical or research settings.

Some discrepancy between participants’ actual BMI and BSP was observed (see online supplementary table 1) where individuals inaccurately perceived their own body size by means of underestimation or overestimation. The direction of BSP inaccuracy, as underestimation or overestimation of BSP, in conjunction with gender specific BMI in clinical or research settings. For either condition. Further research is required for understanding what constitutes this gender difference. Considering the increase in the incidence rates of EDs among men who also seem to present different set of symptoms of EDs, screening and treating men with EDs is becoming more and more a priority. Current reliance on a diagnostic framework based on thinness fails in identification of musculature-oriented pathology of EDs in male population, in clinical or research settings.

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between BSP, BSP accuracy, BMI and intention to lose weight require full exploration that is beyond the scope of current study but is being investigated in a parallel study conducted (by the authors) on determinants of dieting in a Norwegian community sample (the HUNT Study).

**Strengths and limitations**

Strengths of this study include the large sample size derived from a total Norwegian adolescent population with a homogenous ethnic background. Further, anthropometric measurements were carried out by trained nurses. To date, most studies on EDs have relied on clinical data or patient registries of adult populations which leaves out the adolescents in the general population in the time period when psychological distress and disorders often manifest. With the median age of onset for developing EDs reported as low as 12–13 years old, the importance of studying younger affected individuals could not be more emphasised. Studies on male ED sufferers are fewer and far in between, with adolescent male participants usually lumped into adult populations. Our results are of general relevance since our observations were made in a large, population-based adolescent dataset that included both males and females.

Conclusions should be drawn in the light of certain limitations in the current study. The use of shortened and self-reported measures of DE (EAT-7) or mental distress (SCL-5), and not standardised psychiatric interviews, has in effect rendered our findings less generalisable to clinical populations. SI was assessed by a single item question. Due to temporal bias in a cross-sectional design, we are not able to assess potential causal relationships between DE traits and SI. We do not interpret our results as causal but rather associative, hence, the importance of conducting future longitudinal studies on causality in larger populations. One interesting line of enquiry is to look at various DE traits clustered in smaller groups based on participants’ BMI or BSP, which was not possible to perform in the current study given small number of participants in each cluster. Conducting a follow-up study on a larger dataset from the HUNT Study including adolescents from the most recent data collection, HUNT4 Survey (2017–2019), may reach a higher statistical power and hence more conclusive results. Using single-item question on SI in future studies provides an opportunity of validity and to confirm the results obtained here and is hence encouraged by the authors; however, to overcome miscalculation or misinterpretation errors, adding follow-up questions will supplement information derived from a single-item question on SI. Time lapse since YH1 makes prevalence reports from that time less reflective of the current situation; however, authors found no evidence that suggested pooling data from YH1 and YH3 would render the study findings less valid. On the other hand, older cohorts such as YH1 are useful in retrospective research on potential time trends in DE manifestations or their potential impact on prevalence of SI among adolescence. Furthermore, such retrospective studies can provide inferential insight into, for example, how environmental changes might have associated with time trends of DE traits among adolescents.

**CONCLUSION**

An individually tailored approach to suicide risk assessment and management seems to be more appropriate in subpopulations of adolescents with DE and its related traits. Our findings on difference between female and male adolescents may have potential implications in the way clinicians address SI across genders. Shifting focus from maintaining a healthy BMI to addressing individuals’ attitudes towards their own body shape and size is important in designing treatment plans that reduce burden of SI or attempts. Timely identification of associated factors for SI in high-risk but non-clinical populations is important in designing strategic and preventive measures that intend to cut human and economic costs of SI and attempts. Future longitudinal research in both clinical and community populations, preferably with data on onset, frequency and severity of SI in comparison to that of DE traits could help in overcoming current methodological and interpretational difficulties in drawing more conclusive results on temporal relationship between these factors.

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**Contributors**

FSS has conceived the idea, performed the analyses and drafted the manuscript. FSS, TLH, NM, ERS, OB and KK have contributed to interpretation of results and critical revision of manuscript. FSS, TLH, NM, ERS, OB and KK have read and approved of the final version of manuscript before its submission. FSS, TLH, NM, ERS, OB and KK can be held accountable for all aspects of the work.

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**Competing interests**

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