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Accumulation of sensory difficulties predicts fear of falling in older women

Abstract

Objectives: To explore whether the accumulation of sensory difficulties predicts fear of falling (FOF), and whether the traits correlate with each other regardless of familial factors. 

Methods: Self-reported hearing, vision and balance difficulties, and FOF were assessed using structured questionnaires at the baseline and after a three-year follow-up in 63-76 year-old women (n=434). Results: Among the women without FOF at baseline (n=245), 41% reported FOF at follow-up. Increasing numbers of sensory difficulties at baseline predicted higher incidence of FOF. The relationship between accumulated sensory difficulties and FOF was not mediated by familial factors. Discussion: The accumulation of multiple sensory difficulties may hinder older people from receiving compensatory information about body position and environment, thus jeopardizing a person’s confidence in maintaining a balanced position. Regular screening of sensory functions followed by appropriate actions may prevent the development of FOF, and thus contribute to prevention of falls and promotion of healthy aging.

Keywords: aging, fear of falling, hearing, postural balance, vision
Accumulation of sensory difficulties predicts fear of falling in older women

Fear of falling (FOF) is defined as “a lasting concern about falling that leads to an individual avoiding activities that he/she remains capable of performing” (Tinetti & Powell, 1993). Prevalence rates for FOF in community-living older persons range from 20 to above 80%, depending on the methods and samples used (Arfken, Lach, Birge, & Miller, 1994; Curcio, Gomez, & Reyes-Ortiz, 2009; Howland et al., 1998; Scheffer, Schuurmans, van Dijk, van der Hooft, & de Rooij, 2008; Tinetti, Mendes de Leon, Doucette, & Baker, 1994; Zijlstra, van Haastregt, van Eijk et al., 2007). FOF and falls are interrelated problems, each constituting a risk factor for the other (Friedman, Munoz, West, Rubin, & Fried, 2002). However, FOF may also emerge without the occurrence of falls (Arfken et al., 1994; Friedman et al., 2002; Tinetti et al., 1994). In addition to falls, FOF may lead to decreased physical activity and physical performance, reduced social activity, depression as well as decreased quality of life (Deshpande et al., 2008; Friedman et al., 2002; Legters, 2002; Li, Fisher, Harmer, McAuley, & Wilson, 2003; Scheffer et al., 2008).

Knowledge on the role of sensory difficulties in FOF is limited. Some of the earlier studies have suggested that vision (Arfken et al., 1994; Fletcher & Hirdes, 2004; Guthrie et al., 2012; Martin, Hart, Spector, Doyle, & Harari, 2005; Murphy, Dubin, & Gill, 2003) and balance difficulties (Guthrie et al., 2012; Kressig et al., 2001; Lach, 2005; Murphy et al., 2003; Vellas, Wayne, Romero, Baumgartner, & Garry, 1997) are associated with prevalent FOF, but opposite results have also been reported (Friedman et al., 2002; Howland et al., 1998; Kempen, van Haastregt, McKee, Delbaere, & Zijlstra, 2009; Murphy et al., 2003; Reelick, van Iersel, Kessels, & Rikkert, 2009). Only a few prospective studies have reported on the effects of sensory functions on incident FOF (Austin, Devine, Dick, Prince, & Bruce, 2007; Friedman et al., 2002; Lach, 2005; Murphy et al., 2003). According to Austin et al. (2007) and Lach (2005) poor standing balance was cross-sectionally associated with FOF, but
balance impairment did not predict incident FOF over follow-up of one to three years. Similarly, vision did not predict FOF in a study by Friedman et al. (2002), whereas Murphy et al. (2003) supported the predictive value of visual impairment on FOF. The potential association between hearing difficulties and FOF has been supported by Viljanen et al. (2012), and by studies on hearing and falls (Evci, Ergin, & Beser, 2006; Grue et al., 2009; Kulmala et al., 2009; Viljanen, Kaprio, Pyysko, Sorri, Pajala et al., 2009). In addition, while among older people sensory difficulties often coincide, no previous studies have demonstrated the effect of accumulated sensory difficulties on FOF. Viljanen et al. (2012) provided preliminary evidence for the association between accumulated sensory difficulties and FOF, and also demonstrated that older women who have several sensory difficulties combined with FOF have an increased risk for walking difficulties.

Previous twin studies have demonstrated that individual differences in visual acuity (Lopes, Andrew, Carbonaro, Spector, & Hammond, 2009), hearing acuity (Christensen, Frederiksen, & Hoffman, 2001; Viljanen et al., 2007; Wingfield et al., 2007), postural balance (El Haber et al., 2006; Pajala et al., 2004; Wagner, Melhus, Pedersen, & Michaelsson, 2009), as well as falls (Pajala et al., 2006), are either modestly or largely accounted for by familial factors, that is, by either additive genetic factors or common environmental factors. Fears, phobias and anxiety (Chantarujikapong et al., 2001; Distel et al., 2008; Hettema, Neale, & Kendler, 2001; Marks, 1986), as well as posttraumatic stress disorder (Afifi, Asmundson, Taylor, & Jang, 2010), also have a familial background, although no heritability studies on FOF exist. Information on whether sensory functions and FOF are influenced by same familial effects is also lacking. By identifying and comparing twin pairs discordant for sensory difficulties, information about whether sensory difficulties and FOF correlate with each other because of or regardless of familial factors can be obtained.
Although FOF and sensory difficulties are acknowledged problems among the older population, knowledge of the association between sensory functions and FOF is limited. In particular, prospective studies and studies on the combined effects of sensory difficulties on FOF are lacking. The purpose of this study is to investigate whether self-reported hearing, vision and/or balance difficulties are associated with FOF at baseline, and whether sensory deficits predict the incidence of FOF in a three-year follow-up among community-dwelling older women. Furthermore, the effects of familial factors for the possible association between sensory functions and FOF are estimated.

**Method**

**Participants**

Participants were recruited through the nationwide Finnish Twin Cohort, which comprises all same-sex twin pairs born before 1958 with both co-twins alive in 1975. Inclusion in the Finnish Twin Study on Aging (FITSA) required that both individuals in the twin pair had to be willing to participate and to be able to travel to the research laboratory from their town of residence. Consequently the sample consists of 434 relatively high functioning 63 to 76 year-old women from 103 monozygotic and 114 dizygotic twin pairs. The follow-up study was conducted after three years with 419 women (96.5%). During the follow-up, 7 participants died and 8 participants dropped out for health reasons. The recruitment procedure has been described in detail elsewhere (Kaprio & Koskenvuo, 2002; Viljanen, Kaprio, Pyykko, Sorri, Koskenvuo et al., 2009). The study was approved by the Ethics Committee of the Central Finland Health Care District.

**Fear of falling**

FOF was assessed at baseline and at follow-up with the question “Are you afraid of falling?”. Possible answers to the question were: "never", "occasionally", "often", or "constantly ". The participant was categorized as having FOF, if she reported FOF at least
occasionally. FOF was used as a dichotomous variable (yes/no FOF) as very few participants reported FOF often or constantly.

**Sensory functions**

Perceived sensory functions were assessed at baseline using questionnaires. **Hearing** was assessed by the question, “Do you have difficulties hearing, when you have a conversation with several people simultaneously?” The response options were “No difficulties”, “Sometimes, minor difficulties”, and “Yes, major difficulties”. These were subsequently dichotomized into “No difficulties” and “Difficulties”. **Vision** was assessed by the question, “How well can you see from a distance?” The response options were “Well”, “Reasonably well”, and “Poorly”, and dichotomized into “Well” and “Not well”. **Balance** was assessed by the question, ”Are you dizzy or do you suffer from poor balance?” The response options were ”Rarely or never”, ”Sometimes, causing me some distress”, ”Often, causing me much distress”, and dichotomized into ”Rarely or never” and ”At least sometimes”. The number of sensory difficulties was calculated by summing the responses describing the presence (scored as 1) or absence (scored as 0) of difficulties in vision, hearing and balance (range 0-3).

**Descriptive variables**

Self-reported chronic conditions and use of medications were confirmed by a physician during the baseline clinical examination. The Mini-Mental state examination (MMSE) was used to test cognitive capacity. Information on total length of education (years) was gathered using a structured questionnaire.

Separate variables on falls were used in the cross-sectional baseline analyses, and prospective longitudinal analyses. At baseline, history of severe falls was assessed retrospectively by the question, “Have you ever fallen so that it caused you a fracture or other severe injury?” (yes/no).
Information on fall incidence post-baseline was gathered at two time-points during the three-year follow-up. First, information on falls was gathered prospectively for the first year of the follow-up using the fall-calendar method. Participants marked daily on a calendar whether they fell or not, and at the end of each month they mailed the calendar page to the research center. If a fall was reported, the participant was interviewed over the phone about the circumstances, causes, and consequences of the fall (Pajala et al., 2006). A fall was defined as severe if it required treating by a physician. Second, information on falls was gathered retrospectively for the last year of the follow-up by questionnaire, according to the question, “Have you fallen during the last year so that it required physician’s treatment” (yes/no).

**Statistical analysis**

The differences in the proportions of participants with hearing, vision or balance difficulties with respect to FOF were tested with the Wald test adjusted for statistical within-pair dependency resulting from the sampling of twin pairs. The proportion of persons with a history of a previous serious fall, as well as mean differences in age, cognitive function, number of chronic diseases and number of prescribed medications in the two FOF categories were tested in a similar way.

Logistic regression models were used to analyse whether sensory difficulties were associated with FOF cross-sectionally at baseline and whether sensory difficulties at baseline predicted onset of FOF at follow-up three years later among those without FOF at baseline. Regression models were adjusted for age and number of chronic diseases. Furthermore, the cross-sectional baseline analyses were adjusted for history of a previous severe fall, and prospective longitudinal analyses were adjusted for incidence of a severe fall during the follow-up.
We identified twin pairs discordant for sensory difficulties to compare the presence of FOF of the sister with no sensory difficulties with that of her co-twin with two or three sensory difficulties. By using discordant twin pairs it is possible to control for the familial factors, i.e. genetic or environmental factors shared by the siblings, which may contribute to the association between sensory functions and FOF, and this case-control analysis provides information about whether the studied traits correlate with each other because of or regardless of familial factors. Lower odds ratio (OR) among discordant twin pairs compared to OR of the individual based analyses would indicate that familial factors are influencing on the association between traits.

The modelling was performed using Stata statistical software taking into account the within-pair dependency of twin individuals (Stata Corp., College Station, TX). P-values of <0.05 were considered as statistically significant.

Results

A total of 173 women (40%) reported FOF at baseline. Participants with and without FOF did not differ according to age, MMSE score, education or number of prescribed medications. Participants with FOF reported more chronic diseases than participants without FOF. Participants with FOF also reported a history of a previous severe fall more often than those without FOF (48% vs. 32%, \( p = .001 \)) (Table 1). Increasing numbers of sensory difficulties were associated with increasing FOF (Table 2). No single sensory difficulty was associated with FOF, but all possible combinations of two sensory difficulties were associated with FOF. The highest OR for FOF was found for participants who had both vision and balance difficulties or who had all three sensory difficulties compared to participants with no sensory difficulties. Models were adjusted for age, number of chronic diseases and history of a previous severe fall (Figure 1).
Among the 245 women without FOF at baseline, 101 (41%) participants reported FOF in the three-year follow-up. Increasing numbers of sensory difficulties at baseline predicted higher incidence of FOF (Table 3). According to the sensory specific analyses, the highest OR for incident FOF was observed among the participants who had all three sensory difficulties compared to those with no sensory difficulties (Figure 2). Models were adjusted for age, number of chronic diseases and incidence of a severe fall during the follow-up ($n=46$).

Altogether 32 twin pairs, 21 monozygotic and 11 dizygotic pairs, were discordant for sensory difficulties, with one sister reporting no sensory difficulties and other sister reporting two or three sensory difficulties. The age adjusted OR for FOF among the sister with two or three sensory difficulties compared to the sister reporting no sensory difficulties was 3.5 (95% CI 1.3-9.4), indicating no difference between the pairwise estimate and the estimate derived from all individuals.

**Discussion**

Results of this study showed that the accumulation of multiple sensory difficulties predicted FOF. When controlled for shared familial effects within twin pair comparisons, the sister with accumulated sensory difficulties had a significantly higher odds for FOF compared to her sister with no sensory difficulties. The odds for FOF in the discordant twin pair analysis was of the same magnitude as the odds in the whole sample, suggesting that the relationship between accumulated sensory difficulties and FOF is not mediated by familial factors, which may be either shared genetic factors or environmental factors experienced in common by siblings.

According to our results, persons who simultaneously had balance, vision and hearing difficulty had over eight-fold higher risk for FOF compared to persons who did not have any of these three sensory difficulties. Persons who had only one sensory difficulty were not at
increased risk for FOF. The results suggest that the lack of environmental information caused by sensory difficulties induces FOF, but also that, at least to some extent, difficulties in a single sensory modality can be compensated for by another modality. This is supported, for example, by previous studies among deaf and blind people and animals, where adaptive and compensatory changes have been observed in the processing of information by the remaining sensory modalities (Merabet & Pascual-Leone, 2010). However, very little is still known about the plasticity of the brain and consequent compensatory mechanisms in older adults whose vision or hearing, or, in the worst case both, are decreasing progressively and who have maintained some degree of residual sensory function (Merabet & Pascual-Leone, 2010), as was the case in this study.

In addition to accumulated sensory difficulties, severe falls were significant predictors of FOF in this study. The participants who had experienced a severe fall during the three-year follow up had almost four-fold higher risk for FOF compared to those persons who did not report severe falls. However, according to our results, sensory difficulties were associated with FOF independently of severe falls. Many previous prospective studies have shown falls, injurious falls or recurrent falls to be important risk factors for FOF (Austin et al., 2007; Curcio et al., 2009; Friedman et al., 2002; Lach, 2005; Murphy et al., 2003). In this study, severe falls were selected for analysis as they were more strongly associated with FOF than the number of non-injurious falls (Results not shown). It is also theoretically reasonable to consider that falls with serious consequences are more likely than non-injurious falls to induce FOF. Further, it is likely that in retrospective analyses participants recall severe falls that have required treatment by a physician better than non-injurious falls.

FOF may push older people into a spiral of loss of confidence, restriction of physical and social activities, physical frailty, falls, and eventually loss of independence. It is important to intervene in such a downward spiral by trying to influence the factors involved
Interventions that have been shown to be the most effective in reducing FOF are multifactorial cognitive behavioral programs (Tennstedt et al., 1998; Zijlstra et al., 2009), tai chi interventions, exercise interventions, and a hip protector intervention (Bula, Monod, Hoskovec, & Rochat, 2011; Zijlstra, van Haastregt, van Rossum et al., 2007). Several previous studies have found support for the positive effect of balance training on FOF, but studies with no improvements have also been reported (Bula, Monod, Hoskovec, & Rochat, 2011; Zijlstra, van Haastregt, van Rossum et al., 2007). The importance of vision in FOF is also recognized. The randomized trial by Clemson et al. (2004) was based on a multifaceted community-based fall-prevention program. The results indicated that regular visual screening can reduce falls and maintain confidence in the ability to avoid a fall during a variety of functional daily living tasks. Our present study suggested that interventions targeted to improve, correct, or accommodate vision, hearing and balance may help to reduce FOF. A regular ophthalmic examination and audiometric screening followed by appropriate treatment and rehabilitation, such as surgery, use of spectacles or a hearing aid, as well as environmental modifications, could help prevent FOF in older people. Furthermore, attention should be paid to the prevention and proper treatment of diseases, such as diabetes and cardiovascular diseases, which affect sensory systems.

FOF may also serve as a protective factor for falls through avoidance of hazardous environmental situations. For example, a person with poor vision may avoid walking in poor lightning conditions and thus reduce exposure to potential fall risk factors. Environmental modifications, such as better lighting, may reduce FOF and so support the functioning of persons with sensory impairments. However, further studies are needed to determine whether environmental interventions are effective at the population level.

This study comprised a population-based sample of well-functioning, community-dwelling women. To be recruited for this study, participants had to be able to travel to the
research centre from their town of residence for the baseline measurements. Therefore, the present sample was composed of relatively healthy older people, and it is possible that some women with FOF or sensory difficulties dropped out. FOF was determined according to a single question instead of activity-related multi-dimensional questionnaires, and this may in part modify the results. However, it has been argued that a one-item FOF measure may accurately capture the generalized dimension of fear across many different situations and activities (Lachman et al., 1998). The results of this study are based on self-reported evaluations of sensory functions. It has been suggested that perceived and objectively assessed sensory functions are related but emphasize different dimensions of functioning. Self-reports provide information about perceived difficulties in the everyday environment and are thus clinically relevant (Kempen et al., 1996; Viljanen et al., 2007). The participants in this study were cognitively high functioning, which supports the validity of their self-assessments (Kempen et al., 1996).

The prevalence of self-reported FOF and sensory difficulties in this twin-sample were in line with those of the previous non-twin population-based studies (Agrawal, Carey, Della Santina, Schubert, & Minor, 2009; Chia et al., 2007; Steinman & Allen, 2012; Zijlstra, van Haastregt, van Eijk et al., 2007). However, exact comparison between studies is challenging due to the different methods and samples used. Because only very few participants reported constant FOF or severe sensory difficulties, the variables were dichotomized, and thus the severity of difficulties or FOF could not be taken into account in the analyses. Had the sample consisted of participants with more severe sensory difficulties or more constant FOF, the associations found between sensory functions and FOF might have been even stronger. It is also worth of notice that by using the present data it is not possible to disentangle participants who reported FOF as a wise, protective reaction for transitory dangerous situations, for example icy roads, from participants who suffer with debilitating, restrictive
fear. Further studies with larger, more heterogeneous study populations, including men, are warranted to better understand the complex, multidimensional associations between sensory functions, FOF and falls.

**Conclusion**

According to our results, the accumulation of sensory difficulties predicts FOF. Such accumulation may hinder older people from receiving compensatory information about body position and the environment, thus jeopardizing a person’s confidence in maintaining a balanced position. Regular screening of sensory functions followed by appropriate actions may prevent the development of FOF, and thus contribute to the prevention of falls and promotion of healthy aging. Alongside person-related interventions, environmental modifications can be introduced to create neighbourhoods for older people that are accessible, and visually and auditorily mobility-promoting. However, further experimental studies are warranted to determine whether such interventions are effective.
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References


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Table 1

Baseline Characteristics of Participants with and without Fear of Falling

<table>
<thead>
<tr>
<th>Variable</th>
<th>FOF</th>
<th>no FOF</th>
<th>Wald test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( n=173 )</td>
<td>( n=261 )</td>
<td></td>
</tr>
<tr>
<td>Number of sensory difficulties (min 0 – max 3), ( n=431 )</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>29 (17)</td>
<td>84 (32)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>One</td>
<td>52 (30)</td>
<td>102 (39)</td>
<td></td>
</tr>
<tr>
<td>Two</td>
<td>63 (37)</td>
<td>59 (23)</td>
<td></td>
</tr>
<tr>
<td>Three</td>
<td>28 (16)</td>
<td>14 (5)</td>
<td></td>
</tr>
<tr>
<td>History of a previous severe fall</td>
<td>83 (48)</td>
<td>83 (32)</td>
<td>.001</td>
</tr>
<tr>
<td>mean (SD)</td>
<td>68.7 (3.5)</td>
<td>68.6 (3.4)</td>
<td>.732</td>
</tr>
<tr>
<td>Number of chronic diseases</td>
<td>2.3 (1.6)</td>
<td>1.8 (1.4)</td>
<td>.002</td>
</tr>
<tr>
<td>Number of prescribed medications</td>
<td>2.1 (2.1)</td>
<td>1.9 (1.9)</td>
<td>.354</td>
</tr>
<tr>
<td>MMSE (score)</td>
<td>26.9 (2.6)</td>
<td>27.0 (2.1)</td>
<td>.751</td>
</tr>
<tr>
<td>Education in years</td>
<td>8.6 (3.0)</td>
<td>8.6 (3.1)</td>
<td>.955</td>
</tr>
</tbody>
</table>

*Note. FOF = Fear of falling*
### Odds Ratios and 95% Confidence Intervals for Fear of Falling at Baseline

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate logistic regression models for FOF</th>
<th>Multivariate logistic regression model for FOF&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of sensory difficulties</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1 (-)</td>
<td>1 (-)</td>
</tr>
<tr>
<td>One</td>
<td>1.5 (0.8-2.6)</td>
<td>1.4 (0.8-2.6)</td>
</tr>
<tr>
<td>Two</td>
<td>3.1 (1.8-5.5)</td>
<td>2.9 (1.6-5.1)</td>
</tr>
<tr>
<td>Three</td>
<td>5.8 (2.7-12.5)</td>
<td>5.0 (2.3-11.2)</td>
</tr>
<tr>
<td>History of a previous severe fall</td>
<td>2.0 (1.3-3.0)</td>
<td>1.9 (1.2-2.9)</td>
</tr>
<tr>
<td>Number of chronic diseases</td>
<td>1.3 (1.1-1.5)</td>
<td>1.2 (1.0-1.4)</td>
</tr>
<tr>
<td>Age</td>
<td>1.0 (1.0-1.1)</td>
<td>1.0 (0.9-1.1)</td>
</tr>
<tr>
<td>Number of prescribed medications</td>
<td>1.0 (1.0-1.2)</td>
<td>-</td>
</tr>
<tr>
<td>MMSE -score</td>
<td>1.0 (0.9-1.1)</td>
<td>-</td>
</tr>
<tr>
<td>Education in years</td>
<td>1.0 (0.9-1.1)</td>
<td>-</td>
</tr>
</tbody>
</table>

<sup>a</sup> Number of sensory difficulties, history of a previous severe fall, number of chronic diseases and age were included in the model.

*Note.* FOF = Fear of falling, OR = Odds ratio, CI = Confidence interval.
### Odds Ratios and 95% Confidence Intervals for Incident Fear of Falling in the Three-year Follow-up.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate logistic regression models for incident FOF</th>
<th>Multivariate logistic regression model for incident FOF&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Number of sensory difficulties</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1 -</td>
<td>1 -</td>
</tr>
<tr>
<td>One</td>
<td>1.4 (0.7-2.7)</td>
<td>1.4 (0.7-2.8)</td>
</tr>
<tr>
<td>Two</td>
<td>2.3 (1.1-4.8)</td>
<td>2.3 (1.1-4.9)</td>
</tr>
<tr>
<td>Three</td>
<td>8.1 (2.0-31.8)</td>
<td>8.3 (1.9-35.1)</td>
</tr>
<tr>
<td>Incident of a severe fall during the follow-up</td>
<td>3.7 (1.6-8.5)</td>
<td>3.9 (1.6-9.5)</td>
</tr>
<tr>
<td>Number of chronic diseases</td>
<td>1.0 (0.8-1.2)</td>
<td>0.9 (0.7-1.1)</td>
</tr>
<tr>
<td>Age</td>
<td>1.1 (1.0-1.2)</td>
<td>1.0 (0.9-1.1)</td>
</tr>
</tbody>
</table>

*Note.* FOF = Fear of falling, OR = Odds ratio, CI = Confidence interval.

<sup>a</sup> Number of sensory difficulties, incident of a severe fall during follow-up, number of chronic diseases and age were included in the model.
Figure 1. Odds ratios (OR) and their 95% confidence intervals for fear of falling (FOF) according to sensory difficulties at baseline. Logistic regression model is adjusted for age, number of chronic diseases and history of a previous severe fall.
Figure 2. Odds ratios (OR) and their 95% confidence intervals for fear of falling (FOF) in the three-year follow-up according to baseline sensory difficulties. Logistic regression model is adjusted for age, number of chronic diseases and incident of a severe fall during the follow-up.
AUTHOR’S NOTE

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Conflict of interests:

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Author contributions:

The authors are justifiably credited with authorship, according to the authorship criteria. Anne Viljanen: study concept and design, acquisition of data, analysis and interpretation of data, drafting the article, approval of manuscript. Jenni Kulmala and Merja Rantakokko: study concept and design, analysis and interpretation of data, revising critically the article, approval of manuscript. Markku Koskenvuo, Jaakko Kaprio and Taina Rantanen: study concept and design, acquisition of data, analysis and interpretation of data, revising critically the article, approval of manuscript.

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either the design, execution, analysis or interpretation of the data, or in the writing of this report.