Change in β₂-agonist use after severe life events in adults with asthma: A population-based cohort study
Life events and bronchodilator usage among adults with asthma

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ABSTRACT

Objective: This prospective, population-based cohort study of 1102 Finnish adults with asthma, examined whether exposure to stressful life events is associated with the intensity of usage of inhaled short-acting β₂-agonists.

Methods: Survey data was collected by two postal questionnaires. Baseline characteristics were obtained in 1998 and data on 19 specific stressful events (e.g. death of a child or spouse or divorce) within the six preceding months in 2003. Exposure to life events was indicated by a sum score weighted by mean severity of the events. Participants were linked to records of filled prescriptions for inhaled short-acting β₂-agonists from national registers from 2000 through 2006. The rates of purchases of short-acting β₂-agonists before (2000–2001), during (2002–2003) and after (2004–2006) the event exposure were estimated using repeated-measures Poisson regression analyses with the generalized estimating equation.

Results: Of the 1102 participants, 162 (15%) were exposed to highly stressful events, 205 (19%) to less stressful events. During the 7-year observation period, 5955 purchases of filled prescription for inhaled short-acting β₂-agonists were recorded. After exposure to highly stressful events, the rate of purchases of β₂-agonists was 1.50 times higher (95% confidence interval (CI): 1.05, 2.13) than before the stressful event occurred. Among those with low or no exposure to life events, the corresponding rate ratios were not elevated (rate ratio 0.81, 95% CI: 0.66, 0.99 and 0.95, 95% CI: 0.83, 1.09 respectively).

Conclusion: An increase in β₂-agonist usage after severe life events suggests that stressful experiences may worsen asthma symptoms.

1. Introduction

Asthma is a chronic intermittent inflammation of the large airways [1,2] with the reported population prevalence varying from 2% in Estonia to 21% in Australia [3]. Its prevalence is increasing in many countries [4]. A large number of studies on the biological risk factors for asthma morbidity have found evidence of the etiological importance of respiratory infections, allergens, air pollutants, and tobacco smoke [5,6]. Recently, the role of psychosocial stress as a contributor of asthma morbidity has gained increased attention [7,8]. Stress is considered to affect the exacerbation of asthma through multiple immune, endocrine, neural, and behavioural processes [9,10]. Stress also accentuates the individual's immune response and induces changes in inflammatory processes in the airways [11].

Some longitudinal cohort studies suggest an association between negative stressful life events in the family and elsewhere and asthma onset [12-14], while others have not found any association [15]. The most recent study suggests that both work stress and family related life events are positively associated with asthma in women [16]. In addition, life events may lead to a worsening of asthma among asthmatic...
2.2. Participants with asthma

Hospital Ethics Committee. All participants signed an informed consent up survey. (Fig. 1) The study was approved by the Turku University rerence of new life events within the preceding six months in the follow-

January 1, 2000 onward who had provided information on the occur-


2.1. Study design and participants

The Health and Social Support Study, a longitudinal cohort study, is based on a representative sample of the Finnish population in the age groups: 20–24, 30–34, 40–44, and 50–54 years at baseline [24]. The baseline postal survey was conducted in 1998, and a total of 25,901 respondents returned the questionnaire. Of them, 19,629 respondents = 1102, 73% women) at the beginning of the 7-year observation window from January 1, 2000 onward who had provided information on the occur-

of new life events within the preceding six months in the follow-

survey. (Fig. 1) The study was approved by the Turku University Hospital Ethics Committee. All participants signed an informed consent form.

2.2. Participants with asthma

We used the unified personal identification code system, covering all Finnish citizens, to link and obtain records from three administrative and comprehensive Finnish national health registers to identify in-

dividuals with asthma and their purchases of prescribed asthma medi-

We hypothesized that people with asthma inhale short-acting β2-agonists when they are symptomatic and that high exposure to recent stressful life events would be associated with worsening symptoms, resulting in increased purchase of inhaled short-

In this prospective study, we hypothesized that people with asthma inhale short-acting β2-agonists when they are symptomatic and that high exposure to recent stressful life events would be associated with worsening symptoms, resulting in increased purchase of inhaled short-

In Finland, inhaled asthma medications are only available by pre-

scription. The National Health Insurance Scheme, run by the SII of Finland, provides prescription drug coverage for all (~5.5 million) community-dwelling residents of Finland. All reimbursed prescriptions are registered in the Drug Prescription Register managed by the SII [25]. For each drug, the dispensing date and the World Health Orga-

3.2. Recent stressful life events

2.3. Assessment of filled prescription for asthma medication during the 7-year follow-up

In Finland, inhaled asthma medications are only available by pre-

scription. The National Health Insurance Scheme, run by the SII of Finland, provides prescription drug coverage for all (~5.5 million) community-dwelling residents of Finland. All reimbursed prescriptions are registered in the Drug Prescription Register managed by the SII [25]. For each drug, the dispensing date and the World Health Organization Anatomical Therapeutic Chemical (ATC) code are recorded. We derived the date and the ATC classification code of purchases of inhaled β2-agonists and corticosteroids during a seven-year observation period covering the years 2000 to 2006 from the Drug Prescription Register. For observation, we determined the number of purchases for inhaled short-acting β2-agonists (ATC R03AC02, R03AC03 R03AC04) and combinations of short-acting β2-agonists with anticholinergics (ATC R03AK03, R03AK04).

Because the need for short-acting β2-agonists may depend on the simultaneous usage of inhaled anti-inflammatory medication, we de-

terminated the number of purchases for inhaled corticosteroids (ATC R03BA01, R03BA02, R03BA05) and long-acting β2-agonists (ATC R03AC12, R03AC13) in non-combination inhalers and fixed dose combination inhalers of inhaled corticosteroids and long-acting β2-

agonists (ATC R03AK06, R03AK07). The number of purchases in every year of observation was handled as a categorical factor in the model.

2.4. Recent stressful life events

We measured the occurrence of recent stressful life events in the follow-up survey conducted in 2003 by using 19 life events from a list of 21 events [27,28]. The excluded events (i.e., “illness causing work disability of over 21 days” and “disability retirement”) might have been a consequence of asthma exacerbation (see Appendix 1). For the timing of each event, the questionnaire included four response alternatives (never, within the previous 6 months, within the previous 5 yrs. and > 5 yrs. ago), and the respondents were instructed to select only one of them. The focus of this study is in recent events, those that had occurred during the previous six months. We assessed the level of
exposure to recent life events for each individual by calculating a cumulative mean sum score weighted by the average severity of the event (for weights, see Vahtera et al. [28]). The cumulative severity ratings ranged from 2.74 to 24.64. Those respondents with a 0 (zero) score were defined as having no exposure. Those who had been exposed were divided into two groups using the median of the cumulative severity score as the cut-off point (low exposure < 5, high exposure ≥ 5).

As shown in Appendix 1, only a small proportion of participants had reported the corresponding event in the 1998 survey (e.g. 14% of those who were victims of violence in 2003 reported to have been victims in 1998 also). Events with highest recurrence - breakup of long-term friendship (43%), severe financial difficulties (40%) and death of a close relative (35%) - were rated much less severe and, thus, had a lower weight in the cumulative mean sum score.

2.5. Baseline characteristics

Baseline characteristics, measured in the baseline survey in 1998 before exposure to the life events included socio-demographic variables – sex, age group, marital status, and level of education – behaviour-related health risks, sensitivity to stress and depression. The behaviour-related health risks were smoking (never/ex/current), high alcohol intake (≥ 175 g of alcohol for women and ≥ 263 g of alcohol for men per week) [29], obesity (Body Mass Index (BMI) ≥ 30 kg/m²) and physical inactivity (the Metabolic Equivalent Task index < 2 MET-hours/day) [30]. Individual differences in sensitivity to stress were measured by general feelings of stressfulness in daily life [28,31]. The mean scores of the scale were divided with tertiles, with the highest third used as an indicator of sensitivity to stress. Depression, a potential mediator between a stressful life event and asthma, was assessed using the Beck Depression Inventory (sum score > 18) [32] and the Drug Prescription Register [ ≥ 1 antidepressant (ATC-code N06A) purchases in 1998]. Participants showing depression in any of these measurements were classified as cases of pre-existing depression.

2.6. Statistical analysis

The association between background variables (demographics, health-related factors, and psychological factors) (measured in 1998) and recent stressful life-event exposure (measured in 2003) categories were studied using the Pearson’s chi-squared tests. For the analyses, we divided the seven-year follow-up time into three periods in relation to the timing of the life-event exposure: ‘before’ (i.e., year − 3 and − 2, 2000–2001), ‘during’ (i.e. year − 1 and 0, 2002–2003) and ‘after’ (i.e. year + 1 to + 3, 2004–2006). We applied a repeated-measures Poisson regression analysis with the generalized estimating equation (GEE) method and autoregressive correlation structure [33]. The GEE takes into account the correlation of annual medication purchases within persons, and is not very sensitive to missing cases at repeated measurements. We applied a repeated-measures Poisson regression analysis with the generalized estimating equation (GEE) method and autoregressive correlation structure [33]. The GEE takes into account the correlation of annual medication purchases within persons, and is not very sensitive to missing cases at repeated measurements. We first examined the purchases of inhaled short-acting bronchodilators by baseline characteristic by calculating the mean rates of purchases over the seven-year observation period for each characteristic.

We used contrasts to estimate the rate ratios and their 95% confidence intervals (95% CI) during and after the exposure compared with the period before the exposure - within each exposure group using
models including the interaction term “stressful life-event exposure*period”. The rate ratios for purchases of inhaled short-acting β2-agonists were calculated in the three time periods around the life-event exposure. The analyses were adjusted for all baseline characteristics. An additional adjustment was made for inhaled anti-inflammatory medication. In order to examine whether changes in purchases of inhaled short-acting β2-agonists following exposure to life events varied between the subgroups (e.g. by sex, age group, education, behaviour-related health risks, depression or sensitivity to stress) we calculated the rate ratios for each subgroup by using the same model. All tests were 2-tailed.

All analyses were performed using the SAS Enterprise Guide 6.100 (6.100.0.2870) statistical software (SAS Institute Inc., Cary, NC, USA, 2013).

3. Results

3.1. Characteristics of the study population

The sample included 296 (27%) men and 806 (73%) women with prevalent asthma at baseline. Of these individuals, 367 (33%) reported an occurrence of new recent stressful life events in the follow-up survey. The events reported most often were: ‘major increase in marital problems’ (n = 83), ‘severe financial difficulties’ (n = 77) or/and ‘death of another close relative’ (n = 60). (Appendix 1).

Table 1 shows the associations between the severity of life events exposed (no/low/high) and the characteristics of participants; a young age, current or ex-smoking, and physical activity were associated with high life-event exposure.

Table 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All participants</th>
<th>No</th>
<th>Low</th>
<th>High</th>
<th>Purchases 2000–2006</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. %</td>
<td>No. %</td>
<td>No. %</td>
<td>No. %</td>
<td>P Value&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Total</td>
<td>1102 100</td>
<td>73 66</td>
<td>205 19</td>
<td>162 15</td>
<td>0.54</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>296 27</td>
<td>200 27</td>
<td>58 28</td>
<td>38 23</td>
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</tr>
<tr>
<td>Women</td>
<td>806 73</td>
<td>535 73</td>
<td>147 72</td>
<td>124 77</td>
<td>0.001</td>
</tr>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>20–24</td>
<td>242 22</td>
<td>135 18</td>
<td>57 28</td>
<td>50 31</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>30–34</td>
<td>239 22</td>
<td>145 20</td>
<td>53 26</td>
<td>41 25</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>40–44</td>
<td>252 23</td>
<td>171 23</td>
<td>48 23</td>
<td>33 20</td>
<td>0.015</td>
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<td>50–54</td>
<td>369 33</td>
<td>284 39</td>
<td>47 23</td>
<td>38 24</td>
<td>0.015</td>
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<tr>
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<td></td>
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<td>129 18</td>
<td>29 14</td>
<td>19 12</td>
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</tr>
<tr>
<td>College</td>
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<td>211 29</td>
<td>74 37</td>
<td>50 31</td>
<td>0.001</td>
</tr>
<tr>
<td>Vocational school</td>
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<td>158 22</td>
<td>34 17</td>
<td>45 28</td>
<td>0.001</td>
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<tr>
<td>Basic</td>
<td>336 31</td>
<td>225 31</td>
<td>64 32</td>
<td>47 29</td>
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</tr>
<tr>
<td>Marital status</td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>Single/divorced/widowed</td>
<td>326 30</td>
<td>199 27</td>
<td>65 32</td>
<td>62 38</td>
<td>0.001</td>
</tr>
<tr>
<td>Married/cohabiting</td>
<td>775 70</td>
<td>535 73</td>
<td>140 68</td>
<td>62 62</td>
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<td></td>
<td></td>
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<tr>
<td>Never-smoker</td>
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<td>328 49</td>
<td>72 39</td>
<td>49 32</td>
<td>0.001</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>296 29</td>
<td>186 28</td>
<td>56 30</td>
<td>54 36</td>
<td>0.001</td>
</tr>
<tr>
<td>Current smoker</td>
<td>266 26</td>
<td>161 24</td>
<td>57 31</td>
<td>48 32</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Physical inactivity</td>
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<td></td>
</tr>
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<td>532 73</td>
<td>171 83</td>
<td>123 76</td>
<td>0.008</td>
</tr>
<tr>
<td>Yes</td>
<td>270 25</td>
<td>198 27</td>
<td>34 17</td>
<td>38 24</td>
<td>0.003</td>
</tr>
<tr>
<td>Obesity (BMI ≥ 30)&lt;sup&gt;d&lt;/sup&gt;</td>
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<td>609 83</td>
<td>173 84</td>
<td>139 87</td>
<td>0.53</td>
</tr>
<tr>
<td>Yes</td>
<td>175 16</td>
<td>122 17</td>
<td>32 16</td>
<td>21 13</td>
<td>0.001</td>
</tr>
<tr>
<td>High alcohol intake&lt;sup&gt;e&lt;/sup&gt;</td>
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<tr>
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<td>701 96</td>
<td>193 94</td>
<td>152 94</td>
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</tr>
<tr>
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<td>31 4</td>
<td>12 6</td>
<td>10 6</td>
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<td></td>
</tr>
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<td>981 89</td>
<td>659 90</td>
<td>183 89</td>
<td>139 86</td>
<td>0.36</td>
</tr>
<tr>
<td>Yes</td>
<td>121 11</td>
<td>76 10</td>
<td>22 11</td>
<td>23 14</td>
<td>0.036</td>
</tr>
<tr>
<td>Sensitivity to stress</td>
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<td></td>
<td></td>
<td></td>
<td>0.066</td>
</tr>
<tr>
<td>No</td>
<td>720 66</td>
<td>496 68</td>
<td>127 62</td>
<td>97 60</td>
<td>0.066</td>
</tr>
<tr>
<td>Yes</td>
<td>374 34</td>
<td>232 32</td>
<td>77 38</td>
<td>65 40</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index.
<sup>a</sup> P value for difference between the exposure groups (Pearson's chi-squared test).
<sup>b</sup> Annual average purchases of inhaled short-acting β2-agonists per 100 person years derived from Poisson regression generalized estimating equation (GEE) analysis for covariate.
<sup>c</sup> P value from Poisson regression GEE analysis for mean rates.
<sup>d</sup> BMI was calculated as weight (kg)/height (m)<sup>2</sup>
<sup>e</sup> High alcohol intake refers to consumption of > 175 g/week for women and > 263 g/week for men.

3.2. Purchases of inhaled short-acting β2-agonists

During the seven-year observation period, 5955 purchases of inhaled short-acting β2-agonists were recorded for the participants. A high annual purchase rate was observed among smokers, as well as those with depression, obesity and those with a basic level of education (Table 1).

3.3. Inhaled short-acting β2-agonists and recent stressful life events

Table 2 shows the rate ratios for purchases of inhaled short-acting β2-agonists in the time periods during (year − 1 and 0) and after (year 0).
participants who had encountered highly stressful recent life events, the rate of 
recurrence was non-existing or rare (e.g. only 14% of those who were 
exposed to recent stressful events, no increase between periods existed. 

A limitation of the study is that 

4 Discussion 

In this population-based 7-year follow-up study on adults with 
asthma, records of filled prescriptions of inhaled short-acting β₂-ago 
nists before, during and after exposure to stressful life-events were used 
as an indicator of asthma symptoms. Among those who had encoun 
tered recent highly stressful life events, the rate for inhaled short-
acting β₂-agonists purchases was 1.5 times higher after the life event 
compared to the pre-event levels. No such increase was observed among 
those with no or low exposure to stressful life events. These findings 
support the hypothesis that psychosocial stress may exacerbate asthma 
symptoms in working-aged adults. 

Our results are consistent with the biopsychosocial model of stress, 
which suggests that stressful life events may alter the psychological, 
immunological and endocrine systems in ways that lead to the ex 
acerbation of asthma [9,34]. Moreover, the results of this study are in 
line with the few studies which investigated the association between 
stressful life events and the exacerbation of asthma symptoms in adults. 

A case-control study by Kolbe et al. [19] found that life events were 
reported more often among patients admitted to hospital with acute 
asthma compared to a control group of non-hospitalized asthmatics. In 
a prospective population based study by Wainwright et al. [18] life 
events experienced in adulthood were associated with increased rates of 
asthma-related hospital admissions. Although earlier studies provide 
important insight on asthma exacerbation, hospital admissions for 
asthma are considered very rare [21], representing only the tip of an 
iceberg of asthma morbidity. In this study, the finding that the utili 
zation of inhaled short-acting β₂-agonists varies depending on the 
extent to which asthmatic adults are exposed to life stress has not been 
previously reported. 

Stress may have an impact on individuals’ life management and thus 
affects asthma self-care and adherence to treatment [34], and increases 
the risk of inappropriate use of asthma medications [35]. A recent study 
found that many patients perceived stress was an important determi 
nant of uncontrolled asthma [36]. One indicator of such a development is 
high use of short-acting bronchodilators with low use of inhaled 
steroids [35]. As we were able to control in the analysis simultaneous 
usage of anti-inflammatory medication, poor self-care of asthma is an 
unlikely explanation for our time-dependent findings. 

The strengths of this study are its large sample size and a study 
design that allowed the determination of temporary order between 
exposure to recent stressful life events and purchases of asthma medi 
cation. The number of filled prescriptions of inhaled short-acting β₂-
agonists and the measurement of asthma were based on national health 
registers. In Finland, the validity of the national registers has been 
found to be high [37], reasonably accurate, and highly reliable for 
epidemiological study purposes [38]. We were also able to control a 
number of socio-demographic elements and etiological factors of 
asthma. 

A limitation of the study is that filled prescriptions do not equate to 
actual medication utilization. Because we did not have information on 
total amounts of drugs per prescription or recommended doses of the 
asthma treatment, we were not able to use more fine-grained measures 
such as increased daily doses of inhaled short-acting bronchodilators use. 
However, short-acting beta-agonist prescription fills can be used as 
a marker for asthma morbidity [39]. At baseline, the response rate was 
relatively low (40%), and there may have been differences between 
respondents and non-respondents regarding the frequency of asthma 
and recent stressful life events, although no major health-related se 
lection has been detected in a non-response analysis [24]. How 
ever, > 80% of the baseline respondents participated in the follow-up 
survey, and practically all of them (96%) consented to the linking of data 
from national health registers. Thus, it is unlikely that the long-
itudinal association between recent stressful life events and asthma 
exacerbation would be biased due to low participation at baseline. 
Additionally, due to the applied survey methodology, we did not have 
any additional information of the reported life events and their stress-
fulness. However, by using average severity rating instead of individual 
perception of the severity of the event our measure was not confounded 
by the consequences of the event for the individual.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Rate Ratios for Purchases of Inhaled Short-Acting β₂-Agonists Comparing Different Time Periods According to Life-Event exposure, The Health and Social Support Study in Finland, 1998-2006.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjustment level of stressful life-event exposure</td>
<td>Time in relation to life-event exposure</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted</td>
<td></td>
</tr>
<tr>
<td>No exposure</td>
<td>0.98</td>
</tr>
<tr>
<td>Low exposure</td>
<td>0.84</td>
</tr>
<tr>
<td>High exposure</td>
<td>1.46</td>
</tr>
<tr>
<td>Baseline adjusted</td>
<td></td>
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<tr>
<td>No exposure</td>
<td>0.99</td>
</tr>
<tr>
<td>Low exposure</td>
<td>0.84</td>
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<tr>
<td>High exposure</td>
<td>1.47</td>
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<tr>
<td>Additionally adjusted</td>
<td></td>
</tr>
<tr>
<td>No exposure</td>
<td>0.97</td>
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<tr>
<td>Low exposure</td>
<td>0.79</td>
</tr>
<tr>
<td>High exposure</td>
<td>1.43</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; RR, rate ratio. 
² During refers to year – 1 and 0 in relation to the timing of the life-event exposure. 
² After refers to year + 1 to + 3 in relation to the timing of the life-event exposure.
² Rate ratio (RR) and their 95% confidence limits (CI) derived from Poisson regression 
generalized estimating equation analysis for time periods.
² Adjusted for sex, age, educational level, marital status, smoking, sedentary lifestyle, obesity, high alcohol intake, depression and sensitivity to stress. 
² Additionaly adjusted for inhaled corticosteroids and long-acting β₂-agonists in combination or separate as time dependent variable. 
² + 1 to + 3, compared with the period before (year – 3 and – 2), 
exposure to stressful life events adjusted for the baseline characteristics (demographics, health risk behaviours, depression and sensitivity to stress) and, additionally, for inhaled anti-inflammatory medication. 
² Among those with no exposure to recent stressful life events, the rate of 
purchases did not significantly vary between the time periods. Among 
participants who had encountered highly stressful recent life events, the 
purchases of inhaled short-acting β₂-agonists increased by 46% during 
the life event exposure and 52% after the exposure compared with the 
pre-exposure levels. This rate ratio remained unchanged after taking 
into account adjustments for all baseline characteristics. Additionally, 
adjustment for inhaled anti-inflammatory medication only slightly at 
tenuated the association (p < 0.06). Among participants who had low 
exposure to recent stressful events, no increase between periods existed. 

Results from the subgroup analyses are shown in Table 3. Compared 
with the pre-exposure level, the rate of purchases of inhaled short-
acting β₂-agonists increased in all subgroups of participants during and 
after high life-event exposure. One exception was related to age; after 
exposure, the youngest age group showed no increase in the rate of 
purchases of inhaled short-acting β₂-agonists. Interestingly, among depressive participants (n = 121), the post-exposure increase was ex 
tensively high, 4.4-fold compared to the pre-exposure level. 

Appendix 1 presents how many of the 367 participants reporting a 
recent event at the follow-up survey in 2003 reported the corresponding 
event also in the 1998 survey. As can be seen, for the most severe events 
recurrence was non-existing or rare (e.g. only 14% of those who were 
victims of violence in 2003 reported to have been victims in preceding 
six months in 1998 also). Highest recurrence was found for ‘breakup of 
long-term friendship’ (43%), ‘severe financial difficulties’ (40%) and 
‘death of a close relative’ (35%), events rated much less severe.
supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.jpsychores.2017.07.003.

5. Conclusions

To the best of our knowledge, this is the first study to investigate the longitudinal associations between recent stressful life events and purchase levels in a population sample of adults with asthma at middle age. Our finding that exposure to highly-stressful life events is associated with an increase in inhaled short-acting β2-agonists purchases suggests a worsening of asthma symptoms in the aftermath of stressful experiences. These results highlight the potential importance of taking into account psychosocial stress in guiding asthma self-care.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.jpsychores.2017.07.003.

Competing Interest Statement

All authors have completed the Unified Competing Interest Form at http://www.icmje.org/coi_disclosure.pdf and declare that (1) Dr. Kivimäki received support from NordForsk, the Medical Research Council, and the Economic and Social Research Council, during the conduct of the study; (2) authors have no relationships with companies or other competing interests in the past three years that could be perceived to constitute a conflict of interest; (3) spouses, partners, or children of authors have no financial relationships that may be relevant to the submitted work; and (4) authors have no non-financial interests that may be relevant to the submitted work.

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