of this second treatment, defined as the difference in pain ratings on the ointment-treated site and the untreated site, was compared between the positive and the negative treatment history groups. In addition, functional magnetic resonance imaging (fMRI) was performed to assess pain-related brain activity as a physiological measure of analgesia. Specifically, we tested whether the difference in pain-related responses between the treated and untreated sites differed depending on treatment history (interaction effects). The fMRI data were analyzed using SPM8 (http://www.fil.ion.ucl.ac.uk/spm/). The study was approved by the local ethics committee.

Results | The therapeutic effect of the ointment treatment was significantly lower in the negative than in the positive treatment history group (negative group: mean ΔVAS = 27, from a mean [standard error of the mean] of 81 [3] to 54 [3]; positive group: mean ΔVAS = 41, from 81 [2] to 40 [4]; unpaired t test, P = .007; Figure, B). In the brain, this adverse effect of a negative treatment history on analgesia was paralleled by more activation in the bilateral posterior insular cortices (t = 4.0), known to reflect afferent nociceptive processing (Figure, C), and reduced engagement of the right dorsal lateral prefrontal cortex, implicated in pain inhibition.

Discussion | To our knowledge, we provide the first behavioral and neurobiological evidence that the influence of treatment history transfers over time and over therapeutic approach. Our results therefore emphasize that therapeutic outcome is not solely determined by the genuine (eg, pharmacological) properties of a treatment but is substantially modulated by contextual factors, including treatment history. Such carryover effects might be particularly relevant in chronic diseases in which treatments often fail repeatedly and negative treatment experiences accumulate along the course of the disease. Moreover, our data suggest that prior treatment experience should also be assessed in clinical trials because it might explain part of the response to the treatment under investigation. Although these experimental findings require replication in larger clinical populations, we believe that awareness of this effect is important for every physician and that concerted effort is required to avoid or overcome the negative effects of prior experience on treatment outcome. These findings may even challenge the use of common step care approaches in which treatment failure must precede the prescription of next-in-line interventions.

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Somatic Symptoms in Patients With Coronary Heart Disease: Prevalence, Risk Factors, and Quality of Life

A broad spectrum of somatic symptoms is common in primary care, and more than half of medical visits are due to nonspecific symptoms (eg, nausea, headache, dizziness). Patients with frequent somatic symptoms show increased health care use, functional impairment, and a decreased quality of life. Although patients with coronary heart disease (CHD) might present with more than only cardiac symptoms (such as angina pectoris), research on the prevalence of somatic symptoms and their burden on health is rare and historic. Numerous studies showing that the somatic-affective component of depression predicts worse cardiac outcomes underpin the importance of examining somatic symptom severity in CHD.

To our knowledge, this is the first study in patients with CHD that investigates the prevalence and the spectrum of perceived somatic symptoms and tests their associations with quality of life and cardiac and psychological risk factors.
Methods | The present study is based on cross-sectional data from the DEPSCREEN-INFO trial (Increasing the Efficiency of Depression Screening Using Patient-Targeted Feedback: Randomized Controlled Trial), which is described in detail elsewhere (German Clinical Trials Register: Identifier: DRKS00003277). Between September 2011 and May 2012, patients from 5 cardiac outpatient clinics were consecutively approached. Patients were invited to participate if they had a clinically confirmed CHD, were 18 years or older, and had sufficient language skills (German). Exclusion criteria included (1) life-threatening health status; (2) severe somatic or psychiatric disorder that needs urgent treatment; (3) severe cognitive, motor, or visual difficulties; or (4) no written informed consent. The study was approved by a local ethics committee. Patients completed questionnaires assessing sociodemographic data, health-related quality of life (5-dimensional EuroQol index [EQ-5D index]), anxiety (Generalized Anxiety Disorder Scale-7), and depression (Patient Health Questionnaire [PHQ]-9). Due to the overlap between depression and somatic symptoms, the 2 somatic items (sleep difficulty and energy loss) were excluded from the PHQ-9. Somatic symptom severity was measured with the PHQ-15, which assesses the frequency and the severity of the 15 most frequent somatic symptoms in outpatient settings. Diabetes, dyslipidemia, heredity, hypertension, obesity, and smoking behavior were assessed as cardiac risk factors. History of myocardial infarction, hospital admission, and the New York Heart Association (NYHA) class were obtained as measures of overall cardiac health. First, the prevalence of individual somatic symptoms was determined. Second, multivariate linear regressions were performed to identify predictors of somatic symptom severity and to test the impact of somatic symptom severity on quality of life. Models were adjusted for sociodemographic data, depression, anxiety, cardiac health, and risk factors.

Results | In total, 387 patients gave informed consent (participation rate, 92%) and had the following characteristics: the mean (SD) age was 68 (10.3) years; 71.1% were male; 91.4% spoke German as their first language; 72.1% were not living alone; and the mean (SD) total years of education was 13.7 (2.6) years. Concerning cardiac health, 50.1% of patients had a history of myocardial infarction; 83.8% were already treated as cardiac inpatients; and 75.2% had an NYHA class I rating, 17.9% had an NYHA class II rating, and 6.9% had an NYHA class III rating. In terms of cardiac risk factors, 63.0% had hypertension, 57.1% had dyslipidemia, 29.4% were obese, 47.5% had a family history of heart disease, and 13.5% smoked. Of the 15 somatic symptoms, 11 were frequently experienced by at least 30% of patients (Table). At least 5 somatic symptoms were present in 50.0% of patients. Chest pain as a core symptom of CHD was reported by less than every second patient (45.2%). Of those patients reporting symptoms, shortness of breath (40.4%) was indicated among the 5 most bothersome symptoms. In contrast, chest pain (21.1%) was rated among the least bothersome symptoms. In multivariate regression analyses, higher somatic symptom severity (adjusted $R^2 = 0.59$; $P < .001$) was independently associated with depression severity ($\beta = 0.48$; $P < .001$), NYHA class ($\beta = 0.23$; $P < .001$), anxiety ($\beta = 0.18$; $P < .001$), heredity ($\beta = 0.08$; $P = .02$), hypertension ($\beta = 0.08$; $P = .03$), lower education ($\beta = -0.08$; $P = .03$), and female sex ($\beta = 0.07$; $P = .04$). Lower quality of life (adjusted $R^2 = 0.27$; $P < .001$) was associated with higher somatic symptom severity ($\beta = -0.37$; $P < .001$), lower education ($\beta = 0.13$; $P = .01$), and obesity ($\beta = -0.12$; $P = .02$).

Discussion | First, results show that a number of somatic symptoms are highly prevalent and burdensome in patients with CHD. Compared with the data from the general population, prevalence of somatic symptoms is very high and

### Table. Prevalence of Somatic Symptoms in 387 Patients With Coronary Heart Disease

<table>
<thead>
<tr>
<th>Somatic Symptoms</th>
<th>All Symptoms Reported</th>
<th>Bothered a Little*</th>
<th>Bothered a Lot*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>95% CI, %</td>
<td>No. (%)</td>
</tr>
<tr>
<td>Trouble sleeping</td>
<td>297 (76.7)</td>
<td>72.5-81.0</td>
<td>193 (49.9)</td>
</tr>
<tr>
<td>Feeling tired or having low energy</td>
<td>274 (70.8)</td>
<td>66.3-75.3</td>
<td>158 (40.8)</td>
</tr>
<tr>
<td>Pain in arms, legs or joints</td>
<td>244 (63.0)</td>
<td>58.2-67.9</td>
<td>138 (35.7)</td>
</tr>
<tr>
<td>Back pain</td>
<td>237 (61.2)</td>
<td>56.4-66.1</td>
<td>151 (39.0)</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>230 (59.4)</td>
<td>54.5-64.3</td>
<td>137 (35.4)</td>
</tr>
<tr>
<td>Feeling your heart pound or race</td>
<td>177 (45.7)</td>
<td>40.8-50.7</td>
<td>138 (35.7)</td>
</tr>
<tr>
<td>Chest pain</td>
<td>175 (45.2)</td>
<td>40.3-50.2</td>
<td>138 (35.7)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>174 (45.0)</td>
<td>40.0-49.9</td>
<td>137 (35.4)</td>
</tr>
<tr>
<td>Nausea, gas, indigestion</td>
<td>140 (36.2)</td>
<td>31.4-41.0</td>
<td>110 (28.4)</td>
</tr>
<tr>
<td>Constipation, diarrhea, loose bowels</td>
<td>129 (33.3)</td>
<td>28.6-38.0</td>
<td>98 (25.3)</td>
</tr>
<tr>
<td>Headaches</td>
<td>118 (30.5)</td>
<td>25.9-35.1</td>
<td>98 (25.3)</td>
</tr>
<tr>
<td>Pain during sexual intercourse</td>
<td>76 (19.6)</td>
<td>15.7-23.6</td>
<td>47 (12.1)</td>
</tr>
<tr>
<td>Stomach pain</td>
<td>66 (17.1)</td>
<td>13.3-20.8</td>
<td>52 (13.4)</td>
</tr>
<tr>
<td>Menstrual problems or crampsb</td>
<td>7 (6.3)</td>
<td>3.8-8.7</td>
<td>5 (4.5)</td>
</tr>
<tr>
<td>Fainting spells</td>
<td>19 (4.9)</td>
<td>2.8-7.1</td>
<td>15 (3.9)</td>
</tr>
</tbody>
</table>

* Patients could respond from “not bothered at all” to “bothered a little” to “bothered a lot.”

b Only women were asked about menstrual symptoms (n = 112).
almost as high as in chronically ill patients with comorbid pain or affective disorders. Second, after adjustment for sociodemographic, cardiac health, and risk factors, psychological factors show the strongest associations with somatic symptom severity. Future studies, however, should carefully evaluate these findings while controlling for cardiac biomarkers (eg, left ventricular function) and comorbidities (eg, cancer). Third, the present study demonstrates that above and beyond sociodemographic, cardiac, or psychological factors, somatic symptom severity has the greatest impact on quality of life. Therefore, it is vital that effective patient-centered care targets the whole spectrum of somatic symptoms in patients with CHD.

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