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Anne Hway Ann Yee MPsychMed, Chong Guan Ng MPsychMed, Rusdi Abd Rashid MPsychMed & Mohamad Hussain Habil MPsychMed

a Department of Psychological Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

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The Prevalence and Correlates of Nicotine Use Disorder Among Bipolar Patients in a Hospital Setting, Malaysia

Anne Hway Ann Yee, MPyschMed, Chong Guan Ng, MPyschMed, Rusdi Abd Rashid, MPyschMed, and Mohamad Hussain Habil, MPyschMed

Objective: The authors sought to determine the prevalence of nicotine use disorder, related demographic characteristic features, and associated correlates of nicotine use disorder among bipolar patients who attended inpatient and outpatient services in a university hospital setting in Malaysia. Methods: In this cross-sectional study conducted from March 2009 to September 2010, a total of 121 bipolar patients, whose diagnoses were based on the Mini International Neuropsychiatric Interview (bipolar version 5.0.0), were recruited. Their nicotine use disorders were assessed with the Mini International Neuropsychiatric Interview (plus version) and the Fagerström Test for Nicotine Dependence. The associated correlates of nicotine use disorder were assessed with the Addiction Severity Index-Lite-Clinical Factors version. The number of lifetime hospitalizations and the survival days (defined as the number of days between the last discharge and the most current readmission for all patients who had been readmitted to the hospital) were calculated. Results: The prevalence of nicotine use disorder among bipolar patients was 22.3% (n = 27). Male gender was the only demographic factor that was statistically associated with nicotine use disorder (p < .001). Patients with nicotine use disorder had significantly more psychiatric hospitalizations than those without nicotine use disorder after adjusting for gender, race, employment status, education level and duration of illness (p < .001). Conclusions: The rate of nicotine use disorder among bipolar patients in this study is similar to that of the general population in Malaysia but lower than that of hospitalized bipolar patients in other parts of the world. Male bipolar patients had higher risk of nicotine use disorder, which was also associated with a higher rate of prior psychiatric hospitalizations. Because there is a high prevalence of nicotine use disorder among bipolar patients, as well as potential interactions with the course of the disorder, nicotine use should be addressed in these patients. (Journal of Dual Diagnosis, 8:28–34, 2012)

Keywords: bipolar disorder, smoking, nicotine, outcomes, substance use

Cigarette smoking has a high prevalence among bipolar patients. In the Systematic Treatment Enhancement Program for Bipolar Disorder (Waxmonsny et al., 2005), 31.4% of the 1,904 patients were smokers. In the National Epidemiologic Survey on Alcohol and Related Conditions (Grant, Hasin, Chou, Stinson, & Dawson, 2004), the odds ratio for nicotine dependence in bipolar I and II disorders was 3.9 and 3.5, respectively, compared to the general population. In the National Comorbidity Survey (Morris, Giese, Turnbull, Dickinson, & Johnson-Nagel, 2006), a community study in the U.S., 50.7% of the 14,759 bipolar patients were smokers, compared to about 20% in the general population (Garrett, Dube, Trosclair, Caraballo, & Pechacek, 2011).

Although it is not known why patients with bipolar disorder are more likely to smoke, some studies report that smoking is used to either alleviate unpleasant psychiatric symptoms (e.g., agitation) or to induce pleasurable feelings (e.g., euphoria; Grant et al., 2004). In addition, nicotine withdrawal has been linked to increased mania, depression, and irritability, potentially making it more difficult for smokers with bipolar disorder to quit (Benazzi, 1989; Cohen, 1990; Waxmonsny et al., 2005). Berk et al. (2008) note that cigarettes contain nicotine, which is a nicotinic cholinergic receptor agonist that causes the release of neurotransmitters such as dopamine, noradrenaline, serotonin, and glutamate. The activation of the mesolimbic dopaminergic pathways (reward pathway) plays an important role in reinforcement of smoking. The sensitization of nicotinic cholinergic, dopaminergic, and other downstream receptors are altered with prolonged nicotine exposure (Berk et al., 2008). Bipolar disorder, especially during manic episodes, is associated with increased dopamine and noradrenaline transmitters, which may make people with the disorder more susceptible to the rewarding effects of substances such as nicotine (Anand et al., 2000).

Many studies have also examined associations between smoking and the course of bipolar disorder. However, the results have been inconsistent. Some studies have found that lifetime smoking is significantly related to an earlier onset of bipolar disorder, poorer functioning, increased lifetime history of suicide attempts, greater symptomatic severity, greater number of hospitalizations, greater comorbidity with other psychiatric disorders, and use of more types of medication.
(Cassidy, Ahearn, & Carroll, 2001; Waxmonsky et al., 2005; Ostacher et al., 2006; Berk et al., 2008). Smoking in bipolar disorder is also associated with poorer control of mood episodes, contributing to a greater severity of the illness (Law et al., 2009). Singh, Mattoo, Sharan, & Basu (2005) also found that quality of life in terms of physical health, psychological health, and environmental and social relationships was lower in bipolar patients with nicotine use disorder compared to bipolar patients without nicotine use disorder. However, in contrast to these studies, Gumattira et al. (2010) recently reported that patients with bipolar disorder and nicotine use disorder had fewer previous episodes, briefer hospital stays, and more days in the community between hospital admissions when compared to those without nicotine use disorder.

The current study was conducted to estimate the prevalence of nicotine use disorder among bipolar patients in a university hospital in Malaysia and to examine associated demographic factors and clinical correlates of nicotine use disorder in this group of patients.

METHODS

Sample

Patients were recruited from March 2009 to September 2010 from the psychiatric unit (outpatient and inpatient) in a semi-privatized, local teaching hospital in Kuala Lumpur, Malaysia. Inclusion criteria were (a) met DSM-IV-TR (American Psychiatric Association, 2000) criteria for bipolar disorder I or bipolar disorder II, (b) was at least 18 years of age, (c) provided informed consent, and (d) was able to understand and communicate in English or Bahasa Malaysia to complete study measurements. Exclusion criteria were (a) had Axis I diagnosis other than bipolar disorder or substance use disorder, (b) had an organic mental disorder, (c) had a diagnosis of mental retardation, and (d) was experiencing unstable general medical conditions.

All patients who were identified as having bipolar disorder in the clinic and ward were approached. Written informed consent was obtained from patients who chose to participate in the study, after a discussion of study details with the researchers. The study was conducted in accordance with the Declaration of Helsinki and the Medical Ethics Committee of the hospital, which approved and monitored the study (Ethical committee reference number 721.7).

Study Design

This was a cross-sectional study, including a face-to-face interview using the Mini International Neuropsychiatric Interview, bipolar and plus version 5.0.0 (Sheehan et al., 1998), the Fagerström Test for Nicotine Dependence-English and Malay version (subsequently referred to as Fagerström; Heatherton, Kozlowski, Frecker, & Fagerström, 1991; Yee et al., 2011), and the Addiction Severity Index-Lite-Clinical Factors version (ASI-Lite; Cacciola, Alterman, McLellan, Lin, & Lynch, 2007).

The Mini International Neuropsychiatric Interview, bipolar version was used to establish the diagnosis of bipolar disorder, age at onset, and family history of bipolar disorder. The Mini International Neuropsychiatric Interview, plus version 5.0.0 (MINI) was used to assess and screen for substance use disorders (dependence and abuse), including alcohol, cannabis, stimulants, opioids, cocaine, hallucinogens, sedatives/hypnotics/anxiolytics, nicotine, and other substances. A person is classified as having substance dependence when he or she fulfills more than three of the following seven criteria: tolerance, withdrawal symptoms, persistent desire or unsuccessful efforts to reduce the use of substances, excessive time spent to obtain substance or recover from the effects, social, occupational and recreational pursuits are reduced because of the substance use, and continued use of the substance despite knowledge of substance-related harm. Previous research has shown that 39.4% of smokers fail to meet the DSM-IV-TR criteria for nicotine dependence (Donny & Dierker, 2007). Hence, the Fagerström was used to further assess nicotine dependence among bipolar patients. This easy-to-use self-report questionnaire is noninvasive, low-cost, and easy to score and has good sensitivity and specificity for nicotine dependence in smokers. The Fagerström was validated in Malay, which is a local language in Malaysia (Yee, Ng, & Rusdi, 2011). The optimal cutoff for nicotine dependence on the Fagerström is a score of more than two (Heatherton et al., 1991; Yee et al., 2011). Patients who had scores that met the Fagerström cutoff or who fulfilled the MINI criteria for nicotine dependence were defined as having nicotine use disorder.

The ASI-Lite-Clinical Factors version was used to assess four areas of each patient’s life: medical, employment/support, family/social, and psychiatric (Cacciola et al., 2007). On the ASI-Lite, each problem area is divided into two parts, corresponding to objective and subjective items. Examples of objective items in the medical domain include the number of hospitalizations for medical problems and the number of prescription medications for medical issues. A composite score, ranging from 0 (no problem) to 1 (extreme severity), is calculated for each of the domains based on the objective items (McGahan, Griffith, Parente, & McLellan, 1986; Samuel, Cacciola, Carise, Alterman, & McLellan, 2006). For the subjective items, patients indicate the severity of the problem by rating two items (how bothered they are and how much they wish to receive additional treatment) on a 5-point scale (“not at all” to “extremely”). Demographic data, number of lifetime psychiatric hospitalizations, lifetime suicide attempts, and number of psychiatric medications prescribed were also obtained from the ASI-Lite.

For the purposes of statistical analysis of suicide attempts, patients were grouped into those who had made one or more suicide attempts during their lifetime compared to those who had never made such an attempt. For the analysis of psychiatric medications, patients were divided into those who
were prescribed zero to two medications compared to those who were prescribed more than two medications.

Survival days were defined as the total number of days between the last discharge and the most current readmission for all patients who had been readmitted to the hospital. The date of the last discharge and most current readmission were obtained from case notes. The number of lifetime hospitalizations was determined from patient self-report and case records.

Statistical Analyses

All analyses were conducted by using the Statistical Package for the Social Sciences version 16.0 (SPSS, Chicago, Illinois, USA). Descriptive statistics were computed for the baseline characteristics of the study patients. Demographic characteristics such as age, personal income, gender, race, education level, employment status, and marital status were compared between the nicotine use disorder and non-nicotine use disorder groups. ASI-Lite scores in the medical, employment/support, family/social, and psychiatric domains were calculated by using ASI-Lite composite score calculation, and were compared between the nicotine use disorder and non-nicotine use disorder groups. Chi-square or Fisher exact tests were used to compare categorical variables between the nicotine use disorder and non-nicotine use disorder groups. Odds ratios and their 95% confidence intervals were calculated. The means of the continuous variables for the two groups were compared using Student’s t-test. The odds ratios and means were then adjusted for demographic and clinically relevant factors (i.e., age, gender, race, duration of illness, employment status, education level, and comorbid substance use disorder other than nicotine) by using either linear or binary logistic regression models. The Kaplan-Meier survival method was used for the analysis of the survival days. All statistical tests were two-tailed at the significant level of .05.

RESULTS

Demographic Data

A total of 130 bipolar patients who fulfilled the inclusion criteria were approached to participate in the study, and 121 of them consented to be in the study (9 eligible patients refused to participate). The mean age of the sample was 42.13 (SD = 13.4) and 49.6% were female. The largest proportion of study patients were Chinese (45.5%), followed by Indians (25.5%), and Malays (24%). Fifty percent of the patients were married, 10.7% were divorced, 4.1% were separated, and the rest were widowed. About half of the study patients (52.9%) had completed secondary education and only 27.3% were unemployed. The majority of the patients were earning around MYR2400 monthly, which converts to approximately US$755. The majority of the patients had bipolar I disorder diagnosed (96.7%), and about half had a family history of mood disorders (44.6%).

Prevalence of Nicotine Use Disorder

The overall prevalence of nicotine use disorder was 22.3% (n = 27) based on the MINI and Fagerström. Nicotine use disorder was present in 41% (n = 25) of the male patients, compared to only 3.3% (n = 2) of the female patients. Several study patients had multiple substance use disorders, including 5.8% (n = 7) with nicotine and alcohol use disorders, 3.3% (n = 4) with nicotine and marijuana use disorders, and 2.5% (n = 3) with nicotine, alcohol, and marijuana use disorders.

Comparison of Non-nicotine Use Disorder and Nicotine Use Disorder Groups

Differences between the nicotine use disorder and non-nicotine use disorder patients on demographic variables are displayed in Tables 1 and 2. Male patients were more likely to have current nicotine use disorder, with an odds ratio of 16.83 (p < .001) after adjusting for race, duration of illness, education level, employment status, and other substance use disorder (such as alcohol and marijuana use disorder). Differences between the non-nicotine use disorder and nicotine use disorder groups in age at onset of bipolar disorder, number of lifetime psychiatric hospitalizations, and ASI-Lite scores are displayed in Table 3, and differences between the groups in the number of medications used and the number of lifetime suicide attempts are summarized in Table 4. The nicotine use disorder group differed significantly only in number of lifetime psychiatric hospitalizations.

### Table 1

Comparison Between Nicotine Use Disorder and Non-nicotine Use Disorder Groups Among Bipolar Patients: Age and Personal Income per Month

<table>
<thead>
<tr>
<th>Variables</th>
<th>Non-nicotine mean (SD)</th>
<th>Nicotine mean (SD)</th>
<th>Difference of means</th>
<th>Adjusted difference of means</th>
<th>t</th>
<th>95% Confidence interval</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>41.9 (13.6)</td>
<td>42.8 (13.1)</td>
<td>0.879</td>
<td>2.690</td>
<td>0.299</td>
<td>−3.32 to 8.703</td>
<td>.377</td>
</tr>
<tr>
<td>Personal income per month (MYR/month)</td>
<td>2496.4 (2490.3)</td>
<td>2203.0 (1985.6)</td>
<td>−292.462</td>
<td>−252.560</td>
<td>0.561</td>
<td>−1338.3 to 833.21</td>
<td>.646</td>
</tr>
</tbody>
</table>

*Adjusted for use of other substances with or without nicotine.*
TABLE 2
Comparison Between Nicotine Use Disorder and Non-nicotine Use Disorder Groups Among Bipolar Patients: Gender, Ethnicity, Employment Status, Marital Status, and Education Level

<table>
<thead>
<tr>
<th>Variables</th>
<th>Non-nicotine n (%)</th>
<th>Nicotine n (%)</th>
<th>OR</th>
<th>Adjusted OR</th>
<th>( \chi^2 )</th>
<th>95% Confidence interval</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 94</td>
<td>n = 27</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>36 (38.3)</td>
<td>25 (92.6)</td>
<td>20.139</td>
<td>16.83⁴</td>
<td>24.735</td>
<td>3.707 to 26.494</td>
<td>&lt; .001*</td>
</tr>
<tr>
<td>Female</td>
<td>58 (61.7)</td>
<td>2 (74)</td>
<td>0.683</td>
<td>0.610⁴</td>
<td>0.612</td>
<td>0.222 to 1.671</td>
<td>.336</td>
</tr>
<tr>
<td>Malay</td>
<td>21 (22.3)</td>
<td>8 (29.6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Malay</td>
<td>73 (77.7)</td>
<td>19 (70.4)</td>
<td>2.39</td>
<td>2.252⁴</td>
<td>3.651</td>
<td>0.789 to 6.427</td>
<td>1.129</td>
</tr>
<tr>
<td>Indian</td>
<td>21 (22.3)</td>
<td>11 (40.7)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Indian</td>
<td>73 (77.7)</td>
<td>16 (59.3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>41 (43.6)</td>
<td>9 (33.3)</td>
<td>1.547</td>
<td>1.195⁴</td>
<td>0.915</td>
<td>0.498 to 3.275</td>
<td>.408</td>
</tr>
<tr>
<td>Not married/divorced/single</td>
<td>53 (56.4)</td>
<td>18 (66.7)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>69 (73.4)</td>
<td>19 (70.4)</td>
<td>1.162</td>
<td>0.622⁴</td>
<td>0.097</td>
<td>0.252 to 1.524</td>
<td>.303</td>
</tr>
<tr>
<td>Not employed</td>
<td>25 (26.6)</td>
<td>8 (29.6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Below secondary education</td>
<td>41 (43.6)</td>
<td>15 (55.6)</td>
<td>0.619</td>
<td>0.622⁴</td>
<td>1.202</td>
<td>0.253 to 1.534</td>
<td>.303</td>
</tr>
<tr>
<td>Above secondary education</td>
<td>53 (56.4)</td>
<td>12 (44.4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

aAdjusted for use of other substances with or without nicotine.
*p < .01.

hospitalizations (\( p < .001 \)) compared to the non-nicotine use disorder group. When survival days of both groups were compared by using Kaplan-Meier Survival analysis, the difference was also not statistically significant (log-rank chi square = 2.113; df = 1; \( p = .146 \)).

DISCUSSION

This cross-sectional study examined the prevalence of nicotine use disorder in a group of bipolar patients in a hospital setting, as well as demographic and clinical correlates. The prevalence of nicotine use disorder was 22.3%, which was similar to that of the general population in Malaysia (21.5%) (Nationmaster, 2006). However, this prevalence was lower than that reported for hospitalized bipolar patients in other parts of the world, which range from 31% to 52.6% (Grant et al., 2004; Waxmonsky et al., 2005; Morris et al., 2006). Male patients were more likely to be smokers (\( p < .001 \)), consistent with the previous research (Waxmonsky et al., 2005). Bipolar patients with nicotine use disorder also tended to have more psychiatric hospitalizations in their lifetime than those without nicotine use disorder (\( p < .001 \)), but no other significant clinical correlates were found.

The reasons for the lower prevalence of nicotine use disorder in this study could be related to the lower prevalence

TABLE 3
Comparison Between Nicotine Use Disorder and Non-nicotine Use Disorder Groups Among Bipolar Patients: Onset of Bipolar Disorder, Number of Lifetime Psychiatric Hospitalizations, and ASI-Lite Scores

<table>
<thead>
<tr>
<th>Correlates</th>
<th>Non-nicotine mean (SD) n = 94</th>
<th>Nicotine mean (SD) n = 27</th>
<th>Difference of means</th>
<th>t</th>
<th>95% Confidence interval</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset of bipolar disorder (year)</td>
<td>28.36 (11.16)</td>
<td>29.89 (9.72)</td>
<td>1.53</td>
<td>1.59⁴</td>
<td>0.644</td>
<td>−3.76 to 6.94</td>
</tr>
<tr>
<td>Number of lifetime psychiatric hospitalizations</td>
<td>2.88 (2.28)</td>
<td>5.63 (5.04)</td>
<td>2.75</td>
<td>3.00⁴</td>
<td>2.752</td>
<td>1.574 to 4.415</td>
</tr>
<tr>
<td>Medical</td>
<td>0.08 (0.20)</td>
<td>0.09 (0.17)</td>
<td>0.01</td>
<td>0.011⁴</td>
<td>0.357</td>
<td>−0.106 to 0.084</td>
</tr>
<tr>
<td>Employment/Support</td>
<td>0.37 (0.33)</td>
<td>0.28 (0.29)</td>
<td>−0.09</td>
<td>−0.042⁴</td>
<td>−1.317</td>
<td>−0.188 to 0.124</td>
</tr>
<tr>
<td>Family/Social</td>
<td>0.26 (0.16)</td>
<td>0.29 (0.21)</td>
<td>0.03</td>
<td>0.016⁴</td>
<td>0.965</td>
<td>−0.070 to 0.102</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>0.30 (0.20)</td>
<td>0.31 (0.17)</td>
<td>0.01</td>
<td>0.005⁴</td>
<td>0.173</td>
<td>−0.092 to 0.103</td>
</tr>
</tbody>
</table>

Note. ASI-Lite = Addiction Severity Index-Lite-clinical factor version.

aAdjusted for gender, race, education level, employment status, and use of other substances with or without nicotine.

bAdjusted for gender, race, duration of illness, education level, employment status, and use of other substances with or without nicotine.

cAdjusted for age, gender, race, education level, employment status, and use of other substances with or without nicotine.

*p < .01.
of nicotine use among the Malaysian general population, estimated to be 21.5% (Nationmaster, 2006), compared to other countries, which range from 22.3% to 35.9% (Lasser et al., 2000; Ma et al., 2009). Another potentially important reason is that the bipolar patients in this study were more educated (more than half of them completed secondary education), married (50%), and older (mean age of 42 years old) than in other studies. These demographic factors have been found to be negatively associated with nicotine use disorder in the general population (Escobedo, Anda, Smith, Remington, & Mast, 1990; Stinson, Grant, Ruan, & Pickering, 2006; Lin et al., 2010) and among people with bipolar disorder.

The patients with bipolar disorder may have been more educated, older, and more likely to be married because this study was conducted in a semi-privatized hospital in which patients had to pay for their treatment. Therefore, socially disadvantaged patients may have been underrepresented in this sample as they may have been more likely to seek free treatment at public hospitals (Waxmonsky et al., 2005; Grunebaum et al., 2006).

Bipolar patients with nicotine use disorder also showed a twofold increase in number of psychiatric hospitalizations over their lifetime when compared to bipolar patients without nicotine use disorder. This result is consistent with previous studies (Cassidy et al., 2001; Waxmonsky et al., 2005; Ostacher et al., 2006; Berk et al., 2008). Bipolar patients who smoke may have more unstable mood cycles, which in turn may require more psychiatric hospitalizations compared to bipolar patients who do not smoke (Law et al., 2009). In this study, there was no difference between nicotine use disorder and non-nicotine use disorder patients in either number of suicide attempts or number of prescribed medications, in contrast to previous research (Ostacher et al., 2006; Baethge, Tondo, Lepri, & Baldessarini, 2009). Our failure to replicate these previous findings could be due in part to the small sample size of the study, which limited power to detect statistically significant differences.

Many previous studies have found that bipolar patients with nicotine use disorder have poorer employment histories, more impaired social functioning, lower quality of life, and more medical illnesses than non-nicotine use disorder patients (Reich, Davies, & Himmelhoch, 1974; Kilbourne, Brar, Drayer, Xu, & Post, 2007; Mazza et al., 2009). In contrast, this study found no significant differences between nicotine use disorder and non-nicotine use disorder patients in these domains. Again, the small sample size could be the limiting factor.

**Limitations and Conclusions**

The primary limitation of this study was that it was conducted in a private hospital where patients had to pay for treatment. This resulted in a study sample that had higher socioeconomic status than the general population of people with bipolar disorder, which may have limited the generalizability of the study findings. Last, this was a cross-sectional study that did not allow us to explore the cause and effect relationship between clinical correlates of nicotine use disorder in bipolar disorder.

Thus, for example, it is unknown whether nicotine use disorder contributes to more psychiatric hospitalizations, whether more severely ill patients are more likely to have nicotine use disorder, or both.

The rate of nicotine use disorder among bipolar patients in this study is similar to that of the general population in Malaysia but lower than that reported for hospitalized bipolar patients in other parts of the world. Male patients were more likely to be smokers. Nicotine use disorder was associated with a higher rate of psychiatric hospitalization, although there were no other significant clinical differences between nicotine use disorder and non-nicotine use disorder patients. Given the high
prevalence of nicotine use disorder among bipolar patients and its potential interactions with the course of the disorder, nicotine use should be addressed in the management of these patients.

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DISCLOSURES

All the authors report no financial relationships with commercial interests.

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