Association between tobacco waterpipe smoking and head and neck conditions
A systematic review

Teja Munshi, BDS, MPH; Carolyn J. Heckman, PhD; Susan Darlow, PhD

Worldwide, tobacco use causes more than 5 million deaths annually, and current trends suggest that tobacco use will cause more than 8 million deaths annually by 2030.1,2 It is well known that cigarette smoking is harmful for overall health, and the global trend for its use is either stable or declining in countries with high income levels but still increasing in countries with low income levels.3 Unfortunately, there is also an upward global trend for some other forms of tobacco consumption, such as waterpipe smoking (WPS).3 WPS is a traditional form of tobacco consumption that originated in India 400 years ago and later spread to the eastern Mediterranean region.3,4 There, it was modified to its current form. Worldwide, the waterpipe used for tobacco smoking is known by various names such as hookah, hubble-bubble, shisha, nargileh, arghileh, and goza. Initially, the tobacco smoked through the waterpipe did not contain any additives. In the past decade, flavored tobacco, also known as shisha or maassel (tobacco combined with flavoring and sweetener), was introduced.55 This tobacco comes in various flavors such as strawberry (and other fruit flavors), cotton candy, and spiced chai.

WPS, especially with the addition of flavored shisha, is becoming increasingly popular among youth in several parts of the world.15 The lifetime prevalence of WPS in the Eastern Mediterranean region ranges from
6% to 34% among 13- to 15-year-olds, whereas the lifetime prevalence of WPS in the United States ranges from 7% to 20% among university students. The results of laboratory studies show that a typical WPS session can last from 20 to 80 minutes, during which the smoker may take 50 to 200 puffs, which range from approximately 0.15 to 1.0 liter of smoke per puff. A typical cigarette smoking session, on the other hand, lasts approximately 5 to 7 minutes, with approximately 40 to 75 puffs per session, and the smoker inhales 0.5 to 0.6 liters of smoke per cigarette. Therefore, a waterpipe smoker may inhale the equivalent of 100 cigarettes or more in 1 session.

Investigators have conducted a number of studies regarding WPS and its long-term effects on health. The results of systematic reviews and meta-analyses conducted in 2010 and 2014 show that WPS is associated with a risk of experiencing lung cancer, chronic obstructive pulmonary disease, other respiratory illnesses, bladder cancer, coronary artery diseases, and low birth weight. We were unable to identify any systematic reviews or meta-analyses focusing on conditions, diseases, or both, that occur in the head and neck region. We identified 3 articles that focused only on oral health outcomes, and we noted that none of these articles focused more broadly on head and neck health, areas that are also of relevance to dental practitioners. Rastam and colleagues hypothesized the potential pathophysiology of oral cancers among waterpipe users on the basis of the tobacco carcinogenesis process. Warnakulasuriya described and commented only on the oral tissue findings of the investigators of a previous systematic review that had focused on WPS and its effect on overall health. Shah and colleagues provided information on the effects of WPS on oral health and recommended cessation interventions for waterpipe smokers.

The aim of our review was to systematically review the literature to identify the potential health effects of WPS on the head and neck region. The authors of numerous studies suggested that cigarette, cigar, and pipe smoking are some of the main risk factors for periodontitis, precancerous lesions in the oral cavity and vocal cords, as well as head and neck cancers. Hence, we hypothesized that WPS would be associated with conditions of the head and neck tissues such as dry socket, periodontitis, precancerous lesions, and head and neck cancers.

METHODS

Search strategy. For our search strategy, we used the following terms in combination with the word "health": waterpipe, bubble-bubble, shisha, narghileh, arghileh, hookah, and goza. We considered studies for inclusion only if the study’s investigators assessed any association between WPS and health conditions seen in the head and neck region (that is, oral cavity, larynx, pharynx, vocal cords, and middle ear). We excluded from our review studies whose investigators did not distinguish between WPS and other forms of smoking, studies whose investigators did not report any measure of association, and studies whose investigators did not publish the results in English. We searched for articles published from 1990 (when the first article about WPS was published) to March 2014. We used 3 databases (that is, PubMed/MEDLINE, PsycINFO, Google Scholar) and 2 sources of gray literature (that is, www.greynet.org, www.greylit.org). We also e-mailed the Society for Research on Nicotine and Tobacco listerv (www.srnt.org/mem_only/list/index.cfm) to identify any additional unpublished data. We checked the bibliographies of included studies and relevant review articles to uncover studies that the electronic databases did not identify. Using the aforementioned methods, we identified 220 citations in our database search. We identified no additional citations using the gray literature search or the listserv request.

The first author (T.M.) reviewed all of the 220 abstracts to see if the studies assessed any association between WPS and health outcomes in the head and neck region. The results of this review reduced the number of eligible studies to 20 studies.

Data abstraction and coding. The first author (T.M.) and a trained research assistant independently coded the data. These 2 raters agreed on 82% of codes and resolved any disagreements by consensus. These 2 Rammah Mre- viewers independently extracted data using specifically designed data coding forms. We used the following variables for coding: year of publication; geographic location of the study; participant characteristics (sex and age); sample size; type of smoking (for example, cigarette smoking, smokeless tobacco, WPS); WPS duration; WPS frequency in runs per days, per weeks, or per years; type of study design (for example, case report, cross-sectional, case-control); and details on the health outcomes reported (for example, vertical bone defects, dry socket).

RESULTS

Overview. Studies were mainly observational and conducted mostly in Middle Eastern, Asian, and North African countries (for example, case-control [n = 10], cross-sectional [n = 17], experimental [n = 2], and case report [n = 1]). We further categorized these citations by bodily region and disease type as follows: oral tissues (n = 10), head and neck cancers and precancers (n = 7), and others that focused on the voice, larynx, and middle ear (n = 3). Health conditions reported were gingivitis,

periodontitis, dry socket, premalignant lesions, head and neck cancers, and precancerous lesions (for example, esophageal squamous cell carcinoma, lip carcinoma), attic retraction in the middle ear (that is, a condition in which the tympanic membrane lies deeper in the ear than its normal position), and tympanometric and vocal cord differences. The table provides detailed characteristics of all the included studies.

**Description of included studies.** **Oral tissues.** We identified 10 studies as focusing on the impact of WPS on oral tissues. Most of the studies were cross-sectional (n = 7), followed by case-control studies (n = 2), and 1 experimental study. These were conducted in Middle Eastern countries, specifically Saudi Arabia (n = 5), Egypt (n = 2), Yemen (n = 1), Iran (n = 1), and an unspecified location. The health conditions assessed were microscopic differences in the oral mucosa (n = 4), periodontal health (n = 4), dry socket (n = 1), and gingival health (n = 1). The results of 4 studies showed that, at the microscopic level, WPS can affect cells negatively. Specifically, the investigators of these 4 studies noted that WPS was associated with lower cell proliferation, as well as greater micronuclei (potential biomarkers of early carcinogenesis), inflammation, cell doubling time, other histopathologic changes, and oral candidiasis. In addition, WPS users had high plaque levels as well high levels of gingival indexes. The investigators of all 5 studies that focused on periodontal and gingival health reported on the same cohort of patients from Saudi Arabia–found that WPS is associated with periodontitis. Lastly, WPS was associated with dry socket when it occurred on the day of tooth extraction.

**Oral cancers and precancerous lesions.** We identified 7 studies whose investigators focused on oral cancers and precancerous lesions. Most of the studies were case-control (n = 6), and 1 was a case report. Investigators conducted these studies in India (n = 3), North Africa (n = 2), Iran (n = 1), and Saudi Arabia (n = 1). The investigators of these studies examined the association between WPS and head and neck cancers (n = 6) and precancerous lesions (n = 1). The investigators of 1 study found that blood levels of the carcinogens chromium and nickel were greater in waterpipe smokers. The investigators of 4 of 5 studies focusing on head and neck cancer found that WPS was associated with cancer; the most common type being squamous cell carcinoma, mainly of the esophagus, followed by carcinoma of the lip and oral mucosa. The investigators of 1 study did not find any association between WPS and nasopharyngeal carcinoma, and the investigators of 1 study reported that WPS was associated with oral dysplasia.

**Voice, larynx, and middle ear.** We identified 3 studies in this category: 2 were case-control and 1 was experimental. Studies focused on the effects of WPS on the voice (n = 1), larynx (n = 1), and middle ear (n = 1). The geographic location for 2 of these studies was unspecified, but we believe that the location for 1 of these studies likely was Lebanon, which is where the authors were located, and the location for the other likely was Egypt. The investigators of 1 experimental study found that short-term use of WPS (specifically, WPS for 30 minutes) can cause a temporary decrease in vocal pitch and voice turbulence index. We noted that across the studies, long-term WPS was associated with greater attic retraction, benign lesions of the vocal cords, thick mucus secretion, edema, cysts, and acoustic alterations (for example, lower voice turbulence index and greater phonation time).

**DISCUSSION**

The purpose of our study was to evaluate the potential effects of WPS on head and neck tissues. A systematic review of the 20 available studies revealed that WPS is associated with various conditions in the head and neck region. The results showed that acute waterpipe use by chronic users (that is, using a waterpipe for 30 minutes) is associated with lower habitual vocal pitch and voice turbulence index, as well as a risk of experiencing dry sockets (if the waterpipe use occurs on the day of extraction). In addition, chronic waterpipe use is associated with a greater manifestation of periodontal diseases, number of suspicious lesions (that is, any red, painless, firm, indurated lesion that was unresolved for more than 14 days) in the oral cavity, oral candidiasis, and blood levels of chromium and nickel (known carcinogens). However, the same investigative team conducted all of the studies on gingival conditions, and they used the same cohort; therefore, their study results should be replicated. Chronic waterpipe use also is associated positively with precancerous lesions, oral cancers such as squamous cell carcinoma and keratoacanthoma of the lip, and esophageal squamous cell carcinoma. Lastly, the investigators of 1 study found no association between waterpipe use and nasopharyngeal cancer. Although the results of these studies (most of which were correlational studies) show that WPS is associated with various conditions in the head and neck region, there may be other causal factors. However, given such evidence, it is important to generate awareness and educate the public regarding the potential health effects of WPS. For the past 20 years, WPS has been gaining popularity mostly among young adults in North America, the United Kingdom, and Europe. The popularity of WPS could be attributed partially to the fact that many college users believe that WPS is less harmful than cigarette smoking and that it is not addictive. The perceived safety of WPS may be attributed to the lack of regulation on package labeling as well as its nicotine content, the smoothness of flavored tobacco compared with cigarettes, the availability of flavors designed to appeal to children (for example, gummi bear and tutti-frutti), water filtration, and the rise in the number of waterpipe cafés. Moreover, because
### Characteristics of included studies.

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<th>MALE SEX, %</th>
<th>POPULATION (NO.)</th>
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<th>HEALTH OUTCOMES†</th>
<th>RESULTS</th>
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<tr>
<td>El-Hakim and Colleagues, 1999</td>
<td>Saudi Arabia, Egypt</td>
<td>Case report</td>
<td>3 100</td>
<td>WP³ smokers, corner of mouth (2), versus WP smokers, lower lip (1)</td>
<td>Case 1 &gt; 20 y (33%) Case 2 = 5 y (33%) Case 3 = 4 y (33%)</td>
<td>+ Carcinoma of lip or oral mucosa</td>
<td>Not statistically significant</td>
<td></td>
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<tr>
<td>Al-Belasy, 2004</td>
<td>Egypt</td>
<td>Case-control</td>
<td>300 100</td>
<td>WP smokers (100) versus cigarette smokers (100) versus nonsmokers (100)</td>
<td>Unknown</td>
<td>+ Dry socket</td>
<td>For WP smokers who smoked the day of surgery compared with nonsmokers (P &lt; .001)</td>
<td></td>
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<tr>
<td>Effat, 2004</td>
<td>Egypt</td>
<td>Case-control</td>
<td>75 100</td>
<td>WP smokers (40) versus cigarette smokers (35)</td>
<td>≥ 5 y</td>
<td>+ Attic retraction ( tympanic membrane lies deeper in the ear than its normal position)</td>
<td>P &lt; .01</td>
<td></td>
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<tr>
<td>Natto and Colleagues, 2004</td>
<td>Saudi Arabia</td>
<td>Cross-sectional</td>
<td>244 66</td>
<td>WP smokers (76) versus cigarette smokers (49) versus mixed smokers (49) versus nonsmokers (70)</td>
<td>Unknown</td>
<td>+ Plaque index + Gingival index</td>
<td>Fisher exact test = 15.6 (P &lt; .001) for WP smokers’ plaque index compared with cigarette smokers’ plaque index, and Fisher exact test = 5.8 (P &lt; .01) compared with mixed smokers. Statistically significantly higher gingival index for WP smokers compared with nonsmokers (unknown P value).</td>
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<tr>
<td>Baljoon and Colleagues, 2005</td>
<td>Saudi Arabia</td>
<td>Cross-sectional</td>
<td>355 71</td>
<td>WP smokers (80) versus cigarette smokers (50) versus mixed smokers (54) versus nonsmokers (78)</td>
<td>Unknown</td>
<td>+ Vertical bone defects</td>
<td>OR³ = 2.9 (95% CI, 1.2-7.0; P = .06) for WP smokers compared with nonsmokers</td>
<td></td>
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<tr>
<td>Natto and Colleagues, 2005</td>
<td>Saudi Arabia</td>
<td>Cross-sectional</td>
<td>355 71.83</td>
<td>WP smokers (117) versus cigarette smokers (72) versus mixed smokers (67) versus nonsmokers (99)</td>
<td>Unknown</td>
<td>- Periodontal bone height</td>
<td>P &lt; .001 for WP smokers compared with nonsmokers</td>
<td></td>
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<tr>
<td>Natto and Colleagues, 2005</td>
<td>Saudi Arabia</td>
<td>Cross-sectional</td>
<td>262 64.88</td>
<td>WP smokers (81) versus cigarette smokers (50) versus mixed smokers (54) versus nonsmokers (77)</td>
<td>Unknown</td>
<td>- Periodontal disease</td>
<td>RR⁴ = 5.1 (P &lt; .001) for WP smokers compared with nonsmokers</td>
<td></td>
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* WPS: Waterpipe smoking.
† Health outcomes described as higher amount (+), lower amount (-), or no association (=).
‡ WP: Waterpipe.
§ OR = Odds ratio.
¶ CI = Confidence interval.
# RR = Relative risk.
** ESCC: Esophageal squamous cell carcinoma.
†† VTI: Voice turbulence index.
‡‡ MPT: Maximum phonation time.
§§ Suspicious lesions: Any lesion that was red, painless, firm, indurated, and had a history of being unresolved for more than 14 days.
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<tr>
<td>Natto and Colleagues,24 2005</td>
<td>Saudi Arabia</td>
<td>Cross-sectional</td>
<td>198</td>
<td>62.62</td>
<td>WP smokers (58) versus cigarette smokers (35) versus mixed smokers (25) versus nonsmokers (80)</td>
<td>Unknown</td>
<td>Changes in subgingival microflora</td>
<td>Not statistically significant</td>
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<tr>
<td>Ali,17 2007</td>
<td>Yemen</td>
<td>Cross-sectional</td>
<td>33</td>
<td>81.8</td>
<td>WP smokers (11) versus cigarette smokers (11) versus nonsmokers (11)</td>
<td>Unknown</td>
<td>Histopathologic changes</td>
<td>Ranged from 0% to 90% on the WPS side of the mouth versus 0% to 54.5% on the contralateral side of the mouth</td>
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<td>El-Setouhy and Colleagues,18 2008</td>
<td>Egypt</td>
<td>Case-control</td>
<td>206</td>
<td>100</td>
<td>WP smokers (128) versus nonsmokers (78)</td>
<td>≤ 14 y = 70 (54.6%) &gt; 14 y = 58 (45.3%)</td>
<td>Micronuclei (products of early events in the carcinogenic processes)</td>
<td>(P = .001)</td>
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<tr>
<td>Nasrollahzadeh and Colleagues,30 2008</td>
<td>Iran</td>
<td>Case-control</td>
<td>871</td>
<td>51</td>
<td>ESCC** patients (300) versus healthy controls (571)</td>
<td>≤ 19 y = 27 (62.8%) &gt; 19 y = 16 (37.2%)</td>
<td>ESCC</td>
<td>Nearly significant OR = −1.85 (95% CI, 0.95-3.58) for regular WPS and P = .03 for higher average intensity of use</td>
</tr>
<tr>
<td>Feng and Colleagues,31 2009</td>
<td>North Africa</td>
<td>Case-control</td>
<td>1,251</td>
<td>69.46</td>
<td>Nasopharyngeal carcinoma patients (636) versus healthy controls (615)</td>
<td>Unknown</td>
<td>Nasopharyngeal carcinoma</td>
<td>Not statistically significant</td>
</tr>
<tr>
<td>Hamdan and Colleagues,15 2010</td>
<td>Unknown (probably Lebanon)</td>
<td>Case-control</td>
<td>110</td>
<td>65.45</td>
<td>WP smokers (42) versus cigarette smokers (27) versus nonsmokers (41)</td>
<td>Mean (standard deviation) = 8.09 y (6.45 y)</td>
<td>Edema; Excessive or thick mucus of vocal folds – VTI†† – MPT‡‡</td>
<td>P = .012 for edema; P = .026 for mucus; P = .009 for VTI; and P = .037 for MPT in WP smokers versus nonsmokers</td>
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<td>Hamdan and Colleagues,13 2011</td>
<td>Unknown (probably Lebanon)</td>
<td>Experimental</td>
<td>18</td>
<td>38.88</td>
<td>Study participants before 30 min of WPS (18) versus after WPS (18)</td>
<td>&lt; 1 y = 3 (17.7%) 1-5 y = 11 (58.7%) &gt; 5 y = 4 (23.6%)</td>
<td>VTI – Habitual pitch</td>
<td>P = .03; P = .07</td>
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<td>Khan and Colleagues,29 2011</td>
<td>India</td>
<td>Case-control</td>
<td>200</td>
<td>73</td>
<td>ESCC patients (100) versus healthy controls (100)</td>
<td>Unknown</td>
<td>Esophageal carcinoma</td>
<td>P = .000 in WP smokers (n = 81) compared with cigarette smokers (n = 33)</td>
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<td>Dangi and Colleagues,32 2012</td>
<td>India</td>
<td>Case-control</td>
<td>761</td>
<td>49.8</td>
<td>Cases with suspicious oral lesions (42) versus healthy controls (719)</td>
<td>Unknown</td>
<td>Suspicious oral lesions§§</td>
<td>OR = 4.42 (P = .01) for WP smokers (n = 163) compared with nonsmokers (n = 598)</td>
</tr>
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<td>Dar and Colleagues,27 2012</td>
<td>India</td>
<td>Case-control</td>
<td>2,365</td>
<td>55.43</td>
<td>ESCC (702) versus matched healthy controls (1,663)</td>
<td>1-33 y = 318 (28.5%) 34-45 y = 423 (37.9%) ≥ 46 y = 376 (33.7%)</td>
<td>ESCC</td>
<td>OR = 1.85 (95% CI, 1.41-2.44) for WP smokers (n = 1,119) compared with nonsmokers (n = 1,246)</td>
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<td>Khli and Colleagues,26 2013</td>
<td>North Africa</td>
<td>Case-control</td>
<td>520</td>
<td>76.53</td>
<td>Head and neck cancer patients (169) versus healthy controls (351)</td>
<td>&gt; 1 y</td>
<td>Blood chromium and nickel (carcinogens)</td>
<td>P &lt; .001 in WP smokers (n = 77) compared with nonsmokers (n = 443)</td>
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</table>
WPS is a traditional method of smoking tobacco that has deep cultural roots among people living in Asia and particularly in the Middle East, public health professionals will find it difficult to alter the behavior of people who smoke waterpipes.

Public health professionals could use community-level recommendations for tobacco control made by the US Preventive Services Task Force to attempt to decrease WPS, such as increasing the taxation of waterpipe tobacco products, conducting mass media campaigns, and using stronger governmental regulations targeted toward retailers. There are no regulations on the percentage of nicotine content, age restrictions for entering hookah bars or cafés, or even buying WPS paraphernalia or tobacco. There also are no bans or regulations on advertising.

Although WPS has been in practice for many years, relatively few researchers have published the results of studies on this topic in the English language. We identified a sample that included enough studies to conduct a systematic review of the literature on the association between WPS and conditions of the head and neck; however, our review had some limitations. For example, we did not formally assess the quality of the studies. A few of the studies were experimental, and some others may have been of poor quality. Some of the study investigators did not adequately describe certain aspects of some of the studies, such as the study design and methods, population, sample size justification, measurement of exposure, and statistical analyses. In addition, investigators did not use standardized methods for reporting waterpipe usage, such as the number of runs per day, week, month, and year. Because investigators did not report the impact of confounding variables consistently across all the studies, we were unable to take them into account. In addition, all of the studies were conducted outside of the United States. Hence, the generalizability of the results to the US population may be limited, and readers should interpret the results of this systematic review accordingly. Investigators should conduct similar studies in locations other than the Middle East and Asia to track more recent trends of WPS.

Although the results of the included studies help clarify the association between WPS and various health conditions of the head and neck, determining the results of high-quality, prospective, longitudinal and experimental studies is necessary to identify additional causal effects. Finally, more information also is needed regarding the health effects of the various flavorings of waterpipe tobacco, as flavoring is believed to be appealing and popular among younger populations.

**CONCLUSION**

In this systematic review, we identified various conditions of head and neck tissues associated with WPS. As the practice of WPS is gaining momentum among young adults in the Western world, it is important to alert medical and dental professionals about the potential dangers of WPS so that they can help affected waterpipe smokers by providing proper education as well as treatment options as necessary. Preventive measures such as implementing increased taxation, offering media campaigns and advertising regulations, providing stronger regulations targeted toward retailers, regulating nicotine content, and setting age restrictions for buying and using WPS products are some measures that could be implemented in the community with the help of local, state, and national governments. Finally, investigators should conduct future studies on this topic in areas of the world where WPS is gaining popularity.

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<td>Seifi and Colleagues, 2014</td>
<td>Iran</td>
<td>Cross-sectional</td>
<td>120</td>
<td>Unknown</td>
<td>WP smokers (40) versus cigarette smokers (40) versus nonsmokers (40)</td>
<td>3-5 y</td>
<td>+ Inflammation + Candida</td>
<td>$P = .002$ for smokers compared with nonsmokers</td>
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<td>Shihadeh and Colleagues, 2014</td>
<td>Unknown (probably Lebanon)</td>
<td>Experimental</td>
<td>15</td>
<td>Unknown</td>
<td>Study participants with &gt; 45 min of tobacco WPS and tobacco-free WPS, counterbalanced (15)</td>
<td>≥ 6 mo</td>
<td>– Cell proliferation (caused cell cycle arrest) + Cell doubling time (seen for both conditions)</td>
<td>By 43% By 22%</td>
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