# Sleep Disordered Breathing and Hypertension: Does Self-Reported Sleepiness Modify the Association?

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**Study Objectives:** Epidemiologic studies that demonstrate increased risk of hypertension in persons with sleep disordered breathing indicate that only a minority of these persons report significant subjective sleepiness. Studies also suggest that presence of self-reported sleepiness may identify a subset of persons with sleep disordered breathing who are at greatest risk of cardiovascular sequelae, including hypertension. We explore whether self-reported sleepiness modifies the relationship between sleep disordered breathing and prevalent hypertension.

**Design:** Cross-sectional

**Setting:** Multicenter study

**Participants:** 6046 subjects from the Sleep Heart Health Study

**Measurements:** Polysomnography, systolic and diastolic blood pressure, antihypertensive medication use, questionnaire determined excessive sleepiness and Epworth Sleepiness Scale, and covariates.

**Results:** The odds of hypertension at higher apnea hypopnea index categories were larger in participants identified as sleepy based on responses to a frequency of sleepiness question or the Epworth score. For example, for those with AHI ≥30 compared to AHI <1.5, the adjusted odds ratio for hypertension was 2.83 (1.33-6.04) among those reporting sleepiness ≥5 days per month, but only 1.22 (0.89-1.68) among those reporting less frequent daytime sleepiness. In adjusted logistic regression models, there was statistical evidence for effect modification by frequency of sleepiness (P = 0.033) of the association between apnea hypopnea index and hypertension. In adjusted models that included the Epworth score as a continuous variable, the interaction term fell slightly short of statistical significance (β = 0.010, P = 0.07).

**Conclusion:** This study finds that the association of sleep disordered breathing with hypertension is stronger in individuals who report daytime sleepiness than in those who do not.

**Keywords:** Sleepiness, hypertension, Epworth, epidemiology, apnea, interaction, effect, modification, cardiovascular

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EPIDEMIOLOGICAL STUDIES INDICATE THAT PEOPLE WITH SIGNIFICANT LEVELS OF SLEEP DISORDERED BREATHING (SDB) ARE AT INCREASED RISK FOR developing hypertension and may have increased risk for other cardiovascular events.[1-3] In contrast to patients referred for clinical evaluation of SDB, however, only a small proportion of participants in these epidemiologic studies who had an elevated apnea-hypopnea index (AHI) complained of significant sleepiness.[4] Among Sleep Heart Health Study (SHHS) participants with moderate to severe SDB (AHI ≥ 15), only 46% reported an elevated score on the Epworth Sleepiness Scale (ESS) or frequent feelings of sleepiness or feeling unrested.[5]

Several epidemiologic studies have shown a relation between self-reported sleepiness and cardiovascular disease, though these studies have not used polysomnography to measure SDB. In the Cardiovascular Health Study, daytime sleepiness was the only sleep disturbance symptom associated with incident myocardial infarction, heart failure, overall cardiovascular morbidity and mortality, and all-cause mortality.[6] The risk of stroke was independently associated with taking frequent daytime naps in the first National Health and Nutrition Survey.[7] In the Caerphilly cohort, a population-based study of older men, daytime sleepiness was found to be associated with increased ischemic heart disease events.[8] A prospective study of 157 healthy older adults found significant relationships between an elevated Epworth Sleepiness Scale score (ESS ≥ 10) and blood pressure, as well as incident diagnosed hypertension.[9]

Studies in clinical patient samples in which polysomnography was performed also point to a relation between self-reported sleepiness and cardiovascular disease. Higher ESS was related to lower stroke volume index and cardiac index in middle-aged obstructive sleep apnea patients after controlling for polysomnographic measures of sleep apnea severity.[10] A review of randomized trials evaluating the effect of continuous positive airway pressure (CPAP) on blood pressure in persons with SDB found that studies with less sleepy participants show a smaller decrease in blood pressure on CPAP therapy.[11-13] These findings suggest that the symptom of excessive self-reported sleepiness may identify a subset of individuals with SDB at greatest risk of cardiovascular sequelae, including hypertension. If so, this would have important implications for the clinical management of the large proportion of individuals with polysomnographic evidence of SDB who report no significant daytime sleepiness. We use cross-sectional data from the Sleep Heart Health Study (SHHS) to explore whether self-reported sleepiness modifies the relationship between SDB and prevalent hypertension.

**Disclosure Statement**

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## METHODS

The subjects in this analysis include all SHHS participants with information on sex, age, ethnicity, systolic and diastolic blood pressure, antihypertensive medication use, body mass index (BMI), AHI, and questionnaire-determined excessive sleepiness and Epworth Sleepiness Scale (N = 6046). Subjects from all participating sites provided informed consent, and the study was approved by the Institutional Review Boards of each institution. The design of the SHHS has been described, and additional documentation can be found at http://www.jhucct.com/shhs/.[14,15,16]

### Study Variables

The average of the second and third of 3 consecutive measurements was used as the BP value in this report. Following standard recommendations, hypertension was defined as systolic BP of at least 140 mm Hg, diastolic BP of at least 90 mm Hg, or current treatment with antihypertensive medications.[17,18]

Participants had a single night of unattended PSG.[15,16] Sleep disordered breathing was quantified using the AHI, defined as the average number of apneic plus hypopneic episodes associated with ≥ 4% decrease in oxygen saturation per hour of sleep.[1] In our analyses, AHI was categorized based on severity (< 1.5, 1.5-4.9, 5-14.9, 15-29.9, ≥ 30). Clinically, SDB severity is commonly categorized using AHI cut-offs of < 5 (non-diagnostic), 5 ≥ and < 15 (mild), 15 ≥ and < 30 (moderate), ≥ 30 (severe).[19]

The ESS score was calculated for each participant.[20] An ESS score > 10, which has been proposed as the upper limit of normal, was used to define sleepy participants in this report.[4,20] A second measure of sleepiness was based on the response to the single question, "How often do you feel excessively (overly) sleepy during the day." A response of "often" (5-15 days/month) or "almost always" (16-30 days/month) was defined as "frequently sleepy." A response of "never"(0), "rarely" (≤ 1 day/month), or "sometimes" (2-4 days/month) was defined as "not frequently sleepy." This question was adapted from the Wisconsin Sleep Cohort Study Sleep Survey for use in the SHHS.[21,22] It has been widely used and shown consistent correlations with variables that contribute to daytime sleepiness, including snoring, and apnea-hypopnea index categories.[5,21-23]

### Statistical Analysis

Statistical analyses were performed using SAS 9.1 (SAS Institute, Inc., Cary, NC). Clinical and demographic characteristics were compared between sleepy and non-sleepy subjects using the Pearson chi-square test or analysis of variance. A P-value ≤ 0.05 was used as a cut-off for statistical significance.

Using separate models for sleepy and non-sleepy groups, logistic regression was used to calculate the odds ratio (OR) of hypertension comparing each AHI severity category to the category AHI < 1.5, adjusted for possible confounders. As the odds of hypertension showed a reasonably linear increase across AHI categories, AHI severity categories were coded as a single variable (integer values 0-4 to represent each category) in subsequent logistic regression models. Demographics (age, gender, ethnicity), BMI, neck circumference, waist-to-hip ratio, smoking history, and alcohol use were included in fully adjusted models as possible confounders. These variables have been considered in prior studies as possible confounders of the relationship between hypertension and sleep disordered breathing.[1] The results of these separate logistic regression models for sleepy and non-sleepy groups are presented in tables 2A and 2B to allow the reader to assess effect modification.

Logistic regression analyses were also performed on the entire cohort and interaction terms were evaluated in models. Interaction terms (sleepiness × AHI) were used to evaluate whether there were statistically significant interactions (i.e., whether the relationship between increased odds of hypertension with increased AHI was modified by sleepiness.

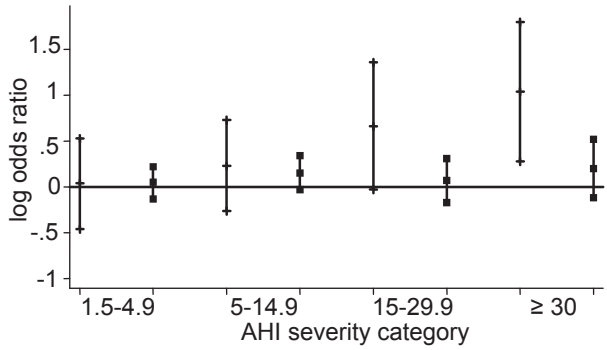


**Figure 1**—Log odds ratio for hypertension and 95% confidence interval by AHI category.
This is a graph of results of the fully adjusted logistic regression comparing the log odds ratio for hypertension vs. AHI severity category separately for frequently sleepy (+ sleepy ≥ 5 days/month) and not frequently sleepy (■ sleepy < 5 days/month) participants. Frequently sleepy subjects show an increase in log odds ratio with increase in AHI severity in contrast to not frequently sleepy subjects.

## RESULTS

The two self-reported sleepiness classification schemes produced different prevalence of sleepy subjects (Tables 1A and 1B): 13% reported frequently feeling sleepy (≥ 5 days/month) while 25% had an ESS > 10. There was a significant association between the two classification schemes, though only 26.8% of those with ESS > 10 also reported frequently feeling sleepy (Table 1B). Sleepy subjects by either classification scheme had higher AHI, BMI, and neck circumference, but were slightly younger than subjects without sleepiness. In subjects who reported frequently feeling sleepy, there was a slightly higher prevalence of hypertension and antihypertensive medication use. Among hypertensive subjects, 76% were taking antihypertensive medications.

Tables 2A shows the adjusted odds ratios for the relationship between AHI severity category and prevalent hypertension, with separate models for subjects who reported frequently and not frequently feeling sleepy. In models adjusted for demographic variables only, a progressive increase in odds of hypertension was seen across AHI categories in both frequently and not frequently sleepy subjects. After adjustment

**Table 1A**—Comparison of Subjects Based on Self-Reported Frequency of Sleepiness

| Characteristics | Frequently sleepy (≥ 5 days/mo) N = 787 | Not frequently sleepy (< 5 days/mo) N = 5259 |
|---|---|---|
| **Men** (%) | 44.9 | 47.6 |
| **AHI Category** (%)*** | | |
| < 1.5 | 22.2 | 28.2 |
| 1.5-4.9 | 24.8 | 26.3 |
| 5-14.9 | 31.0 | 28.4 |
| 15-29.9 | 12.2 | 11.5 |
| ≥ 30 | 9.8 | 5.7 |
| **Race** (%) | | |
| White | 80.1 | 77.3 |
| Black | 6.0 | 7.3 |
| American Indian | 9.0 | 9.9 |
| Other | 5.0 | 5.5 |
| **Smoking** (%)** | | |
| Never | 44.6 | 45.9 |
| Former | 40.9 | 43.3 |
| Current | 14.5 | 10.8 |
| **ESS > 10** (%)*** | 51.5 | 21.1 |
| **ESS**, mean (SD)*** | 10.7 (5.0) | 7.3 (4.1) |
| **Sleepy**, mean (SD)*** | 4.21 (0.4) | 2.17 (0.7) |
| **Hypertension** (high BP or med.) (%) | 55.5 | 52.2 |
| **Hypertension medication** (%)* | 43.5 | 39.2 |
| **Age**, mean (SD)** | 61.8 (10.9) | 63.2 (10.9) |
| **AHI**, mean (SD)*** | 11.1 (15.2) | 8.5 (12.0) |
| **% time < 90%**, mean (SD)*** | 4.9 (12.4) | 3.4 (10.1) |
| **Arousal index**, mean (SD) | 19.8 (12.2) | 19.1 (10.3) |
| **BMI**, kg/m,$^2$ mean (SD)*** | 29.3 (6.0) | 28.4 (5.3) |
| **Neck circumference**, cm, mean (SD)* | 38.3 (4.4) | 37.9 (4.2) |

Overall N = 6046: Includes participants with information on sex, age, ethnicity, systolic and diastolic blood pressure, antihypertensive medications, body mass index (BMI), AHI, sleepy frequency, and Epworth Sleepiness Scale.
P-value based on Pearson chi-square test for categorical variables and ANOVA for continuous variables.
*P < 0.05
**P < 0.01
***P < 0.001
SD: Standard deviation

**Table 1B**—Comparison of Subjects Based on Epworth Sleepiness Score

| Characteristics | ESS > 10 N = 1513 | ESS ≤ 10 N = 4533 |
|---|---|---|
| **Men** (%)*** | 55.9 | 44.3 |
| **AHI Category** (%)*** | | |
| < 1.5 | 21.6 | 29.4 |
| 1.5-4.9 | 24.4 | 26.7 |
| 5-14.9 | 30.6 | 28.1 |
| 15-29.9 | 13.7 | 10.8 |
| ≥ 30 | 9.7 | 5.0 |
| **Race** (%)* | | |
| White | 76.5 | 78.0 |
| Black | 8.9 | 6.6 |
| American Indian | 9.3 | 10.0 |
| Other | 5.3 | 5.5 |
| **Smoking** (%) | | |
| Never | 44.1 | 46.3 |
| Former | 44.9 | 42.4 |
| Current | 11.1 | 11.3 |
| **Frequently Sleepy** (%)*** | 26.8 | 8.4 |
| **ESS**, mean (SD)*** | 13.8 (2.8) | 5.7 (2.6) |
| **Sleepy**, mean (SD)*** | 2.93 (1.0) | 2.27 (0.9) |
| **Hypertension** (high BP or med.) (%) | 53.9 | 52.2 |
| **Hypertension medication** (%) | 41.6 | 39.2 |
| **Age**, mean (SD)* | 62.6 (10.3) | 63.2 (11.0) |
| **AHI**, mean (SD)*** | 11.3 (14.9) | 8.0 (11.4) |
| **% time < 90%**, mean (SD)*** | 5.1 (13.1) | 3.1 (9.4) |
| **Arousal index**, mean (SD)** | 19.9 (11.8) | 19.0 (10.2) |
| **BMI**, kg/m,$^2$ mean (SD)*** | 29.3 (5.6) | 28.2 (5.3) |
| **Neck circumference**, cm, mean (SD)*** | 38.9 (4.3) | 37.7 (4.2) |

Overall N = 6046: Includes participants with information on sex, age, ethnicity, systolic and diastolic blood pressure, antihypertensive medications, body mass index (BMI), AHI, sleepy frequency, and Epworth Sleepiness Scale.
P-value based on Pearson chi-square test for categorical variables and ANOVA for continuous variables.
*P < 0.05
**P < 0.01
***P < 0.001
SD: Standard deviation

for body habitus, smoking history and alcohol consumption, however, only subjects reporting frequent daytime sleepiness showed a significant relationship between AHI category and likelihood of having hypertension. Additional logistic models were constructed using the entire cohort, with AHI severity category (coded as a continuous variable with values 0-4 to test for trend) and presence or absence of sleepiness as predictor variables and adjusting for the same covariates as in the stratified models. In the fully adjusted model, both AHI ($\beta$ = 0.07, P = 0.017) and sleepiness (frequency of sleepiness: $\beta$ = 0.219, P = 0.017) were significantly associated with hypertension prior to adding the interaction term (AHI × sleepiness). The interaction term when added to this model was significant ($\beta$ = 0.167, P = 0.033), suggesting that frequency of sleepiness modifies the AHI-hypertension relationship (AHI category: $\beta$ = 0.047, P = 0.12; frequency of sleepiness $\beta$ = −0.040, P = 0.79). Figure 1 graphs the results of the fully adjusted logistic regression comparing the log odds ratio for hypertension vs. AHI severity category separately for frequently sleepy and not frequently sleepy participants.

In contrast, sleepiness as measured by the Epworth Sleepiness Scale appeared to modify the AHI-hypertension association less strongly than sleepiness measured by reported frequency of daytime sleepiness based on stratified analyses (Table 2B). In models that included the entire cohort, ESS score (> 10 or ≤ 10) was not significantly related to the likelihood of having hypertension and did not significantly modify the relation between AHI severity and odds of hypertension. The analyses were repeated using an alternative cut-off for ESS (> 13 or ≤ 13). This cut-off was chosen because a similar percentage of sub-

**Table 2A**—Adjusted Odds Ratios for Hypertension Stratified by Frequency of Excessive Sleepiness

| AHI | Frequently sleepy (≥ 5 days/mo) OR (95%) CI | | | Not frequently sleepy (< 5 days/mo.) OR (95%) CI | | |
|---|---|---|---|---|---|---|
| | N | Demographics only | Fully Adjusted† | N | Demographics only | Fully Adjusted† |
| < 1.5 | 175 | 1.00 | 1.00 | 1483 | 1.00 | 1.00 |
| 1.5-4.9 | 195 | 1.22 (0.79-1.86) | 1.04 (0.63-1.70) | 1385 | 1.22 (1.04-1.43) | 1.05 (0.88-1.25) |
| 5-14.9 | 244 | 1.40 (0.92-2.14) | 1.26 (0.77-2.07) | 1491 | 1.46 (1.25-1.71) | 1.16 (0.97-1.40) |
| 15-29.9 | 96 | 2.03 (1.16-3.54) | 1.94 (0.97-3.89) | 602 | 1.49 (1.21-1.84) | 1.07 (0.84-1.36) |
| ≥ 30 | 77 | 3.04 (1.64-5.75) | 2.83 (1.33-6.04) | 298 | 2.05 (1.56-2.71) | 1.22 (0.89-1.68) |

†Adjusted for demographics (age, gender, and ethnicity) plus BMI, neck circumference, waist-to-hip ratio, smoking history, alcohol use
Clinically, AHI is commonly categorized using AHI cut-offs of < 5 (non-diagnostic), 5 ≥ and <15 (mild), 15 ≥ and < 30 (moderate), and ≥ 30 (severe) to indicate severity.

**Table 2B**—Adjusted Odds Ratios for Hypertension Stratified by Epworth Sleepiness Scale Score

| AHI | ESS > 10 OR (95%) CI | | | ESS ≤ 10 OR (95%) CI | | |
|---|---|---|---|---|---|---|
| | N | Demographics only | Fully Adjusted† | N | Demographics only | Fully Adjusted† |
| < 1.5 | 327 | 1.00 | 1.00 | 1331 | 1.00 | 1.00 |
| 1.5-4.9 | 369 | 1.53 (1.11-2.11) | 1.31 (0.92-1.87) | 1211 | 1.15 (0.97-1.36) | 0.98 (0.81-1.18) |
| 5-14.9 | 463 | 1.57 (1.15-2.14) | 1.15 (0.80-1.65) | 1272 | 1.45 (1.22-1.71) | 1.20 (0.99-1.46) |
| 15-29.9 | 207 | 1.81 (1.24-2.64) | 1.35 (0.86-2.10) | 491 | 1.48 (1.18-1.86) | 1.08 (0.84-1.40) |
| ≥ 30 | 147 | 2.70 (1.75-4.18) | 1.66 (0.98-2.82) | 228 | 2.08 (1.52-2.85) | 1.32 (0.93-1.87) |

†Adjusted for demographics (age, gender, and ethnicity) plus BMI, neck circumference, waist-to-hip ratio, smoking history, alcohol use
Clinically, AHI is commonly categorized using AHI cut-offs of <5 (non-diagnostic), 5 ≥ and < 15 (mild), 15 ≥ and < 30 (moderate), and ≥ 30 (severe) to indicate severity.

jects (11%) had ESS > 13 as reported frequently feeling sleepy (13%). Stratified analyses demonstrated that odds ratios for the most severe category of SDB (AHI ≥ 30) differed even more between sleepy and non-sleepy subjects (2.91 vs. 1.23 in fully adjusted models). In regression models, the presence of ESS > 13 was not significantly associated with hypertension and did not significantly modify the effect of AHI on odds of hypertension. Finally, ESS was introduced into fully adjusted models as a continuous variable. It was not significantly associated with hypertension ($\beta = -0.007$, $P = 0.33$). When added to the model, the interaction term for ESS × AHI category fell short of statistical significance ($\beta = 0.010$, $P = 0.07$) but was suggestive of an effect modification (AHI category: $\beta = -0.10$, $P = 0.89$; ESS $\beta = -0.023$, $P = 0.04$).

Additional exploratory analyses were performed to assess whether effect modification by sleepiness may differ by gender. The analyses done to create Tables 2A and B were repeated separately for men and women (results not shown). The small number of subjects that resulted in specific AHI categories (at lower AHI in men and higher AHI in women) precluded any definite judgment on whether there were differences by gender. The interaction between sleepiness and AHI category was more noticeable in men than in women. For example, in fully adjusted logistic models, the odds ratios for hypertension comparing highest to lowest AHI category in frequently and not frequently sleepy men was 3.63 (1.27-10.34) vs. 1.32 (0.88-1.97), while for women the corresponding odds ratios were 1.74 (1.46-6.50) vs. 0.89 (0.50-1.53)

## DISCUSSION

The intent of our analyses was to evaluate whether the presence or absence of subjective sleepiness modifies the association of polysomnographically detected SDB with hypertension. Participants with SDB who frequently felt excessively sleepy were more likely to have hypertension than were subjects who were not frequently sleepy. Among subjects with AHI ≥ 30, the odds of hypertension relative to those with AHI < 1.5 was 2.8 in frequently sleepy participants, but only 1.2 in not frequently sleepy participants. A similar trend was seen between those with high and low Epworth scores, though of smaller magnitude. Therefore, the presence of daytime sleepiness appears to modify the association of SDB with hypertension, with sleepiness identifying a group of people with moderate to severe SDB who are more likely to have hypertension than people who are asymptomatic. Our results are consistent with the observation that, in randomized trials evaluating the effect of continuous positive airway pressure (CPAP) on blood pressure in persons with SDB, studies with less sleepy participants show a smaller decrease in blood pressure on CPAP therapy.[11,12]

There may be common mechanisms relating exposure to SDB with both sleepiness and hypertension. Intermittent hypoxia has been shown to cause sympathetic activation, oxidative stress, and endothelial dysfunction that may eventually lead to chronic hypertension.[24-28] It has also been proposed that damage to wake-promoting neurons by intermittent hypoxia-induced oxidative stress may cause sleepiness.[29] Sleep fragmentation by the arousals that characteristically terminate obstructive respiratory

events are believed to result in sleepiness, and arousals may also contribute to sympathetic activation independent of hypoxemia.[30] Genetic or acquired susceptibility to the disruptive effects of SDB may influence whether an exposed individual develops any clinical sequelae of SDB. Alternatively, sleepiness may simply be a better marker of the physiological significance of SDB than are polysomnographic measures of SDB severity.

In additional exploratory analyses, effect modification was more noticeable in men than in women. These results must be interpreted with caution, as a gender effect was not an a priori hypothesis, and stratification by gender resulted in small samples sizes in specific AHI categories. The previously noted treatment studies that suggest less sleepy participants show a smaller blood pressure decrease included very few women.[12,13] There is a need for studies that include significant numbers of women to determine whether it is reasonable to generalize findings about OSA and hypertension to women.

Strengths of this study include the large, community-based sample and standardized assessment of SDB, blood pressure, antihypertensive medication use, and sleepiness. One limitation of the study is the cross-sectional design, which precludes assessment of the relation of sleepiness to incident hypertension or cardiovascular disease. Another limitation is the use of self-report measures of sleepiness; however, such measures are highly relevant to clinical practice, as objective measures such as multiple sleep latency or maintenance of wakefulness testing are too expensive and burdensome to be practical for the routine clinical assessment of patients with SDB. The majority of our hypertensive subjects (76%) were using antihypertensive medications. While the use of antihypertensive medications can cause sleepiness, the proportion of hypertensive subjects on therapy did not differ systematically between sleepy and non-sleepy groups and was similar across AHI categories.

We have previously reported that fewer than half of subjects with polysomnographically moderate-to-severe SDB (AHI > 15) report excessive sleepiness. If the findings of the present study are substantiated by prospective studies of incident hypertension risk, this will have important implications for management of the very large group of individuals with asymptomatic or minimally symptomatic SDB; invasive, uncomfortable and expensive therapies such as surgery, CPAP, and oral appliances may not be warranted in these patients.

In conclusion, this study finds that the association of SDB with hypertension is stronger in individuals who report daytime sleepiness than in those who do not. This suggests that the possible cardiovascular benefits of treatment for SDB may be greatest in symptomatic individuals. Prospective studies that incorporate measures of pathophysiologic intermediates and individual susceptibility are needed to more definitively answer this question and help elucidate the mechanisms common to these disparate consequences of SDB.

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**IHS Disclaimer:**

The opinions expressed in the paper are those of the author(s) and do not necessarily reflect the views of the IHS.

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