

# The impact of SHS exposure on health status and exacerbations among patients with COPD

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**Abstract:** Secondhand smoke (SHS) is a major contributor to indoor air pollution. Because it contains respiratory irritants, it may adversely influence the clinical course of persons with chronic obstructive pulmonary disease (COPD). We used data from nonsmoking members of the FLOW cohort of COPD (n = 809) to elucidate the impact of SHS exposure on health status and exacerbations (requiring emergency department visits or hospitalization). SHS exposure was measured by a validated survey instrument (hours of exposure during the past week). Physical health status was measured by the SF-12 Physical Component Summary Score and disease-specific health-related quality of life (HRQL) by the Airways Questionnaire 20-R. Health care utilization for COPD was determined from Kaiser Permanente Northern California computerized databases. Compared to no SHS exposure, higher level SHS exposure was associated with poorer physical health status (mean score decrement -1.78 points; 95% confidence interval [CI] -3.48 to -0.074 points) after controlling for potential confounders. Higher level SHS exposure was also related to poorer disease-specific HRQL (mean score increment 0.63; 95% CI 0.016 to 1.25) and less distance walked during the Six-Minute Walk test (mean decrement -50 feet; 95% CI -102 to 1.9). Both lower level and higher level SHS exposure was related to increased risk of emergency department (ED) visits (hazard ratio [HR] 1.40; 95% CI 0.96 to 2.05 and HR 1.41; 95% CI 0.94 to 2.13). Lower level and higher level SHS exposure were associated with a greater risk of hospital-based care for COPD, which was a composite endpoint of either ED visits or hospitalizations for COPD (HR 1.52; 95% CI 1.06 to 2.18 and HR 1.40; 95% CI 0.94 to 2.10, respectively). In conclusion, SHS was associated with poorer health status and a greater risk of COPD exacerbation. COPD patients may comprise a vulnerable population for the health effects of SHS.

**Keywords:** chronic obstructive pulmonary disease, chronic bronchitis, pulmonary emphysema, tobacco smoke pollution

Chronic obstructive pulmonary disease (COPD) is a common and disabling condition. Although the major cause of COPD is direct cigarette smoking, other factors may influence the clinical course of established disease. Emerging evidence suggests that the indoor environment may be one of these factors. A cross-sectional study of COPD patients found that higher indoor level of fine particles (PM<sub>2.5</sub>) was associated with greater respiratory symptoms.<sup>1</sup> Other recent data indicate that combustion of wood or charcoal for heating or cooking in the home may contribute to COPD morbidity.<sup>2</sup> Despite these intriguing initial observations, scant knowledge exists about the indoor environment and COPD.

Secondhand smoke (SHS) is a major source of indoor pollution. Existing evidence indicates that SHS exposure is an important cause of asthma exacerbation among children and, to a lesser extent, adults.<sup>3-5</sup> In COPD, however, there are few studies that

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address the impact of SHS exposure on clinical course.<sup>1,6,7</sup> We used data from a large prospective cohort study of COPD to evaluate the impact of SHS exposure on health status and disease exacerbation.

## Methods

### Overview

The FLOW (Function, Living, Outcomes, and Work) study of COPD is an ongoing prospective cohort study of adult members of an integrated health care delivery system with a physician's diagnosis of COPD. The long-term goal is to determine what factors are responsible for the development of disability in COPD. At baseline assessment, we conducted structured telephone interviews that ascertained COPD-related health status, sociodemographic characteristics, and SHS exposure. Research clinic visits included spirometry and other physical assessments. In this report, we evaluated the impact of recent SHS exposure on health status and the future risk of emergency health care utilization for COPD. The study was approved both by the University of California, San Francisco Committee on Human Research and the Kaiser Foundation Research Institute's institutional review board and all participants provided written informed consent.

### Subject recruitment

We studied adult members of Kaiser Permanente Medical Care Program (KPMCP), the nation's largest nonprofit managed care organization. In northern California, the KPMCP provides the full spectrum of primary-to-tertiary care to approximately 3.2 million members. In northern California, KPMCP's share of the regional population ranges from 25 to 30%.<sup>8</sup> The demographic characteristics of KPMCP members are similar to the overall northern California population, except for the extremes of income distribution.<sup>9</sup>

Recruitment methods have been previously reported in detail.<sup>10,11</sup> We identified all adult KPMCP members who were recently treated for COPD using a previously described approach. The age range was restricted to 40–65 years because a key study outcome includes work disability.<sup>12</sup> Using KPMCP computerized databases, we identified all subjects who met each of two criteria: one based on health care utilization and the second based on medication prescribing. The health care utilization criterion was one or more ambulatory visits, emergency department (ED) visits, or hospitalizations with a principal International Classification of Disease (ICD-9) diagnosis code for COPD (chronic bronchitis [491], emphysema [492], or COPD

[496] during a recent 12-month time period. The medication criterion was two or more prescriptions for a COPD-related medication during a 12-month window beginning six months before the index utilization date and ending six months after index date. The criterion medications included: inhaled anticholinergic medications, inhaled beta agonists, inhaled corticosteroids, or theophylline. Based on medical record review, we demonstrated that this algorithm is a valid method for identifying adults with COPD.<sup>12</sup> To facilitate attendance at the research clinic, we restricted the sample to persons living within a 30 mile geographic radius of the research clinic where the study examinations took place.

Persons identified by the algorithm who were no longer KPMCP members or who had moved away were considered ineligible for study. The primary care physicians for all patients were contacted and given the opportunity to decline contact of any identified patients under their care. Potential subjects were then contacted by a letter describing the study and given an opportunity to decline participation. Those not declining were contacted by telephone to arrange an interview. At the end of the interview, subjects were invited to participate in the research clinic visit. Persons who were found at the time of interview to have severe communication difficulties attributable to advanced dementia or aphasia were excluded.

A total of 5,800 subjects were initially identified using the computerized algorithm. Of these, 298 died before they could be recruited into the study. Another 1,011 did not meet study inclusion criteria or were excluded at the time of interview contact as noted above. The completion rate for structured telephone interviews was 2,310 out of a remaining eligible group of 4,491 (51%). This is comparable to our earlier cohort study of adult asthma conducted at KPMCP and compares favorably for other survey-based epidemiologic studies conducted in the US.<sup>13,14</sup> Among the 2,310 respondents, 112 were not eligible for the clinic visit and 1,216 completed the research clinic visit (55% of those interviewed and eligible). An additional 10 subjects were excluded because they did not meet the GOLD criteria for COPD after interviews and spirometry were performed.<sup>15</sup> Four additional subjects were excluded from this analysis because they could not perform spirometry due to previous tracheostomy placement. Ultimately, there were 1,202 subjects with COPD who completed both interviews and research clinic visits. Previous reports compared respondents and nonrespondents.<sup>10,11,16</sup>

The current analysis of SHS exposure and COPD outcomes was restricted to current nonsmokers (n = 809).

## Structured telephone interviews

Each subject underwent a 30–40 minute structured telephone interview that used customized computer-assisted telephone interview (CATI) software. Interviews ascertained sociodemographic characteristics. Cigarette smoking was measured using questions developed for the National Health Interview Survey.<sup>17</sup> As in previous studies, we defined educational attainment as high school or less, some college, or college/graduate degree.<sup>18</sup> Race/ethnicity was defined based on self-report as a series of categories: white/non-Hispanic, Black, Asian or Pacific Islander, Hispanic or Latino, and other.<sup>18</sup> For analysis, we classified subjects as white, non-Hispanic vs all others.

## SHS exposure measurement

We previously developed and validated a survey instrument that assesses recent SHS exposure for adults with obstructive lung disease.<sup>19</sup> The instrument ascertains exposure during the past seven days in seven microenvironments: the respondent's home, another person's home, traveling in a car or another vehicle, workplace (including dedicated smoking areas), bars and nightclubs, outdoor locations, and other locations. In each area, the instrument queries the total duration (in hours) of exposure during the past seven days. Based on the distribution of responses, we defined three ordinal categories of exposure: no exposure, lower level exposure (up to 1 hour/week), and higher level ( $\geq 1$  hour/week) exposure. The lower level and higher level exposure categories were divided at the median among those with any exposure to ensure approximately equal numbers of subjects in each group.

## Study outcomes: Health status measures

We used a combined approach with disease-specific and generic health status measurements to assess COPD-related health status. At the time of telephone interview, generic physical health status was measured with the Short Form (SF)-12 Physical Component Summary (PCS) score. The SF-12 is derived from the Medical Outcomes Study SF-36 instrument, which is the most widely used measure of generic health status. The SF-36 has been extensively validated in the general population<sup>20</sup> and among adults with COPD.<sup>21</sup> Defined from the eight SF-36 subscales by factor analysis, the PCS score reflects an underlying physical dimension of physical HRQL.<sup>22</sup> Higher scores reflect more favorable health states.

We used the Airways Questionnaire 20 revised (AQ-20R) to measure disease-specific HRQL.<sup>23,24</sup> This validated instrument has excellent psychometric properties for assessing

HRQL in persons with airway disease, including COPD. Higher scores correspond to poorer HRQL.<sup>23,25</sup>

Submaximal exercise performance was measured using the Six-Minute Walk Test, which was developed by Guyatt and has been widely used in studies of COPD.<sup>26,27</sup> We used a standardized flat, straight course of 30 meters in accordance with American Thoracic Society (ATS) Guidelines.<sup>28</sup> Subjects who routinely used home oxygen or who had a resting oxygen saturation  $< 90\%$  were supplied with supplemental oxygen during the test. Every two minutes, the technician used standardized phrases to encourage effort, as recommended by the ATS guidelines. The primary outcome measured was the total distance walked in six minutes.

## Longitudinal outcomes: Disease exacerbation

We used ED visits and hospitalization for COPD as proxy measures of severe disease exacerbation. These outcomes were ascertained during prospective follow-up, after completion of baseline interviews. COPD-related hospitalization was defined as those with a principal ICD-9 discharge diagnosis code for COPD (491, 492, or 496). COPD-related ED visits were identified as those with an ICD-9 code for COPD. In contrast to hospital discharge diagnoses, ED visits do not distinguish primary or secondary diagnoses within the Kaiser system. A composite outcome for hospital-based care was defined as either an ED visit or hospitalization for COPD. The median duration of follow-up was 2.1 years (25th–75th interquartile range 1.7 to 2.6 years). During the follow-up period, there were 50 hospitalizations and 153 ED visits for COPD.

## Measurement of disease severity

Disease severity can confound the study of SHS exposure. Although SHS exposure may increase COPD severity, persons with greater COPD-related breathing symptoms might selectively avoid exposure (the “healthy passive smoker” effect). Consequently, we explicitly considered disease severity in our analysis.

To measure disease severity, we used a combined approach. We employed a disease-specific COPD severity score that we had previously developed and validated for use in epidemiologic and outcomes research.<sup>29</sup> Based on survey responses, the COPD severity score is comprised of five overall aspects of COPD severity: respiratory symptoms, systemic corticosteroid use, other COPD medication use (including inhaled corticosteroids), previous hospitalization or intubation for respiratory disease, and home supplemental

oxygen use. Each item was weighted based on clinical aspects of the disease and its expected contribution to overall COPD severity. Possible total scores range from 0 to 35, with higher scores reflecting more severe COPD.

We also used the validated BODE index, which is a multi-modal measure of disease severity.<sup>30</sup> The BODE index is based on the body mass index (B), the degree of airflow obstruction (O) measured by forced expiratory volume in 1 second ( $FEV_1$ ), grade of dyspnea (D) assessed by the modified MRC Dyspnea Scale, and exercise capacity (E) measured by the Six-Minute Walk Test. Each component is assigned a specific score and the total score ranges from 0 to 10 points (higher scores indicate greater severity). The BODE index predicts death and other poor outcomes in COPD.<sup>30–32</sup>

To assess respiratory impairment, which is a component of the BODE index, we conducted spirometry according to ATS Guidelines.<sup>33,34</sup> We used the EasyOne™ Frontline spirometer (ndd Medical Technologies, Chelmsford, MA), which is known for its reliability, accuracy, and durability.<sup>35,36</sup> The Easyone spirometer has been used by two large scale multicenter international epidemiologic studies of COPD: the BOLD Study (Burden of Obstructive Lung Disease) and the Platino Study (Latin American Project for the Investigation of Obstructive Lung Disease).<sup>36,37</sup> Percent predicted values were calculated using predictive equations derived from NHANES III.<sup>38</sup>

## Statistical analysis

Statistical analysis was conducted using SAS software, version 9.1 (SAS Institute, Inc., Cary, NC). The relationship between SHS exposure category (none, lower level, and higher level) and variables of study interest was examined using the chi-square test for categorical variables and analysis of variance for continuous variables. We used multivariable linear regression analysis to elucidate the association between SHS exposure categories and health status outcomes (physical health status, disease-specific quality of life, and distance walked in six minutes). In these analyses, we controlled for key variables that might confound the relationship between SHS exposure and health outcomes, including age, sex, race, educational attainment, marital status, COPD severity, and previous smoking history (all subjects were current nonsmokers).<sup>39,40</sup> We also performed a secondary analysis using backwards selection to identify covariates after forcing the SHS exposure variables into the model ( $p$  value cut-off for covariate removal was 0.10). In all analyses, a two-tailed  $p$  value of 0.05 was considered to represent the conventional threshold of statistical significance.

We used Cox proportional hazards regression to elucidate the impact of SHS exposure on the prospective risk of ED visits, hospitalizations, and hospital-based care (composite of ED visits and hospitalizations). Control for confounding variables was performed as described for linear regression analysis (above). The proportional hazards assumption was verified by evaluating interaction terms between time and SHS exposure ( $p > 0.40$  in all cases, indicating no violation).

We also carried out a secondary analysis to further control for confounding. We used logistic regression analysis to create propensity scores for SHS exposure. The propensity score is the probability of SHS exposure based on known personal characteristics. To control for confounding, we then re-estimated the linear regression analysis and Cox proportional hazards analysis including adjustment for the propensity score.<sup>41</sup> There was no substantive difference compared to the primary analysis (data not shown).

## Results

### Baseline characteristics and SHS exposure

Nearly half of current nonsmokers with COPD reported SHS exposure during the past week ( $n = 364$ ; 45%; 95% confidence interval [CI] 42 to 49%) (Tables 1 and 2). Of those reporting any SHS exposure, 55% and 45% were in the lower level and higher level exposure categories, respectively. Females were somewhat less likely to report SHS exposure ( $p = 0.09$ ); there was an inverse relationship between educational attainment and SHS exposure ( $p = 0.01$ ) (Table 1). Notably, a history of prior smoking and COPD severity (as measured by both the COPD severity score and BODE score) were not related to SHS exposure status (Table 1). Table 2 provides the distribution of self-reported SHS exposure during the past 7 days.

### Impact of SHS exposure on health status in COPD

Compared to no SHS exposure, higher level SHS exposure was associated with poorer physical health status (mean score decrement  $-1.78$  points; 95% CI  $-3.48$  to  $-0.074$  points) (Table 3). Higher level SHS exposure was also related to poorer disease-specific HRQL (mean score increment 0.63; 95% CI 0.016 to 1.25) and less distance walked during the Six-Minute Walk test (mean decrement  $-50$  feet; 95% CI  $-102$  to 1.9). In the model using backwards selection to identify covariates, the confidence interval excluded the no effect level for the high level SHS category and distance walked (mean decrement  $-55$  feet;  $-3.4$  to  $-106$ ;  $p = 0.037$ ).

**Table 1** Baseline characteristics of the nonsmoking FLOW cohort by SHS exposure status (n = 809)

| Characteristic               | No SHS exposure<br>(n = 445) | Low level SHS<br>exposure (n = 200) | High level SHS<br>exposure (n = 164) | P value for<br>comparison |
|------------------------------|------------------------------|-------------------------------------|--------------------------------------|---------------------------|
| Age (years)                  | 58 (6.3)                     | 59 (6.1)                            | 59 (5.9)                             | 0.31                      |
| Sex (female)                 | 269 (61%)                    | 106 (53%)                           | 86 (52%)                             | 0.088                     |
| White, non-Hispanic          | 304 (68%)                    | 131 (66%)                           | 106 (65%)                            | 0.62                      |
| Smoking history              |                              |                                     |                                      |                           |
| Never smoked                 | 100 (23%)                    | 37 (19%)                            | 28 (17%)                             | 0.25                      |
| Ex-smoker                    | 348 (78%)                    | 163 (82%)                           | 136 (83%)                            |                           |
| Educational attainment       |                              |                                     |                                      | 0.014                     |
| High school or less          | 111 (25%)                    | 46 (23%)                            | 62 (38%)                             |                           |
| Some college                 | 183 (41%)                    | 88 (44%)                            | 61 (37%)                             |                           |
| College or graduate degree   | 151 (34%)                    | 66 (33%)                            | 41 (25%)                             |                           |
| Married or cohabiting        | 286 (64%)                    | 130 (65%)                           | 113 (69%)                            | 0.56                      |
| COPD severity score          | 10.1 (6.1)                   | 11.0 (6.5)                          | 10.5 (5.6)                           | 0.71                      |
| BODE score                   | 3.0 (2.4)                    | 2.9 (2.5)                           | 2.6 (2.2)                            | 0.23                      |
| FEV <sub>1</sub> % predicted | 62 (23)                      | 62 (24)                             | 65 (22)                              | 0.32                      |

**Notes:** Results are mean (sd) for age, COPD severity score, and BODE score; n (%) for all others – column proportions are reported.

**Abbreviations:** COPD, chronic obstructive pulmonary disease; FEV<sub>1</sub>, forced expiratory volume in one second; FLOW, Function, Living, Outcomes, and Work study; SHS, secondhand smoke.

## Prospective impact of SHS exposure and COPD exacerbation

SHS exposure was longitudinally associated with a greater risk of COPD exacerbation, as measured by ED visits for COPD. Both lower level and higher level SHS exposure was related to increased risk of ED visits (hazard ratio [HR] 1.40; 95% CI 0.96 to 2.05 and HR 1.41; 95% CI 0.94 to 2.13, respectively) (Table 4). Although there was no clear relationship between SHS exposure and hospitalization for COPD, lower level and higher level SHS exposure were associated with a greater risk of hospital-based care for COPD, which was a composite endpoint of either ED visits or hospitalizations for COPD (HR 1.52; 95% CI 1.06 to 2.18 and HR 1.40; 95% CI 0.94 to 2.10, respectively).

When we redefined SHS exposure as any exposure vs none during the past seven days, SHS exposure was associated with a greater risk of ED visits (HR 1.41; 95% CI 1.02 to 1.94; p = 0.036) and hospital-based care for COPD (HR 1.47; 95% CI 1.08 to 2.00; p = 0.015). Although the risk estimate for hospitalization was elevated (HR 1.29; 95% CI 0.73 to 2.27) the confidence interval included the no effect level.

## Discussion

SHS exposure was common among patients with COPD. Nonetheless, exposure intensity was generally low, which likely reflects the low prevalence of current smoking and the

statewide workplace smoking ban in California. Despite the relatively low intensity of exposure, SHS was associated with poorer health status and a greater risk of COPD exacerbation. Consequently, patients with COPD appear to be vulnerable to adverse health effects of low-level SHS exposure.

Our study adds to the emerging literature that SHS exposure may adversely affect the clinical course of COPD. We previously reported in another cohort that short-term SHS exposure, as evidenced by urine cotinine, was related to poorer COPD severity and health status measures.<sup>6</sup> In a previous cohort study of adults hospitalized for COPD, self-reported SHS exposure was also a risk factor for re-hospitalization.<sup>7</sup>

**Table 2** SHS exposure during the past seven days among adults with COPD

| Group of subjects               | Median<br>(hours) | 25th–75th IQR<br>(hours) |
|---------------------------------|-------------------|--------------------------|
| All subjects (n = 809)          | 0                 | 0–4.0                    |
| Subgroup with any SHS exposure  |                   |                          |
| Entire subgroup (n = 364)       | 1.0               | 0.5–3.0                  |
| Lower level exposure (n = 200)* | 0.7               | 0.3 to 1.0               |
| Higher level exposure (n = 164) | 4.0               | 2.0–6.0                  |

**Notes:** \*SHS exposure was assessed using a validated survey instrument that assessed duration of SHS exposure (hours) during the past seven days in a variety of microenvironments. The hours of SHS exposure during the past seven days in each microenvironment were summed to calculate the total. Lower level and higher level were divided at the median among those with any exposure.

**Abbreviations:** COPD, chronic obstructive pulmonary disease; IQR, interquartile range; SHS, secondhand smoke.

**Table 3** Impact of SHS exposure on health status in COPD

| SHS exposure category*              | Health status outcome <sup>†</sup>              |   |   |
|-------------------------------------|---|---|---|
|                                     | Physical health status                          | Disease-specific HRQL                       | Submaximal exercise performance           |
|                                     | Mean points (95% CI)                            | Mean points (95% CI)                        | Mean feet walked in six minutes (95% CI)  |
| None (n = 838)                      | 0 (referent)                                    | 0 (referent)                                | 0 (referent)                              |
| Lower level SHS exposure (n = 200)  | 0.007 (-1.56 to 1.57) P = 0.99                  | 0.36 (-0.21 to 0.93) P = 0.22               | -0.62 (-49 to 47) P = 0.98                |
| Higher level SHS exposure (n = 164) | -1.78 (-3.48 to -0.074) P = 0.041 <sup>##</sup> | 0.63 (0.016 to 1.25) P = 0.04 <sup>##</sup> | -50 (-102 to 1.9) P = 0.059 <sup>##</sup> |

**Notes:** Multivariable linear regression controlling for age, sex, race, educational attainment, smoking history, COPD severity score, and BODE score. Results are mean change in health status outcome variable for lower level SHS exposure vs none; higher level SHS exposure vs none; \*Based on validated survey instrument that assessed duration of SHS exposure (hours) during the past seven days in a variety of microenvironments. Lower level and higher level were divided at the median among those with any exposure; <sup>†</sup>Physical health status was assessed using the SF-12 Physical Component Summary Score; Disease-specific health-related quality of life with the Airways Questionnaire 20-Revised; Submaximal exercise performance with the Six-Minute Walk Test; <sup>##</sup>p < 0.05 in linear regression analysis using backwards selection (to eliminate covariates with p value ≥ 0.10).

**Abbreviations:** CI, confidence interval; COPD, chronic obstructive pulmonary disease; HRQL, health-related quality of life; SHS, secondhand smoke.

Another population-based US study found that self-reported SHS exposure was related to a greater risk of “chronic respiratory disease exacerbation,” defined as activity limitation or a physician visit due to asthma, chronic bronchitis, emphysema, or chronic sinusitis.<sup>42</sup> More recently, indoor PM<sub>2.5</sub> levels, a proxy measure of home SHS exposure, was associated with poorer disease-specific quality of life among persons with COPD.<sup>1</sup> The present findings add significant additional evidence that SHS exposure is deleterious for patients with COPD.

A significant study strength is the large sample of clinically well-characterized COPD patients who manifest a broad spectrum of disease severity, ranging from mild to severe. The cohort is also diverse in terms of gender, race-ethnicity, and socioeconomic status. Recruitment from a large health plan that covers a substantive proportion of the regional population helps to ensure generalizability to patients who are being treated for COPD in clinical practice.

Our study is also subject to several limitations. Although the inclusion criteria required health care utilization for

COPD, misclassification of COPD could have occurred. To minimize this, our COPD definition required concomitant treatment with COPD medications to increase the specificity of our definition. In addition, all patients had a physician diagnosis of COPD and reported having the condition. The observed lifetime smoking prevalence was similar to that in other population-based epidemiologic studies of COPD, supporting the diagnosis of COPD rather than asthma.<sup>39,43</sup> We also previously demonstrated the validity of our approach using medical record review.<sup>12</sup> Nonetheless, we acknowledge this potential misclassification as a study limitation.

We used self-reported SHS exposure which could have resulted in misclassification of exposure. The SHS survey exposure instrument has been previously validated against a direct measurement of exposure.<sup>19</sup> Based on our previous work, however, we know that self-reported SHS exposure tends to underestimate actual exposure.<sup>5</sup> To the extent that exposure misclassification is nondifferential with respect to respiratory status, the bias would be conservative

**Table 4** Prospective impact of SHS exposure on emergency health care utilization for COPD

| SHS exposure category*              | Emergency department visit for COPD            | Hospitalization for COPD        | Any hospital-based care for COPD <sup>‡</sup>  |
|-------------------------------------|--|---------------------------------|--|
|                                     | Hazard ratio (95% CI)                          | Hazard ratio (95% CI)           | Hazard ratio (95% CI)                          |
| None (n = 445)                      | 1.0 (referent)                                 | 1.0 (referent)                  | 1.0 (referent)                                 |
| Lower level SHS exposure (n = 200)  | 1.40 (0.96 to 2.05)<br>P = 0.078               | 1.37 (0.72 to 2.61)<br>P = 0.34 | 1.52 (1.06 to 2.18)<br>P = 0.023               |
| Higher level SHS exposure (n = 164) | 1.41 (0.94 to 2.13)<br>P = 0.097 <sup>††</sup> | 1.15 (0.51 to 2.59)<br>P = 0.73 | 1.40 (0.94 to 2.10)<br>P = 0.099 <sup>††</sup> |

**Notes:** Multivariable Cox proportional hazards analysis controlling for age, sex, race, educational attainment, smoking history, COPD severity score, and BODE score. Results are hazard ratio for lower level SHS exposure vs none; higher level SHS exposure vs none; \*Based on validated survey instrument that assessed duration of SHS exposure (hours) during the past six days in a variety of microenvironments. Lower level and higher level were divided at the median among those with any exposure; <sup>†</sup>Emergency department visits and hospitalizations for COPD were ascertained from Kaiser Permanente Northern California computerized databases (see Methods); <sup>‡</sup>Combined endpoint of either hospitalization or emergency department visit for COPD; <sup>††</sup>p = 0.08 from Cox model using backwards selection; <sup>##</sup>p = 0.085 from Cox model using backwards selection.

**Abbreviations:** COPD, chronic obstructive pulmonary disease; SHS, secondhand smoke.

(ie, “towards the null”). If persons with greater disease severity were more likely to remember or report SHS exposure, the estimates of SHS-related health effects would be inflated. Because we used two complementary methods to control for the effects of disease severity, which included both traditional multivariable regression and propensity scoring, we explicitly controlled for this possible bias.

In addition, some subjects could have inaccurately reported their current personal smoking status. We observed no relationship between past smoking and reported SHS exposure, which is reassuring that there is no confounding by direct personal smoking. We cannot, however, fully exclude the possibility of residual confounding.

Selection bias could have been introduced by nonparticipation in the study. There were some differences among subjects who did and did not participate in the interviews and clinic visits, but they were modest in scope and not likely to affect the relation between SHS exposure and health outcomes. Even so, we acknowledge the potential for selection bias as a limitation of our study.

In sum, SHS exposure appears to increase the risk of adverse health outcomes, including poorer physical health status, HRQL, exercise capacity, and disease exacerbation resulting in emergency health care utilization. These poor health outcomes were observed at low levels of SHS exposure. Patients with COPD may comprise a vulnerable population who are at especially high risk of the respiratory health effects of SHS exposure. Promotion of smoke-free indoor environments, including the home and public places, will likely benefit persons with COPD and other chronic respiratory diseases.

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