Risk of COPD From Exposure to Biomass Smoke: A Metaanalysis

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Wood and other forms of biomass (animal dung, crop residues, and so forth) are commonly used as sources of energy in developing countries and are estimated to be used for 50% of household cooking and heating fuels worldwide. Combustion of biomass produces a large amount of smoke that spreads into the environment as air pollutants. Exposure to such biomass smoke has been documented as playing an important role in mortality and morbidity globally.

Over the past decade, COPD has become a major public health problem, with increasing prevalence throughout the world, and this prevalence results from an interaction between host and environmental factors. Although many studies have suggested that biomass smoke is a risk factor for COPD, the relationship between the two has not been firmly established. In particular, the extent of the association between exposure of biomass smoke and COPD in different populations, as well as the relationship between biomass smoke and cigarette smoke, is not clear. To ascertain the relationship between biomass smoke and COPD, we performed a meta-analysis.

**Background:** Although many studies have suggested that biomass smoke is a risk factor for COPD, the relationship between the two has not been firmly established. In particular, the extent of the association between exposure of biomass smoke and COPD in different populations, as well as the relationship between biomass smoke and cigarette smoke, is not clear. To ascertain the relationship between biomass smoke and COPD, we performed a meta-analysis.

**Methods:** We searched MEDLINE, EMBASE, and the Latin American and Caribbean Literature in Health Sciences Database and analyzed 15 epidemiologic (11 cross-sectional and four case-control) studies that met our criteria. Data were extracted and analyzed independently by two investigators using a standardized protocol.

**Results:** Overall, people exposed to biomass smoke have an odds ratio (OR) of 2.44 (95% CI, 1.9-3.33) for developing COPD, relative to those not exposed to biomass smoke. Biomass smoke exposure was clearly identified as a risk factor for developing COPD in both women (OR, 2.73; 95% CI, 2.28-3.28) and men (OR, 4.30; 95% CI, 1.85-10.01), and in both the Asian population (OR, 2.31; 95% CI, 1.41-3.78) and the non-Asian population (OR, 2.56; 95% CI, 1.71-3.83). This risk factor has also been revealed in patients with chronic bronchitis (OR, 2.56; 95% CI, 1.77-3.70) and COPD (OR, 2.65; 95% CI, 1.75-4.03), and in cigarette smokers (OR, 4.39; 95% CI, 1.40-4.66) and non-cigarette smokers (OR, 2.55; 95% CI, 2.06-3.15).

**Conclusions:** Exposure to biomass smoke is a risk factor for COPD.

**Abbreviations:** OR = odds ratio

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factors. As widely recognized, tobacco smoke is the most important risk factor for COPD; however, exposure to biomass smoke can be as hazardous where indoor ventilation is inefficient.\textsuperscript{2,5} Recently, considerable attention has been devoted to the relationship between smoke from biomass combustion and declined pulmonary function in COPD.\textsuperscript{6-32} Although most studies did show an association, controversies over this issue remain. Moreover, the extent of such an association remains largely unknown. We searched the literature on the association between biomass smoke and COPD to determine whether ethnicity, sex, smoking status, study design, phenotype of COPD, and duration of exposure to biomass smoke have different effects on the development of COPD.

**Materials and Methods**

**Search of the Literature**

Papers published in the MEDLINE database, the Latin American and Caribbean Literature in Health Sciences Database, and EMBASE were searched (up to January 2009) with key words including "COPD," "chronic bronchitis," "emphysema," "chronic obstructive pulmonary disease," "biomass fuel," "biofuel," "organic fuel," "wood," and "indoor air pollution." Articles about relevant studies in the references were also obtained. Only studies published in the English language were included in the analysis. We communicated with some of the authors for additional data that did not appear in the text, and also communicated with the Chinese COPD Alliance and e-mailed researchers on COPD outside China for data from unpublished or ongoing studies.

**Study Selection**

All potentially relevant manuscripts were reviewed independently by two investigators. Areas of disagreement or uncertainty were adjudicated by other investigators. For studies to be included in the metaanalysis, they had to meet the following criteria: (1) they had to contain a case-control or cross-sectional study design; (2) they had to have compared at least two groups (COPD vs control, or biomass smoke vs control); (3) they had to show odds ratios (ORs) to estimate the association between COPD and biomass smoke with corresponding 95% CIs, or with sufficient data for calculation; and (4) they had to be independent from other studies. Studies with the same data sets as already published studies were not deemed to be independent. As such, only studies with large sample sizes and sufficient information for data extraction were metaanalyzed. No limitations were set for participants' ages or definition of exposure to biomass smoke as used in individual studies. Two major phenotypes of COPD, emphysema and chronic bronchitis, were included, although some cases are not characterized by airflow limitation that is not fully reversible. Chronic bronchitis was clinically diagnosed as chronic productive cough for 3 months in each of 2 successive years with no known causative factors. Because epidemiologic surveys have shown undiagnosed COPD in about two-thirds of subjects,\textsuperscript{33,34} studies in which the diagnostic criterion was a history of ever-diagnosed COPD, chronic bronchitis, or emphysema were excluded from the primary metaanalysis but used in a sensitivity analysis. This is because if some undiagnosed COPD were included in the control group, it could result in a differential diagnostic bias between biomass-exposed and non-exposed subjects. Case-control studies with a demonstrated source and matching control, criteria of exposure, and definition of COPD, or cross-sectional studies with demonstrated criteria of exposure and definition of COPD, were considered high-quality studies.

**Data Extraction**

All data were extracted independently by two investigators using a standardized protocol and data-collection forms. Disagreements were resolved by discussion. The studies were recorded as follows: first author, year of publication, study design (case-control study or cross-sectional study), characteristics of the study subjects (definition of exposure and nonexposure to biomass smoke, diagnosis criteria of COPD, sample size, age, gender, ethnicity, status of cigarette smoking, and duration of exposure to biomass smoke), measures of outcome and exposure, the ORs of COPD associated with biomass smoke, and standard errors (overall and in each subgroup, according to gender and smoking status).

**Statistical Analysis**

Metaanalysis was performed using Stata, version 7.0, statistical software (Stata Corporation; College Station, TX). The heterogeneity among studies was examined with the \( \chi^2 \)-based Q statistic.\textsuperscript{35} Depending on the presence of heterogeneity between studies, either a random effect model or a fixed effect model was used.\textsuperscript{36} The ORs of COPD associated with biomass smoke were estimated using nonexposure to biomass smoke as the reference. Subgroup analyses were performed with stratifications by cigarette-smoking status, sex, study design, ethnicity, duration of biomass smoke, and the phenotypes (lung function test-diagnosed COPD, emphysema, or chronic bronchitis). We further examined the relationship between exposure to biomass smoke and COPD by including the studies in which the diagnostic criterion was a history of having been given a diagnosis of COPD, chronic bronchitis, or emphysema. The significance of pooled ORs was determined by z test. All statistical tests were rendered two tailed, and \( P < .05 \) was considered significant. Potential for publication bias was assessed using the Egger test and funnel plots.\textsuperscript{37} Another method of identifying publication bias was the number of unpublished studies that would have to exist to negate the results of the metaanalysis.

**Results**

**Characteristics of the Included Studies**

A detailed flow chart of the review process is presented in Figure 1. The initial search resulted in 984 hits of potential interest. Nine hundred fifty-seven studies were excluded upon review of the titles and abstracts. Among the remaining 27 articles\textsuperscript{6-32} on biomass smoke and the incidence of COPD, some were further excluded because of duplicated publication,\textsuperscript{6} lack of adequate data for the metaanalysis,\textsuperscript{25,30,31} or inclusion/exclusion criteria that made the study unrepresentative of the population.\textsuperscript{22-24,26-29,32} The data from the article by Liu et al\textsuperscript{6} is part of the data used by Zhong et al.\textsuperscript{7} The article by Liu et al\textsuperscript{6} provided information about the association between biomass smoke and COPD in female and cigarette nonsmokers, which was not provided by Zhong et al's\textsuperscript{5} article. Therefore, the article by Liu et al\textsuperscript{6} was excluded from the primary metaanalysis but was used in a subgroup analysis. Subsequently,
only 15 articles were included in our primary metaanalysis, comprising four case-control and 11 cross-sectional studies of 3,719 COPD patients and 34,969 healthy controls. The characteristics of the included studies are presented in Table 1. Studies included five publications that dealt with the phenotype of chronic bronchitis, six with COPD, and four with both chronic bronchitis and COPD. The reasons for excluding studies are presented in Table 2. No unpublished or ongoing studies were included.

Association Between Exposure to Biomass Smoke and COPD

Fifteen studies examined the association between exposure to biomass smoke and COPD. A random effect model was used for the analysis because heterogeneity existed among the studies ($\chi^2 = 126.11; P < .001$). The pooled analysis found a significant elevation in risk (OR, 2.44; 95% CI, 1.79-3.33; $z = 5.65; P < .001$) of COPD for those exposed to biomass smoke, compared with those without the exposure (Fig 2).

No significant heterogeneity was observed after stratification of the group of OR by gender, heterogeneity was found among three studies in which the participants were male ($\chi^2 = 6.50; P = .039$). The pooled results showed that biomass smoke was a significant risk factor for men for developing COPD (OR, 4.30; 95% CI, 1.85-10.01; $z = 3.38; P = .001$) (Table 3). No heterogeneity was observed in 11 studies (for chronic bronchitis studies: $\chi^2 = 15.48; P = .116$). Using a fixed effect model, the pooled analysis revealed that biomass smoke was a significant risk factor for women for developing COPD (OR, 2.73; 95% CI, 2.28-3.28; $z = 10.75; P < .001$) (Fig 3, Table 3).

According to the definition of COPD, patients can be classified into three subgroups: COPD, emphysema, and chronic bronchitis. However, the studies included in our metaanalysis only have two phenotype groups: COPD and chronic bronchitis. Significant heterogeneity was observed among eight chronic bronchitis studies, and nine COPD studies (for chronic bronchitis studies: $\chi^2 = 28.59; P < .001$; and for COPD studies: $\chi^2 = 80.06; P < .001$) (Table 3). The pooled result showed that biomass smoke was a risk factor for chronic bronchitis and COPD (for chronic bronchitis: OR = 2.57; 95% CI, 1.79-3.70; $z = 5.12; P < .001$; and for COPD: OR = 2.77; 95% CI, 1.50-4.27; $z = 4.605; P < .001$).

Another study not included in our metaanalysis showed that the incidence of COPD decreased markedly after household coal stoves were improved, suggesting biomass smoke as a risk factor for COPD.

Sensitivity of the Analysis

We further examined the relationship between exposure to biomass smoke and COPD by including...
three studies in which diagnostic criteria included a history of ever-diagnosed COPD, chronic bronchitis, or emphysema. Eighteen studies, examined for association between exposure to biomass smoke and COPD, and heterogeneity was found among the studies ($\chi^2 = 177.720; P = .000$). Therefore, a random effect model was used for the analysis. The pooled analysis showed a significant elevation in the risk (OR, 2.23; 95% CI, 1.70-2.93; $z = 5.74; P = .000$) of developing COPD for those exposed to biomass smoke, compared with those without the exposure. (Fig 4).

Table 4 shows the subgroup analysis of the association between exposure to biomass smoke and COPD when we included three studies that were based on a history of having received a diagnosis of COPD, chronic bronchitis, or emphysema. All these subgroup analyses showed that biomass smoke was a risk factor for developing COPD, except for the male sex subgroup, for which no statistical significance was reached.

### Duration of Biomass Smoke and COPD

Exposure-response data were available in seven studies of COPD, examined for association between exposure to biomass smoke and COPD, and heterogeneity was found among the studies ($\chi^2 = 177.720; P = .000$). Therefore, a random effect model was used for the analysis. The pooled analysis showed a significant elevation in the risk (OR, 2.23; 95% CI, 1.70-2.93; $z = 5.74; P = .000$) of developing COPD for those exposed to biomass smoke, compared with those without the exposure. (Fig 4).

Table 4 shows the subgroup analysis of the association between exposure to biomass smoke and COPD when we included three studies that were based on a history of having received a diagnosis of COPD, chronic bronchitis, or emphysema. All these subgroup analyses showed that biomass smoke was a risk factor for developing COPD, except for the male sex subgroup, for which no statistical significance was reached.

### Table 1—Studies Included in the Metaanalysis

<table>
<thead>
<tr>
<th>Study</th>
<th>Location</th>
<th>Population</th>
<th>Study Design</th>
<th>Definition of Biomass Smoke Exposure</th>
<th>Definition of Biomass Smoke Nonexposure</th>
<th>COPD Definitions</th>
<th>Sex</th>
<th>Smoking Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ekici et al</td>
<td>Turkey</td>
<td>Non-smoking</td>
<td>Cross-sectional</td>
<td>History of exposure to biomass cooking</td>
<td>No history of biomass cooking</td>
<td>CB and/or FEV1/FVC $\geq 70%$</td>
<td>F</td>
<td>N</td>
</tr>
<tr>
<td>Behera and Jindal</td>
<td>India</td>
<td>Non-smoking</td>
<td>Cross-sectional</td>
<td>Cooking with “chulla” in which biomass fuels are used</td>
<td>Cooking with gas stove operated by LPG</td>
<td>CB</td>
<td>F</td>
<td>N</td>
</tr>
<tr>
<td>Regalado et al</td>
<td>Mexico</td>
<td>Women</td>
<td>Cross-sectional</td>
<td>Using biomass as cooking fuel</td>
<td>Using gas as cooking fuel</td>
<td>FEV1/FVC $&lt; 70%$</td>
<td>F</td>
<td>B</td>
</tr>
<tr>
<td>Caballero et al</td>
<td>Colombia</td>
<td>Adults</td>
<td>Cross-sectional</td>
<td>Using wood for cooking at some time</td>
<td>Not using wood for cooking at all</td>
<td>FEV1/FVC $&lt; 70%$</td>
<td>FM</td>
<td>B</td>
</tr>
<tr>
<td>Goel et al</td>
<td>India</td>
<td>Population</td>
<td>Cross-sectional</td>
<td>Using wood/cow dung as cooking fuel</td>
<td>No exposure to cooking fuel</td>
<td>CB</td>
<td>FM</td>
<td>B</td>
</tr>
<tr>
<td>Zhong et al</td>
<td>China</td>
<td>Population</td>
<td>Cross-sectional</td>
<td>Exposure to biomass fuel for cooking or heating</td>
<td>Nonexposure to biomass fuel for cooking or heating</td>
<td>GOLD criteria</td>
<td>FM</td>
<td>B</td>
</tr>
<tr>
<td>Akhtar et al</td>
<td>Pakistan</td>
<td>Rural population</td>
<td>Cross-sectional</td>
<td>Using solid biomass fuels for cooking</td>
<td>Using LPG for cooking</td>
<td>CB</td>
<td>FM</td>
<td>N</td>
</tr>
<tr>
<td>Menezes et al</td>
<td>Brazil</td>
<td>Adults</td>
<td>Cross-sectional</td>
<td>Exposure to biomass stove for cooking or heating</td>
<td>Nonexposure to biomass stove for cooking or heating</td>
<td>FEV1/FVC $&lt; 70%$</td>
<td>FM</td>
<td>B</td>
</tr>
<tr>
<td>Pandey et al</td>
<td>Nepal</td>
<td>Rural population</td>
<td>Cross-sectional</td>
<td>Time near the fireplace $&gt; 1$ h/d</td>
<td>Time near the fireplace $\leq 0.9$ h/d</td>
<td>CB</td>
<td>FM</td>
<td>B</td>
</tr>
<tr>
<td>Albalak et al</td>
<td>Bolivia</td>
<td>Population</td>
<td>Cross-sectional</td>
<td>Cooking done indoors</td>
<td>Cooking done outdoors using biomass</td>
<td>CB</td>
<td>FM</td>
<td>B</td>
</tr>
<tr>
<td>Kiraz et al</td>
<td>Turkey</td>
<td>Housewives</td>
<td>Cross-sectional</td>
<td>Heating home and cooking meals using a traditional stove, heated with dung and sticks</td>
<td>Heating home and cooking meals using central heating and modern stoves powered with fuel oil</td>
<td>CB; COPD was defined as reversibility $&lt; 12%$, FEV1/FVC $&lt; 88%$, FEV1 $&lt; 70%$ predicted</td>
<td>F</td>
<td>B</td>
</tr>
<tr>
<td>Dissing et al</td>
<td>Saudi Arabia</td>
<td>Adults</td>
<td>Case-control</td>
<td>Exposure to open fire (wood biomass fuel)</td>
<td>Nonexposure to open fire (biomass fuel)</td>
<td>FEV1/FVC $&lt; 70%$; FEV1 $&lt; 70%$ predicted</td>
<td>FM</td>
<td>B</td>
</tr>
<tr>
<td>Dennis et al</td>
<td>Colombia</td>
<td>Women</td>
<td>Case-control</td>
<td>Using wood as cooking fuel</td>
<td>Not using wood as cooking fuel</td>
<td>FEV1/FVC $&lt; 70%$; FEV1 $&lt; 70%$ predicted; CB and/or FEV1 $&lt; 75%$ predicted</td>
<td>F</td>
<td>B</td>
</tr>
<tr>
<td>Pérez-Padilla et al</td>
<td>Mexico</td>
<td>Women</td>
<td>Case-control</td>
<td>Cooking with a wood stove</td>
<td>Not cooking with a wood stove</td>
<td>CB and/or FEV1 $&lt; 75%$ predicted</td>
<td>F</td>
<td>B</td>
</tr>
<tr>
<td>Orozco-Levi et al</td>
<td>Spain</td>
<td>Adults</td>
<td>Case-control</td>
<td>Exposure to wood and charcoal smoke</td>
<td>Nonexposure to wood and charcoal smoke</td>
<td>FEV1/FVC $&lt; 70%$; FEV1 $&lt; 70%$ predicted</td>
<td>F</td>
<td>B</td>
</tr>
</tbody>
</table>

B = both cigarette smokers and nonsmokers; CB = chronic bronchitis (defined as cough or phlegm on most days for $> 3$ months per year for at least 2 consecutive years; F = female; FM = both female and male; GOLD = Global Initiative on Obstructive Lung Disease; LPG = liquid petroleum gas; N = nonsmoker.
standard errors among all populations and among women. For all 15 studies, the $P = .025$ that was derived using the Egger test and the asymmetry of the

### Funnel Plot Analysis

Figures 5 and 6 show funnel plots of the natural logarithm of OR estimates for the studies against their

```plaintext
Figure 2. Odds ratios and 95% CIs for COPD comparing biomass smokers with biomass nonsmokers among the whole population.
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distribution suggest the potential for publication bias (Fig 5A). Further investigation showed that another seven unpublished articles may be needed to negate the results of the metaanalysis (Fig 5B). When we included only the 11 studies in which the subjects were women, the Egger test value of $P = .133$ and the symmetry of the distribution suggested that a publication bias was not likely to be a problem in this analysis (Fig 6A). Further investigation showed that only one additional unpublished article could negate the results of the metaanalysis (Fig 6B).

**DISCUSSION**

Metaanalytic methods are powerful tools for studying cumulative data from individual studies with small sample sizes and low statistical power. Pooling the
its benefits. Our analyses showed a risk association between biomass smoke and COPD. In our analyses of racial/ethnic subgroups, we detected a significant association between biomass smoke and COPD in both Asian and non-Asian subjects, and we also showed that this association did not differ across ethnic groups. The pooled OR was increased to 2.31 (95% CI, 1.41-3.78) for Asian subjects and 2.56 (95% CI, 1.71-3.83) for non-Asian subjects.

effects from individual studies by a metaanalysis may increase the statistical power and can help detect modest risk differences among study groups. The large data set of this pooled analysis enabled us to investigate aspects of biomass smoke and subgroup-specific associations that could not be addressed adequately in previous studies. Although the metaanalysis can be a useful tool in environmental epidemiology, problems associated with the methodology may limit its use.

Table 4—Association Between Biomass Smoke and COPD in Total and by Subgroups When Including the Three Articles Whose Diagnostic Criterion Is a History of Ever-Diagnosed COPD, Chronic Bronchitis, or Emphysema

<table>
<thead>
<tr>
<th></th>
<th>No. of Subjects</th>
<th>No. of Studies</th>
<th>Heterogeneity Test (Q test)</th>
<th>Biomass Smoker vs Niomass Nonsmoker</th>
<th>Pooled OR test (z test)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Ethnicity (all)</td>
<td>5,556</td>
<td>36,930</td>
<td>18</td>
<td>Q = 177.88; P = .000</td>
<td>2.22</td>
</tr>
<tr>
<td>Asian</td>
<td>4,205</td>
<td>29,082</td>
<td>8</td>
<td>Q = 89.75; P = .000</td>
<td>1.98</td>
</tr>
<tr>
<td>Non-Asian</td>
<td>1,351</td>
<td>7,848</td>
<td>10</td>
<td>Q = 45.39; P = .000</td>
<td>2.41</td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cigarette smoker</td>
<td>576</td>
<td>2,007</td>
<td>4</td>
<td>Q = 4.83; P = .185</td>
<td>4.29</td>
</tr>
<tr>
<td>Cigarette nonsmoker</td>
<td>623</td>
<td>10,064</td>
<td>8</td>
<td>Q = 6.95; P = .44</td>
<td>2.54</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1,872</td>
<td>10,292</td>
<td>13</td>
<td>Q = 55.29; P = .000</td>
<td>2.46</td>
</tr>
<tr>
<td>Male</td>
<td>1,330</td>
<td>2,329</td>
<td>4</td>
<td>Q = 106.06; P = .000</td>
<td>2.75</td>
</tr>
<tr>
<td>Study design</td>
<td>5,556</td>
<td>36,930</td>
<td>18</td>
<td>Q = 177.88; P = .000</td>
<td>2.22</td>
</tr>
<tr>
<td>Case-control</td>
<td>2,120</td>
<td>2,127</td>
<td>6</td>
<td>Q = 76.48; P = .000</td>
<td>3.25</td>
</tr>
<tr>
<td>Cross-sectional</td>
<td>3,436</td>
<td>34,803</td>
<td>12</td>
<td>Q = 90.50; P = .000</td>
<td>1.96</td>
</tr>
<tr>
<td>Phenotype</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>COPD</td>
<td>2,921</td>
<td>26,201</td>
<td>11</td>
<td>Q = 93.51; P = .000</td>
<td>2.50</td>
</tr>
<tr>
<td>CB</td>
<td>5,696</td>
<td>10,940</td>
<td>9</td>
<td>Q = 101.74; P = .000</td>
<td>2.28</td>
</tr>
</tbody>
</table>

See Table 1 for expansion of abbreviation.

a Analyzed with a random effect.
b Analyzed with a fixed effect model.
COPD usually arises from an interaction between host and environmental factors. Cigarette smoke is an important risk factor. To investigate whether there is an interaction between biomass smoke and cigarette smoke, and to investigate the source of heterogeneity, we stratified the group by cigarette-smoking status, and found that there was no significant heterogeneity among cigarette smoking studies and non-cigarette smoking studies, which showed that the heterogeneity among all the 15 studies may arise from the difference in smoking status. We also showed that associations differed with cigarette-smoking status. The pooled OR increased to 4.39 (95% CI, 3.38-5.70) for those exposed to biomass smoke or cigarette smoke. For those exposed to biomass smoke but not cigarette smoke, the pooled OR only increased to 2.55 (95% CI, 2.06-3.05). Our results imply that biomass smoke may interact with cigarette smoking in the pathogenesis of COPD.

Biomass fuels such as crop residues or woods are used in more than one-half the world’s households and a significant proportion of this activity takes place in conditions where much of the airborne effluent is released into the indoor living area. The persons most frequently affected are women, who do most of the cooking for households in rural villages. We made a subgroup analysis stratified by sex. Heterogeneity was found among the male studies, but not among the female studies. Our results also showed a stronger association between biomass smoke and COPD among men than among women (for men: OR = 4.30; 95% CI, 1.85-10.01; and for women: OR = 2.73; 95% CI, 2.28-3.28). A possible explanation may be the difference in cigarette-smoking status, although there was no statistically significant difference in the distribution of cigarette smoking between the case and control groups in each study. In the female studies, the number of cigarette smokers was very small, or there were no cigarette smokers at all, compared with the large and varying number of cigarette smokers in the male studies. Also, biomass smoke may interact with cigarette smoking in the pathogenesis of COPD, which may lead to heterogeneity among male studies and a stronger association between biomass smoke and COPD among men than among women. Although we could not combine the results across studies, all the present studies showed a positive trend of COPD with increasing level or duration of exposure to biomass smoke.

We stratified the group by study design and found that biomass smoke was a risk factor in both case-control and cross-sectional studies. However, we also observed a stronger risk association with biomass smoke pooled from case-control studies than pooled from cross-sectional studies. The reason may be the difference in duration of exposure to biomass smoke. The current spirometric classification for severity of COPD includes four stages: stage I, mild; stage II, moderate; stage III, severe; stage IV, very severe.
The cross-sectional studies included patients in all four stages of COPD, whereas the case-control studies included fewer stage I patients. Thus, the patients in the case-control studies may have had a longer duration of biomass smoke exposure. Finally, with improvements in living standards, more and more people use liquefied petroleum gas as the cooking fuel, and the participants in some studies reported only their current use of cooking fuels, ventilating fans, and winter heating, rather than a combination of current and historical use, which may be another confounding factor.

COPD patients include three subpopulations, based on how the disease is diagnosed: emphysema, chronic bronchitis, and spirometry-diagnosed COPD. Our results showed that biomass smoke is a risk factor for developing chronic bronchitis (OR = 2.57) and COPD diagnosed according to lung function (OR = 2.77). According to epidemiology studies, about two-thirds of COPD patients have not been given this diagnosis. Using a history of ever having received a diagnosis of COPD, chronic bronchitis, or emphysema as a diagnostic criterion can lead to many COPD patients being included in the healthy control group. We did a sensitivity analysis including the three studies in which the diagnostic criterion was a history of having received a diagnosis of COPD, and showed that biomass smoke is still a risk factor for COPD. In addition, all the subgroup analyses showed that biomass smoke is a risk factor for COPD, except for the subgroup analysis that included only men, which showed no association between biomass smoke and COPD. However, we still believe that exposure to...
biomass smoke is a risk factor for COPD in men because this subgroup analysis was part of a sensitivity analysis and the main analysis showed a strong association between biomass smoke and COPD in men. The study by Chapman et al.²⁹ showed that the incidence of COPD decreased markedly after household coal stoves were improved, which also showed that biomass smoke is a risk factor for COPD.

There are several limitations that should be considered when interpreting our results. First, some pooled ORs were obtained from heterogeneous studies. Second, the studies included in our metaanalysis were case-control and cross-sectional studies, not cohort studies, in which biomass smoke is assessed after disease onset. Thus, biomass smoke information in these studies is likely to be less accurate and possibly influenced by recall bias. Third, we must consider the possibility of a publication bias involved in our analysis, given that we combined data only from published reports, and that we may have excluded important unpublished data that did not show results consistent with our findings, although we did our best to contact the researchers for data from unpublished or ongoing studies, and although our result showed that only one additional unpublished article could negate the results of the metaanalysis in women. Finally, in most studies included in our metaanalysis, exposure was assessed using crude proxies such as whether the households were using solid fuels. This has proved useful, but better quantifying exposure will be necessary for establishing exposure-response relationships and for quantifying health risks more precisely.

Conclusions

In conclusion, our metaanalysis suggests that biomass smoke is associated with an increase in the risk of COPD. Given the high prevalence of biomass smoke, especially in rural areas, the public health consequences of biomass smoke with regard to COPD are important and suggest that COPD incidence could be reduced by interventions targeting biomass smoke.
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