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Biomass Fuel Use and Risk of Cataract: Systematic Review and Meta-Analysis

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Authors' contributions

This work was carried out in collaboration among all authors. Author HK conceptualized and designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors UWN and NDS participated in the analyses as well as contributed the unpublished data. Authors HK, UWN, ST and NDS independently reviewed the studies. Author SNU performed additional statistical analyses. All authors read and approved the final manuscript.

Research Article

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ABSTRACT

Aims: There is an increasing recognition of the putative association between the use of biomass fuels and the risk of cataracts. However, the exact strength of this association is currently unknown. Our aim was to synthetically quantify the association between biomass fuel use and cataract.
Study Design: Systematic review and meta-analysis.
Methodology: Using results from the MEDLINE®, Scopus®, Web of Science® and Google® searches, we conducted a random-effects meta-analysis of the published studies. We also conducted subgroup meta-analyses, meta-regressions and sensitivity analyses to determine the contribution of potential confounders to between-study heterogeneity which was measured by the tau-squared and I^2 statistics. Summary effect sizes (SES) were estimated using the DerSimonian and Laird method and the 95%

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confidence intervals (CI) and 95% prediction intervals (PI) were also estimated. Publication bias was examined using funnel plots and Egger's test.
Results: In spite of significant between-study heterogeneity (I^2 70%, $p=8.1\times10^{-5}$), biomass fuel use was associated with a significantly increased risk of cataract (SES 2.12; 95% CI 1.61-2.80; 95% PI 0.88-5.09). Age-, gender- and other methodological differences did not significantly contribute to between-study heterogeneity but Indian studies showed a statistically significant association between biomass fuel use and cataract. Statistically homogeneous studies (n = 8) showed an SES of 2.01 (95% CI and PI 1.67-2.41).
Conclusion: Synthetic evidence from observational studies indicates that biomass fuel use may increase the risk of cataract. Public health initiatives aimed at avoidance of biomass fuel use may reduce the burden of cataracts especially in settings where biomass fuels are commonly used.

Keywords: Biomass; cataract; energy; indoor air pollution; meta-analysis.

1. INTRODUCTION

Exposure to indoor air pollution (IAP) is a vexing problem on many counts. Nearly 3 billion people worldwide use solid fuels (including biomass and coal) to meet their routine, household energy demands [1]. The prevalence of biomass fuel use is reported to be high in Sub-Saharan Africa (76%), Asia (65%) and Latin America (23%) [2]. The World Health Organization reported that household air pollution from solid fuel use accounted for 2.7% of the global burden of disease in 2000 [3]. Additionally, 1.6 million global deaths were attributable to IAP in 2002 [4]. India bears a heavy brunt of this environmental menace where 78% of the population still uses solid fuels for household cooking.[5] Further, an estimated 28% of the worldwide IAP-related deaths are contributed by Indian women and children who die due to IAP-associated respiratory disorders [6].

With regard to eye health, the past couple of decades have witnessed emerging evidence that the incidence and prevalence of cataracts may be strongly and significantly associated with the practice of solid biomass use [7,8]. It has been posited from elegant animal studies that the smoke-induced lenticular damage may be mediated through systemic absorption and dissemination of the toxic components to several tissues, but especially to the lens where the metabolic turnover is slow. As a result, there is chronic accumulation of these condensates in the lens leading to an oxidative injury to the lenticular tissue [9]. Given the proportion of world population partaking in biomass fuel use, it is conceivable that the global burden of cataracts can be partially explained by IAP if there is synthetic evidence to support such an association. However, the exact strength and significance of this conjecture is currently unknown. We therefore conducted a systematic review and meta-analysis of published literature on the association of the risk of cataract with biomass fuel use.

2. MATERIALS AND METHODS

2.1 Data Extraction

We aimed to include all the observational studies that have been published in this field. To identify these studies we searched the MEDLINE®, Scopus® and Web of Science® databases for published observational epidemiological studies dealing with biomass fuel use and risk of cataract and published before Dec 31, 2012. The search strategy and the search protocol are detailed in Table 1.

Table 1. Literature search strategy used in this study

Strategy	# Papers
1. ((biomass) OR ("indoor air pollution") OR (fuel) OR ("household air pollution"))	53785
2. 1 and cataract	13
3. 2 and NOT review	9
4. 3 and reporting effect size for association with biomass fuel use	6
5. Additional studies through Web of Science® and Scopus® using the same strategy outlined in steps 1-4	5
6. Unpublished primary data from a previous study by authors	1
Total number studies included	12
Total number of comparisons*	13

**, one study reported data from two centers thus the number of comparisons was higher than the number of studies*

We used the same search strategy on all the three databases. Our additional inclusion criteria (not a review, presence of a control group not using biomass fuels and explicitly stating the association between biomass fuel use and cataract) resulted in further narrowing of the search. In addition, we searched the internet using the Google search engine to ensure that we did not miss any studies. Lastly, we included the results of a study that we had recently conducted in which we had estimated the prevalence of cataract in women using biomass fuels to different degrees [10]. After locating the studies, the authors independently reviewed the studies; any discrepancies in the study evaluations were discussed and resolved during one-to-one meetings. Whenever available, we used the multivariate-adjusted estimates of odds ratios (OR) reported in each study. When multivariate results were not reported we used the univariate estimates of the OR and if a study did not report OR, we used the cell frequencies in a constructed two-by-two contingency table to estimate the OR and 95% confidence interval (CI). This report is provided in line with the PRISMA® guidelines (http://www.prisma-statement.org/index.htm).

2.2 Meta-Analysis

The primary outcome being studied here was the risk of cataract irrespective of the types of cataract. For the meta-analysis we used the random effects model of DerSimonian and Laird [11,12]. For quantifying heterogeneity, we used two statistics: the I^2 statistic and the τ^2 statistic that represents the among-study variance. We used the τ^2 statistic because it is required to estimate the 95% prediction intervals (PI) for the global distribution of the estimated summary effect measure (odd ratio) [13,14]. Publication bias was examined using funnel plot and the regression intercept method [15]. We determined the potential contribution of each study to the heterogeneity using sensitivity analyses. To investigate if known confounding factors like age, area of residence, gender distribution and type of cataract explain significant proportion of between-study heterogeneity we conducted sub-group meta-analyses and meta-regression using linear meta-regression models. Statistical analyses were conducted using the Stata 10.2 (Stata Corp, College Station, TX) software package. For meta-analyses we used the metan.ado program written by Bradburn [16].

3. RESULTS

3.1 Studies Used

We included a total of 12 studies [10, 17-27] that reported an association between biomass fuel use and risk of cataract. One of these studies [24] reported data from two geographically distinct areas and therefore we had a total of 13 comparisons on which we conducted the meta-analyses. These 13 comparisons pertained to a total of 4025 cases of cataract and 7048 controls. Detailed description of the study comparisons included in this meta-analysis is provided in Table 2.

Table 2. Summary of the studies included in this meta-analysis

#	Study [Ref]	Place	Cases			Controls		
			N	Mean age (y)	% female	N	Mean age (y)	% female
1	Mohan et al. [20]	New Delhi, India	1441	54.48	---	549	48.92	---
2	Badrinath et al. [17]	Madras, India	244	---	49.6	264	---	42.8
3	Ughade et al. [26]	Nagpur, India	262	60.46	48.9	262	59.96	48.1
4	Sreenivas et al. [24]	Kerala, India	258	53.34	62.8	308	47.55	52.9
5	Sreenivas et al. [24]	West Bengal, India	301	54.99	54.5	591	46.66	55.2
6	Zodpey et al. [27]	Nagpur, India	223	60.56	100	223	60.56	100
7	Ranasinghe and Mahanama [22]	Sri Lanka	197	62.06	76.7	190	55.44	77.9
8	Krishnaiah et al. [19]	Andhra Pradesh, India	459	---	100	2702	---	100
9	Pokhrel et al. [21]	India-Nepal	206	46.11	100	203	46.22	100
10	Saha et al. [23]	Western India	120	---	---	353	---	---
11	Haq et al. [18]	Aligarh, India	110	62.43	62.1	388	36.33	58.4
12	Tanchangya et al. [25]	Bangladesh	153	42.47	52.3	306	42.04	52.3
13	Sukhsohale et al. [10]	Nagpur, India	51	61.61	100	709	30.42	100

#, Comparison; N, subjects; Ref, Reference

As expected from known distribution of the practice of biomass fuel use, all the studies included in this meta-analysis were published from India, Bangladesh and Nepal. We also examined key methodological features from each study (Table 3) and found that eight of the 13 comparisons included in this meta-analysis did not use a matched design. Also, of the studies that used matching none used a pair-matched design. All studies used the definition of exposure to biomass fuels as ever- or regular-use of the specified fuel for cooking however the comparison group varied across studies. Additional study-specific methodological issues are shown in Table 3 (see column titled "Comments").

Table 3. Methodological features of the studies included in this meta-analysis

#	Study [Ref]	Age Diff (y)	Matching variables	Source of controls	Definition of exposure	Comments
1	Mohan et al. [20]	5.6	None	Hospital	Cow dung, wood versus gas	Risk factor for cortical, nuclear and mixed cataracts but nor for posterior subcapsular cataracts
2	Badrinath et al. [17]	4.7	None	Hospital	Cheap fuels (cow dung, wood coal, kerosene) versus others	Although age-matching was done, there was difference in mean ages of cases and controls. Analyses have adjusted for age and sex
3	Ughade et al. [26]	0.5	Age, sex	Hospital	Cheaper fuels versus others	Population attributable risk proportion for cheaper fuels as a risk factor of cataract was 0.37 (95% confidence interval 0.33 – 0.41)
4	Sreenivas et al. [24]	5.8	None	Community	Cheap fuels (cow dung, wood) versus others	Subjects from Angamally, Kerala in south India
5	Sreenivas et al. [24]	8.3	None	Community	Cheap fuels (cow dung, wood) versus others	Subjects from Calcutta, West Bengal in east India
6	Zodpey et al. [27]	0	Age	Hospital	Cheaper fuels (cow dung, wood, kerosene) versus gas	Population attributable risk proportion for cheaper fuels as a risk factor of cataract was 0.29 (95% confidence interval 0.12 – 0.49)
7	Ranasinghe and Mahanama [22]	6.6	None	Hospital	Firewood versus others	Cases also showed a longer duration of exposure
8	Krishnaiah et al. [19]	---	None	Community	Cheaper cooking fuels versus others	Smoking was a potential confounder
9	Pokhrel et al. [21]	-0.1	Age	Hospital	Solid fuels versus clean burning stove	Lack of kitchen ventilation worsened the association of solid-fuel with cataract
10	Saha et al. [23]	---	None	Hospital	Traditional fuels (wood, cattle dung and coal) versus gas	Males had a reduced risk of cataract
11	Haq et al. [18]	26.1	None	Community	Wood, cow dung and coal versus gas	Cataract unrelated to gender, residence or social class
12	Tanchangya et al. [25]	0.4	Age, sex	Hospital	Solid biomass versus gas	Associations were different when cases were compared to non-eye disease controls and non-cataract eye-disease controls.
13	Sukhsohale et al. [10]	31.2	None	Community	Solid biomass fuels versus gas	Cross-sectional study design

#, Comparison; Ref, Reference; Age Diff, mean age difference between cases and controls in years

3.2 Summary Effect Size

We found that the synthetic combination of the results from these 13 comparisons yielded a summary effect size of 2.12 (95% CI 1.61 – 2.80, Fig. 1A). However, there was a high degree of heterogeneity across the studies as indicated by the τ^2 (0.1675) and I^2 (70%) statistics; which was statistically significant ($p = 8.1 \times 10^{-5}$). We therefore estimated the 95% prediction interval for this summary effect size. We found that the prediction interval did not straddle unity and was therefore statistically not significant. These results indicated that due to the significant heterogeneity across the published results the summary effect size of 2.12 that was synthesized from these comparisons may not generalize to all the populations in the light of the estimated prediction interval. We also investigated the potential of a publication bias in this regard but found (Fig. 1B) that there was no evidence for such a bias ($p = 0.258$). For these reasons we conducted two sets of analyses – fist, we investigated the possible reasons for the observed heterogeneity among studies and second, we conducted sensitivity analyses to examine the influence of the observed heterogeneity on the robustness of the summary effect size.

3.3 Investigation into Heterogeneity

We next tried to identify the potential sources of heterogeneity in the published studies. For this, we first identified six potential contributors: age, gender, type of cataract, country, matching and source of controls. We observed (Table 2) that in 7 of the 10 studied that reported group-wise mean age of cases and controls, the mean age of cases was substantially higher than that of the controls [10,17,18,20,22,24,26]. Also, 4 of the 10 studies that reported the proportion of females in cases and controls had recruited more females than males [17,18,24,26] while four other studies [10,21,27,28] conducted exclusively in women. Only one study [25] reported the effect sizes separately for males and females but for inconsistent categories of fuel types. We therefore conducted meta-analysis in studies that recruited females only and found that the summary effect size was 1.91 (95% CI 1.24-2.97; I^2 = 54.8%, τ^2 = 0.1079, 95% PI 0.86-4.27). This summary effect was similar to the overall summary effect estimated from all studies (Fig. 1A). We also conducted meta-regression analyses to determine if the between-study heterogeneity can be partially explained by the differential age and gender distributions. However, our results of meta-regression (Fig. 1C) showed that neither of these two variables was significantly associated with the study-specific effect sizes ($P = 0.586$ for age-difference between cases and controls and 0.282 for proportion of females in the study). These results indicate that the increased risk of cataract in users of biomass fuels is unlikely due to the case-control differences with respect to age and gender.

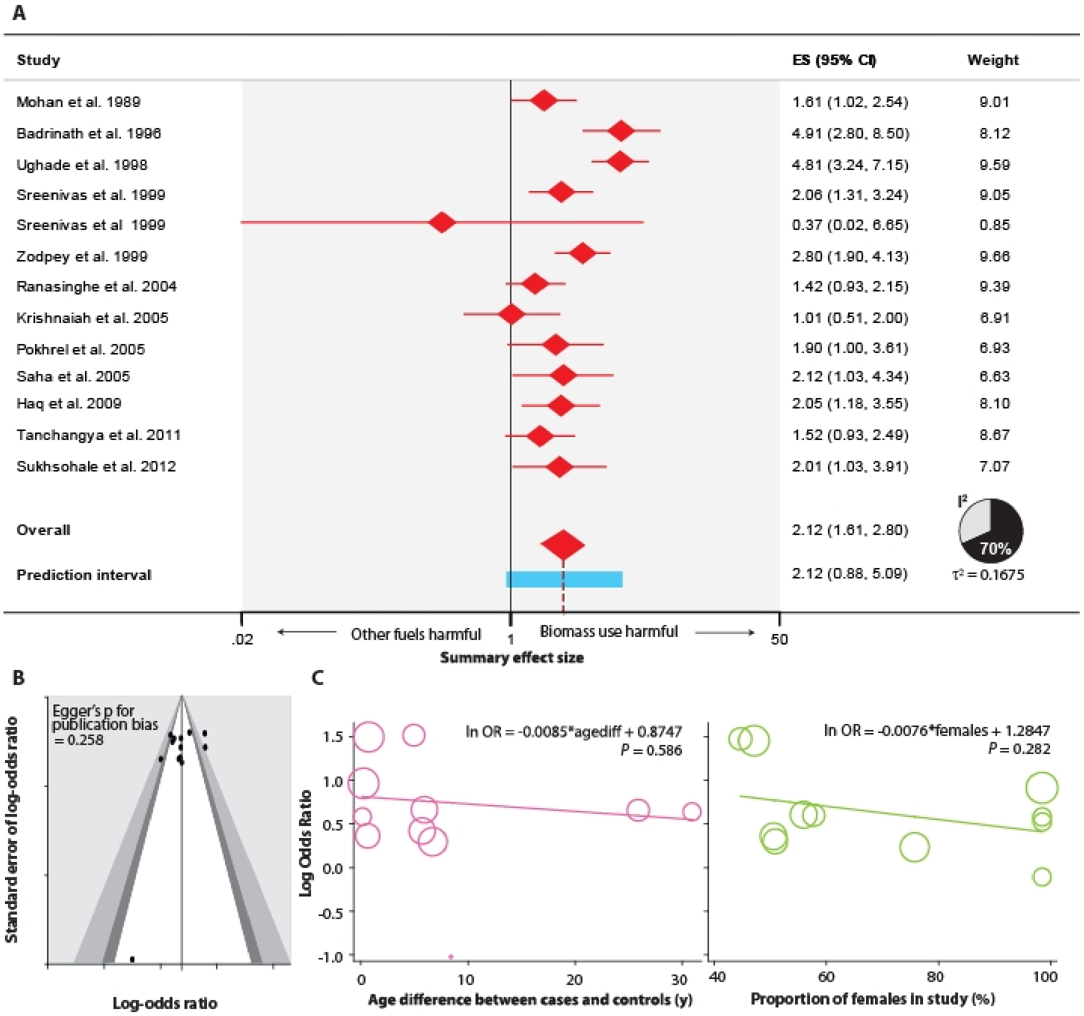

Fig. 1. Meta-analysis of the association of biomass fuel use with the risk of cataract

(A) Forest plot. Colored diamonds and error bars for each study indicate the study-specific effect size and 95% confidence interval. Filled diamond at the bottom indicates the summary effect size (center of the diamond) and 95% confidence interval (width of the diamond). The blue band at the bottom indicates the width of the 95% prediction interval around the summary effect size. Pie-diagram at the bottom-right shows the between-study heterogeneity as measured by the I^2 *statistic (black slice). The estimated* τ^2 *is also shown. (B) Determination of publication bias using funnel plot. Egger's P indicates the statistical significance of the publication bias. (C) Results of meta-regression on the age difference between cases and controls (left panel) and the proportion of females in the study (right panel). The plots show study-specific effect sizes (log odds ratios) and a meta-regression fitted line. The diameters of the circles for each study are proportional to the study-specific standard error of log-odds ratios. Shown at the top are the fitted regression equations and the statistical significance. agediff, age difference between cases and controls; females, proportion of females in the study; P, statistical significance for the meta-regression coefficient departing from zero.*

3.4 Other Potential Confounders

With regards the type of cataract only one study reported the type-specific ORs for the biomass fuel-cataract association [20]. However, this study did not report the 95%

confidence intervals for all the ORs. For these reasons a subgroup analysis on the potential association of the type of cataract with biomass fuel use could not be carried out. We next considered if the country of study origin contributed to the between-study heterogeneity. We found that 11 of the 13 comparisons originated partially or fully from India [10,17,20,21,24,26-28]. The Indian studies showed a summary effect size of 2.30 (95% confidence interval 1.70 – 3.12), a τ^2 of 0.1645 and an I^2 of 67.9%% (*P* = 0.001) while the studies from outside India [22,25] had a smaller but significant summary effect size of 1.46 (95% confidence interval 1.06 – 2.01). When we considered the potential association of matched versus unmatched study designs, we found that the matched studies yielded somewhat higher summary effect size (2.57, 95% confidence interval 1.54 – 4.31) as compared to unmatched studies (1.91, 95% confidence interval 1.41 – 2.59). However, in meta-regression this variable only accounted for a decrease of 3.0% in the I^2 which was not statistically significant (p = 0.307). The source of controls also did not significantly explain the heterogeneity in effect sizes (meta-regression *P* = 0.271) – studies using hospital controls yielded a summary effect size of 2.36 (95% confidence interval 1.63 – 3.42) while those using community-based controls yielded a summary effect size of 1.77 (95% confidence interval 1.30 – 2.40). Lastly, there were 4 studies (5 comparisons) conducted entirely in rural settings [10,23-25], 2 studies in urban settings [20, 29] and 6 studies included subjects from rural as well as urban settings [18,19,21,22,26,27]. Subgroup meta-analyses revealed the summary effect sizes (95% confidence interval) for the studies conducted in rural, urban and mixed settings were 1.73 (1.01 – 2.97), 1.76 (1.23 – 2.51) and 2.45 (1.77 – 2.33), respectively. Again, however, this variable only accounted for 2.2% decrease in the I^2 statistic and was not statistically significant (P = 0.615) in the meta-regression analyses.

3.5 Sensitivity Analyses

Alternatively, we took the approach of sensitivity analyses to determine the contribution of each comparison to the overall between-study heterogeneity. In these analyses, we first excluded each study separately to find out studies that maximally influenced the heterogeneity. Next, we combined the most contributory studies and excluded these combinations to end up with the most homogeneous set of comparisons. We observed that (Table 4) four studies [17,22,26,28] contributed significantly to the between-study heterogeneity as indicated by a significant change in the Q statistic (Table 4, columns ΔQ and Δ*P*). Interestingly, these four studies included three Indian studies and one non-Indian study. After excluding these four studies the summary effect size was 2.01 with 95% confidence interval and 95% prediction intervals (Table 4) that did not straddle unity.

Table 4. Sensitivity analyses for contribution of each study to among-study heterogeneity

Comparison excluded	ES	95% CI	τ^2	95% PI	Q	ΔQ	Δ*P*
1	2.17	1.61 – 2.93	0.1803	0.87 – 5.43	37.60	2.09	0.148
2	1.98	1.52 – 2.58	0.1326	0.90 – 4.35	31.26	8.43	0.0034
3	1.96	1.55 – 2.48	0.0848	1.03 – 3.70	23.08	16.61	<0.001
4	2.12	1.56 – 2.88	0.1946	0.82 – 5.47	39.65	0.04	0.842
5	2.15	1.63 – 2.84	0.1650	0.90 – 5.15	38.30	1.39	0.238
6	2.05	1.51 – 2.79	0.1923	0.80 – 5.27	38.25	1.44	0.230
7	2.21	1.66 – 2.95	0.1636	0.92 – 5.29	34.62	5.07	0.024
8	2.24	1.70 – 2.95	0.1487	0.98 – 5.16	34.37	5.32	0.021
9	2.13	1.59 – 2.87	0.1817	0.85 – 5.33	39.56	0.13	0.718
10	2.12	1.57 – 2.84	0.1821	0.84 – 5.30	39.76	0.00	1.000
11	2.12	1.57 – 2.86	0.1877	0.84 – 5.38	39.69	0.00	1.000
12	2.19	1.63 – 2.93	0.1750	0.89 – 5.37	37.22	2.47	0.116
13	2.12	1.58 – 2.86	0.1830	0.85 – 5.32	39.69	0.00	1.000
3 & 2	1.82	1.52 – 2.18	0.0130	1.35 – 2.45	11.68	28.01	<0.001
3, 2 & 8	1.90	1.61 – 2.24	0.0000	1.61 – 2.24	8.59	31.10	<0.001
3, 2, 8 & 7	2.01	1.67 – 2.41	0.0000	1.67 – 2.41	6.35	25.34	<0.001

ES, effect size; CI, confidence interval; PI, prediction interval; ΔQ, change in the Q statistic by excluding the indicated comparison(s); ΔP, statistical significance of ΔQ using χ^2 *test*

4. DISCUSSION

4.1 Interpretations and Implications

Over a decade ago Smith [6] identified an urgent need to programmatically stamp out the ill-effects of biomass fuels. Since then several meta-analyses relating to the association of biomass fuel use and outcomes like acute lower respiratory tract infections, chronic obstructive pulmonary diseases, pneumonia, still birth and tuberculosis have established that biomass usage poses a significant health risk [30-35]. In the context of eye health, Fletcher [36] points out that biomass fuels are an important external source of reactive oxygen species, an observation that has also recently been demonstrated in Indian women using biomass fuels [37]. Our results demonstrate a possible epidemiological link between biomass fuel use and cataracts. In spite of the between-study heterogeneity observed in this meta-analysis, the summary effect size was statistically significant, especially when gleaned from statistically homogeneous studies. Our sensitivity analyses showed that after exclusion of studies contributing to heterogeneity this significant summary effect was still evident (Table 4, last row). Since we included studies published before December 31, 2012, we could not include a recent cross-section study [38] which found an odds ratio of 2.58 (95% confidence interval 1.22-5.46) for the risk of nuclear cataracts in Nepalese women associated with the use of biomass stoves as compared to the use of gas stoves. Notably, the results of this Nepalese study are in line with the inferences our meta-analyses. The mechanism of cataract precipitation in response to biomass fuel use is currently not fully understood but the associative epidemiological evidence from various published studies in this regard is indicative of the importance of indoor air pollutants in the pathogenesis of cataracts independently of age and gender.

4.2 Methodological Implications

Studies included in this meta-analysis together point towards three important methodological issues that future studies need to consider. First, it should be noted that the definition of exposure used by all the studies included in this meta-analysis is simplistic – ever use of biomass fuel. Existence of a dose-response relationship between biomass fuel use and cataract risk, albeit plausible, could not be meta-analytically confirmed based on the current evidence. Two recent studies [25,38] have shown that length of exposure to biomass fuels may associate with the risk of cataract development but more intensive investigation of this association is needed. Secondly, the use of this definition of exposure also precludes estimation of fuel-specific associations. For example, the relative strengths of association of wood, cow dung and coal in with cataract risk are currently unknown. Whether such a risk differential exists across biomass fuel types and, if so, would it have public health relevance are under-researched questions at this time. Thirdly, age and sex are important potential confounders that only four studies have matched for. When possible future studies should match on these confounders. Minimally, future studies need to report the age and gender distribution in enough details to permit estimation of association between biomass fuel use and cataract within each stratum of age and gender.

4.3 Limitations

In addition to all the limitations implicit in any meta-analysis there are some other issues that must also be considered. First, the available literature linking biomass fuel use and cataracts mainly originates from developing countries and therefore these results should not be generalized to the scenarios where biomass fuels are not commonly used. Second, the inferences arrived at in this meta-analysis hinge upon observational studies. As pointed out in the previous section, there are several methodological issues that future studies need to improve upon. As a result of these lacunae, the results of this meta-analysis, while statistically reliable, need more epidemiological credence. Third, the meta-analysis uses the effect sizes as reported in the primary studies. As many of the studies are cross-sectional in nature it would be more accurate to use prevalence ratios as a better measure of effect size rather than the odds ratios as reported by the primary studies. However, prevalence ratios have not been reported by any study nor was it possible to estimate the prevalence ratios from the information provided by the studies. Since odds ratios can somewhat overestimate the strength of association our estimates of the effect size may be slightly higher than truth. We tried to offset this limitation by estimating prediction intervals; however some degree of overestimation may still be operative. Fourth, potentially differential risks of cataract subtypes could not be estimated in this study. This was important since it could have provided some insights into the pathogenesis of biomass-related cataract. Therefore, no claim implying biomass fuel use in the pathogenesis can be made from the findings of this study. Finally, inclusion of all the studies in this meta-analysis resulted in a statistically significant heterogeneity, the source of which could not be resolved. That the heterogeneity may not affect the interpretations of this study is substantiated by most of the prediction intervals however there does remain a significant amount of heterogeneity when Indian and other studies are combined together. Nutritional status, environmental factors and genetic make-up can all contribute to cataract development but relative quantification of these influences was not possible in this meta-analysis since majority of the primary studies have not reported these additional observations.

5. CONCLUSION

Notwithstanding these limitations, our results indicate a need to take public health initiatives to eliminate or reduce the use of biomass fuels. Our results provide conceptual substantiation to the premise [39] that interventions aimed at substitution of biomass fuel use with cleaner sources of energy are also likely to reduce societal burden of cataracts. Further studies and efforts in this direction are both vital and required for improvement in the eye health.

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

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Dr. Uday Narlawar wishes to dedicate this work to the fond memory of his father Late Mr. Wasudeorao Narlawar.

COMPETING INTERESTS

None of the authors have any competing interests to declare.

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