An Association of Household Air Pollution and Eye Diseases

GRADUATE SCHOOL OF PUBLIC HEALTH

CAPSTONE PROJECT

BY:

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TOPIC:

AN ASSOCIATION OF HOUSEHOLD AIR POLLUTION AND EYE DISEASES.

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A CAPSTONE PROJECT REPORT SUBMITTED TO THE GRADUATE SCHOOL OF PUBLIC HEALTH IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF THE DEGREE OF MASTER OF PUBLIC HEALTH OF ST. LUKE'S INTERNATIONAL UNIVERSITY, TOKYO, JAPAN.

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Introduction:

According to World Health Organization (W.H.O) October 2019 Fact Sheets[1], at least 2.2 billion people have a vision impairment or blindness, of whom at least 1 billion have a vision impairment that could have been prevented or has yet to be addressed. This 1 billion people include those with moderate and severe distance vision impairment or blindness due to unassessed refractive error as well as near vision impairment cause by unaddressed presbyopia. Globally, the leading cause of vision impairment are uncorrected refractive factors and cataracts. The majority of people with vision impairment are over the age of 50 years. In this updated systematic review paper, eye diseases being reviewed are: cataract, Age related Macular Degeneration (AMD), trachoma, dry eye disease, blindness and other ocular outcome such as tears and eye irritation.

In terms of regional difference, the prevalence of distance vision impairment in low- and middle-income regions is estimated to be four times higher than high income regions[2]. This is from previous studies and action plan such Global Action Plan 2014 – 2019 which was adopted by W.H.O member states at the World Health Assembly in 2013, with the main goal being to reduce vision impairment as a global public health problem and to secure access to rehabilitation for people with vision impairment[2].

Low- and middle-income countries are also the main users of solid fuels (biomass and coal) for cooking and heating[3]. Traditional stoves which are inefficient in terms of fuel use, are highly polluting, leading to high concentrations of particulate matter, carbon monoxide and other organic compounds[4]. Women are traditionally known to work in the kitchen as they prepare meals for their families. However, this contributes to the main exposure to high concentrations of particulate matter emitted from frying foods, open flame and smoke from these inefficient biomass fuels thus leading to eye diseases and other ocular outcome such as tears and eye irritation.

High levels of Household Air Pollution according to W.H.O results from usage of polluting fuels, including biomass fuels (dung, wood, agricultural residues, coal and kerosene) for their energy needs. Cooking and heating with polluting fuels on open fires and traditional stoves results in high levels of Household Air Pollution. Indoor smoke contains a range of health-damaging pollutants, such as small particles, carbon monoxide and particulate pollution levels may be twenty times higher than expected guideline values. Exposure terms for this systematic

review include: indoor air pollution, household air pollution, biomass, cookstove, cooking, smoke, stove and fuel.

There is scarce research linking eye diseases and indoor solid fuel use, although good evidence exists linking inefficient use of these fuels and a wide range of health effects, including pneumonia, cancer, chronic obstructive pulmonary disease, low birthweight and cardiovascular disease[5] . This paper seeks to find out if there is an association between eye diseases and other ocular outcome such as tears and eye irritation as a result of exposure from Household Air Pollution.

Methods:

Following (Preferred Reporting Items for Systematic Reviews and Meta-analyses) PRISMA 2009 checklist[15], the eligibility criteria for study selection was in line with the following exposure search terms/MeSH terms/key words: “indoor air pollution”, “household air pollution”, “biomass”, “cookstove”, “cooking”, “smoke”, “fuel” and “stove”. The outcome search terms/MeSH terms/key words were: “dry eye”, “Cataract”, “Macular degeneration”, “blindness”, “tears” and “eye disease”. The protocol for this updated systematic review was registered in PROSPERO[16] (registration number CRD42020193675).

As for data extraction (selection and coding), RefWorks software was used to remove any duplicate studies during the study selection process. For each ocular outcome, all variables were defined, that is the type of biomass solid fuel exposure resulting in household air pollution. Full text papers were included in this systematic review. The means used for recording data, extraction and management was by use of RefWorks reference manager.

Sources included but were not limited to bibliographic databases, reference lists of the systematic review being updated. Electronic bibliographic databases used included: PubMed, EMBASE, Google Scholar and hand search on key journals. Restrictions included papers published in English Language. There was no time restriction for the publication period. Prior to the final analysis, searches were re-run. Unpublished papers were not sought. In the types of study designs included, all study designs were included. As for inclusion criteria, this included studies that examined people with eye diseases and other ocular outcome resulting from exposure to Household Air Pollution from solid fuel use. Exclusion criteria for this updated systematic review was studies on children were not included due to ethical reasons, infectious

diseases like trachoma were excluded, studies on tobacco smoke were excluded because the main exposure investigation was household air pollution from biomass solid fuel use and not tobacco smoking, studies on eye diseases with other exposure terms other than household air pollution, as well as air pollution in occupational/work places occurring outside of the home setting were also excluded.

The measure of effect for this paper was odds ratio (OR) for the main outcome i.e., eye diseases and other ocular outcome. There was no additional outcome measured other than the listed outcome terms in this review.

Literature review with risk of bias[8] assessment was done using the Critical Appraisal Skills Programme (CASP) checklist[8]. The CASP checklist used comprised of eleven to twelve questions with three outcome measures; yes, no and can't tell and an overall numeric score for each question asked, which classifies the quality of the study conducted. CASP checklist has appraisal checklist designed for use with systematic reviews and other study designs (case control studies, cohort studies).

The results from the study selection informed data synthesis, that is, relative risks for eye diseases and other ocular outcome resulting from Household Air Pollution, were used in generating a forest plot to show the overall picture of risk ratios from studies selected.

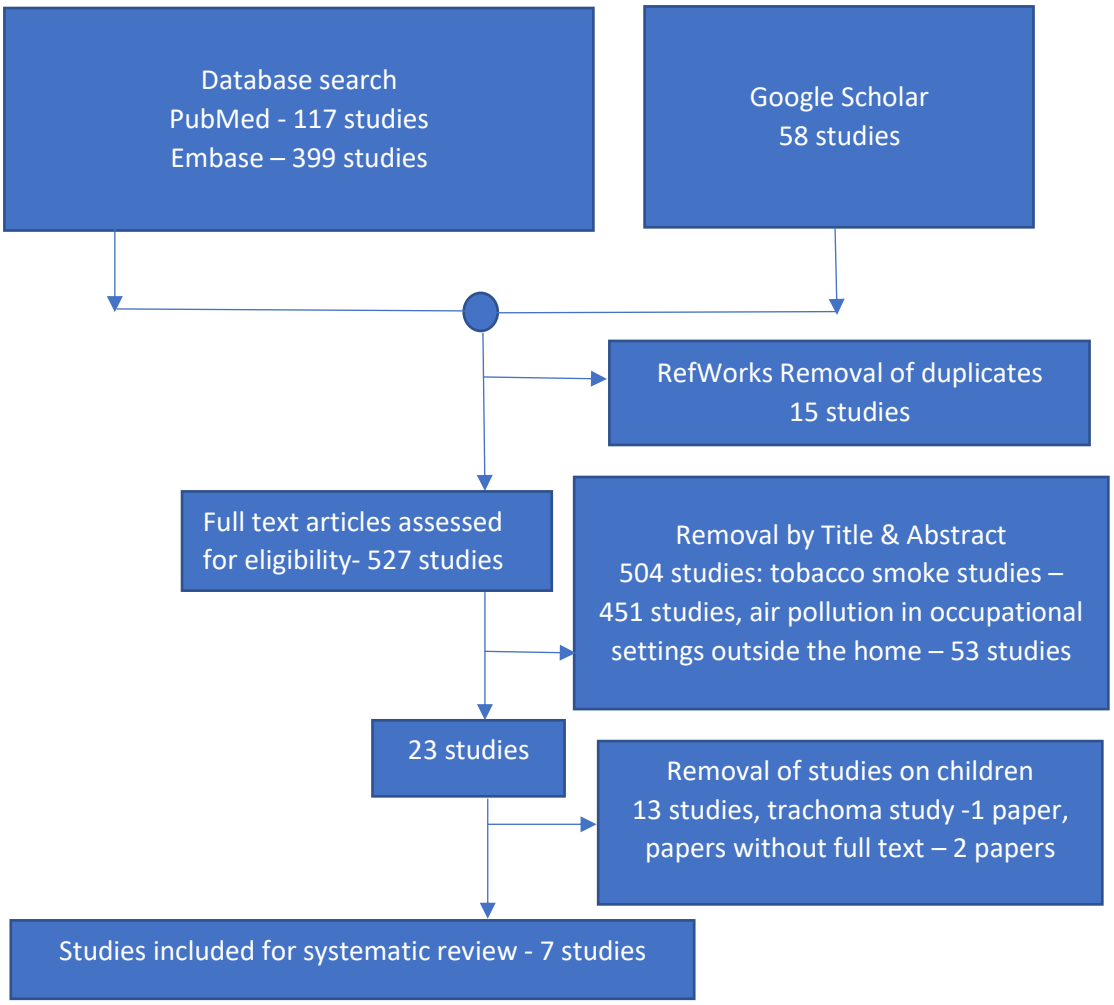


Figure 1: Flowchart showing the screening process of published studies for this updated systematic review

Results:

Table 1: Summary of relevant literature for Household Air Pollution and eye diseases and other ocular outcome

Reference	**Study design**	**Location**	**Study population (N)**	**Exposure measure**	**Outcome**	**Adjusted for:**	**Strengths**	**Limitations**
(Ravilla et al., 2016)	CS	North & South India	7,518 people, both sexes, 60 years old and above	Biomass cooking fuels	Cataract	Age, study center, socioeconomic status, tobacco use, sun exposure, malnutrition, vitamin c deficiency, diabetes, other sources of indoor air pollution (mosquito repellants and incense)	Large random population-based sample, clinical information, detailed information on key confounders.	Information on kitchens was limited to current kitchens without details of ventilation or proximity to eating and sleeping areas, data on passive smoking was not collected.

(Das et al., 2019)	CC	East Delhi, India	90/90, both sexes, 18-40 years	Indoor and or outdoor fuel exposure and other risk factors	Cataract	Age, occupation, sociodemographic profile, amount of fuel exposure per day, smoking, use of smokeless tobacco, alcohol use, dietary pattern, systemic disorders, long term drug therapy, ocular trauma, hair dye use.	Clinical information.	Small sample size, inability to fully adjust for various confounders, data collection based on recall basis may have led to recall bias.
(Vashist et al., 2020)	CS	India	9,735 participants, both sexes, 40 years and older.	Sun exposure and other environmental risk factors such as exposure to indoor kitchen smoke	Cataract	Educational status.	Clinical information, large sample size from three different geographic locations in India.	Recall bias with regard to history of risk factors.
(Li et al., 2016)	RCT	Peru	334 women	Indoor wood stove	Red eye	Woman age, stove type, CO, wood type, second-hand smoke, home-to-road distance, pesticide use, fertilizer use, enclosed kitchen, grilled food,	Clinical confirmation	Small sample size, Exposure assessment was not conducted before new stove installation in the

						Creatinine level in urine sample to assess exposure to Household Air Pollution		intervention households, the study could not assess factors and barriers affecting the adoption of new stoves, recall bias could occur in participant's self-reported health symptoms.
(Sukhsohale et al., 2013)	CS	Raipura village, Nagpur district, India	760 women, aged 15 years and above.	Indoor cooking smoke	Eye irritation	Not available.	Clinical information.	Small sample size. Self-reported symptoms.
(Aung et al., 2018)	CC	Rural India	199 women, above 25 years old followed up out of original participants of 222 women (i.e. 90%)	Solid fuel smoke from traditional stoves	Eye irritation	Chimney, room numbers in household, age, caste, BMI.	First study to independently evaluate the health impacts from an ongoing climate financed stove intervention program.	Self-reported eye symptoms. Small sample size.

(Walker et al., 2019)	CS	Rural Honduras	150 women aged from 25 to 56 years old. 74 using Justa stoves and 76 using traditional stoves.	Household Air Pollution from biomass cookstoves	Eye irritation	Age, BMI, household assets.	Stove type considered separately.	Possible selection bias during study recruitment. Recall bias.	CC: Case-Control study, CS: Cross-sectional, RCT:

Randomized control trial, BMI: Body mass index,

N:Number

The final list of study papers was seven studies which were included in this systematic review. Three study papers were for cataract. One study was for red eye ocular outcome and three studies were for eye irritation. Generally, for most of these studies, fuel type category was mentioned, that is, traditional stove, improved Justa traditional stove as seen in the Honduras study (Walker et al., 2019). Out of the list of eye diseases used in the MeSH terms/ keywords/ search terms, the results after meeting exclusion criteria did not capture dry eye disease or macular degeneration. From the final list of study papers, most studies conducted in India showed cataract as the disease outcome following Household Air Pollution exposure as shown in Table 1. One study conducted in India showed an additional environmental risk factor of sun exposure in addition to Household Air Pollution from indoor kitchen smoke with relation to cataract as the eye disease outcome. We present a summary of the findings of this review below.

Cataract

Three studies showed cataract as the eye disease outcome. These three studies also showed positive association for cataract eye disease outcome following exposure to household air pollution from biomass solid fuel use. This eye disease involves an opacification of the lens of the eye which leads to decrease in vision. Cataracts often develop slowly and can affect one or both eyes. Cataract is highly prevalent in India and the major cause of vision loss ((Ravilla et al., 2016). Though evidence linking biomass fuel use and cataract is limited. The Odds ratio for nuclear cataract following exposure to biomass cooking fuels according to (Ravilla et al., 2016) was 1.28 with 95% confidence interval of (1.10- 1.48) (Table 1). This is a similar finding to (West et al., 2013) reference paper whereby 11 studies suggested an association between biomass fuel use and cataract with relative risk estimates almost greater than 1.0. As for presenile cataract occurrence, fuel exposure greater than 2 hours a day had a higher odds ratio of 8.25 with a p-value of 0.004 which shows a significant association (Das et al., 2019). The studies conducted in India in this review was for both sexes and mainly adjusted for age, sociodemographic status, smoking, diabetes, sun exposure, educational status as possible confounders. Subtypes for cataract included nuclear cataract, presenile cataract and posterior subcapsular cataract. Patients who had complicated, congenital, developmental, traumatic and drug induced cataracts were excluded as seen in (Das et al., 2019) case-control study. (Vashist et al., 2020) cross-sectional study reported an odds ratio of 1.2 with a confidence interval of

(1.0-1.4) for indoor kitchen smoke exposure, sun exposure was an odds ratio of 9.4 with a confidence interval of (7.9-11.2) for nuclear cataract, as it sought to investigate sun exposure and other environmental risk factors such as exposure to indoor kitchen smoke as a risk factor for nuclear cataract (Table 1). Sun exposure was categorized into four quartiles ranging from the lowest duration exposure to the highest duration exposure in (Vashist et al., 2020) cross-sectional study as one of the major potential confounder of biomass fuels and cataract in three geographically different areas in India.

Red eye

One study showed red eye ocular outcome following exposure to household air pollution from biomass solid fuel use. This one study showed a positive association between red eye outcome and the exposure to household air pollution. Red eye is an ocular outcome commonly resulting from smoke/household air pollution whereby the white appearance of the eyes turns red in color and often is accompanied with tears. (Li et al., 2016) cross sectional study conducted in Peru with 334 women as study participants, reported an adjusted higher odds ratio of 3.80 [1.32- 10.9] 95% confidence interval, of experiencing red eyes resulting from indoor wood stove exposure. This study adjusted for woman age, stove type, CO, wood type, second-hand smoke, home-to-road distance, pesticide use, fertilizer use, enclosed kitchen, grilled food and Creatinine level in urine sample to assess exposure to Household Air Pollution.

Eye irritation

Three studies showed eye irritation outcome. Two studies showed a positive association between eye irritation outcome following exposure to household air pollution. Eye irritation is a general term used to describe the feeling when something is bothering your eyes or the surrounding area and causing discomfort. (Sukhsohale et al., 2013) cross sectional study conducted in India with 760 women aged 15 years and above reported eye irritation as a result of exposure to indoor cooking smoke. The relative risk/odds ratio was not reported. (Aung et al., 2018) case-control study conducted in rural India, with 199 women above 25 years old followed up from the original number of 222 women (i.e. 90% follow-up) reported an odds ratio of 0.48 (0.24- 0.96) 95% confidence interval, in the control group as a result of exposure to solid fuel smoke from traditional stove while adjusting for chimney, room numbers in

household, age, caste, BMI (see Table 1). (Walker et al., 2019) cross sectional study conducted in rural Honduras on 150 women aged from 25 to 56 years old. 74 using Justa stoves and 76 using traditional stoves, reported an odds ratio of 3.23 (1.41-7.40) in the traditional

stove group resulting from exposure to Household Air Pollution from biomass cookstoves (see Table 1) while adjusting for age, BMI and household assets.

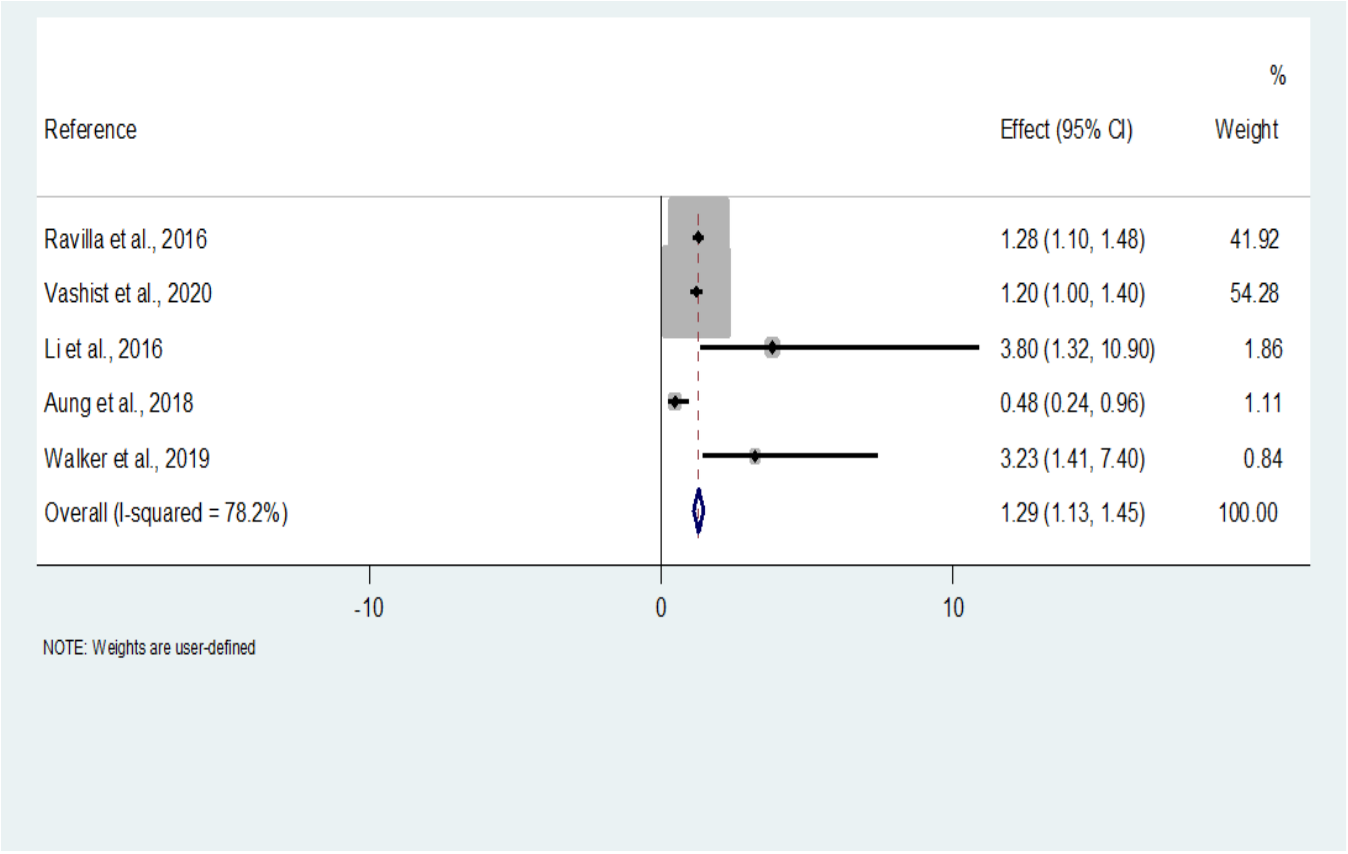
Table 2: Risk of bias analysis using The Critical Appraisal Skills Programme (CASP) checklist.

Study	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12	Score	Classification of quality
Ravilla et al., 2016 (CS)	**Yes**	**Yes**	**Yes**	**No**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**		**10**	**High**
Das et al., 2019 (CC)	**Yes**	**Yes**	**Yes**	**Yes**	**No**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**		**10**	**High**
Vashist et al., 2020 (CS)	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**		**11**	**High**
Li et al., 2016 (CS)	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	**No**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**		**10**	**High**
Sukhsohale et al., 2013 (CS)	**Yes**	**Yes**	**Yes**	**No**	**Yes**	**No**	**Can't tell**	**Yes**	**Yes**	**Yes**	**No**		**7**	**Moderate**
Aung et al., 2018 (CC)	**Yes**	**Yes**	**Yes**	**Yes**	**No**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**		**10**	**High**
Walker et al., 2019 (CS)	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	**No**	**Yes**	**Yes**	**Yes**	**Yes**	**No**		**9**	**High**

CC: Case-Control study, CS: Cross-sectional study, Cohort: Cohort study.

Risk of bias assessment in individual studies was conducted using the Critical Appraisal Skills Program (CASP) checklist(Ma et al., 2020) with focus on case-control studies, cross sectional studies and cohort study in this systematic review paper. Six studies had high quality assessment score and one study had a moderate quality score. This was based on the CASP checklist, comprising of eleven to twelve critical appraisal questions with answer choices such as yes, no and can't tell and the summary is as shown in Table 2. The critical appraisal questions of the CASP checklist are in Supplement 1 of this systematic review paper.

A summary of the results in a forest plot to visualize the odds ratios.



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.  admetan or lower95ci upper95ci , wgt( samplesize ) label(namevar= reference )

Studies included: 5
Participants included: Unknown

Meta-analysis pooling of aggregate data
using the fixed-effect inverse-variance model
and with user-defined weights Sample size
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Reference	Effect	[95% Conf.	Interval]	% Weight
Ravilla et al., 2016	1.280	1.100	1.480	41.92
Vashist et al., 2020	1.200	1.000	1.400	54.28
Li et al., 2016	3.800	1.320	10.900	1.86
Aung et al., 2018	0.480	0.240	0.960	1.11
Walker et al., 2019	3.230	1.410	7.400	0.84
Overall effect	1.291	1.127	1.454	100.00

```
Test of overall effect = 0:  z =  15.477  p = 0.000

Heterogeneity Measures  and on standard inverse-variance weights)
```

	Value	df	p-value
Cochran's Q	18.37	4	0.001
I² (%)	78.2%		
Modified H²	3.593		
tau²	0.1022		

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I² = between-study variance (tau²) as a percentage of total variance
Modified H² = ratio of tau² to typical within-study variance

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Using STATA software, I generated a forest plot to visualize the reported odds ratios in the included studies. Due to inconsistent findings of positive associations between household air pollution and eye disease, we concluded that there is an association.

Discussion:

The biological mechanism of eye diseases and other ocular outcome and exposure to household air pollution is as follows; the ocular surface is composed of the surface and glandular epithelia of the cornea, conjunctiva, lacrimal gland, accessory lacrimal glands, the eyelashes and the nasolacrimal duct. Each of this surface is in contact with air pollution, in this case, household air pollution and this affects human health. Various chemical components present in household air pollution including small particulate matter, may have an irritant effect on the membranes in which a very thin tear film separates the corneal and conjunctival epithelia from the air

pollutants. Dysfunction of any component of the ocular surface system can lead to ocular symptoms through two interrelated mechanisms of abnormality, that is, the hyper-osmolarity and the instability of the lacrimal film. Lacrimal hyper-osmolarity may cause lesions on the epithelial surface by activating a series of inflammatory events on the ocular surface, which leads to production of inflammatory mediators in the lacrimal film. Subsequent damage to the epithelium includes cell death due to apoptosis, loss of goblet cells and disorder of mucin expression, resulting in instability of the lacrimal film. This instability exacerbates the hyper-osmolarity of the eye surface.

In this systematic review paper, cataract was found to have an association with Household Air Pollution as seen in most studies conducted in India. This was mostly because of household biomass fuel use without fitted chimneys in the kitchen area and women were more at risk for cataract following Household Air Pollution exposure (Ravilla et al., 2016)). The well conducted large population-based eye study (Ravilla et al., 2016) conducted in India to investigate use of cooking fuels and cataract is advantageous for cost-benefit analysis and clarification of the contribution of Household Air Pollution to the global burden of cataract (West et al., 2013). Quantification of lens opacity as seen in (Vashist et al., 2020) in relation to the degree of exposure to smoke from solid biomass fuel use was considered and this may provide evidence of exposure-response relationships and the risk of individual cataract subtypes i.e., presenile cataract, cortical cataract and nuclear cataract. One of the strengths of the studies conducted in India was a large sample size as seen in these population-based studies (Vashist et al., 2020) which also added sun exposure in geographically diverse populations of India while investigating nuclear cataract subtype and indoor kitchen smoke exposure.

Red eye condition as seen in the Peru study (Li et al., 2016) was unique in that a cross-sectional study within the framework of a community randomized stove intervention trial was conducted, while investigating for red eye condition (self-reported health symptoms) using Household Air Pollution exposure biomarkers in the non-smoking Peruvian women population. Red eye condition was found to have an association with longer duration to smoke from indoor wood stove exposure. The biomarker of exposure used was creatinine level in urine sample to assess exposure to Household Air Pollution (Li et al., 2016).

Eye irritation symptom was reported in three studies and the biomass cook stove type was considered separately as seen in (Walker et al., 2019) in rural Honduras whereby Household Air Pollution had a positive association with eye irritation. This was also seen in (Aung et al.,

2018) study in India whereby traditional stoves using solid fuel had a positive association between Household Air Pollution and eye irritation symptoms; this study showed discrepant result mainly due to study bias and population specificity. Since there was no prospective study in this systematic review, study bias such as recall bias in study participants may have occurred and this is the reason for discrepant results.

In this systematic review paper, indoor air pollution at the household level was the main inclusion criteria of the selected studies, thus eye diseases and other ocular symptoms resulting from air pollution outside the household setting such as in industrial areas were excluded. Household Air Pollution showed a positive association with cataract, red eye and eye irritation in the household setting especially as a result of solid fuel use/biomass in traditional cooking stoves.

How I interpret the results of this systematic review, is that, cataract shows positive association with household air pollution resulting from solid fuel use as compared to eye irritation and red eye condition. This is especially seen in the forest plot which showed positive association. This is a similar finding to the (West et al., 2013) reference paper study which found out that cataract had positive association following exposure to biomass solid fuel use. Following this result, replacing biomass solid fuel use with clean energy should be considered, so as to eliminate household air pollution.

The strength of this updated systematic review is that, an additional risk of bias analysis was done using the Critical Appraisal Skills Program (CASP) checklist. Also, this paper included most recent studies studying the association between household air pollution and the risk of eye diseases. The limitation of this study paper is that, there is still limited evidence of eye diseases resulting from household air pollution as a result of solid fuel use and appropriate investigations are still needed using better study design such as prospective studies. There was no prospective study in this review and cross-sectional studies captured in this review had an element of recall bias thus the quality of such studies is not that high.

Conclusion:

There is limited evidence, however, Household Air Pollution resulting from solid fuel use showed a positive association with cataract, red eye and eye irritation although strongest association was with cataract. The wide spread use of solid fuel results in Household Air

Pollution especially in traditional stoves mostly used by women in rural areas of developing countries. Appropriate investigations are needed to investigate the plausibility of the association between Household Air Pollution and eye diseases resulting from widespread use of solid fuels for cooking using better study designs such as prospective studies.

As for policy implications, replacing biomass solid fuel use to clean energy should be considered with the aim of reducing household air pollution. Given the current situation, I recommend altering traditional cooking stoves to efficient cooking stoves.

Conflicts of Interest:

The authors of this paper declare no conflict of interest.

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Supplement 1:

Critical Appraisal Skills Program (CASP) checklist with focus on case-control studies, cross sectional studies and cohort study in this systematic review paper with the following items as shown below:

CASP checklist: 12 questions to help you make sense of a Cohort study

1. Did the study address a clearly focused issue?

2. Was the cohort recruited in an acceptable way?

3. Was the exposure accurately measured to minimize bias?

4. Was the outcome accurately measured to minimize bias?

5. Have the authors identified all important confounding factors in the design and/or analysis? Have they taken account of the confounding factors in the design and/or analysis?

6. Was the follow-up of subjects complete enough? Was the follow-up of subjects long enough?

7. What are the results of this study?

8. How precise are the results?

9. Do you believe the results?

10. Can the results be applied to the local population?

11. Do the results of this study fit with other available evidence?

12. What are the implications of this study for practice?

CASP checklist: 11 questions to help you make sense of a Case-control study

1. Did the study address a clearly focused issue?

2. Did the authors use an appropriate method to answer their question?

3. Were the cases recruited in an acceptable way?

4. Were the controls selected in an acceptable way?

5. Was the exposure accurately measured to minimize bias?

6. Aside from the experimental intervention, were the groups treated equally? Have the authors taken account of the potential confounding factors in the design and/or in their analysis?

7. How large was the treatment effect?

8. How precise was the estimate of the treatment effect?

9. Do you believe the results?

10. Can the results be applied to the local population?

11. Do the results of this study fit with other available evidence?

CASP checklist: 11 questions to help you make sense of descriptive/cross-sectional studies

1. Did the study address a clearly focused issue?

2. Did the authors use an appropriate method to answer their question?

3. Were the subjects recruited in an acceptable way?

4. Were the measures accurately measured to reduce bias?

5. Were the data collected in a way that addressed the research issue?

6. Did the study have enough participants to minimize the play of chance?

7. How are the results presented and what is the main result?

8. Was the data analysis sufficiently rigorous?

9. Is there a clear statement of findings?

10. Can the results be applied to the local population?

11. How valuable is the research?