# **BMJ Open**

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<u>http://bmjopen.bmj.com</u>).

If you have any questions on BMJ Open's open peer review process please email <u>editorial.bmjopen@bmj.com</u>

BMJ Open

# **BMJ Open**

# **Coronary Heart Disease, Hypertension and Use of Biomass Fuel among Women: Comparative Cross-sectional Study.**

Journal:	BMJ Open
Manuscript ID	bmjopen-2019-030881
Article Type:	Research
Date Submitted by the Author:	04-Apr-2019
Complete List of Authors:	Fatmi, Zafar; Aga Khan University, Department of Community Health Sciences Ntani, G; University of Southampton and Southampton University Hospitals NHS Trust, MRC Lifecourse Epidemiology Unit Coggon, David; University of Southampton, MRC Lifecourse Epidemiology Unit
Keywords:	Coronary heart disease < CARDIOLOGY, biomass fuel, Hypertension < CARDIOLOGY, women



# **Coronary Heart Disease, Hypertension and Use of Biomass Fuel among Women: Comparative Cross-sectional Study.**

# Zafar Fatmi,<sup>1,2</sup> Georgia Ntani,<sup>2</sup> David Coggon<sup>2</sup>

<sup>1</sup>Department of Community Health Sciences, Aga Khan University, PO Box 3500, Karachi 74800, Pakistan.

<sup>2</sup>MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK.

\*Correspondence should be addressed to Zafar Fatmi; zafar.fatmi@aku.edu;

# Abstract

*Objectives:* To explore the associations of coronary heart disease (CHD) and hypertension with use of biomass fuel for cooking.

Design: Comparative cross-sectional study.

Setting: Rural villages in Sindh, Pakistan.

*Participants:* Women aged  $\geq$ 40 years who had used biomass fuel for cooking for at least the past year (n = 436), and a comparison group (n=414) who had cooked only with non-biomass fuel over the same period were recruited through door-to-door visits. None of those who were invited to take part declined.

**Primary and secondary outcome measures:** CHD was assessed by three measures: history of angina (Rose angina questionnaire), previous history of 'heart attack', and definite or probable changes of CHD on electrocardiogram (ECG). Hypertension was determined from blood pressure measurements and use of medication. Potentially confounding risk factors were ascertained by questionnaire and anthropometry. Associations of CHD and hypertension with use of biomass and other risk factors were assessed by logistic regression, and summarised by odds ratios (ORs) with 95% confidence intervals (CIs).

**Results:** After adjustment for potential confounders, there was no association of angina (OR: 1.0, 95% CI 0.8-1.4), heart attack (OR: 1.2, 95% 0.7 - 2.2), ECG changes of CHD (OR: 0.8, 95% CI 0.6 - 1.2) or hypertension (OR: 1.0, 95% CI 0.8 - 1.4) with current use of biomass for cooking. Nor were any associations apparent when analyses were restricted to long-term ( $\geq$ 10 years) users and non-users of biomass fuel.

*Conclusions:* A linked air monitoring study indicated substantially higher airborne concentrations of fine particulate matter in kitchens where biomass was used for cooking. It is possible that associations with CHD and hypertension were missed because most of the comparison group had used biomass for cooking at some time in the past, and risk remains elevated for many years after last exposure.

# Strengths and limitations of this study:

• The study was well-powered with a high response rate from those invited to take part, and large contrasts in recent exposure to indoor air pollution.

- Comparisons were based on recent cooking practices, but some exposures may have changed since the onset of CHD.
- Many women who did not currently use biomass for cooking, had done so in the past, and this may have obscured associations with health outcomes if effects of exposure persist long-term.
- Errors may have occurred in the assessment of outcome measures, biasing risk estimates towards the null.
- Recall of some potentially confounding factors may have been inaccurate, leading to uncontrolled residual confounding.

# **Funding Statement**

This research was supported by a fellowship from the Colt Foundation for the conduct of a PhD by Professor Zafar Fatmi. Professor David Coggon and Dr Georgia Ntani were supported by funding from the UK Medical Research Council (MRC\_MC\_UU\_12011/5).

# **Conflicts of Interest**

The authors declare that there is no conflict of interest regarding the publication of this paper.

# Authors' contributions

ZF led the design and conduct of the study, carried out the initial statistical analyses, and wrote the first draft of the manuscript.

GN oversaw and guided the statistical analysis.

DC supervised the project and amended the first draft of the manuscript.

All authors approved the final version of the manuscript.

# Introduction

Much of the world's population still uses biomass fuel (wood, cow-dung, crop residues etc.) in open fires or simple stoves for domestic cooking and heating [1,2]. The household air pollution (HAP) which this generates is a major cause of respiratory infections among children [3-5], chronic obstructive pulmonary disease [6-7] and lung cancer [8-10]. In addition, several studies have suggested a hazard of coronary heart disease (CHD), but evidence for this is more limited [11].

We, therefore, carried out a cross-sectional survey to explore the association between CHD and cooking with biomass in a sample of women drawn from the general population in rural areas of Pakistan. The objective of the study was to compare the prevalence of angina, previous history of heart attack, electrocardiographic (ECG) changes indicative of CHD, and hypertension in women  $\geq$ 40 years of age who used biomass fuel for cooking with that in women of similar age who cooked using other types of fuel.

# Materials and Methods

# Study Setting

The survey was conducted during January to September 2015 in villages surrounding the main urban area of Nawabshah district (recently renamed as Shaheed Benazirabad) in the province of Sindh, Pakistan. These were selected to give a mix in the fuels used for cooking within the study sample. Some of the villages had been supplied with natural gas for at least 10 years, whereas in others biomass fuel (wood and/or cow dung) was still being used.

# Recruitment of households and subjects

Within each village, trained field workers made door-to-door visits, and asked the heads of households whether their families would be willing to assist with the study, and if so, what type of fuel was used for cooking, and whether food preparation was regularly undertaken by a woman  $\geq$ 40 years of age. In this way, the study team identified quotas of the required numbers of households in each of the two categories of fuel use (biomass and other). The heads of these households were then asked to complete a consent form, and to identify and introduce the woman of the household aged  $\geq$ 40 years who had carried out the most cooking in the house over the past 10 years. The study was explained to her, and she was invited to participate and to give signed consent.

# Inclusion criteria

Women aged 40 years or older were eligible for inclusion if they gave informed consent, and had been cooking in the household for at least the past year, using only one of biomass fuel or non-biomass fuel (natural gas).

# Questionnaire, examination and measurements

A standardized questionnaire was used to collect information at interview about: demographic and socio-economic characteristics, birth weight, smoking history, whether another member of the household was a regular smoker, relevant aspects of diet, physical activity, lifetime history of cooking using different types of fuel, any previous diagnosis of a "heart attack" by a doctor, symptoms of angina (through the Rose angina questionnaire [12]), and any current use of medication for hypertension. In addition, measurements were made of height, weight, waist circumference, hip circumference and blood pressure.

Socioeconomic status was characterized by the literacy of the participant (no vs. any literacy), the type of employment of her father during her childhood (manual or non-manual), the ownership and construction of her house ('pucca' i.e. made of concrete walls and roof or 'katcha/semi-pucca' i.e. made fully or partially of thatched walls and roof), the income level of the household, and the number of household assets owned from a list of seven. Birth weight was determined from participants' recall as being 'higher than normal vs. normal vs. lower than normal'.

The questions on smoking covered use of cigarettes, *bidi* (locally made cigarettes without filters) or a huqqa (pipe) regularly (at least once a week for a month or longer). The number of other people in the household who smoked provided a measure of domestic exposure to environmental tobacco smoke (ETS), which was classified according to whether at least one other household member smoked cigarettes, bidi, or a huqqa in the home.

Dietary questions covered the use of oil or ghee for cooking and eating, and weekly consumption of meat and eggs. The former was categorized to three levels: only or mostly use oil; mixed use of oil and ghee; only or mostly use ghee. Frequencies of consuming meat and eggs were each categorized to two levels: at least once per week vs. less than once per week.

Level of physical activity was assessed through questions on the frequency per week of shopping, fetching water, washing clothes, collecting wood for cooking, agricultural work on a farm and any other regular heavy physical work. Each of these activities was categorized to two levels: zero days per week or at least once per week. A composite physical activity score was then derived as the number of activities carried out at least once per week, with values ranging from 0 to 6.

Height, weight, and waist and hip circumference were measured using a stadiometer, digital weighing scale and measuring tape, following standardized methods. Body mass index (BMI) (weight in kilograms per squared height in meters) and waist-to-hip ratio (WHR) were then calculated from the measurements. BMIs  $\geq$ 25kg/m<sup>2</sup> were considered abnormally high (overweight or obese), as were WHRs  $\geq$ 0.85.

#### Categories of exposure to biomass:

Use of biomass was classed to two main categories; biomass users who currently used firewood and/or cow dung for cooking; and non-users of biomass who did not (other sorts of biomass for example coal were not used for cooking in the community studied).

In addition, two subsets of these main categories were distinguished: long-term biomass users who currently used firewood and/or cow dung for cooking <u>and</u> had done so for at least the past 10 years; and long-term non-users of biomass who currently did not use either firewood or cow dung for cooking <u>and</u> had not done so for at least10 years.

#### *Outcome measures:*

Four outcome measures were specified.

Hypertension: Three measurements of blood pressure were made at five-minute intervals, using an Omron upper arm blood pressure monitor, and mean values for systolic and diastolic blood pressure were derived. Women were deemed to have hypertension if they met at least one of three criteria: mean systolic blood pressure  $\geq$ 140 mm Hg; mean diastolic blood pressure  $\geq$ 90 mm Hg; regular use of medication for blood pressure.

Angina: Experience of angina was assessed through the WHO's Rose angina questionnaire [12], which comprises seven questions relating to chest pain, its anatomical distribution, precipitating and relieving factors, and duration. A diagnosis of angina required report of pain, pressure or discomfort

in the chest centrally, or in both the left anterior chest and left arm, that occurred when walking uphill or hurrying, that caused the participant to stop or slow down when it occurred while walking, and that was then relieved within 10 minutes by standing still.

Heart attack: Previous diagnosis of "heart attack" by a doctor was ascertained through a single question: "In the past, have you ever been told by a health care provider that you had a 'heart attack'?"

Definite or probable CHD on ECG: A 12-lead ECG was recorded according to a standard protocol, and coded for the presence of definite or probable CHD, using the Minnesota Code Manual of Electrocardiographic Findings, second edition [13]. This corresponded to the presence of any of codes 1-1 to 1-3, 3-1, 4-1 to 4-4, 5-1 to 5-3, 7-1-1 and 9-2. In order to check the repeatability of the coding, two of us (ZF and DC) coded all of the ECGs independently. We used the same scanned ECG traces, without information about the type of cooking fuel used by the participant. Levels of agreement between the observers were assessed, using kappa statistics. Where differences occurred in the classification of an ECG trace, they were then resolved by discussion between the two observers.

#### Statistical analysis

Data were double-entered in Epidata 3.1 software [14] for validation. All discrepancies were corrected by reference to the original questionnaire or record sheet. Statistical analysis was carried out with Stata version 12.0 [15].

As a first step, several variables were reclassified or combined, based on their distribution in the full study sample, and without knowledge of participants' use of biomass fuel. Thus, a combined index was derived for frequency of consuming meat and eggs with three levels: neither meat nor eggs as much as once per week; one of meat or eggs at least once per week; both meat and eggs at least once per week. Scores for physical activity were categorized into three levels: low (0-1 activities); medium (2-3); high (4 or more). Similarly, BMI and WHR were combined as a single variable with three categories: neither BMI nor WHR high; one of BMI or WHR high; both BMI and WHR high.

Descriptive statistics were produced for women in each of the four categories of exposure to biomass, summarizing their demographic and socioeconomic characteristics, current and past cooking arrangements, types and durations of fuel use, hours of cooking per day, types of stove and kitchen, and exposures to potentially confounding risk factors. The prevalence of the main outcomes was determined for the study sample overall, and the relationship of ECG changes to angina and history of heart attack was explored.

Logistic regression analysis was then used to assess the association of each of the four outcome variables with use of biomass fuel for cooking and other possible risk factors. First, associations with each potential risk factor were determined after adjustment for age. The main exposure of interest (user or non-user of biomass) was then carried forward into a mutually adjusted model along with all other risk factors which showed associations ( $p \le 0.1$ ) when examined individually. In addition, a second mutually adjusted model was fitted that compared long-term use and non-use of biomass for cooking.

#### Sample size

The size of the study sample was determined by a power calculation which assumed an outcome prevalence of at least 6% for definite CHD among non-users of biomass fuel, based on a previous study in Pakistan [16] (the prevalence of other outcomes was expected to be higher). This indicated that we would require at least 876 women (438 users and 438 non-users of biomass) for 80% power to detect an odds ratio of 2.0 for the use of biomass fuel with a 5% level of statistical significance.

# Ethical approval

The study was approved by Ethics Review Committee of Aga Khan University, Karachi, Pakistan.

# Results

A total of 24 villages were visited in order to recruit the number of households required for the survey. In 14 villages all households used biomass for cooking, in three, all used natural gas, and in the other seven, both types of fuel were used. The number of participating households per village ranged from as few as three to as many as 210. Interviews were completed with women from a total of 1073 households, 536 of which currently used biomass fuel, and 537 natural gas. No-one declined to participate in the study, but 77 women could not be interviewed because they were not at home at the time when the survey team visited (mostly because they were engaged in agricultural work).

Among the 1073 women who completed interviews, 44 indicated that they were in fact aged less than 40 years of age, and were therefore excluded from the analysis. An additional 151 women had not made meals regularly (at least one meal per day on most days of the week) during the past year, and were also excluded. We further excluded 28 women who did not currently use firewood or cow dung for cooking, but whose time since last use of biomass was <2 years (this was done to ensure distinct exposure categories). Thus, further analysis was based on 850 women: 436 users and 414 non-users of biomass. Among them, 430 were long-term biomass users, and 263 were long-term non-users.

Table 1 summarizes the demographic and socioeconomic characteristics of the participants in the study sample overall, and according to categories of exposure to biomass fuel. In comparison with users of biomass, non-users were marginally younger (63% versus 60% <50 years), and somewhat more advantaged socioeconomically.

Table 2 describes the current and past cooking arrangements of participants, including type and duration of fuel use, intensity of cooking, and type of stove and kitchen. Even among the long-term non-users of biomass, 88% had cooked with biomass fuels at some time in their life. Among the biomass users, the large majority had used wood (93%) and cow dung (88%) for longer than 20 years. Few participants (3.7% of biomass users and 6.3% of non-users) had ever used kerosene as a cooking fuel. Most participants (approximately 60%) currently cooked for 2-3 hours per day, the average duration of cooking per day being similar in users and non-users of biomass. Where biomass was used for cooking, it was also more likely to be used to heat the home.

Table 3 shows the distribution of potentially confounding risk factors for CHD in the four categories of exposure to biomass. In comparison with non-users of biomass, slightly higher proportions of women using biomass reported having been born with 'lower than normal' birth weight, having lost weight at some time during childhood, ever having smoked, and being exposed to environmental tobacco smoke in the home.

#### Prevalence of outcome measures

Supplementary Table 1 shows the prevalence of the main outcome measures that were investigated. In total, 297 women (35%) were classed as having hypertension, two thirds of whom were taking regular medication for blood pressure. About 27% had symptoms indicative of angina based on Rose's questionnaire. Fifty-four (6.4%) reported a previous history of heart attack, and 19% of women had findings of definite or probable CHD on ECG.

# Validity of ECG classification and interrelationships of outcome measures:

Supplementary Table 2 compares the classification of ECGs by the two observers. Satisfactory ECG traces were obtained for 841 (98.9%) of the participants, but four were missing from the file used to assess inter-observer agreement, and were later assessed jointly by the two observers. The overall agreement between the two observers was 85.2% (kappa = 0.57). Most disagreements were related to

cases in which the exceedance of a threshold in, for example, ST elevation, ST depression or the width (duration) of a Q wave was borderline. In some cases, it was questionable whether there was a small R wave or a QS pattern. Also, there was some disagreement about whether T waves were negative or flat. Following discussion between the two observers, all of the discrepancies were reconciled, and it was finally agreed that 181 women (21.5%) showed changes indicative of definite or probable CHD. However, in 22 of these cases, it appeared that the abnormality had occurred only because the ECG leads had been placed incorrectly, and those traces were reclassified as normal. Thus in further analyses, 159 (19%) of women were considered to have definite or probable CHD on ECG.

Supplementary Table 3 shows the prevalence of definite or probable CHD on ECG according to symptoms of angina and history of heart attack. It was somewhat more frequent in participants who reported an earlier heart attack (26%) than in those who did not and had no symptoms of angina (18%). However, there was no association with angina in the absence of heart attack.

#### Association of outcome measures with use of biomass and other risk factors

Associations of hypertension and the three CHD outcomes (angina, heart attack and definite or probable CHD on ECG) with potential risk factors are presented in Supplementary Tables 4 to 7, from which the risk estimates for use of biomass fuel for cooking are summarized in Table 4. The first column of each table gives odds ratios adjusted only for age, while the second column presents mutually adjusted risk estimates from a single model that included use of biomass and all of the risk factors that showed associations ( $p \le 0.1$ ) in the analyses adjusted only for age. The last column shows findings from a similar analysis but restricted to women who were long-term users or non-users of biomass.

In analyses that adjusted only for age, hypertension was associated ( $p \le 0.1$ ) with older age, a higher number of household assets, higher frequency of consuming meat and eggs, and having a high BMI or WHR (Supplementary Table 4). When these variables were carried forward to the mutually adjusted analysis, the association with consumption of meat and eggs was diminished, but the others remained. Thus, the risk of hypertension increased 40% with every 10-year increase in age, was 2.3 times higher in women with  $\ge 4$  household assets than in those with 0 or 1, and was increased 1.9-fold in women who had both high BMI and high WHR as compared with those in whom neither BMI nor WHR were elevated. However, hypertension was not associated with use of biomass (OR 1.0 in the fully adjusted model). When analysis was restricted to long-term users and non-users of biomass, results were similar, with an OR of 1.1 for long-term use of biomass.

In analyses that adjusted only for age, the odds of angina increased with age and regular smoking, and were significantly lower with more frequent consumption of meat and eggs (Supplementary Table 5). Moreover, this pattern was maintained when risk estimates were mutually adjusted. Thus, the odds of angina increased by 30% per 10-year increase in age, and with ever having smoked regularly (OR 2.0, 95%CI 1.2-3.2), and were significantly lower in women who ate both meat and eggs at least once per week (OR 0.5, 95%CI 0.3-0.7). There was, however, no association with use of biomass (OR 1.0, 95%CI 0.8-1.4). When analysis was restricted to long-term users and non-users of biomass, results were similar except that there was a suggestion of a weak association with exposure to biomass (OR 1.3, 95%CI 0.9-1.9).

In corresponding analyses with previous history of heart attack (diagnosed by a physician) as an outcome, initial models with adjustment only for age indicated associations (p<0.1) with age, higher household income, higher number of household assets, and high BMI or WHR (Supplementary Table 6). After mutual adjustment, age remained a significant risk factor (OR 1.5, 95%CI 1.2-2.0, for each 10-year increase in age). However, the other associations, although still positive, were not significant at a 5% level. Nor was there an association with use of biomass for cooking (OR 1.2, 95%CI 0.7-2.2). In the mutually adjusted model for long-term use of biomass, results were very similar.

In analyses adjusted only for age, household income was the only variable significantly associated with definite or probable CHD on ECG, and it remained significant in the fully adjusted model (OR 1.6, 95%CI 1.1-2.4 for household income >10,000PKR) (Supplementary Table 7). However, there was no association with use of biomass for cooking, either overall or in the long-term (ORs 0.8 and 0.9).

#### Discussion

This study found no association between use of biomass fuel and any of the four outcomes studied (angina, previous history of heart attack, definite or probable CHD on ECG and hypertension), even when comparison was with women who had not used biomass for at least the last 10 years. The strongest hint of an association was for angina in long-term users as compared with long-term non-users of biomass, but the elevation of risk was small (30%) and not statistically significant at a 5% level.

The choice of villages from which to recruit participants ensured a balance in the fuels currently used for cooking, and cooperation in the survey was good with high response rates from the households and women that were invited to take part. Inevitably, recruitment was to some extent opportunistic and limited to one province of Pakistan. However, there seems no reason to expect that the study sample would have been seriously unrepresentative in the associations of hypertension and CHD with use of biomass and other risk factors.

A linked air monitoring study found that in the kitchens of houses using biomass for cooking, the mean 24-hour average  $PM_{2.5}$  concentrations was 531 µg/m<sup>3</sup>, with a median of 136 µg/m<sup>3</sup> and interquartile range 34-615 µg/m<sup>3</sup> (paper in preparation). Corresponding concentrations in houses not using biomass for cooking were 69.9, 24.2, and 13.5-53.3 µg/m<sup>3</sup>. Thus, while individual exposures may have been influenced also by time spent cooking and whether biomass was burned in a closed or open kitchen, the absence of associations with CHD and hypertension is unlikely to reflect inadequate contrasts in recent intensity of exposure.

Our aim was as far as possible to recruit households that had used the same fuel for cooking exclusively for at least 10 years. Villages were selected with this criterion in mind, and it was covered in preliminary inquiries that were addressed to local community representatives. In practice, however, it turned out that where natural gas was available in villages, some participants had not yet switched to cleaner fuel, or had done so at a later date than others. A pragmatic decision was therefore made to include women even if they had changed their cooking fuel within the past 10 years, provided that they had used their current fuel for at least a year. This seemed reasonable since trials had suggested that interventions to reduce household air pollution from use of biomass for cooking can produce reductions in blood pressure and changes in ECGs over the short to medium term [17-19]. However, to check that it did not obscure associations, additional analyses were carried out with restriction to long-term users and non-users of biomass, and still no relationship was found with the health outcomes.

The sample size achieved for the study was close to that planned, and the prevalence of the four outcomes was higher than had been assumed in the power calculations. Moreover, the upper confidence limits for the odds ratios relating to use of biomass were almost all <2. Thus, the absence of associations with biomass does not reflect a lack of statistical power.

Ascertainment of current use of biomass is likely to have been highly accurate, and while there may have been some errors in recall of the times when biomass had been used in the past, it is difficult to conceive that any resultant misclassification would have obscured important associations with CHD. Generally, switches in the use of fuel were only in one direction – towards cleaner natural gas from biomass. The timing of changes was usually well recalled because in most instances the entire village

received the new source of fuel in a particular year. However, the duration of using cow dung and firewood may not always have been remembered reliably, and switches between these types of fuel could also have occurred. Many women reported using cow dung and firewood for the same duration, and no attempt was made to analyse them separately.

Recall of some potentially confounding exposures may also have been inaccurate – particularly those pertaining to childhood. If so, the errors would be expected to be non-differential with respect to CHD, and therefore to bias risk estimates towards the null, possibly leading to uncontrolled residual confounding. However, the assessment of BMI and WHR used standardized methods, and should have been reasonably reliable. The interviewers were trained in how to make the measurements, and their technique was piloted in the field before the start of data collection.

A greater concern is the possibility of error in the ascertainment of outcomes. Blood pressure was objectively measured according to a standardized protocol, and was taken as the average of three readings. Moreover, most of the women who were classed as having hypertension were taking treatment for the disorder, which supports the validity of its assessment. Angina was determined through the well-established Rose questionnaire, but it is possible that symptoms in some cases arose from other pathology. Previous research has suggested that the Rose angina questionnaire may not be as reliable among women as in men [20]. Although the question to participants about history of heart attack referred specifically to diagnoses that had been given by a health professional, errors could have occurred in interpretation of the term "heart attack" (e.g. to include symptoms from dysrhythmias and acute heart failure as well as myocardial infarction). However, ascertainment of heart attack had been previously carried out by the same method in a similar population, where it was found to be reasonably accurate [21].

The diagnosis of CHD from ECGs showed only a weak relationship to history of medically diagnosed heart attack, and none at all to symptoms of angina (Supplementary Table 3). Between observer agreement in the classification of ECGs was reasonably good (kappa = 0.57) (Supplementary Table 2), but it is notable that unlike angina and history of heart attack, CHD diagnosed from ECGs did not show the expected association with age (Supplementary Table 7).

To the extent that errors did occur in the ascertainment of outcomes, they are unlikely to have differed systematically in relation to use of biomass, and therefore would be expected to tend to obscure any true associations.

Because the study had a cross-sectional design, consideration must be given to the possibility of reverse causation. For risk factors related to childhood (e.g. birthweight, father's occupation and education), this is less of a concern. However, it is plausible that characteristics such as diet, physical activity and time spent cooking could have changed as a consequence of CHD. Depending on the circumstances, this might bias associations either upwards or downwards.

Another limitation of the study was that it did not determine when past heart attacks had occurred. Even if not as a consequence of an earlier heart attack, some of the exposures studied (e.g. BMI and WHR) may have changed in the interval since such an attack occurred. If so, this might obscure true associations.

A further possible source of error was uncontrolled residual confounding. To minimize this problem, information was collected about a range of potentially confounding variables, and as in most studies of biomass fuel, socio-economic status tended to be higher in women using cleaner fuels [22]. Although several socio-economic indicators were evaluated as possible factors for adjustment, residual confounding could still have occurred. To explain the absence of associations with biomass, such confounding would have to be inverse (i.e. the under-ascertained confounder would have to be less prevalent in women who used biomass than in non-users).

The study found expected associations with several established risk factors for CHD. Thus, the odds of hypertension, angina and previous history of heart attack were all higher with older age (by 30-50% for every 10 year increase), although this was not found for definite or probable CHD on ECG. The relationship of CHD to age is well documented in the literature [23], and in women, the incidence of CHD increases rapidly after the menopause, reaching up to three times that in premenopausal women [24].

Two of the outcome measures – hypertension and previous history of heart attack – were significantly associated with affluence as measured by number of household assets. This relationship has also been observed before. In a population-based study in Pakistan, history of 'angina or heart attack' was estimated to have 3-fold higher prevalence among affluent participants than in those who were poor [25]. The direction of the association, which is the inverse of that observed in western populations, accords with a higher prevalence of diabetes, hypertension and dyslipidaemias in more educated and affluent groups, which was found in a recent study conducted in South Asian countries, including Pakistan [26].

In further support of an effect of affluence, we found that high BMI and/or WHR was associated with greater risk of hypertension, and (non-significantly) with history of heart attack. Obesity has been shown to increase the risk of hypertension in several studies [27, 28], and partly through this mechanism, also increases the risk and progression of CHD [29]. The INTERHEART study suggested that WHR (abdominal obesity) is a better marker of risk for CHD than BMI [30], but the two were correlated in our study sample, and we opted to use a combined measure.

In contrast, we found that more frequent consumption of meat and eggs was associated with reduced risk of angina. This was unexpected given the known relationship of CHD to consumption of saturated fat [31], and may have been a chance finding. It did not extend to the other outcomes investigated. However, a recent large review suggests that the relationship may be inconsistent [32].

Smoking has consistently been found to increase the risk of CHD in many studies [33]. However, in our investigation it was associated only with angina. This might be because intensity of tobacco use among female smokers in Pakistani population is low [34].

Despite the finding of several expected associations, the failure to demonstrate more consistent relationships to known risk factors is a further indication for caution in the interpretation of our results.

Several earlier studies have indicated links between use of biomass for cooking and CHD, although the finding has not been entirely consistent [11]. As already discussed, one explanation for our failure to demonstrate such associations in the current study could be inaccuracies in the diagnosis of CHD. Another possibility, however, is that adverse effects of exposure to pollutants from the use of biomass persist many years after last exposure. In this survey, even among women who had not used biomass during the last 10 years, most had done so earlier, and often for a long time. Only a few participants (about 3.5% overall) had never used biomass, which was too few for meaningful risk estimates. While it would be possible to compare rural users of biomass with lifelong users of cleaner fuels in urban settings, interpretation would be complicated by other important differences between those living in rural and urban areas.

# Conclusions

This study evaluated the association of hypertension and three measures of CHD – angina, previous history of heart attack and definite or probable CHD on ECG - with use of biomass for cooking. We found no clear associations with any of the health outcomes. However, the weak relationship of ECG abnormalities to the other two measures of CHD, and the inconsistency of their associations with well-established risk factors, suggest that this could have been because of diagnostic misclassification. Alternatively, it could be that an effect was missed because most of the women who were not

currently using biomass for cooking had used it in the past, and risk remains elevated for many years after last exposure.

#### **Data Availability**

The data [stata.dta format] underpinning the findings of this study are available from the corresponding author upon reasonable request.

#### Acknowledgments

This study reported in this paper formed part of a PhD project carried out by Dr Zafar Fatmi under the supervision of Professor David Coggon at the University of Southampton.

Mr Syed Nayab Ali Shah coordinated the data collection. Ms Shereen Jamali, Ms Fozia Jamali, Ms Iqra Memon and Ms Sana Memon administered the questionnaires at interview and recorded the ECGs. We are grateful also to Professor Keith Palmer and Professor M. Masood Kadir for their advice on various aspects of the study.

# References

- Bonjour S, Adair-Rohani H, Wolf J, Bruce NG, Mehta S, Prüss-Ustün A, Lahiff M, Rehfuess 1. EA, Mishra V, Smith KR. Solid fuel use for household cooking: country and regional estimates for 1980-2010. Environ Health Perspect. 2013;121:784-90.
- World Health Organization. Household air pollution and health. Geneva, Switzerland. (Accessed 2. on 4 April 2018). http://www.who.int/mediacentre/factsheets/fs292/en/
- 3. Smith KR, Samet JM, Romieu I, Bruce N. Indoor air pollution in developing countries and acute lower respiratory infections in children. Thorax. 2000 Jun;55(6):518-32.
- 4. Smith KR. Mehta S. Maeusezahl-Feuz M. Indoor air pollution from household use of solid fuels: comparative quantification of health risks. In: Ezzati MLA, Rodgers A, Murray CJL, editors. Global and regional burden of disease attributable to selected major risk factors. Geneva, Switzerland: World Health Organization; 2004. pp. 1435–1493.
- Torres-Duque C, Maldonado D, Pérez-Padilla R, Ezzati M, Viegi G; Forum of International 5. Respiratory Studies (FIRS) Task Force on Health Effects of Biomass Exposure. Biomass fuels and respiratory diseases: a review of the evidence. Proc Am Thorac Soc. 2008 Jul 15;5(5):577-90.
- Liu Y, Lee K, Perez-Padilla R, Hudson NL, Mannino DM. Outdoor and indoor air pollution and 6. COPD-related diseases in high- and low-income countries. Int J Tuberc Lung Dis. 2008;12(2):115-27.
- Kurmi OP, Semple S, Simkhada P, Smith WC, Ayres JG. COPD and chronic bronchitis risk of 7. indoor air pollution from solid feul: a systematic review and meta-analysis. Thorax. 2010; 65(3):221-8.
- 8. Liu Q, Sasco AJ, Riboli E et al. Indoor air pollution and lung cancer in Guangzhou, People's Republic of China. Am. J. Epidemiol. 1993; 137: 145-54.
- Kleinerman R, Wang Z, Lubin J, Zhang S, Metayer C, Brenner A. Lung cancer and indoor air 9. pollution in rural china. Ann Epidemiol. 2000;10(7):469.
- 10. Behera D, Balamugesh T. Indoor air pollution as a risk factor for lung cancer in women. J Assoc Physicians India. 2005; 53:190-2.
- 11. Fatmi Z, Coggon D. Coronary heart disease and household air pollution from use of solid fuel: a systematic review. Br Med Bull. 2016 Jun;118(1):91-109.
- 12. Rose G, McCartney P, Reid DD. Self-administration of a questionnaire on chest pain and intermittent claudication. Br J Prev Soc Med. 1977; 31:42-48.
- 13. Prineas RJ, Crow RS, Zhang Z-h. The Minnesota code manual of electrocardiographic findings. 2<sup>nd</sup> Edition. London. Springer London; 2010.
- 14. Christiansen TB and Lauritsen JM. (Ed.) EpiData Comprehensive Data Management and Basic Statistical Analysis System. Odense Denmark, EpiData Association, 2010-. http://www.epidata.dk
- 15. Stata Corp LP 2012, Stata Statistical Software: Release 12.0, College Station TX, USA.
- 16. Jafar TH, Qadri Z, Chaturvedi N. Coronary artery disease epidemic in Pakistan: more electrocardiographic evidence of ischaemia in women than in men. Heart. 2008;94(4):408-13.
- 17. McCracken J, Smith KR, Stone P, Diaz A, Arana B, Schwartz J. Intervention to lower household wood smoke exposure in Guatemala reduces ST-segment depression on electrocardiograms. Environ Health Perspect 2011;119:1562-8.
- 18. McCracken JP, Smith KR, Díaz A, Mittleman MA, Schwartz J. Chimney stove intervention to reduce long-term wood smoke exposure lowers blood pressure among Guatemalan women. Environ Health Perspect 2007;115:996-1001.
- 19. Alexander D, Larson T, Bolton S, Vedal S. Systolic blood pressure changes in indigenous Bolivian women associated with an improved cookstove intervention. Air Qual Atmos Health 2015;8:47-53.
- 20. Wilcosky T, Harris R, Weissfeld L. The prevalence and correlates of Rose questionnaire angina among women and men in the Lipid Research Clinics Program Prevalence Study. Am J Epidemiol. 1987;125 (3):400-409.
- 21. Jafar TH, Jafary FH, Jessani S, Chaturvedi N. Heart disease epidemic in Pakistan: women and men at equal risk. Am Heart J. 2005;150(2):221-6.

2
3
-
4
5
6
7
/
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
57
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
58 59
59

- 22. Khushk WA, Fatmi Z, White F, Kadir MM. Health and social impacts of improved stoves on rural women: a pilot intervention in Sindh, Pakistan. Indoor Air. 2005 Oct;15(5):311-6.
- 23. Castelli WP. Epidemiology of coronary heart disease: The Framingham study. American Journal of Medicine 1984, page 4.
- 24. Gordon T, Kannel WB, Hjortland MC, McNamara PM. Menopause and coronary heart disease. The Framingham Study. Ann Intern Med. 1978; 89:157–61.
- 25. Hameed K, Kadir M, Gibson T, Sultana S, Fatima Z, Syed A. The frequency of known diabetes, hypertension and ischaemic heart disease in affluent and poor urban populations of Karachi, Pakistan. Diabet Med. 1995;12(6):500-3.
- 26. Ali MK, Bhaskarapillai B, Shivashankar R, Mohan D, Fatmi Z, Pradeepa R, Masood Kadir M, Mohan V, Tandon N, Narayan KM, Prabhakaran D; CARRS investigators. Socioeconomic status and cardiovascular risk in urban South Asia: The CARRS Study. Eur J Prev Cardiol. 2016 Mar;23(4):408-19.
- 27. Hubert HB, Feinleib M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. Circulation 1983; 67:968–77.
- 28. Todd Miller M, Lavie CJ, White CJ. Impact of obesity on the pathogenesis and prognosis of coronary heart disease. J Cardiometab Syndrome 2008; 3:162–7.
- 29. Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet. 2002;360: 1903-13.
- 30. Yusuf S, Hawken S, Ounpuu S, Bautista L, Franzosi MG, Commerford P, Lang CC, Rumboldt Z, Onen CL, Lisheng L, Tanomsup S, Wangai P Jr, Razak F, Sharma AM, Anand SS; INTERHEART Study Investigators. Obesity and the risk of myocardial infarction in 27,000 participants from 52 countries: a case-control study. Lancet 2005;366(9497):1640-9.
- 31. The World Health Report 2002: reducing risks, promoting healthy life. Geneva, World Health Organization, 2002.
- 32. Chowdhury R, Warnakula S, Kunutsor S, Crowe F, Ward HA, Johnson L, Franco OH, Butterworth AS, Forouhi NG, Thompson SG, Khaw KT, Mozaffarian D, Danesh J, Di Angelantonio E. Association of dietary, circulating, and supplement fatty acids with coronary risk: a systematic review and meta-analysis. Ann Intern Med. 2014 Mar 18;160(6):398-406. doi: 10.7326/M13-1788.
- 33. Huxley RR, Woodward, M. Cigarette smoking as a risk factor for coronary heart disease in women compared with men: a systematic review and meta-analysis of prospective cohort studies. Lancet. 2011;378(9799):1297-305.
- 34. Global Adult Tobacco Survey. Pakistan Fact sheet 2014. http://www.who.int/tobacco/surveillance/survey/gats/pakfactsheet.pdf

Characteristic	All we (n=85		Users o (n=436	of biomass )	Non-u bioma (n=414		Long- of bion (n=430			term non- of biomass 3)
	N	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Age (years)										
<50	525	(61.8)	263	(60.3)	262	(63.3)	257	(59.8)	166	(63.1)
≥50	325	(38.2)	173	(39.7)	152	(36.7)	173	(40.2)	97	(36.9)
Educational status				x 2				× × ×		
No literacy	797	(93.8)	419	(96.1)	378	(91.3)	413	(96.1)	239	(90.9)
Any literacy	53	(6.2)	17	(3.9)	36	(8.7)	17	(4.0)	24	(9.1)
Household income/month		6								
≤10000PKR	651	(76.6)	351	(80.5)	300	(72.5)	347	(80.7)	185	(70.3)
>10000PKR	199	(23.4)	85	(19.5)	114	(27.5)	83	(19.3)	78	(29.7)
Household tenure			1					× × ×		· · · · · ·
Rented	70	(8.2)	25	(5.7)	45	(10.9)	25	(5.8)	20	(7.6)
Owned	780	(91.8)	411	(94.3)	369	(89.1)	405	(94.2)	243	(92.4)
Construction of house				CI.		· · ·				
Katcha/ semi-pucca	652	(76.7)	361	(82.8)	291	(70.3)	356	(82.8)	173	(65.8)
Pucca	198	(23.3)	75	(17.2)	123	(29.7)	74	(17.2)	90	(34.2)
Number of household assets										
Low (0-1)	268	(31.5)	140	(32.1)	128	(30.9)	139	(32.3)	84	(31.9)
Medium (2-3)	404	(47.5)	223	(51.2)	181	(43.7)	218	(50.7)	108	(41.1)
High $(\geq 4)$	178	(21.0)	73	(16.7)	105	(25.4)	73	(17.0)	71	(27.0)
Father's occupation in childhood										
Non-manual	39	(4.6)	19	(4.4)	20	(4.8)	18	(4.2)	16	(6.1)
Manual	811	(95.4)	417	(95.6)	394	(95.2)	412	(95.8)	247	(93.9)

Table 1 D staniation of monticinants h 1. а. • :. . **.** .

1	
2	
3 4	
5	
6 7	
8	
9 10	
11	
12 13	
14	
15 16	
17	
18	
20	
21	
11 12 13 14 15 16 17 18 19 20 21 22 23	
24	
25 26	
27	
28 29	
30	
31 32	
33	
32 33 34 35 36	
36 37	
37 38	
39	
40 41	
42	
43 44	
45	

Characteristic	User (n=4	rs of biomass 36)	Non-use biomass (n=414)			g-term users omass 30)	Long-to of biom (n=263	
	n	(%)	n	(%)	n	(%)	n	(%)
Ever used biomass for cooking	436	(100)	382	(92.3)	430	(100)	231	(87.8)
Years since last used biomass for cooking								
Current user	436	(100)	-	-	430	(100)	-	-
2-9	-	-	151	(39.5)	-	-	-	-
≥10	-	-	231	(60.5)	-	-	231	(100)
Ever used wood for cooking	435	(99.8)	358	(86.5)	429	(99.8)	218	(82.9)
Ever used cow dung for cooking	422	(96.8)	358	(86.5)	416	(96.7)	216	(82.1)
Ever used kerosene for cooking	16	(3.7)	26	(6.3)	16	(3.7)	17	(6.5)
Ever used LPG/natural gas for cooking	17	(3.9)	413	(99.8)	15	(3.5)	263	(100)
Average hours per day cooked in past year								
<u>≤</u> 1	129	(29.6)	133	(32.1)	123	(28.6)	75	(28.5)
2-3	270	(61.9)	237	(57.3)	270	(62.8)	165	(62.7)
<u>≥</u> 4	37	(8.5)	44	(10.6)	37	(8.6)	23	(8.8)
Type of stove used for cooking								
Gas/LPG	2	(0.5)	414	(100)	2	(0.5)	263	(100)
Biomass with	166	(38.1)			164	(38.1)		
chimney/improved stove	100	(38.1)	-	-	104	(38.1)	-	-
Biomass with three brick open stove	267	(61.2)	-	-	263	(61.2)	-	-
Other	1	(0.2)	-	-	1	(0.2)	-	-
Type of kitchen								
Closed (four walls – linked with living	88	(20, 2)	116	(28.0)	86	(20.0)	79	(30.0)
room or separate)	00	(20.2)	110	(20.0)	00	(20.0)	/ 7	(30.0)
Semi-open (fewer than four walls)	189	(43.3)	155	(37.4)	187	(43.5)	94	(35.7)
Open (no walls)	159	(36.5)	143	(34.5)	157	(36.5)	90	(34.2)
Heat home with biomass	237	(54.4)	106	(25.6)	236	(54.9)	74	(28.1)

 Table 2. Current and past cooking arrangements according to exposure category.

1 2 3	
3 4	-
5 6	-
7	-
8	
9 10	
11	-
12	
13	
14	
15 16	
16 17	
18	-
18 19 20	
20	
21 22	
23	-
24	
25	
26	-
27 28	
29	
30	-
31	
32	
33 34	
32 33 34 35	-
26	
37	
38	

**Table 3.** Distribution of risk factors across the four exposure categories.

Characteristic	Users of b (n=436)		Non-user (n=414)	s of biomass	0	term users of ss (n=430)		erm non-users nass (n=263)
	n	(%)	n	(%)	n	(%)	n	(%)
Birthweight				· ·				· ·
Lower than normal	117	(26.8)	77	(18.6)	114	(26.5)	54	(20.5)
Normal	239	(54.8)	254	(61.4)	237	(55.1)	156	(59.3)
Higher than normal	80	(18.4)	83	(20.0)	79	(18.4)	53	(20.2)
No	176	(40.4)	176	(42.5)	175	(40.7)	122	(46.4)
Yes	260	(59.6)	238	(57.5)	255	(59.3)	141	(53.6)
Lost weight during childhood		\$ <i>}</i>						
No	162	(37.2)	182	(44.0)	160	(37.2)	119	(45.2)
Yes	274	(62.8)	232	(56.0)	270	(62.8)	144	(54.8)
Ever smoked regularly (any of cigarettes, bidi, huqqa)								
Never	390	(89.4)	378	(91.3)	384	(89.3)	240	(91.3)
Ever	46	(10.6)	36	(8.7)	46	(10.7)	23	(8.7)
Environmental tobacco smoke (at least one other								
household member smoked cigarettes, bidi or huqqa in								
the home)								
No	269	(61.7)	267	(64.5)	265	(61.6)	173	(65.8)
Yes	167	(38.3)	147	(35.5)	165	(38.4)	90	(34.2)
Physical activity score								
0-2	124	(28.4)	205	(49.5)	124	(28.8)	149	(56.7)
3-4	199	(45.6)	156	(37.7)	196	(45.6)	91	(34.6)
5-6	113	(25.9)	53	(12.8)	110	(25.6)	23	(8.7)
Consumption of meat or eggs								
Do not eat either meat or eggs as much as once per week	173	(39.7)	142	(34.3)	172	(40.0)	88	(33.5)
Eat one of meat or eggs as much as once per week	176	(40.4)	163	(39.4)	173	(40.2)	100	(38.0)
Eat both meat and eggs at least once per week	87	(20.0)	109	(26.3)	85	(19.8)	75	(28.5)
Current nutrition <sup>a</sup>								
Neither BMI nor WHR high	183	(42.0)	129	(31.2)	179	(41.6)	79	(30.0)
One of BMI or WHR high	151	(34.6)	160	(38.7)	149	(34.7)	101	(38.4)
Both BMI and WHR high	102	(23.4)	124	(30.0)	102	(23.7)	82	(31.2)
Not known	0	(0)	1	(0.2)	0	(0)	1	(0.4)

<sup>a</sup>BMI ( $kg/m^2$ )  $\geq 25 = high;$  WHR  $\geq 0.85 = high.$ 

2	
3	
4	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
20	
21	
- 77	
22	
24	
24	
25	
26	
27	
28	
29	
29	
30	
31	
32	
33	
24	
34	
35	
36 37	
37	
20	
39	
40	
41	
42	
43	
44	
45	
46	
47	
48	
49	
50	
51	
52	
53	
54	
55	
56	
57	
58	

58 59 60 **Table 4.** Associations of hypertension, angina, history of heart attack, and definite or probable CHD on ECG with current and long-term use of biomass for cooking.

Outcome	Adjuste age (n=	d only for 850)	v	Fully adjusted <sup>a</sup> (n=850)		adjusted and d to long-term and non-users of ss <sup>b</sup> 3)
	OR	(95%CI)	OR	(95% CI)	OR	(95% CI)
Hypertension						
Non-users of biomass	1.0		1.0		1.0	
Users of biomass	1.2	(0.9-1.5)	1.0	(0.8-1.4)	1.1	(0.8-1.6)
Angina						
Non-users of biomass	1.0		1.0		1.0	
Users of biomass	1.0	(0.7-1.3)	1.0	(0.8-1.4)	1.3	(0.9-1.9)
Heart Attack						
Non-users of biomass	1.0		1.0		1.0	
Users of biomass	1.4	(0.8-2.4)	1.2	(0.7-2.2)	1.3	(0.7-2.4)
Definite or probable CHD on	4					
ECG						
Non-users of biomass	1.0		1.0		1.0	
Users of biomass user	0.8	(0.6-1.2)	0.8	(0.6-1.2)	0.9	(0.6-1.3)

<sup>a</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p < 0.1) in analyses adjusted only for age

<sup>b</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p<0.1) in analyses adjusted only for age, but was restricted to women who were long-term users or non-users of biomass

Liezoni

### **Supplementary Materials**

**Supplementary Table 1.** Prevalence of hypertension, history of heart attack, angina and coronary heart disease in study sample.

Characteristic	n	(%)
Hypertension		
Systolic hypertension (systolic BP≥140 mmHg)	133	(15.8)
Diastolic hypertension (diastolic BP≥90 mmHg)	102	(12.1)
Regular medication for high blood pressure	198	(23.5)
Hypertension (any of the above)	297	(35.3)
Angina	227	(27.0)
History of heart attack	54	(6.4)
Definite or probable CHD on ECG <sup>a</sup>	159	(18.9)

Toret review only

<sup>a</sup>Based on 841 women. ECGs for 9 women were missing or could not be coded due to poor quality.

 $\underset{\text{For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml}{18}$ 

Negative         591         30           Positive         94         122           Kappa = 0.57         Image: Constraint of the second seco	Negative         591         30           Positive         94         122           Kappa = 0.57         Image: Constraint of the second seco	Negative         591         30           Positive         94         122           Kappa = 0.57         Image: Second s	Negative         591         30           Positive         94         122           Kappa = 0.57         Image: Constraint of the second seco	Negative         591         30           Positive         94         122           Kappa = 0.57         Image: Constraint of the second seco	Observer 1	Observer 2	
Positive 94 122 Kappa = 0.57	Nagatiya	Negative	Positive				
					Positive		
					Kappa = 0.57		

**Supplementary Table 3.** Prevalence of definite or probable CHD changes on ECG according to history of heart attack and angina.

Other measure of CHD	Definite or probable CHD changes on ECG <sup>a</sup>						
	Yes		No				
	n	(%)	Ν	(%)			
No history of heart attack or angina	105	(18.2)	471	(81.8)			
History of angina	45	(19.8)	182	(80.2)			
History of heart attack	14	(25.9)	40	(74.1)			
History of angina or heart attack	54	(20.4)	211	(79.6)			
History of angina and heart attack	5	(31.3)	11	(68.8)			

<sup>a</sup>ECGs for 9 women were missing or could not be coded due to poor quality.

Risk factor	Adju for a	isted only ge	Fully (n=85	adjusted <sup>a</sup> 50)	Fully adjusted and limited to long- term users and		
	(n=8	50)	(1 000)		non-users of biomass <sup>b</sup>		
					(n=693)		
	OR	(95%CI)	OR	(95%CI)	OR	(95%CI)	
Age (per 10 year increase)	1.4	(1.2-1.6)	1.4	(1.2-1.7)	1.5	(1.2-1.7)	
Educational status							
Illiterate	1.0		-		-		
Any literacy	0.6	(0.3-1.2)					
Household income/month					-		
<3000-10000PKR	1.0		-				
>10000PKR	1.0	(0.7-1.4)					
Household ownership					-		
Rented	1.0		-				
Own	0.8	(0.5-1.3)					
Construction of house					-		
Katcha/semi-pucca	1.0		-				
Pucca	0.9	(0.6-1.2)					
Number of household assets							
0-1	1.0		1.0		1.0		
2-3	1.7	(1.2-2.4)	1.6	(1.2-2.3)	1.8	(1.2-2.6)	
<u>≥</u> 4	2.4	(1.6-3.6)	2.3	(1.5-3.4)	2.7	(1.7-4.3)	
Father's occupation in woman's					-		
childhood							
Non-manual	1.0						
Manual	1.2	(0.6-2.5)					
Birthweight							
Lower than normal	1.0				-		
Normal	1.0	(0.7-1.4)	-				
Higher than normal	1.0	(0.6-1.5)					
Ever hungry during all the time during childhood because there					-		
was not enough food No	1.0		_				
Yes	0.9	(0.7-1.3)	-				
Lost weight during childhood	0.9	(0.7-1.5)					
No	1.0		_		-		
Yes	1.0	(0.9-1.6)	_				
Ever smoked regularly (any of	1.4	(0.9-1.0)					
cigarettes, bidi, huqqa)							
Never	1.0		_		_		
Ever	0.8	(0.5-1.3)					
Even Environmental tobacco smoke (at		(0.5-1.5)					
least one other household member							
smokes cigarettes, bidi or huqqa	L						
in the home)							
No	1.0		_				
Yes	0.8	(0.6-1.1)	-				

1.0		1.0		1.0	
1.4	(1.0-1.9)	1.2	(0.9-1.7)	1.2	(0.8-1.7)
1.4	(1.0-2.1)	1.2	(0.8-1.8)	1.2	(0.8-1.9)
1.0		1.0		1.0	
1.2	(0.9-1.7)	1.2	(0.8-1.6)	1.2	(0.8-1.8)
2.0	(1.4-2.9)	1.9	(1.3-2.8)	1.8	(1.2-2.7)
1.0		1.0			·
1.2	(0.9-1.5)	1.0	(0.8-1.4)		
1.0	· · · · · ·			1.0	
1.2	(0.9-1.7)			1.1	(0.8-1.6)
	1.4 1.4 1.0 1.2 2.0 1.0 1.2 1.0	$\begin{array}{cccc} 1.4 & (1.0-1.9) \\ 1.4 & (1.0-2.1) \\ \hline \\ 1.0 \\ 1.2 & (0.9-1.7) \\ 2.0 & (1.4-2.9) \\ 1.0 \\ 1.2 & (0.9-1.5) \\ 1.0 \\ \end{array}$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$

<sup>a</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p < 0.1) in analyses adjusted only for age

<sup>b</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p < 0.1) in analyses adjusted only for age, but was restricted to women who were long-term users or non-users of biomass

<sup>c</sup>Body mass index (BMI) ( $kg/m^2$ )  $\geq 25 = high$ ; Waist-to-hip ratio (WHR)  $\geq 0.85 = high$ .

Supplementary Table 5.	Associations of angina with risk factors.

Risk factor	Adju for ag	sted only ze	Fully	v adjusted <sup>a</sup>	Fully adjusted and limited to long-		
	(n=850)		(n=850)		term users and non-users of biomass <sup>b</sup>		
					(n=693)		
	OR	(95%CI)	OR	(95%CI)	OR	(95%CI)	
Age (per 10 year increase)	1.3	(1.1-1.6)	1.3	(1.1-1.5)	1.3	(1.1-1.5)	
Educational status							
Illiterate	1.0		-		-		
Any literacy	0.6	(0.3-1.3)					
Household income/month		/			-		
<3000-10000PKR	1.0		-				
>10000PKR	1.1	(0.8-1.6)					
Household ownership	1.1	(0.0 1.0)			-		
Rented	1.0		_		-		
Own	0.8	(0.5-1.3)	-				
Construction of house	0.0	(0.3-1.3)					
	1.0				-		
Katcha/semi-pucca	1.0	(0, 0, 1, 7)	-				
Pucca	1.2	(0.8-1.7)					
Number of household assets					-		
0-1	1.0		-				
2-3	0.9	(0.6-1.3)					
<u>≥</u> 4	1.0	(0.6-1.5)					
Father's occupation in woman's					-		
childhood							
Non-manual	1.0						
Manual	0.7	(0.3-1.4)					
Birthweight							
Lower than normal	1.0				-		
Normal	1.2	(0.8-1.8)	-				
Higher than normal	1.1	(0.7-1.8)					
Ever hungry during all the time		(			-		
during childhood because there							
was not enough food							
No	1.0		-				
Yes	0.8	(0.6-1.1)					
Lost weight during childhood	0.0	(0.0-1.1)					
No	1.0				-		
	1.0	$(0 \ 0 \ 1 \ 4)$	-				
Yes	1.0	(0.8-1.4)					
Ever smoked regularly (any of							
cigarettes, bidi, huqqa)	1.0		1.0		1.0		
Never	1.0	<i>(</i> <b>1 - - )</b>	1.0	<i>(</i> <b>1 - - )</b>	1.0	<i></i>	
Ever	2.1	(1.3-3.3)	2.0	(1.2-3.2)	2.1	(1.3-3.6)	
Environmental tobacco smoke							
(at least one other household							
member smokes cigarettes, bidi							
or huqqa in the home)							
No	1.0		-				
Yes	1.2	(0.9-1.6)					
Consumption of meat or eggs		(					

**Consumption of meat or eggs** 

Do not eat either meat or eggs	1.0		1.0		1.0	
as much as once per week Eat one of meat or eggs as much as once per week	0.6	(0.4-0.8)	0.6	(0.4-0.8)	0.7	(0.5-1.0)
Eat both meat and eggs at least once per week	0.4	(0.3-0.7)	0.5	(0.3-0.7)	0.5	(0.3-0.8)
Current nutrition <sup>c</sup>						
Neither BMI nor WHR high	1.0					
One of BMI or WHR high	0.8	(0.5 - 1.1)	-			
Both BMI and WHR high	0.8	(0.5-1.2)				
Non-user of biomass	1.0					
User of biomass user	1.0	(0.7-1.3)	1.0	(0.8-1.4)		
Long-term non-user of biomass	1.0				1.0	
Long-term non-user of biomass	1.2	(0.9-1.7)			1.3	(0.9-1.9)

<sup>*a*</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p < 0.1) in analyses adjusted only for age

<sup>b</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p < 0.1) in analyses adjusted only for age, but was restricted to women who were long-term users or non-users of biomass

Review only

<sup>c</sup>Body mass index (BMI) ( $kg/m^2$ )  $\geq 25 = high$ ; Waist-to-hip ratio (WHR)  $\geq 0.85 = high$ .

Risk factor	Adju for a	sted only ge	Full	y adjusted <sup>b</sup>	Fully adjusted and limited to long-term			
				850)	users and non-users of			
	( <b>n=850</b> ) <sup>a</sup>					biomass <sup>c</sup>		
					(n=6	593)		
	OR	(95%CI)	OR	(95%CI)	OR	(95%CI)		
Age (per 10 year increase)	1.5	(1.2-2.0)	1.5	(1.2-2.0)	1.5	(1.2-2.0)		
Educational status								
Illiterate	1.0		-		-			
Any literacy	1.5	(0.5-4.5)						
Household income/month								
<3000-10000PKR	1.0		1.0		1.0			
>10000PKR	1.6	(0.9-2.9)	1.4	(0.8-2.5)	1.6	(0.8-3.1)		
Household ownership								
Rented	1.0		-		-			
Own	1.2	(0.4 - 3.4)						
Construction of house	0				-			
Katcha/semi-pucca			-					
Pucca	1.3	(0.7-2.3)						
Number of household assets								
0-1	1.0		1.0		1.0			
2-3	1.4	(0.7-2.7)	1.3	(0.7-2.5)	1.8	(0.8-3.8)		
>4	2.1	(1.0-4.3)	1.8	(0.8-3.8)	2.1	(0.9-5.1)		
Father's occupation in woman's	-			()	-			
childhood								
Non-manual	1.0							
Manual	1.0	(0.2-4.5)						
Birthweight								
Lower than normal	1.0				-			
Normal	1.0	(0.5 - 1.9)	-					
Higher than normal	0.7	(0.3-1.7)						
Ever hungry during all the time		(****			-			
during childhood because there								
was not enough food								
No	1.0		-					
Yes	1.0	(0.6-1.7)						
Lost weight during childhood		(			-			
No	1.0		-					
Yes	1.1	(0.6-1.9)						
Ever smoked regularly (any of		(0.0 1.7)						
cigarettes, bidi, huqqa)								
Never	1.0		_					
Ever	0.9	(0.4-2.1)						
Environmental tobacco smoke (at	0.7	(0.1 2.1)						
least one other household member								
smokes cigarettes, bidi or huqqa in								
the home)								
No	1.0		_					
Yes	1.0 0.9	(0.5-1.6)	-					
Consumption of meat or eggs	0.7	(0.3-1.0)						

**Supplementary Table 6.** Associations of previous history of heart attack (diagnosed by a physician) with risk factors.

**Consumption of meat or eggs** 

Do not eat either meat or eggs as	1.0		-				
much as once per week							
Eat one of meat or eggs as much	1.2	(0.6-2.3)					
as once per week							
Eat both meat and eggs at least	1.8	(0.9-3.5)					
once per week							
Current nutrition <sup>d</sup>							
Neither BMI nor WHR high	1.0		1.0		1.0		
One of BMI or WHR high	1.3	(0.6-2.5)	1.2	(0.6-2.5)	1.6	(0.7-3.4)	
Both BMI and WHR high	2.0	(1.0-4.0)	1.9	(0.9-3.7)	1.7	(0.8-3.6)	
Non-user of biomass	1.0		1.0		-		
Use of biomass	1.4	(0.8-2.4)	1.2	(0.7-2.2)			
Long-term non-user of biomass	1.0				1.0		
Long-term user of biomass	1.5	(0.8-2.7)			1.3	(0.7-2.4)	
							-

<sup>a</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p < 0.1) in analyses adjusted only for age

<sup>b</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p < 0.1) in analyses adjusted only for age, but was restricted to women who were long-term users or non-users of biomass

<sup>a</sup>Body mass index (BMI) (kg/m<sup>2</sup>) ≥25= high; Waist-to-hip ratio (WHR) ≥0.85=high.

Risk factor	Adjusted only for age			Ū	Fully adjusted and limited to long-terr users and non-user		
	(n=84	41)	(n=841	()		omass <sup>b</sup>	
					(n=68	86)	
	OR	(95%CI)	OR	(95%CI)	OR	(95%CI)	
Age (per 10 year increase)	1.1	(0.9-1.3)	1.1	(0.9-1.3)	1.0	(0.8-1.3)	
Educational status							
Illiterate	1.0		-		-		
Any literacy	0.8	(0.4-1.7)					
Household income/month		/					
<3000-10000PKR	1.0		1.0		1.0		
>10000PKR	1.6	(1.1-2.3)	1.6	(1.1-2.4)	1.3	(0.8-2.0)	
Household ownership		()		()	-	()	
Rented	1.0		-				
Own	1.4	(0.7-2.9)					
Construction of house	1.7	(0.7-2.7)					
Katcha/semi-pucca	1.0				-		
Pucca	1.0	(0, 7, 1, 5)	-				
	1.0	(0.7-1.5)					
Number of household assets	1.0						
0-1	1.0	(0,7,1,5)	-				
2-3	1.0	(0.7-1.5)					
$\geq 4$	1.3	(0.8-2.1)					
Father's occupation in woman's					-		
childhood	1.0						
Non-manual	1.0		-				
Manual	1.0	(0.4-2.3)					
Birthweight							
Lower than normal	1.0				-		
Normal	1.1	(0.7-1.7)	- 6				
Higher than normal	1.1	(0.7-1.9)					
Ever hungry during all the time					-		
during childhood because there							
was not enough food							
No	1.0		-				
Yes	1.1	(0.8-1.6)					
Lost weight during childhood		× /			-		
No	1.0		-				
Yes	0.8	(0.6-1.2)					
Ever smoked regularly (any of	0.0	(0.0 1.2)					
cigarettes, bidi, huqqa)							
Never	1.0		_		_		
Ever	1.0	(0.6-1.8)	-		-		
		(0.0-1.0)					
Environmental tobacco smoke (at	,						
least one other household							
member smokes cigarettes, bidi							
or huqqa in the home)	1.0						
No	1.0				-		
Yes	0.9	(0.6-1.3)	-				

Do not eat either meat or eggs as	5 1.0					
much as once per week						
Eat one of meat or eggs as much	h 0.9	(0.6-1.4)				
as once per week						
Eat both meat and eggs at least	1.2	(0.7-1.8)				
once per week						
Current nutrition <sup>c</sup>						
Neither BMI nor WHR high	1.0					
One of BMI or WHR high	0.8	(0.5-1.2)	-			
Both BMI and WHR high	1.1	(0.7-1.6)				
Non-user of biomass user	1.0		1.0			
User of biomass	0.8	(0.6-1.2)	0.8	(0.6-1.2)		
Longterm non-user of biomass	1.0				1.0	
Longterm user of biomass	0.9	(0.6-1.3)			0.9	(0.6-1.3)

<sup>a</sup>ECGs were missing for 9 women or not codable due to poor quality.

<sup>b</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p < 0.1) in analyses adjusted only for age

<sup>c</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p < 0.1) in analyses adjusted only for age, but was restricted to women who were long-term users or non-users of biomass

<sup>*d*</sup>Body mass index (BMI) ( $kg/m^2$ )  $\geq 25 = high$ ; Waist-to-hip ratio (WHR)  $\geq 0.85 = high$ .

 BMJ Open

Section/Topic	ltem #	Recommendation	Reported on page
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2
Objectives	3	State specific objectives, including any prespecified hypotheses	2
Methods		6	
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	3
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	3-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	3-5
Bias	9	Describe any efforts to address potential sources of bias	3-5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	5
		(b) Describe any methods used to examine subgroups and interactions	5
		(c) Explain how missing data were addressed	In relevant tables
		(d) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(e) Describe any sensitivity analyses	N/A

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	6
		confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	Not needed
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6 and Tables 1-3
		(b) Indicate number of participants with missing data for each variable of interest	Tables 1-3
Outcome data	15*	Report numbers of outcome events or summary measures	6
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence	Supplementary
		interval). Make clear which confounders were adjusted for and why they were included	Tables 4-7
		(b) Report category boundaries when continuous variables were categorized	Tables
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	8-9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10
Generalisability	21	Discuss the generalisability (external validity) of the study results	8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on	2
		which the present article is based	

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

# **BMJ Open**

# **Coronary Heart Disease, Hypertension and Use of Biomass Fuel among Women: Comparative Cross-sectional Study.**

Journal:	BMJ Open
Manuscript ID	bmjopen-2019-030881.R1
Article Type:	Research
Date Submitted by the Author:	17-Jun-2019
Complete List of Authors:	Fatmi, Zafar; Aga Khan University, Department of Community Health Sciences Ntani, G; University of Southampton and Southampton University Hospitals NHS Trust, MRC Lifecourse Epidemiology Unit Coggon, David; University of Southampton, MRC Lifecourse Epidemiology Unit
<b>Primary Subject Heading</b> :	Global health
Secondary Subject Heading:	Epidemiology, Occupational and environmental medicine, Public health
Keywords:	Coronary heart disease < CARDIOLOGY, biomass fuel, Hypertension < CARDIOLOGY, women, EPIDEMIOLOGY, Public health < INFECTIOUS DISEASES



# **Coronary Heart Disease, Hypertension and Use of Biomass Fuel among Women: Comparative Cross-sectional Study.**

# Zafar Fatmi,<sup>1,2</sup> Georgia Ntani,<sup>2</sup> David Coggon<sup>2</sup>

<sup>1</sup>Department of Community Health Sciences, Aga Khan University, PO Box 3500, Karachi 74800, Pakistan.

<sup>2</sup>MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK.

\*Correspondence should be addressed to Zafar Fatmi; zafar.fatmi@aku.edu;

# Abstract

*Objectives:* To explore the associations of hypertension and coronary heart disease (CHD) with use of biomass fuel for cooking.

Design: Comparative cross-sectional study.

Setting: Rural villages in Sindh, Pakistan.

**Participants:** Women aged  $\geq$ 40 years who had used biomass fuel for cooking for at least the past year (n = 436), and a comparison group (n=414) who had cooked only with non-biomass fuel during the past year were recruited through door-to-door visits. None of those who were invited to take part declined.

**Primary and secondary outcome measures:** Hypertension was determined from blood pressure measurements and use of medication. CHD was assessed by three measures: history of angina (Rose angina questionnaire), previous history of 'heart attack', and definite or probable changes of CHD on electrocardiogram (ECG). Potentially confounding risk factors were ascertained by questionnaire and anthropometry. Associations of hypertension and CHD with use of biomass and other risk factors were assessed by logistic regression, and summarised by odds ratios (ORs) with 95% confidence intervals (CIs).

**Results:** After adjustment for potential confounders, there was no association of hypertension (OR: 1.0, 95% CI 0.8 – 1.4) angina (OR: 1.0, 95% CI 0.8-1.4), heart attack (OR: 1.2, 95% 0.7 - 2.2) or ECG changes of CHD (OR: 0.8, 95% CI 0.6 – 1.2) with current use of biomass for cooking. Nor were any associations apparent when analyses were restricted to long-term ( $\geq 10$  years) users and non-users of biomass fuel.

*Conclusions:* A linked air monitoring study indicated substantially higher airborne concentrations of fine particulate matter in kitchens where biomass was used for cooking. It is possible that associations with CHD and hypertension were missed because most of the comparison group had used biomass for cooking at some time in the past, and risk remains elevated for many years after last exposure.

# Strengths and limitations of this study:

• The study was well-powered with a high response rate (93%) from those invited to take part, and large contrasts in recent exposure to indoor air pollution.

- Comparisons were based on recent cooking practices, but some exposures may have changed since the onset of coronary heart disease.
- Many women who did not currently use biomass for cooking, had done so in the past, and this may have obscured associations with health outcomes if effects of exposure persist long-term.
- Errors may have occurred in the assessment of outcome measures, biasing risk estimates towards the null.
- Recall of some potentially confounding factors may have been inaccurate, leading to uncontrolled residual confounding.

# **Funding Statement**

This research was supported by a fellowship from the Colt Foundation for the conduct of a PhD by Professor Zafar Fatmi. Professor David Coggon and Dr Georgia Ntani were supported by funding from the UK Medical Research Council (MRC\_MC\_UU\_12011/5).

# **Conflicts of Interest**

The authors declare that there is no conflict of interest regarding the publication of this paper.

Authors' contributions

ZF led the design and conduct of the study, carried out the initial statistical analyses, and wrote the first draft of the manuscript.

GN oversaw and guided the statistical analysis.

DC supervised the project and amended the first draft of the manuscript.

All authors approved the final version of the manuscript.

# Introduction

Much of the world's population still uses biomass fuel (wood, cow-dung, crop residues etc.) in open fires or simple stoves for domestic cooking and heating [1,2]. The household air pollution (HAP) which this generates is a major cause of respiratory infections among children [3-5], chronic obstructive pulmonary disease [6-7] and lung cancer [8-10]. In addition, several studies have suggested a hazard of coronary heart disease (CHD), but evidence for this is more limited [11, 12].

We, therefore, carried out a cross-sectional survey to explore the association between CHD and cooking with biomass in a sample of women drawn from the general population in rural areas of Pakistan. The objective of the study was to compare the prevalence of hypertension, angina, previous history of heart attack, and electrocardiographic (ECG) changes indicative of CHD in women  $\geq$ 40 years of age who used biomass fuel for cooking with that in women of similar age who cooked using other types of fuel.

# Materials and Methods

# Study Setting

The survey was conducted during 2015 in villages surrounding the main urban area of Nawabshah district (recently renamed as Shaheed Benazirabad) in the province of Sindh, Pakistan. These were selected to give a mix in the fuels used for cooking within the study sample. Some of the villages had been supplied with natural gas for at least 10 years, whereas in others biomass fuel (wood and/or cow dung) was still being used.

# Recruitment of households and subjects

Within each village, trained field workers made door-to-door visits, and asked the heads of households whether their families would be willing to assist with the study, and if so, what type of fuel was used for cooking, and whether food preparation was regularly undertaken by a woman  $\geq$ 40 years of age. In this way, the study team identified quotas of the required numbers of households in each of the two categories of fuel use (biomass and other). The heads of these households were then asked to complete a consent form, and to identify and introduce the woman of the household aged  $\geq$ 40 years who had carried out the most cooking in the house over the past 10 years. The study was explained to her, and she was invited to participate and to give signed consent.

#### Inclusion criteria

Women aged 40 years or older were eligible for inclusion if they gave informed consent, and had been cooking in the household for at least the past year, using only one of biomass fuel or non-biomass fuel.

# Questionnaire, examination and measurements

A standardized questionnaire was used to collect information at interview about: demographic and socio-economic characteristics, birth weight, smoking history, whether another member of the household was a regular smoker, relevant aspects of diet, physical activity, lifetime history of cooking using different types of fuel, any previous diagnosis of a "heart attack" by a doctor, symptoms of angina (through the Rose angina questionnaire [13]), and any current use of medication for hypertension. In addition, measurements were made of height, weight, waist circumference, hip circumference and blood pressure.

Socioeconomic status was characterized by the literacy of the participant (no vs. any literacy), the type of employment of her father during her childhood (manual or non-manual), the ownership and construction of her house ('pucca' i.e. made of concrete walls and roof or 'katcha/semi-pucca' i.e. made fully or partially of thatched walls and roof), the income level of the household, and the number of household assets owned from a list of seven. Birth weight was determined from participants' recall as being 'higher than normal vs. normal vs. lower than normal'.

The questions on smoking covered use of cigarettes, *bidi* (locally made cigarettes without filters) or a huqqa (pipe) regularly (at least once a week for a month or longer). The number of other people in the household who smoked provided a measure of domestic exposure to environmental tobacco smoke (ETS), which was classified according to whether at least one other household member smoked cigarettes, bidi, or a huqqa in the home.

Dietary questions covered the use of oil or ghee for cooking and eating, and weekly consumption of meat and eggs. The former was categorized to three levels: only or mostly use oil; mixed use of oil and ghee; only or mostly use ghee. Frequencies of consuming meat and eggs were each categorized to two levels: at least once per week vs. less than once per week.

Level of physical activity was assessed through questions on the frequency per week of shopping, fetching water, washing clothes, collecting wood for cooking, agricultural work on a farm and any other regular heavy physical work. Each of these activities was categorized to two levels: zero days per week or at least once per week. A composite physical activity score was then derived as the number of activities carried out at least once per week, with values ranging from 0 to 6.

Height, weight, and waist and hip circumference were measured using a stadiometer, digital weighing scale and measuring tape, following standardized methods. Body mass index (BMI) (weight in kilograms per squared height in meters) and waist-to-hip ratio (WHR) were then calculated from the measurements. BMIs  $\geq$ 25kg/m<sup>2</sup> were considered abnormally high (overweight or obese), as were WHRs  $\geq$ 0.85.

#### Categories of exposure to biomass:

Use of biomass was classed to two main categories; biomass users who currently used firewood and/or cow dung for cooking; and non-users of biomass who did not (other sorts of biomass were not used for cooking in the community studied).

In addition, two subsets of these main categories were distinguished: long-term biomass users who currently used firewood and/or cow dung for cooking <u>and</u> had done so for at least the past 10 years; and long-term non-users of biomass who currently did not use either firewood or cow dung for cooking <u>and</u> had not done so for at least10 years.

#### Outcome measures:

Four outcome measures were specified.

Hypertension: Three measurements of blood pressure were made at five-minute intervals, using an Omron upper arm blood pressure monitor, and mean values for systolic and diastolic blood pressure were derived. Women were deemed to have hypertension if they met at least one of three criteria: mean systolic blood pressure  $\geq$ 140 mm Hg; mean diastolic blood pressure  $\geq$ 90 mm Hg; regular use of medication for blood pressure.

Angina: Experience of angina was assessed through the WHO's Rose angina questionnaire [13], which comprises seven questions relating to chest pain, its anatomical distribution, precipitating and relieving factors, and duration. A diagnosis of angina required report of pain, pressure or discomfort

in the chest centrally, or in both the left anterior chest and left arm, that occurred when walking uphill or hurrying, that caused the participant to stop or slow down when it occurred while walking, and that was then relieved within 10 minutes by standing still.

Heart attack: Previous diagnosis of "heart attack" by a doctor was ascertained through a single question: "In the past, have you ever been told by a health care provider that you had a 'heart attack'?"

Definite or probable CHD on ECG: A 12-lead ECG was recorded according to a standard protocol, and coded for the presence of definite or probable CHD, using the Minnesota Code Manual of Electrocardiographic Findings, second edition [14]. This corresponded to the presence of any of codes 1-1 to 1-3, 3-1, 4-1 to 4-4, 5-1 to 5-3, 7-1-1 and 9-2. In order to check the repeatability of the coding, two of us (ZF and DC) coded all of the ECGs independently. We used the same scanned ECG traces, without information about the type of cooking fuel used by the participant. Levels of agreement between the observers were assessed, using kappa statistics. Where differences occurred in the classification of an ECG trace, they were then resolved by discussion between the two observers.

#### Statistical analysis

Data were double-entered in Epidata 3.1 software [15] for validation. All discrepancies were corrected by reference to the original questionnaire or record sheet. Statistical analysis was carried out with Stata version 12.0 [16].

As a first step, several variables were reclassified or combined, based on their distribution in the full study sample, and without knowledge of participants' use of biomass fuel. Thus, a combined index was derived for frequency of consuming meat and eggs with three levels: neither meat nor eggs as much as once per week; one of meat or eggs at least once per week; both meat and eggs at least once per week. Scores for physical activity were categorized into three levels: low (0-1 activities); medium (2-3); high (4 or more). Similarly, BMI and WHR were combined as a single variable with three categories: neither BMI nor WHR high; one of BMI or WHR high; both BMI and WHR high.

Descriptive statistics were produced for women in each of the four categories of exposure to biomass, summarizing their demographic and socioeconomic characteristics, current and past cooking arrangements, types and durations of fuel use, hours of cooking per day, types of stove and kitchen, and exposures to potentially confounding risk factors. The prevalence of the main outcomes was determined for the study sample overall, and the relationship of ECG changes to angina and history of heart attack was explored.

Logistic regression analysis was then used to assess the association of each of the four outcome variables with use of biomass fuel for cooking and other possible risk factors. First, associations with each potential risk factor were determined after adjustment for age. The main exposure of interest (user or non-user of biomass) was then carried forward into a mutually adjusted model along with all other risk factors which showed associations ( $p \le 0.1$ ) when examined individually. In addition, a second mutually adjusted model was fitted that compared long-term use and non-use of biomass for cooking.

#### Sample size

The size of the study sample was determined by a power calculation which assumed an outcome prevalence of at least 6% for definite CHD among non-users of biomass fuel, based on a previous study in Pakistan [17] (the prevalence of other outcomes was expected to be higher). This indicated that we would require at least 876 women (438 users and 438 non-users of biomass) for 80% power to detect an odds ratio of 2.0 for the use of biomass fuel with a 5% level of statistical significance.

## Patient and public involvement

There was no involvement of patients or the public in development of this study.

## Ethical approval

The study was approved by Ethics Review Committee of Aga Khan University, Karachi, Pakistan.

## Results

A total of 24 villages were visited in order to recruit the number of households required for the survey. In 14 villages all households used biomass for cooking, in three, all used natural gas, and in the other seven, both types of fuel were used. The number of participating households per village ranged from as few as three to as many as 210. Interviews were completed with women from a total of 1073 households, 536 of which currently used biomass fuel, and 537 natural gas (including LPG). No-one declined to participate in the study, but 77 women could not be interviewed because they were not at home at the time when the survey team visited (mostly because they were engaged in agricultural work).

Among the 1073 women who completed interviews, 44 indicated that they were in fact aged less than 40 years of age, and were therefore excluded from the analysis. An additional 151 women had not made meals regularly (at least one meal per day on most days of the week) during the past year, and were also excluded. We further excluded 28 women who did not currently use firewood or cow dung for cooking, but whose time since last use of biomass was <2 years (this was done to ensure distinct exposure categories). Thus, further analysis was based on 850 women: 436 users and 414 non-users of biomass. Among them, 430 were long-term users of biomass users, and 263 were long-term non- users.

Table 1 summarizes the demographic and socioeconomic characteristics of the participants in the study sample overall, and according to categories of exposure to biomass fuel. In comparison with users of biomass, non-users were marginally younger (63% versus 60% <50 years), and somewhat more advantaged socioeconomically.

Table 2 describes the current and past cooking arrangements of participants, including type and duration of fuel use, intensity of cooking, and type of stove and kitchen. Even among the long-term non-users of biomass, 88% had cooked with biomass fuels at some time in their life. Among the biomass users, the large majority had used wood (93%) and cow dung (88%) for longer than 20 years. Few participants (3.7% of biomass users and 6.3% of non-users) had ever used kerosene as a cooking fuel. Most participants (approximately 60%) currently cooked for 2-3 hours per day, the average duration of cooking per day being similar in users and non-users of biomass. Where biomass was used for cooking, it was also more likely to be used to heat the home.

Table 3 shows the distribution of potentially confounding risk factors for CHD in the four categories of exposure to biomass. In comparison with non-users of biomass users, slightly higher proportions of women using biomass reported having been born with 'lower than normal' birth weight, having lost weight at some time during childhood, ever having smoked, and being exposed to environmental tobacco smoke in the home.

## Prevalence of outcome measures

Supplementary Table 1 shows the prevalence of the main outcome measures that were investigated. In total, 297 women (35%) were classed as having hypertension, two thirds of whom were taking regular medication for blood pressure. About 27% had symptoms indicative of angina based on Rose's

 questionnaire. Fifty-four (6.4%) reported a previous history of heart attack, and 19% of women had findings of definite or probable CHD on ECG.

## Validity of ECG classification and interrelationships of outcome measures:

Supplementary Table 2 compares the classification of ECGs by the two observers. Satisfactory ECG traces were obtained for 841 (98.9%) of the participants, but four were missing from the file used to assess inter-observer agreement, and were later assessed jointly by the two observers. The overall agreement between the two observers was 85.2% (kappa = 0.57). Most disagreements were related to cases in which the exceedance of a threshold in, for example, ST elevation, ST depression or the width (duration) of a Q wave was borderline. In some cases, it was questionable whether there was a small R wave or a QS pattern. Also, there was some disagreement about whether T waves were negative or flat. Following discussion between the two observers, all of the discrepancies were reconciled, and it was finally agreed that 181 women (21.5%) showed changes indicative of definite or probable CHD. However, in 22 of these cases, it appeared that the abnormality had occurred only because the ECG leads had been placed incorrectly, and those traces were reclassified as normal. Thus in further analyses, 159 (19%) of women were considered to have definite or probable CHD on ECG.

Supplementary Table 3 shows the prevalence of definite or probable CHD on ECG according to symptoms of angina and history of heart attack. It was somewhat more frequent in participants who reported an earlier heart attack (26%) than in those who did not and had no symptoms of angina (18%). However, there was no association with angina in the absence of heart attack.

## Association of outcome measures with use of biomass and other risk factors

Associations of hypertension and the three CHD outcomes (angina, heart attack and definite or probable CHD on ECG) with potential risk factors are presented in Supplementary Tables 4 to 7, from which the risk estimates for use of biomass fuel for cooking are summarized in Table 4. The first column of each table gives odds ratios adjusted only for age, while the second column presents mutually adjusted risk estimates from a single model that included use of biomass and all of the risk factors that showed associations ( $p \le 0.1$ ) in the analyses adjusted only for age. The last column shows findings from a similar analysis but restricted to women who were long-term users or non-users of biomass.

In analyses that adjusted only for age, hypertension was associated ( $p \le 0.1$ ) with older age, a higher number of household assets, higher frequency of consuming meat and eggs, and having a high BMI or WHR (Supplementary Table 4). When these variables were carried forward to the mutually adjusted analysis, the association with consumption of meat and eggs was diminished, but the others remained. Thus, the risk of hypertension increased 40% with every 10-year increase in age, was 2.3 times higher in women with  $\ge 4$  household assets than in those with 0 or 1, and was increased 1.9-fold in women who had both high BMI and high WHR as compared with those in whom neither BMI nor WHR were elevated. However, hypertension was not associated with use of biomass (OR 1.0 in the fully adjusted model). When analysis was restricted to long-term users and non-users of biomass, results were similar, with an OR of 1.1 for long-term use of biomass.

In analyses that adjusted only for age, the odds of angina increased with age and regular smoking, and were significantly lower with more frequent consumption of meat and eggs (Supplementary Table 5). Moreover, this pattern was maintained when risk estimates were mutually adjusted. Thus, the odds of angina increased by 30% per 10-year increase in age, and with ever having smoked regularly (OR 2.0, 95%CI 1.2-3.2), and were significantly lower in women who ate both meat and eggs at least once per week (OR 0.5, 95%CI 0.3-0.7). There was, however, no association with use of biomass (OR 1.0, 95%CI 0.8-1.4). When analysis was restricted to long-term users and non-users of biomass, results were similar except that there was a suggestion of a weak association with exposure to biomass (OR 1.3, 95%CI 0.9-1.9).

In corresponding analyses with previous history of heart attack (diagnosed by a physician) as an outcome, initial models with adjustment only for age indicated associations (p<0.1) with age, higher household income, higher number of household assets, and high BMI or WHR (Supplementary Table 6). After mutual adjustment, age remained a significant risk factor (OR 1.5, 95%CI 1.2-2.0, for each 10-year increase in age). However, the other associations, although still positive, were not significant at a 5% level. Nor was there an association with use of biomass for cooking (OR 1.2, 95%CI 0.7-2.2). In the mutually adjusted model for long-term use of biomass, results were very similar.

In analyses adjusted only for age, household income was the only variable significantly associated with definite or probable CHD on ECG, and it remained significant in the fully adjusted model (OR 1.6, 95%CI 1.1-2.4 for household income >10,000PKR) (Supplementary Table 7). However, there was no association with use of biomass for cooking, either overall or in the long-term (ORs 0.8 and 0.9).

## Discussion

This study found no association between use of biomass fuel and any of the four outcomes studied (hypertension, angina, previous history of heart attack, and definite or probable CHD on ECG), even when comparison was with women who had not used biomass for at least the last 10 years. The strongest hint of an association was for angina in long-term users as compared with long-term non-users of biomass, but the elevation of risk was small (30%) and not statistically significant at a 5% level.

The choice of villages from which to recruit participants ensured a balance in the fuels currently used for cooking, and cooperation in the survey was good with high response rates from the households and women that were invited to take part. Inevitably, recruitment was to some extent opportunistic and limited to one province of Pakistan. However, there seems no reason to expect that the study sample would have been seriously unrepresentative in the associations of hypertension and CHD with use of biomass and other risk factors.

A linked air monitoring study found that in the kitchens of houses using biomass for cooking, the mean 24-hour average  $PM_{2.5}$  concentration was 531 µg/m<sup>3</sup>, with a median of 136 µg/m<sup>3</sup> and interquartile range 34-615 µg/m<sup>3</sup> (paper in preparation). Corresponding concentrations in houses not using biomass for cooking were 69.9, 24.2, and 13.5-53.3 µg/m<sup>3</sup>. Thus, while individual exposures may have been influenced also by time spent cooking and whether biomass was burned in a closed or open kitchen, the absence of associations with CHD and hypertension is unlikely to reflect inadequate contrasts in recent intensity of exposure.

Our aim was as far as possible to recruit households that had used the same fuel for cooking exclusively for at least 10 years. Villages were selected with this criterion in mind, and it was covered in preliminary inquiries that were addressed to local community representatives. In practice, however, it turned out that where natural gas was available in villages, some participants had not yet switched to cleaner fuel, or had done so at a later date than others. A pragmatic decision was therefore made to include women even if they had changed their cooking fuel within the past 10 years, provided that they had used their current fuel for at least a year. This seemed reasonable since trials had suggested that interventions to reduce household air pollution from use of biomass for cooking can produce reductions in blood pressure and changes in ECGs over the short to medium term [18-20]. However, to check that it did not obscure associations, additional analyses were carried out with restriction to long-term users and non-users of biomass, and still no relationship was found with the health outcomes.

The sample size achieved for the study was close to that planned, and the prevalence of the four outcomes was higher than had been assumed in the power calculations. Moreover, the upper

confidence limits for the odds ratios relating to use of biomass were almost all <2. Thus, the absence of associations with biomass does not reflect a lack of statistical power.

Ascertainment of current use of biomass is likely to have been highly accurate, and while there may have been some errors in recall of the times when biomass had been used in the past, it is difficult to conceive that any resultant misclassification would have obscured important associations with CHD. Generally, switches in the use of fuel were only in one direction – towards cleaner natural gas from biomass. The timing of changes was usually well recalled because in most instances the entire village received the new source of fuel in a particular year. However, the duration of using cow dung and firewood may not always have been remembered reliably, and switches between these types of fuel could also have occurred. Many women reported using cow dung and firewood for the same duration, and no attempt was made to analyse them separately.

Recall of some potentially confounding exposures may also have been inaccurate – particularly those pertaining to childhood. If so, the errors would be expected to be non-differential with respect to CHD, and therefore to bias risk estimates towards the null, possibly leading to uncontrolled residual confounding. However, the assessment of BMI and WHR used standardized methods, and should have been reasonably reliable. The interviewers were trained in how to make the measurements, and their technique was piloted in the field before the start of data collection.

A greater concern is the possibility of error in the ascertainment of outcomes. Blood pressure was objectively measured according to a standardized protocol, and was taken as the average of three readings. Moreover, most of the women who were classed as having hypertension were taking treatment for the disorder, which supports the validity of its assessment. Angina was determined through the well-established Rose questionnaire, but it is possible that symptoms in some cases arose from other pathology. Previous research has suggested that the Rose angina questionnaire may not be as reliable among women as in men [21]. Although the question to participants about history of heart attack referred specifically to diagnoses that had been given by a health professional, errors could have occurred in interpretation of the term "heart attack" (e.g. to include symptoms from dysrhythmias and acute heart failure as well as myocardial infarction). However, ascertainment of heart attack had been previously carried out by the same method in a similar population, where it was found to be reasonably accurate [22].

The diagnosis of CHD from ECGs showed only a weak relationship to history of medically diagnosed heart attack, and none at all to symptoms of angina (Supplementary Table 3). Between observer agreement in the classification of ECGs was reasonably good (kappa = 0.57) (Supplementary Table 2), but it is notable that unlike angina and history of heart attack, CHD diagnosed from ECGs did not show the expected association with age (Supplementary Table 7).

To the extent that errors did occur in the ascertainment of outcomes, they are unlikely to have differed systematically in relation to use of biomass, and therefore would be expected to tend to obscure any true associations.

Because the study had a cross-sectional design, consideration must be given to the possibility of reverse causation. For risk factors related to childhood (e.g. birthweight, father's occupation and education), this is less of a concern. However, it is plausible that characteristics such as diet, physical activity and time spent cooking could have changed as a consequence of CHD. Depending on the circumstances, this might bias associations either upwards or downwards.

Another limitation of the study was that it did not determine when past heart attacks had occurred. Even if not as a consequence of an earlier heart attack, some of the exposures studied (e.g. BMI and WHR) may have changed in the interval since such an attack occurred. If so, this might obscure true associations.

A further possible source of error was uncontrolled residual confounding. To minimize this problem, information was collected about a range of potentially confounding variables, and as in most studies of biomass fuel, socio-economic status tended to be higher in women using cleaner fuels [23]. Although several socio-economic indicators were evaluated as possible factors for adjustment, residual confounding could still have occurred. To explain the absence of associations with biomass, such confounding would have to be inverse (i.e. the under-ascertained confounder would have to be less prevalent in women who used biomass than in non-users).

The study found expected associations with several established risk factors for CHD. Thus, the odds of hypertension, angina and previous history of heart attack were all higher with older age (by 30-50% for every 10 year increase), although this was not found for definite or probable CHD on ECG. The relationship of CHD to age is well documented in the literature [24], and in women, the incidence of CHD increases rapidly after the menopause, reaching up to three times that in premenopausal women [25].

Two of the outcome measures – hypertension and previous history of heart attack – were significantly associated with affluence as measured by number of household assets. This relationship has also been observed before. In a population-based study in Pakistan, history of 'angina or heart attack' was estimated to have 3-fold higher prevalence among affluent participants than in those who were poor [26]. The direction of the association, which is the inverse of that observed in western populations, accords with a higher prevalence of diabetes, hypertension and dyslipidaemias in more educated and affluent groups, which was found in a recent study conducted in South Asian countries, including Pakistan [27].

In further support of an effect of affluence, we found that high BMI and/or WHR was associated with greater risk of hypertension, and (non-significantly) with history of heart attack. Obesity has been shown to increase the risk of hypertension in several studies [28, 29], and partly through this mechanism, also increases the risk and progression of CHD [30]. The INTERHEART study suggested that WHR (abdominal obesity) is a better marker of risk for CHD than BMI [31], but the two were correlated in our study sample, and we opted to use a combined measure.

In contrast, we found that more frequent consumption of meat and eggs was associated with reduced risk of angina. This was unexpected given the known relationship of CHD to consumption of saturated fat [32], and may have been a chance finding. It did not extend to the other outcomes investigated. However, a recent large review suggests that the relationship may be inconsistent [33].

Smoking has consistently been found to increase the risk of CHD in many studies [34]. However, in our investigation it was associated only with angina. This might be because intensity of tobacco use among female smokers in the Pakistani population is low [35].

Despite the finding of several expected associations, the failure to demonstrate more consistent relationships to known risk factors is a further indication for caution in the interpretation of our results.

Several earlier studies have indicated links between use of biomass for cooking and CHD, although the finding has not been entirely consistent [11,12]. As already discussed, one explanation for our failure to demonstrate such associations in the current study could be inaccuracies in the diagnosis of CHD. Another possibility, however, is that adverse effects of exposure to pollutants from the use of biomass persist many years after last exposure. In this survey, even among women who had not used biomass during the last 10 years, most had done so earlier, and often for a long time. Only a few participants (about 3.5% overall) had never used biomass, which was too few for meaningful risk estimates. While it would be possible to compare rural users of biomass with lifelong users of cleaner fuels in urban settings, interpretation would be complicated by other important differences between those living in rural and urban areas.

## Conclusions

This study evaluated the association of hypertension and three measures of CHD – angina, previous history of heart attack and definite or probable CHD on ECG - with use of biomass for cooking. We found no clear associations with any of the health outcomes. However, the weak relationship of ECG abnormalities to the other two measures of CHD, and the inconsistency of their associations with well-established risk factors, suggest that this could have been because of diagnostic misclassification. Alternatively, it could be that an effect was missed because most of the women who were not currently using biomass for cooking had used it in the past, and risk remains elevated for many years after last exposure.

## **Data Availability**

The data [stata.dta format] underpinning the findings of this study are available from the corresponding author upon reasonable request.

## Acknowledgments

This study reported in this paper formed part of a PhD project carried out by Dr Zafar Fatmi under the supervision of Professor David Coggon at the University of Southampton.

Mr Syed Nayab Ali Shah coordinated the data collection. Ms Shereen Jamali, Ms Fozia Jamali, Ms Iqra Memon and Ms Sana Memon administered the questionnaires at interview and recorded the ECGs. We are grateful also to Professor Keith Palmer and Professor M. Masood Kadir for their advice on various aspects of the study.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

# References

- 1. Bonjour S, Adair-Rohani H, Wolf J, Bruce NG, Mehta S, Prüss-Ustün A, Lahiff M, Rehfuess EA, Mishra V, Smith KR. Solid fuel use for household cooking: country and regional estimates for 1980-2010. *Environ Health Perspect*. 2013;121:784-90.
- 2. World Health Organization. Household air pollution and health. Geneva, Switzerland. (Accessed on 4 April 2018). <u>http://www.who.int/mediacentre/factsheets/fs292/en/</u>
- 3. Smith KR, Samet JM, Romieu I, Bruce N. Indoor air pollution in developing countries and acute lower respiratory infections in children. Thorax. 2000 Jun;55(6):518-32.
- 4. Smith KR, Mehta S, Maeusezahl-Feuz M. Indoor air pollution from household use of solid fuels: comparative quantification of health risks. In: Ezzati MLA, Rodgers A, Murray CJL, editors. Global and regional burden of disease attributable to selected major risk factors. Geneva, Switzerland: World Health Organization; 2004. pp. 1435–1493.
- 5. Torres-Duque C, Maldonado D, Pérez-Padilla R, Ezzati M, Viegi G; Forum of International Respiratory Studies (FIRS) Task Force on Health Effects of Biomass Exposure. Biomass fuels and respiratory diseases: a review of the evidence. Proc Am Thorac Soc. 2008 Jul 15;5(5):577-90.
- 6. Liu Y, Lee K, Perez-Padilla R, Hudson NL, Mannino DM. Outdoor and indoor air pollution and COPD-related diseases in high- and low-income countries. Int J Tuberc Lung Dis. 2008;12(2):115-27.
- 7. Kurmi OP, Semple S, Simkhada P, Smith WC, Ayres JG. COPD and chronic bronchitis risk of indoor air pollution from solid feul: a systematic review and meta-analysis. Thorax. 2010; 65(3):221-8.
- 8. Liu Q, Sasco AJ, Riboli E et al. Indoor air pollution and lung cancer in Guangzhou, People's Republic of China. Am. J. Epidemiol. 1993; 137: 145–54.
- 9. Kleinerman R, Wang Z, Lubin J, Zhang S, Metayer C, Brenner A. Lung cancer and indoor air pollution in rural china. Ann Epidemiol. 2000;10(7):469.
- 10. Behera D, Balamugesh T. Indoor air pollution as a risk factor for lung cancer in women. J Assoc Physicians India. 2005; 53:190-2.
- 11. Fatmi Z, Coggon D. Coronary heart disease and household air pollution from use of solid fuel: a systematic review. Br Med Bull. 2016 Jun;118(1):91-109.
- 12. Yu K, Qui G, Chan K-H, Lam K-BH, Kurmi OP, Bennett DA et al. Association of solid fuel use with risk of cardiovascular and all-cause mortality in rural China. JAMA 2018;319:1351-61.
- 13. Rose G, McCartney P, Reid DD. Self-administration of a questionnaire on chest pain and intermittent claudication. Br J Prev Soc Med. 1977; 31:42–48.
- 14. Prineas RJ, Crow RS, Zhang Z-h. The Minnesota code manual of electrocardiographic findings. 2<sup>nd</sup> Edition. London. Springer London; 2010.
- Christiansen TB and Lauritsen JM. (Ed.) EpiData Comprehensive Data Management and Basic Statistical Analysis System. Odense Denmark, EpiData Association, 2010-. <u>http://www.epidata.dk</u>
- 16. Stata Corp LP 2012, Stata Statistical Software: Release 12.0, College Station TX, USA.
- 17. Jafar TH, Qadri Z, Chaturvedi N. Coronary artery disease epidemic in Pakistan: more electrocardiographic evidence of ischaemia in women than in men. Heart. 2008;94(4):408-13.
- 18. McCracken J, Smith KR, Stone P, Diaz A, Arana B, Schwartz J. Intervention to lower household wood smoke exposure in Guatemala reduces ST-segment depression on electrocardiograms. Environ Health Perspect 2011;119:1562-8.
- 19. McCracken JP, Smith KR, Díaz A, Mittleman MA, Schwartz J. Chimney stove intervention to reduce long-term wood smoke exposure lowers blood pressure among Guatemalan women. Environ Health Perspect 2007;115:996-1001.
- 20. Alexander D, Larson T, Bolton S, Vedal S. Systolic blood pressure changes in indigenous Bolivian women associated with an improved cookstove intervention. Air Qual Atmos Health 2015;8:47-53.

2	
3	
4	
5	
6	
7	
8	
-	
9	
1	0
1	1
	2
1	3
1	
	5
1	6
1	7
I	8
1	9
	0
ĥ	1
2	1
2	2
2	3
	4
2	5
2	6
	7
2	8
2	9
	0
3	1
3	2
3	
3	4
3	5
	6
3	7
3	8
3	
	2
4	
4	1
4	2
4	
4	4
4	5
	-
4	
4	7
4	8
4	
5	0
5	1
5	
5	∠ م
5	
5	4
	5
	6
5	7
5	
5	
5	
6	Λ

21. Wilcosky T, Harris R, Weissfeld L. The prevalence and correlates of Rose questionnaire angina among women and men in the Lipid Research Clinics Program Prevalence Study. Am J Epidemiol. 1987;125 (3):400-409.

- 22. Jafar TH, Jafary FH, Jessani S, Chaturvedi N. Heart disease epidemic in Pakistan: women and men at equal risk. Am Heart J. 2005;150(2):221-6.
- 23. Khushk WA, Fatmi Z, White F, Kadir MM. Health and social impacts of improved stoves on rural women: a pilot intervention in Sindh, Pakistan. Indoor Air. 2005 Oct;15(5):311-6.
- 24. Castelli WP. Epidemiology of coronary heart disease: The Framingham study. American Journal of Medicine 1984, page 4.
- 25. Gordon T, Kannel WB, Hjortland MC, McNamara PM. Menopause and coronary heart disease. The Framingham Study. Ann Intern Med. 1978; 89:157–61.
- 26. Hameed K, Kadir M, Gibson T, Sultana S, Fatima Z, Syed A. The frequency of known diabetes, hypertension and ischaemic heart disease in affluent and poor urban populations of Karachi, Pakistan. Diabet Med. 1995;12(6):500-3.
- 27. Ali MK, Bhaskarapillai B, Shivashankar R, Mohan D, Fatmi Z, Pradeepa R, Masood Kadir M, Mohan V, Tandon N, Narayan KM, Prabhakaran D; CARRS investigators. Socioeconomic status and cardiovascular risk in urban South Asia: The CARRS Study. Eur J Prev Cardiol. 2016 Mar;23(4):408-19.
- 28. Hubert HB, Feinleib M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. Circulation 1983; 67:968–77.
- 29. Todd Miller M, Lavie CJ, White CJ. Impact of obesity on the pathogenesis and prognosis of coronary heart disease. J Cardiometab Syndrome 2008; 3:162–7.
- 30. Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet. 2002;360: 1903-13.
- 31. Yusuf S, Hawken S, Ounpuu S, Bautista L, Franzosi MG, Commerford P, Lang CC, Rumboldt Z, Onen CL, Lisheng L, Tanomsup S, Wangai P Jr, Razak F, Sharma AM, Anand SS; INTERHEART Study Investigators. Obesity and the risk of myocardial infarction in 27,000 participants from 52 countries: a case-control study. Lancet 2005;366(9497):1640-9.
- 32. The World Health Report 2002: reducing risks, promoting healthy life. Geneva, World Health Organization, 2002.
- 33. Chowdhury R, Warnakula S, Kunutsor S, Crowe F, Ward HA, Johnson L, Franco OH, Butterworth AS, Forouhi NG, Thompson SG, Khaw KT, Mozaffarian D, Danesh J, Di Angelantonio E. Association of dietary, circulating, and supplement fatty acids with coronary risk: a systematic review and meta-analysis. Ann Intern Med. 2014 Mar 18;160(6):398-406. doi: 10.7326/M13-1788.
- 34. Huxley RR, Woodward, M. Cigarette smoking as a risk factor for coronary heart disease in women compared with men: a systematic review and meta-analysis of prospective cohort studies. Lancet. 2011;378(9799):1297-305.
- 35. Global Adult Tobacco Survey. Pakistan Fact sheet 2014. http://www.who.int/tobacco/surveillance/survey/gats/pakfactsheet.pdf

Characteristic	All we (n=85		(n=436) biomass		Long-term users of biomass (n=430)		Long-term non- users of biomass (n=263)			
	N	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Age (years)										
<50	525	(61.8)	263	(60.3)	262	(63.3)	257	(59.8)	166	(63.1)
≥50	325	(38.2)	173	(39.7)	152	(36.7)	173	(40.2)	97	(36.9)
Educational status				x 2				× × ×		
No literacy	797	(93.8)	419	(96.1)	378	(91.3)	413	(96.1)	239	(90.9)
Any literacy	53	(6.2)	17	(3.9)	36	(8.7)	17	(4.0)	24	(9.1)
Household income/month		6								
≤10000PKR	651	(76.6)	351	(80.5)	300	(72.5)	347	(80.7)	185	(70.3)
>10000PKR	199	(23.4)	85	(19.5)	114	(27.5)	83	(19.3)	78	(29.7)
Household tenure			1					× × ×		· · · · · ·
Rented	70	(8.2)	25	(5.7)	45	(10.9)	25	(5.8)	20	(7.6)
Owned	780	(91.8)	411	(94.3)	369	(89.1)	405	(94.2)	243	(92.4)
Construction of house				CI.		· · ·				
Katcha/ semi-pucca	652	(76.7)	361	(82.8)	291	(70.3)	356	(82.8)	173	(65.8)
Pucca	198	(23.3)	75	(17.2)	123	(29.7)	74	(17.2)	90	(34.2)
Number of household assets										
Low (0-1)	268	(31.5)	140	(32.1)	128	(30.9)	139	(32.3)	84	(31.9)
Medium (2-3)	404	(47.5)	223	(51.2)	181	(43.7)	218	(50.7)	108	(41.1)
High $(\geq 4)$	178	(21.0)	73	(16.7)	105	(25.4)	73	(17.0)	71	(27.0)
Father's occupation in childhood										
Non-manual	39	(4.6)	19	(4.4)	20	(4.8)	18	(4.2)	16	(6.1)
Manual	811	(95.4)	417	(95.6)	394	(95.2)	412	(95.8)	247	(93.9)

Table 1 D staniation of monticinants h 1. а. • :. . **.** .

1	
2	
3 4	
5	
6 7	
8	
9 10	
11	
12 13	
14	
15 16	
17	
18	
20	
21	
11 12 13 14 15 16 17 18 19 20 21 22 23	
24	
25 26	
27	
28 29	
30	
31 32	
33	
32 33 34 35 36	
36 37	
37 38	
39	
40 41	
42	
43 44	
45	

Characteristic	Users of biomass (n=436)		Non-use biomass (n=414)	1		Long-term users of biomass (n=430)		erm non-users 1ass )
	n	(%)	n	(%)	n	(%)	n	(%)
Ever used biomass for cooking	436	(100)	382	(92.3)	430	(100)	231	(87.8)
Years since last used biomass for cooking								
Current user	436	(100)	-	-	430	(100)	-	-
2-9	-	-	151	(39.5)	-	-	-	-
≥10	-	-	231	(60.5)	-	-	231	(100)
Ever used wood for cooking	435	(99.8)	358	(86.5)	429	(99.8)	218	(82.9)
Ever used cow dung for cooking	422	(96.8)	358	(86.5)	416	(96.7)	216	(82.1)
Ever used kerosene for cooking	16	(3.7)	26	(6.3)	16	(3.7)	17	(6.5)
Ever used LPG/natural gas for cooking	17	(3.9)	413	(99.8)	15	(3.5)	263	(100)
Average hours per day cooked in past year								
<u>≤</u> 1	129	(29.6)	133	(32.1)	123	(28.6)	75	(28.5)
2-3	270	(61.9)	237	(57.3)	270	(62.8)	165	(62.7)
<u>≥</u> 4	37	(8.5)	44	(10.6)	37	(8.6)	23	(8.8)
Type of stove used for cooking								
Gas/LPG	2	(0.5)	414	(100)	2	(0.5)	263	(100)
Biomass with	166	(38.1)			164	(38.1)		
chimney/improved stove	100	(38.1)	-	-	104	(38.1)	-	-
Biomass with three brick open stove	267	(61.2)	-	-	263	(61.2)	-	-
Other	1	(0.2)	-	-	1	(0.2)	-	-
Type of kitchen								
Closed (four walls – linked with living	88	(20, 2)	116	(28.0)	86	(20.0)	79	(30.0)
room or separate)	00	(20.2)	110	(20.0)	00	(20.0)	/ 7	(30.0)
Semi-open (fewer than four walls)	189	(43.3)	155	(37.4)	187	(43.5)	94	(35.7)
Open (no walls)	159	(36.5)	143	(34.5)	157	(36.5)	90	(34.2)
Heat home with biomass	237	(54.4)	106	(25.6)	236	(54.9)	74	(28.1)

 Table 2. Current and past cooking arrangements according to exposure category.

Non-users of biomass

(%)

(18.6)

(61.4)

(20.0)

(42.5)

(57.5)

(44.0)

(56.0)

(91.3)

(64.5)

(35.5)

(49.5)

(37.7)

(12.8)

(34.3)

(39.4)

(26.3)

(31.2)

(38.7)

(30.0)

(0.2)

(8.7)

(n=414)

n

77

254

83

176

238

182

232

378

36

267

147

205

156

53

142

163

109

129

160

124

1

Long-term users of

(%)

(26.5)

(55.1)

(18.4)

(40.7)

(59.3)

(37.2)

(62.8)

(89.3)

(10.7)

(61.6)

(38.4)

(28.8)

(45.6)

(25.6)

(40.0)

(40.2)

(19.8)

(41.6)

(34.7)

(23.7)

(0)

biomass (n=430)

n

114

237

175

255

160

270

384

46

265

165

124

196

110

172

173

85

179

149

102

0

79

Long-term non-users

(%)

(20.5)

(59.3)

(20.2)

(46.4)

(53.6)

(45.2)

(54.8)

(91.3)

(8.7)

(65.8)

(34.2)

(56.7)

(34.6)

(8.7)

(33.5)

(38.0)

(28.5)

(30.0)

(38.4)

(31.2)

(0.4)

of biomass (n=263)

n

54

156

53

122

141

119

144

240

23

173

90

149

91

23

88

100

75

79

101

82

1

2	
3	Table 3. Distribution of risk factors across the
4	Characteristic
5	
6	
7	Birthweight
8	Lower than normal
9	Normal
10	Higher than normal
11	Ever hungry all the time during childhood because there
12	was not enough food
13	No
14	Yes
15	Lost weight during childhood
16	No
	Yes
17	Ever smoked regularly (any of cigarettes, bidi, huqqa)
18	Never
19	Ever
20	Environmental tobacco smoke (at least one other
21	household member smoked cigarettes, bidi or huqqa in
22	the home)
23	No
24	Yes
25	Physical activity score
26	0-2
27	3-4
28	5-6
20	Consumption of meat or eggs
	Do not eat either meat or eggs as much as once per week
30	Eat one of meat or eggs as much as once per week
31	Eat both meat and eggs at least once per week
32	Current nutrition <sup>a</sup>
33	Neither BMI nor WHR high
34	One of BMI or WHR high
35	Both BMI and WHR high
36	Not known
37	<sup><i>a</i></sup> BMI ( $kg/m^2$ ) $\geq 25 = high$ ; WHR $\geq 0.85 = high$ .
38	
39	

40 41 42

1

**Table 3.** Distribution of risk factors across the four exposure categories.

Users of biomass

(%)

(26.8)

(54.8)

(18.4)

(40.4)

(59.6)

(37.2)

(62.8)

(89.4)

(10.6)

(61.7)

(38.3)

(28.4)

(45.6)

(25.9)

(39.7)

(40.4)

(20.0)

(42.0)

(34.6)

(23.4)

(0)

(n=436)

n

117

239

80

176

260

162

274

390

46

269

167

124

199

113

173

176

87

183

151

102

2	
3	
4	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
17	
20	
21	
- 77	
22	
24	
24	
25	
26	
27	
28	
29	
29	
30	
31	
32	
33	
24	
34	
35	
36 37	
37	
20	
39	
40	
41	
42	
43	
44	
45	
46	
47	
48	
49	
50	
51	
52	
53	
54	
55	
56	
57	
58	

58 59 60 **Table 4.** Associations of hypertension, angina, history of heart attack, and definite or probable CHD on ECG with current and long-term use of biomass for cooking.

Outcome	Adjuste age (n=	d only for 850)	Fully a (n=850	djusted <sup>a</sup> )	limiteo users a bioma	Fully adjusted and limited to long-term users and non-users of biomass <sup>b</sup> (n=693)		
	OR	(95%CI)	OR	(95% CI)	OR	(95% CI)		
Hypertension								
Non-users of biomass	1.0		1.0		1.0			
Users of biomass	1.2	(0.9-1.5)	1.0	(0.8-1.4)	1.1	(0.8-1.6)		
Angina								
Non-users of biomass	1.0		1.0		1.0			
Users of biomass	1.0	(0.7-1.3)	1.0	(0.8-1.4)	1.3	(0.9-1.9)		
Heart Attack								
Non-users of biomass	1.0		1.0		1.0			
Users of biomass	1.4	(0.8-2.4)	1.2	(0.7-2.2)	1.3	(0.7-2.4)		
Definite or probable CHD on	4							
ECG								
Non-users of biomass	1.0		1.0		1.0			
Users of biomass user	0.8	(0.6-1.2)	0.8	(0.6-1.2)	0.9	(0.6-1.3)		

<sup>a</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p < 0.1) in analyses adjusted only for age

<sup>b</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p<0.1) in analyses adjusted only for age, but was restricted to women who were long-term users or non-users of biomass

Liezoni

## Supplementary Materials

**Supplementary Table 1.** Prevalence of hypertension, history of heart attack, angina and coronary heart disease in study sample.

Characteristic	n	(%)
Hypertension		
Systolic hypertension (systolic BP≥140 mmHg)	133	(15.8)
Diastolic hypertension (diastolic BP≥90 mmHg)	102	(12.1)
Regular medication for high blood pressure	198	(23.5)
Hypertension (any of the above)	297	(35.3)
Angina	227	(27.0)
History of heart attack	54	(6.4)
Definite or probable CHD on ECG <sup>a</sup>	159	(18.9)

<sup>a</sup>Based on 841 women. ECGs for 9 women were missing or could not be coded due to poor quality.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Negative59130Positive94122Kappa = 0.57	Negative         591         30           Positive         94         122
Positive         94         122           Kappa = 0.57         122	Positive 94 122 Kappa = 0.57
Kappa = 0.57	Kappa = 0.57

3
4
5
6
7
8
9
10
11
12
13
14
14
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
44 45
46
47
48
49
50
51
52
53
54
55
56
57
50

1 2 З

Supplementary Table 3. Prevalence of definite or probable CHD changes on ECG according to history of heart attack and angina.

Other measure of CHD	Definite or	probable CHD	changes on	ECG <sup>a</sup>
	Yes		No	
	n	(%)	Ν	(%)
No history of heart attack or angina	105	(18.2)	471	(81.8)
History of angina	45	(19.8)	182	(80.2)
History of heart attack	14	(25.9)	40	(74.1)
History of angina or heart attack	54	(20.4)	211	(79.6)
History of angina and heart attack "ECGs for 9 women were missing or cost	5	(31.3)	11	(68.8)

Risk factor	Adjusted only for age		Fully	adjusted <sup>a</sup>	Fully adjusted and limited to long-		
	(n=8		(n=85	50)	term users and non-users of biomass <sup>b</sup>		
					(n=69		
A ( 10 )	OR	(95%CI)	OR	(95%CI)	OR	(95%CI)	
Age (per 10 year increase)	1.4	(1.2-1.6)	1.4	(1.2-1.7)	1.5	(1.2-1.7)	
Educational status	1.0						
Illiterate	1.0		-		-		
Any literacy	0.6	(0.3-1.2)					
Household income/month	1.0				-		
<3000-10000PKR	1.0		-				
>10000PKR	1.0	(0.7-1.4)					
Household ownership					-		
Rented	1.0		-				
Own	0.8	(0.5-1.3)					
Construction of house					-		
Katcha/semi-pucca	1.0		-				
Pucca	0.9	(0.6-1.2)					
Number of household assets							
0-1	1.0		1.0		1.0		
2-3	1.7	(1.2-2.4)	1.6	(1.2-2.3)	1.8	(1.2-2.6)	
≥4	2.4	(1.6-3.6)	2.3	(1.5-3.4)	2.7	(1.7-4.3)	
Father's occupation in woman's					-		
childhood							
Non-manual	1.0		-				
Manual	1.2	(0.6-2.5)					
Birthweight							
Lower than normal	1.0				-		
Normal	1.0	(0.7-1.4)	-				
Higher than normal	1.0	(0.6-1.5)					
Ever hungry during all the time					-		
during childhood because there							
was not enough food							
No	1.0		-				
Yes	0.9	(0.7-1.3)					
Lost weight during childhood					-		
No	1.0		-				
Yes	1.2	(0.9-1.6)					
Ever smoked regularly (any of		. /					
cigarettes, bidi, huqqa)							
Never	1.0		-		-		
Ever	0.8	(0.5-1.3)					
Environmental tobacco smoke (at		(110 -10)					
least one other household membe							
smokes cigarettes, bidi or huqqa							
in the home)							
No	1.0		_				
Yes	0.8	(0.6-1.1)	_				
100	0.0	(0.0-1.1)					

Do not eat either meat or eggs as	1.0		1.0		1.0	
much as once per week						
Eat one of meat or eggs as much	1.4	(1.0-1.9)	1.2	(0.9-1.7)	1.2	(0.8-1.7)
as once per week						
Eat both meat and eggs at least	1.4	(1.0-2.1)	1.2	(0.8-1.8)	1.2	(0.8-1.9)
once per week						
Current nutrition <sup>c</sup>						
Neither BMI nor WHR high	1.0		1.0		1.0	
One of BMI or WHR high	1.2	(0.9-1.7)	1.2	(0.8-1.6)	1.2	(0.8-1.8)
Both BMI and WHR high	2.0	(1.4-2.9)	1.9	(1.3-2.8)	1.8	(1.2-2.7)
Non-user of biomass	1.0		1.0			
User of biomass	1.2	(0.9-1.5)	1.0	(0.8-1.4)		
Long-term non-user of biomass	1.0				1.0	
Long-term user of biomass	1.2	(0.9-1.7)			1.1	(0.8-1.6)

<sup>*a*</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p < 0.1) in analyses adjusted only for age

<sup>b</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p<0.1) in analyses adjusted only for age, but was restricted to women who were long-term users or non-users of biomass

°Body mass index (BMI) (kg/m²) ≥25= high; Waist-to-hip ratio (WHR) ≥0.85=high.

Supplementary Table	e 5. Asso	ciations of	f angina	with risk factors.
---------------------	-----------	-------------	----------	--------------------

Risk factor		sted only	Fully	adjusted <sup>a</sup>		adjusted and	
	for age (n=850)		( <b>n=8</b>	(n=850)		limited to long- term users and non-users of biomass <sup>b</sup>	
					(n=69		
	OR	(95%CI)	OR	(95%CI)	OR	(95%CI)	
Age (per 10 year increase)	1.3	(1.1-1.6)	1.3	(1.1-1.5)	1.3	(1.1-1.5)	
Educational status							
Illiterate	1.0		-		-		
Any literacy	0.6	(0.3-1.3)					
Household income/month					-		
<3000-10000PKR	1.0		-				
>10000PKR	1.1	(0.8-1.6)					
Household ownership		. /			-		
Rented	1.0		-				
Own	0.8	(0.5-1.3)					
Construction of house		(			-		
Katcha/semi-pucca	1.0		_				
Pucca	1.2	(0.8-1.7)					
Number of household assets	1.2	(0.0 1.7)			_		
0-1	1.0		_		-		
2-3	0.9	(0.6-1.3)	-				
>4	0.9 1.0	(0.6-1.5)					
—	1.0	(0.0-1.3)					
Father's occupation in woman's					-		
childhood Non-manual	1.0						
		(0, 2, 1, 4)					
Manual	0.7	(0.3-1.4)					
Birthweight	1.0						
Lower than normal	1.0				-		
Normal	1.2	(0.8-1.8)	-				
Higher than normal	1.1	(0.7-1.8)					
Ever hungry during all the time					-		
during childhood because there							
was not enough food							
No	1.0		-				
Yes	0.8	(0.6-1.1)					
Lost weight during childhood					-		
No	1.0		-				
Yes	1.0	(0.8-1.4)					
Ever smoked regularly (any of							
cigarettes, bidi, huqqa)							
Never	1.0		1.0		1.0		
Ever	2.1	(1.3-3.3)	2.0	(1.2-3.2)	2.1	(1.3-3.6)	
Environmental tobacco smoke							
(at least one other household							
member smokes cigarettes, bidi							
member smokes cigarettes, bidi or huqqa in the home)							
member smokes cigarettes, bidi or huqqa in the home) No	1.0		_				

**Consumption of meat or eggs** 

Do not eat either meat or eggs	1.0		1.0		1.0	
as much as once per week Eat one of meat or eggs as	0.6	(0.4-0.8)	0.6	(0.4-0.8)	0.7	(0.5-1.0)
much as once per week Eat both meat and eggs at least once per week	0.4	(0.3-0.7)	0.5	(0.3-0.7)	0.5	(0.3-0.8)
Current nutrition <sup>c</sup>						
Neither BMI nor WHR high	1.0					
One of BMI or WHR high	0.8	(0.5-1.1)	-			
Both BMI and WHR high	0.8	(0.5-1.2)				
Non-user of biomass	1.0					
User of biomass user	1.0	(0.7-1.3)	1.0	(0.8-1.4)		
Long-term non-user of biomass	1.0				1.0	
Long-term non-user of biomass	1.2	(0.9-1.7)			1.3	(0.9-1.9)

<sup>a</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p<0.1) in analyses adjusted only for age

<sup>b</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p<0.1) in analyses adjusted only for age, but was restricted to women who were long-term users or non-users of biomass

<sup>c</sup>Body mass index (BMI)  $(kg/m^2) \ge 25 = high$ ; Waist-to-hip ratio (WHR)  $\ge 0.85 = high$ .

Risk factor	Adjusted only for age (n=850) <sup>a</sup>		Full	y adjusted <sup>b</sup>	Fully adjusted and limited to long-term		
			(n=850)		users and non-users of		
					biomass <sup>c</sup>		
	OR	(95%CI)	OR	(95%CI)	(n=6 OR	(93) (95%CI)	
Age (per 10 year increase)	1.5	(1.2-2.0)	1.5	(1.2-2.0)	1.5	(1.2-2.0)	
Educational status	1.5	(1.2-2.0)	1.5	$(1.2^{-2.0})$	1.5	(1.2-2.0)	
Illiterate	1.0		_		_		
Any literacy	1.5	(0.5-4.5)	-		-		
Household income/month	1.5	(0.3-4.3)					
<3000-10000PKR	1.0		1.0		1.0		
<3000-10000PKR	1.0 1.6	(0,0,2,0)		(0, 2, 2, 5)	1.0	(0, 2, 2, 1)	
	1.0	(0.9-2.9)	1.4	(0.8-2.5)	1.0	(0.8-3.1)	
Household ownership	1.0						
Rented	1.0	(0, 4, 2, 4)	-		-		
Own	1.2	(0.4-3.4)					
Construction of house					-		
Katcha/semi-pucca		(0 = 5 = 5	-				
Pucca	1.3	(0.7-2.3)					
Number of household assets							
0-1	1.0		1.0		1.0		
2-3	1.4	(0.7-2.7)	1.3	(0.7-2.5)	1.8	(0.8-3.8)	
<u>≥</u> 4	2.1	(1.0-4.3)	1.8	(0.8-3.8)	2.1	(0.9-5.1)	
Father's occupation in woman's					-		
childhood							
Non-manual	1.0		-				
Manual	1.0	(0.2-4.5)					
Birthweight							
Lower than normal	1.0				-		
Normal	1.0	(0.5-1.9)	-				
Higher than normal	0.7	(0.3-1.7)					
Ever hungry during all the time					-		
during childhood because there							
was not enough food							
No	1.0		-				
Yes	1.0	(0.6-1.7)					
Lost weight during childhood	-				-		
No	1.0		-				
Yes	1.1	(0.6-1.9)					
Ever smoked regularly (any of		(					
cigarettes, bidi, huqqa)							
Never	1.0		-				
Ever	0.9	(0.4-2.1)					
Environmental tobacco smoke (at	0.7	(0.7-2.1)					
least one other household member							
smokes cigarettes, bidi or huqqa in							
the home)	1.0						
No	1.0	$(0 = 1 \leq 1)$	-				
Yes Consumption of meat or eggs	0.9	(0.5-1.6)					

**Supplementary Table 6.** Associations of previous history of heart attack (diagnosed by a physician) with risk factors.

**Consumption of meat or eggs** 

Do not out aither most or access	1.0						
Do not eat either meat or eggs as	1.0		-				
much as once per week							
Eat one of meat or eggs as much	1.2	(0.6-2.3)					
as once per week Eat both meat and eggs at least	1.8	(0.9-3.5)					
once per week	1.0	(0.9-3.3)					
Current nutrition <sup>d</sup>							
Neither BMI nor WHR high	1.0		1.0		1.0		
One of BMI or WHR high	1.3	(0.6-2.5)	1.2	(0.6-2.5)	1.6	(0.7-3.4)	
Both BMI and WHR high	2.0	(1.0-4.0)	1.9	(0.9-3.7)	1.7	(0.8-3.6)	
Non-user of biomass	1.0		1.0		-		
Use of biomass	1.4	(0.8-2.4)	1.2	(0.7-2.2)			
Long-term non-user of biomass	1.0				1.0		
Long-term user of biomass	1.5	(0.8-2.7)			1.3	(0.7-2.4)	

<sup>a</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p<0.1) in analyses adjusted only for age

<sup>b</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p<0.1) in analyses adjusted only for age, but was restricted to women who were long-term users or non-users of biomass

<sup>a</sup>Body mass index (BMI) (kg/m<sup>2</sup>) ≥25= high; Waist-to-hip ratio (WHR) ≥0.85=high.

Risk factor	Adjusted only for age			Ū	Fully adjusted and limited to long-term users and non-users		
	( <b>n=8</b> 4	<b>1</b> 1)	( <b>n=841</b> )			omass <sup>b</sup>	
					(n=68		
	OR	(95%CI)	OR	(95%CI)	OR	(95%CI)	
Age (per 10 year increase)	1.1	(0.9-1.3)	1.1	(0.9-1.3)	1.0	(0.8-1.3)	
Educational status							
Illiterate	1.0		-		-		
Any literacy	0.8	(0.4-1.7)					
Household income/month							
<3000-10000PKR	1.0		1.0		1.0		
>10000PKR	1.6	(1.1-2.3)	1.6	(1.1-2.4)	1.3	(0.8-2.0)	
Household ownership					-		
Rented	1.0		-				
Own	1.4	(0.7-2.9)					
Construction of house		. /			-		
Katcha/semi-pucca	1.0		-				
Pucca	1.0	(0.7-1.5)					
Number of household assets							
0-1	1.0		-				
2-3	1.0	(0.7-1.5)					
>4	1.3	(0.8-2.1)					
Father's occupation in woman's childhood	1.0				-		
Non-manual	1.0	(0, 1, 2, 2)	-				
Manual	1.0	(0.4-2.3)					
Birthweight	1.0						
Lower than normal	1.0				-		
Normal	1.1	(0.7-1.7)	-				
Higher than normal	1.1	(0.7-1.9)					
Ever hungry during all the time during childhood because there was not enough food					-		
No	1.0		-				
Yes	1.1	(0.8-1.6)					
Lost weight during childhood		. ,			-		
No	1.0		-				
Yes	0.8	(0.6-1.2)					
Ever smoked regularly (any of		. /					
cigarettes, bidi, huqqa)							
Never	1.0		-		-		
Ever	1.0	(0.6-1.8)					
Environmental tobacco smoke (at		()					
least one other household							
member smokes cigarettes, bidi							
or huqqa in the home)							
No	1.0				_		

as once per week Eat both meat and eggs at least	1.2	(0.7-1.8)				
once per week		. ,				
Current nutrition <sup>c</sup>						
Neither BMI nor WHR high	1.0					
One of BMI or WHR high	0.8	(0.5-1.2)	-			
Both BMI and WHR high	1.1	(0.7-1.6)				
Non-user of biomass user	1.0		1.0			
User of biomass	0.8	(0.6-1.2)	0.8	(0.6-1.2)		
Longterm non-user of biomass	1.0	. ,			1.0	
Longterm user of biomass	0.9	(0.6-1.3)			0.9	(0.6-1.3)

<sup>a</sup>ECGs were missing for 9 women or not codable due to poor quality.

<sup>b</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p<0.1) in analyses adjusted only for age

<sup>c</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p<0.1) in analyses adjusted only for age, but was restricted to women who were long-term users or non-users of biomass

<sup>*d*</sup>Body mass index (BMI)  $(kg/m^2) \ge 25 = high$ ; Waist-to-hip ratio (WHR)  $\ge 0.85 = high$ .

reziez onz

 BMJ Open

Section/Topic	ltem #	Recommendation	Reported on page
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1-2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods		6	
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	3
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	3-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	3-5
Bias	9	Describe any efforts to address potential sources of bias	3-5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	5
		(b) Describe any methods used to examine subgroups and interactions	5
		(c) Explain how missing data were addressed	In relevant tables
		(d) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(e) Describe any sensitivity analyses	N/A

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	6
		confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	Not needed
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6 and Tables 1-3
		(b) Indicate number of participants with missing data for each variable of interest	Tables 1-3
Outcome data	15*	Report numbers of outcome events or summary measures	6
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence	Supplementary
		interval). Make clear which confounders were adjusted for and why they were included	Tables 4-7
		(b) Report category boundaries when continuous variables were categorized	Tables
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	8-9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10
Generalisability	21	Discuss the generalisability (external validity) of the study results	8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on	2
		which the present article is based	

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

# **BMJ Open**

## **Coronary Heart Disease, Hypertension and Use of Biomass Fuel among Women: Comparative Cross-sectional Study.**

Journal:	BMJ Open
Manuscript ID	bmjopen-2019-030881.R2
Article Type:	Research
Date Submitted by the Author:	03-Jul-2019
Complete List of Authors:	Fatmi, Zafar; Aga Khan University, Department of Community Health Sciences Ntani, G; University of Southampton and Southampton University Hospitals NHS Trust, MRC Lifecourse Epidemiology Unit Coggon, David; University of Southampton, MRC Lifecourse Epidemiology Unit
<b>Primary Subject Heading</b> :	Global health
Secondary Subject Heading:	Epidemiology, Occupational and environmental medicine, Public health
Keywords:	Coronary heart disease < CARDIOLOGY, biomass fuel, Hypertension < CARDIOLOGY, women, EPIDEMIOLOGY, Public health < INFECTIOUS DISEASES



# **Coronary Heart Disease, Hypertension and Use of Biomass Fuel among Women: Comparative Cross-sectional Study.**

## Zafar Fatmi,<sup>1,2</sup> Georgia Ntani,<sup>2</sup> David Coggon<sup>2</sup>

<sup>1</sup>Department of Community Health Sciences, Aga Khan University, PO Box 3500, Karachi 74800, Pakistan.

<sup>2</sup>MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK.

\*Correspondence should be addressed to Zafar Fatmi; zafar.fatmi@aku.edu;

## Abstract

*Objectives:* To explore the associations of hypertension and coronary heart disease (CHD) with use of biomass fuel for cooking.

Design: Comparative cross-sectional study.

Setting: Rural villages in Sindh, Pakistan.

**Participants:** Women aged  $\geq$ 40 years who had used biomass fuel for cooking for at least the past year (n = 436), and a comparison group (n=414) who had cooked only with non-biomass fuel during the past year were recruited through door-to-door visits. None of those who were invited to take part declined.

**Primary and secondary outcome measures:** Hypertension was determined from blood pressure measurements and use of medication. CHD was assessed by three measures: history of angina (Rose angina questionnaire), previous history of 'heart attack', and definite or probable changes of CHD on electrocardiogram (ECG). Potentially confounding risk factors were ascertained by questionnaire and anthropometry. Associations of hypertension and CHD with use of biomass and other risk factors were assessed by logistic regression, and summarised by odds ratios (ORs) with 95% confidence intervals (CIs).

**Results:** After adjustment for potential confounders, there was no association of hypertension (OR: 1.0, 95% CI 0.8 – 1.4) angina (OR: 1.0, 95% CI 0.8-1.4), heart attack (OR: 1.2, 95% 0.7 - 2.2) or ECG changes of CHD (OR: 0.8, 95% CI 0.6 – 1.2) with current use of biomass for cooking. Nor were any associations apparent when analyses were restricted to long-term ( $\geq 10$  years) users and non-users of biomass fuel.

*Conclusions:* A linked air monitoring study indicated substantially higher airborne concentrations of fine particulate matter in kitchens where biomass was used for cooking. It is possible that associations with CHD and hypertension were missed because most of the comparison group had used biomass for cooking at some time in the past, and risk remains elevated for many years after last exposure.

## Strengths and limitations of this study:

• The study was well-powered with a high response rate (93%) from those invited to take part, and large contrasts in recent exposure to indoor air pollution.

- Comparisons were based on recent cooking practices, but some exposures may have changed since the onset of coronary heart disease.
- Many women who did not currently use biomass for cooking, had done so in the past, and this may have obscured associations with health outcomes if effects of exposure persist long-term.
- Errors may have occurred in the assessment of outcome measures, biasing risk estimates towards the null.
- Recall of some potentially confounding factors may have been inaccurate, leading to uncontrolled residual confounding.

## **Funding Statement**

This research was supported by a fellowship from the Colt Foundation for the conduct of a PhD by Professor Zafar Fatmi. Professor David Coggon and Dr Georgia Ntani were supported by funding from the UK Medical Research Council (MRC\_MC\_UU\_12011/5).

## **Conflicts of Interest**

The authors declare that there is no conflict of interest regarding the publication of this paper.

## Authors' contributions

ZF led the design and conduct of the study, carried out the initial statistical analyses, and wrote the first draft of the manuscript.

GN oversaw and guided the statistical analysis.)

DC supervised the project and amended the first draft of the manuscript.

All authors approved the final version of the manuscript.

## Introduction

Three (3) billion people across the globe use solid fuel (such as wood, crop wastes, animal-dung, and charcoal/coal) for cooking and heating the homes [1]. Burning of solid fuels in inefficient stoves or open fires causes household air pollution (HAP) and 3.8 million deaths globally [2]. It primarily affects women and young children in low- and middle income countries (LMICs) who work 4-5 hours daily in the kitchen and spend 90% time at home, respectively [2,3] About 77% of household in Africa and 60% in Southeast Asia use solid fuel in homes [1].

The HAP consists of hundreds of health-damaging pollutants, however, finer particles ( $<2.5\mu$ m – PM<sub>2.5</sub>) and carbon monoxide (CO) are major emissions studied extensively. PM<sub>2.5</sub> and CO affects lungs and absorbed into the blood and causes inflammation of the airways and lungs and impairs immune response [4]. PM<sub>2.5</sub> could be 100 times higher in kitchen and living rooms than acceptable standard of ambient (outdoor) air [5]. HAP is known to cause upper and lower respiratory tract infections among children [6-8], chronic obstructive pulmonary disease [9-10] and lung cancer [11-13]. Also lead to early foetal loss, preterm delivery, low birth weight babies [14,15] and may affect physical and cognitive development of young children [16].

In addition, several studies have suggested a hazard of coronary heart disease (CHD), but evidence for this is more limited and mixed [17, 18]. Several outcomes of cardiovascular diseases were studied including acute coronary syndromes (such as myocardial infarction/unstable angina), coronary heart diseases, and blood pressure. Two small scale case-control studies found significantly high risk of myocardial infarction (MI)/unstable angina with use of solid fuel [19,20]. In addition, a cohort study found association with MI and coal use among women in China [21]. Lee and colleagues [22], in a large cross-sectional self-reported survey of adults in China found a positive association with CHD. On the other hand, two large cohort studies, one in Iran [23] and other in Bangladesh [24] found no association with CHD. However, it was unclear how potential confounders were taken into account. On the other hand, most of the published studies have found significant positive associations with use of solid fuel with higher blood pressure [25-28] or prevalence of hypertension [22, 29-31]. However, few studies were also found insignificant differences in blood pressure [25,32-33].

In Pakistan, 52% households overall and 75% in rural areas use solid fuel for cooking and also for heating, particularly in colder northern part of the country. One pilot case control study was conducted in Pakistan to determine the association of solid fuel use and acute coronary syndrome and found high risk [20]. We, therefore, carried out a cross-sectional survey to explore the association between CHD and cooking with biomass in a sample of women drawn from the general population in rural areas of Pakistan. The objective of the study was to compare the prevalence of hypertension, angina, previous history of heart attack, and electrocardiographic (ECG) changes indicative of CHD in women  $\geq$ 40 years of age who used biomass fuel for cooking with that in women of similar age who cooked using other types of fuel.

## **Materials and Methods**

## Study Setting

The survey was conducted during 2015 in villages surrounding the main urban area of Nawabshah district (recently renamed as Shaheed Benazirabad) in the province of Sindh, Pakistan. These were selected to give a mix in the fuels used for cooking within the study sample. Some of the villages had been supplied with natural gas for at least 10 years, whereas in others biomass fuel (wood and/or cow dung) was still being used.

Recruitment of households and subjects

Within each village, trained field workers made door-to-door visits, and asked the heads of households whether their families would be willing to assist with the study, and if so, what type of fuel was used for cooking, and whether food preparation was regularly undertaken by a woman  $\geq$ 40 years of age. In this way, the study team identified quotas of the required numbers of households in each of the two categories of fuel use (biomass and other). The heads of these households were then asked to complete a consent form, and to identify and introduce the woman of the household aged  $\geq$ 40 years who had carried out the most cooking in the house over the past 10 years. The study was explained to her, and she was invited to participate and to give signed consent.

#### Inclusion criteria

Women aged 40 years or older were eligible for inclusion if they gave informed consent, and had been cooking in the household for at least the past year, using only one of biomass fuel or non-biomass fuel.

#### Questionnaire, examination and measurements

A standardized questionnaire was used to collect information at interview about: demographic and socio-economic characteristics, birth weight, smoking history, whether another member of the household was a regular smoker, relevant aspects of diet, physical activity, lifetime history of cooking using different types of fuel, any previous diagnosis of a "heart attack" by a doctor, symptoms of angina (through the Rose angina questionnaire [34]), and any current use of medication for hypertension. In addition, measurements were made of height, weight, waist circumference, hip circumference and blood pressure.

Socioeconomic status was characterized by the literacy of the participant (no vs. any literacy), the type of employment of her father during her childhood (manual or non-manual), the ownership and construction of her house ('pucca' i.e. made of concrete walls and roof or 'katcha/semi-pucca' i.e. made fully or partially of thatched walls and roof), the income level of the household, and the number of household assets owned from a list of seven. Birth weight was determined from participants' recall as being 'higher than normal vs. normal vs. lower than normal'.

The questions on smoking covered use of cigarettes, *bidi* (locally made cigarettes without filters) or a huqqa (pipe) regularly (at least once a week for a month or longer). The number of other people in the household who smoked provided a measure of domestic exposure to environmental tobacco smoke (ETS), which was classified according to whether at least one other household member smoked cigarettes, bidi, or a huqqa in the home.

Dietary questions covered the use of oil or ghee for cooking and eating, and weekly consumption of meat and eggs. The former was categorized to three levels: only or mostly use oil; mixed use of oil and ghee; only or mostly use ghee. Frequencies of consuming meat and eggs were each categorized to two levels: at least once per week vs. less than once per week.

Level of physical activity was assessed through questions on the frequency per week of shopping, fetching water, washing clothes, collecting wood for cooking, agricultural work on a farm and any other regular heavy physical work. Each of these activities was categorized to two levels: zero days per week or at least once per week. A composite physical activity score was then derived as the number of activities carried out at least once per week, with values ranging from 0 to 6.

Height, weight, and waist and hip circumference were measured using a stadiometer, digital weighing scale and measuring tape, following standardized methods. Body mass index (BMI) (weight in kilograms per squared height in meters) and waist-to-hip ratio (WHR) were then calculated from the measurements. BMIs  $\geq 25$ kg/m<sup>2</sup> were considered abnormally high (overweight or obese), as were WHRs  $\geq 0.85$ .

Categories of exposure to biomass:

Use of biomass was classed to two main categories; biomass users who currently used firewood and/or cow dung for cooking; and non-users of biomass who did not (other sorts of biomass were not used for cooking in the community studied).

In addition, two subsets of these main categories were distinguished: long-term biomass users who currently used firewood and/or cow dung for cooking and had done so for at least the past 10 years; and long-term non-users of biomass who currently did not use either firewood or cow dung for cooking and had not done so for at least10 years.

## Outcome measures:

Four outcome measures were specified.

Hypertension: Three measurements of blood pressure were made at five-minute intervals, using an Omron upper arm blood pressure monitor, and mean values for systolic and diastolic blood pressure were derived. Women were deemed to have hypertension if they met at least one of three criteria: mean systolic blood pressure ≥140 mm Hg; mean diastolic blood pressure ≥90 mm Hg; regular use of medication for blood pressure.

Angina: Experience of angina was assessed through the WHO's Rose angina questionnaire [34], which comprises seven questions relating to chest pain, its anatomical distribution, precipitating and relieving factors, and duration. A diagnosis of angina required report of pain, pressure or discomfort in the chest centrally, or in both the left anterior chest and left arm, that occurred when walking uphill or hurrying, that caused the participant to stop or slow down when it occurred while walking, and that was then relieved within 10 minutes by standing still.

Heart attack: Previous diagnosis of "heart attack" by a doctor was ascertained through a single question: "In the past, have you ever been told by a health care provider that you had a 'heart attack'?"

Definite or probable CHD on ECG: A 12-lead ECG was recorded according to a standard protocol, and coded for the presence of definite or probable CHD, using the Minnesota Code Manual of Electrocardiographic Findings, second edition [35]. This corresponded to the presence of any of codes 1-1 to 1-3, 3-1, 4-1 to 4-4, 5-1 to 5-3, 7-1-1 and 9-2. In order to check the repeatability of the coding, two of us (ZF and DC) coded all of the ECGs independently. We used the same scanned ECG traces, without information about the type of cooking fuel used by the participant. Levels of agreement between the observers were assessed, using kappa statistics. Where differences occurred in the classification of an ECG trace, they were then resolved by discussion between the two observers.

## Statistical analysis

Data were double-entered in Epidata 3.1 software [36] for validation. All discrepancies were corrected by reference to the original questionnaire or record sheet. Statistical analysis was carried out with Stata version 12.0 [37].

As a first step, several variables were reclassified or combined, based on their distribution in the full study sample, and without knowledge of participants' use of biomass fuel. Thus, a combined index was derived for frequency of consuming meat and eggs with three levels: neither meat nor eggs as much as once per week; one of meat or eggs at least once per week; both meat and eggs at least once per week. Scores for physical activity were categorized into three levels: low (0-1 activities); medium (2-3); high (4 or more). Similarly, BMI and WHR were combined as a single variable with three categories: neither BMI nor WHR high; one of BMI or WHR high; both BMI and WHR high.

Descriptive statistics were produced for women in each of the four categories of exposure to biomass, summarizing their demographic and socioeconomic characteristics, current and past cooking arrangements, types and durations of fuel use, hours of cooking per day, types of stove and kitchen, and exposures to potentially confounding risk factors. The prevalence of the main outcomes was determined for the study sample overall, and the relationship of ECG changes to angina and history of heart attack was explored.

Logistic regression analysis was then used to assess the association of each of the four outcome variables with use of biomass fuel for cooking and other possible risk factors. First, associations with each potential risk factor were determined after adjustment for age. The main exposure of interest (user or non-user of biomass) was then carried forward into a mutually adjusted model along with all other risk factors which showed associations ( $p \le 0.1$ ) when examined individually. In addition, a second mutually adjusted model was fitted that compared long-term use and non-use of biomass for cooking.

#### Sample size

The size of the study sample was determined by a power calculation which assumed an outcome prevalence of at least 6% for definite CHD among non-users of biomass fuel, based on a previous study in Pakistan [38] (the prevalence of other outcomes was expected to be higher). This indicated that we would require at least 876 women (438 users and 438 non-users of biomass) for 80% power to detect an odds ratio of 2.0 for the use of biomass fuel with a 5% level of statistical significance.

#### Patient and public involvement

There was no involvement of patients or the public in development of this study.

#### Ethical approval

The study was approved by Ethics Review Committee of Aga Khan University, Karachi, Pakistan.

#### Results

A total of 24 villages were visited in order to recruit the number of households required for the survey. In 14 villages all households used biomass for cooking, in three, all used natural gas, and in the other seven, both types of fuel were used. The number of participating households per village ranged from as few as three to as many as 210. Interviews were completed with women from a total of 1073 households, 536 of which currently used biomass fuel, and 537 natural gas (including LPG). No-one declined to participate in the study, but 77 women could not be interviewed because they were not at home at the time when the survey team visited (mostly because they were engaged in agricultural work).

Among the 1073 women who completed interviews, 44 indicated that they were in fact aged less than 40 years of age, and were therefore excluded from the analysis. An additional 151 women had not made meals regularly (at least one meal per day on most days of the week) during the past year, and were also excluded. We further excluded 28 women who did not currently use firewood or cow dung for cooking, but whose time since last use of biomass was <2 years (this was done to ensure distinct exposure categories). Thus, further analysis was based on 850 women: 436 users and 414 non-users of biomass. Among them, 430 were long-term users of biomass users, and 263 were long-term non-users.

Table 1 summarizes the demographic and socioeconomic characteristics of the participants in the study sample overall, and according to categories of exposure to biomass fuel. In comparison with

users of biomass, non-users were marginally younger (63% versus 60% <50 years), and somewhat more advantaged socioeconomically.

Table 2 describes the current and past cooking arrangements of participants, including type and duration of fuel use, intensity of cooking, and type of stove and kitchen. Even among the long-term non-users of biomass, 88% had cooked with biomass fuels at some time in their life. Among the biomass users, the large majority had used wood (93%) and cow dung (88%) for longer than 20 years. Few participants (3.7% of biomass users and 6.3% of non-users) had ever used kerosene as a cooking fuel. Most participants (approximately 60%) currently cooked for 2-3 hours per day, the average duration of cooking per day being similar in users and non-users of biomass. Where biomass was used for cooking, it was also more likely to be used to heat the home.

Table 3 shows the distribution of potentially confounding risk factors for CHD in the four categories of exposure to biomass. In comparison with non-users of biomass users, slightly higher proportions of women using biomass reported having been born with 'lower than normal' birth weight, having lost weight at some time during childhood, ever having smoked, and being exposed to environmental tobacco smoke in the home.

#### *Prevalence of outcome measures*

Supplementary Table 1 shows the prevalence of the main outcome measures that were investigated. In total, 297 women (35%) were classed as having hypertension, two thirds of whom were taking regular medication for blood pressure. About 27% had symptoms indicative of angina based on Rose's questionnaire. Fifty-four (6.4%) reported a previous history of heart attack, and 19% of women had findings of definite or probable CHD on ECG.

## Validity of ECG classification and interrelationships of outcome measures:

Supplementary Table 2 compares the classification of ECGs by the two observers. Satisfactory ECG traces were obtained for 841 (98.9%) of the participants, but four were missing from the file used to assess inter-observer agreement, and were later assessed jointly by the two observers. The overall agreement between the two observers was 85.2% (kappa = 0.57). Most disagreements were related to cases in which the exceedance of a threshold in, for example, ST elevation, ST depression or the width (duration) of a Q wave was borderline. In some cases, it was questionable whether there was a small R wave or a QS pattern. Also, there was some disagreement about whether T waves were negative or flat. Following discussion between the two observers, all of the discrepancies were reconciled, and it was finally agreed that 181 women (21.5%) showed changes indicative of definite or probable CHD. However, in 22 of these cases, it appeared that the abnormality had occurred only because the ECG leads had been placed incorrectly, and those traces were reclassified as normal. Thus in further analyses, 159 (19%) of women were considered to have definite or probable CHD on ECG.

Supplementary Table 3 shows the prevalence of definite or probable CHD on ECG according to symptoms of angina and history of heart attack. It was somewhat more frequent in participants who reported an earlier heart attack (26%) than in those who did not and had no symptoms of angina (18%). However, there was no association with angina in the absence of heart attack.

#### Association of outcome measures with use of biomass and other risk factors

Associations of hypertension and the three CHD outcomes (angina, heart attack and definite or probable CHD on ECG) with potential risk factors are presented in Supplementary Tables 4 to 7, from which the risk estimates for use of biomass fuel for cooking are summarized in Table 4. The first column of each table gives odds ratios adjusted only for age, while the second column presents mutually adjusted risk estimates from a single model that included use of biomass and all of the risk factors that showed associations ( $p \le 0.1$ ) in the analyses adjusted only for age. The last column shows findings from a similar analysis but restricted to women who were long-term users or non-users of biomass.

In analyses that adjusted only for age, hypertension was associated ( $p \le 0.1$ ) with older age, a higher number of household assets, higher frequency of consuming meat and eggs, and having a high BMI or WHR (Supplementary Table 4). When these variables were carried forward to the mutually adjusted analysis, the association with consumption of meat and eggs was diminished, but the others remained. Thus, the risk of hypertension increased 40% with every 10-year increase in age, was 2.3 times higher in women with  $\ge 4$  household assets than in those with 0 or 1, and was increased 1.9-fold in women who had both high BMI and high WHR as compared with those in whom neither BMI nor WHR were elevated. However, hypertension was not associated with use of biomass (OR 1.0 in the fully adjusted model). When analysis was restricted to long-term users and non-users of biomass, results were similar, with an OR of 1.1 for long-term use of biomass.

In analyses that adjusted only for age, the odds of angina increased with age and regular smoking, and were significantly lower with more frequent consumption of meat and eggs (Supplementary Table 5). Moreover, this pattern was maintained when risk estimates were mutually adjusted. Thus, the odds of angina increased by 30% per 10-year increase in age, and with ever having smoked regularly (OR 2.0, 95%CI 1.2-3.2), and were significantly lower in women who ate both meat and eggs at least once per week (OR 0.5, 95%CI 0.3-0.7). There was, however, no association with use of biomass (OR 1.0, 95%CI 0.8-1.4). When analysis was restricted to long-term users and non-users of biomass, results were similar except that there was a suggestion of a weak association with exposure to biomass (OR 1.3, 95%CI 0.9-1.9).

In corresponding analyses with previous history of heart attack (diagnosed by a physician) as an outcome, initial models with adjustment only for age indicated associations (p<0.1) with age, higher household income, higher number of household assets, and high BMI or WHR (Supplementary Table 6). After mutual adjustment, age remained a significant risk factor (OR 1.5, 95%CI 1.2-2.0, for each 10-year increase in age). However, the other associations, although still positive, were not significant at a 5% level. Nor was there an association with use of biomass for cooking (OR 1.2, 95%CI 0.7-2.2). In the mutually adjusted model for long-term use of biomass, results were very similar.

In analyses adjusted only for age, household income was the only variable significantly associated with definite or probable CHD on ECG, and it remained significant in the fully adjusted model (OR 1.6, 95%CI 1.1-2.4 for household income >10,000PKR) (Supplementary Table 7). However, there was no association with use of biomass for cooking, either overall or in the long-term (ORs 0.8 and 0.9).

#### Discussion

This study found no association between use of biomass fuel and any of the four outcomes studied (hypertension, angina, previous history of heart attack, and definite or probable CHD on ECG), even when comparison was with women who had not used biomass for at least the last 10 years. The strongest hint of an association was for angina in long-term users as compared with long-term non-users of biomass, but the elevation of risk was small (30%) and not statistically significant at a 5% level.

The choice of villages from which to recruit participants ensured a balance in the fuels currently used for cooking, and cooperation in the survey was good with high response rates from the households and women that were invited to take part. Inevitably, recruitment was to some extent opportunistic and limited to one province of Pakistan. However, there seems no reason to expect that the study sample would have been seriously unrepresentative in the associations of hypertension and CHD with use of biomass and other risk factors.

A linked air monitoring study found that in the kitchens of houses using biomass for cooking, the mean 24-hour average  $PM_{2.5}$  concentration was 531 µg/m<sup>3</sup>, with a median of 136 µg/m<sup>3</sup> and interquartile range 34-615 µg/m<sup>3</sup> (paper in preparation). Corresponding concentrations in houses not using biomass for cooking were 69.9, 24.2, and 13.5-53.3 µg/m<sup>3</sup>. Thus, while individual exposures may have been influenced also by time spent cooking and whether biomass was burned in a closed or open

kitchen, the absence of associations with CHD and hypertension is unlikely to reflect inadequate contrasts in recent intensity of exposure.

Our aim was as far as possible to recruit households that had used the same fuel for cooking exclusively for at least 10 years. Villages were selected with this criterion in mind, and it was covered in preliminary inquiries that were addressed to local community representatives. In practice, however, it turned out that where natural gas was available in villages, some participants had not yet switched to cleaner fuel, or had done so at a later date than others. A pragmatic decision was therefore made to include women even if they had changed their cooking fuel within the past 10 years, provided that they had used their current fuel for at least a year. This seemed reasonable since trials had suggested that interventions to reduce household air pollution from use of biomass for cooking can produce reductions in blood pressure and changes in ECGs over the short to medium term [39-41]. However, to check that it did not obscure associations, additional analyses were carried out with restriction to long-term users and non-users of biomass, and still no relationship was found with the health outcomes.

The sample size achieved for the study was close to that planned, and the prevalence of the four outcomes was higher than had been assumed in the power calculations. Moreover, the upper confidence limits for the odds ratios relating to use of biomass were almost all <2. Thus, the absence of associations with biomass does not reflect a lack of statistical power.

Ascertainment of current use of biomass is likely to have been highly accurate, and while there may have been some errors in recall of the times when biomass had been used in the past, it is difficult to conceive that any resultant misclassification would have obscured important associations with CHD. Generally, switches in the use of fuel were only in one direction – towards cleaner natural gas from biomass. The timing of changes was usually well recalled because in most instances the entire village received the new source of fuel in a particular year. However, the duration of using cow dung and firewood may not always have been remembered reliably, and switches between these types of fuel could also have occurred. Many women reported using cow dung and firewood for the same duration, and no attempt was made to analyse them separately.

Recall of some potentially confounding exposures may also have been inaccurate – particularly those pertaining to childhood. If so, the errors would be expected to be non-differential with respect to CHD, and therefore to bias risk estimates towards the null, possibly leading to uncontrolled residual confounding. However, the assessment of BMI and WHR used standardized methods, and should have been reasonably reliable. The interviewers were trained in how to make the measurements, and their technique was piloted in the field before the start of data collection.

A greater concern is the possibility of error in the ascertainment of outcomes. Blood pressure was objectively measured according to a standardized protocol, and was taken as the average of three readings. Moreover, most of the women who were classed as having hypertension were taking treatment for the disorder, which supports the validity of its assessment. Angina was determined through the well-established Rose questionnaire, but it is possible that symptoms in some cases arose from other pathology. Previous research has suggested that the Rose angina questionnaire may not be as reliable among women as in men [42]. Although the question to participants about history of heart attack referred specifically to diagnoses that had been given by a health professional, errors could have occurred in interpretation of the term "heart attack" (e.g. to include symptoms from dysrhythmias and acute heart failure as well as myocardial infarction). However, ascertainment of heart attack had been previously carried out by the same method in a similar population, where it was found to be reasonably accurate [43].

The diagnosis of CHD from ECGs showed only a weak relationship to history of medically diagnosed heart attack, and none at all to symptoms of angina (Supplementary Table 3). Between observer agreement in the classification of ECGs was reasonably good (kappa = 0.57) (Supplementary Table

2), but it is notable that unlike angina and history of heart attack, CHD diagnosed from ECGs did not show the expected association with age (Supplementary Table 7).

To the extent that errors did occur in the ascertainment of outcomes, they are unlikely to have differed systematically in relation to use of biomass, and therefore would be expected to tend to obscure any true associations.

Because the study had a cross-sectional design, consideration must be given to the possibility of reverse causation. For risk factors related to childhood (e.g. birthweight, father's occupation and education), this is less of a concern. However, it is plausible that characteristics such as diet, physical activity and time spent cooking could have changed as a consequence of CHD. Depending on the circumstances, this might bias associations either upwards or downwards.

Another limitation of the study was that it did not determine when past heart attacks had occurred. Even if not as a consequence of an earlier heart attack, some of the exposures studied (e.g. BMI and WHR) may have changed in the interval since such an attack occurred. If so, this might obscure true associations.

A further possible source of error was uncontrolled residual confounding. To minimize this problem, information was collected about a range of potentially confounding variables, and as in most studies of biomass fuel, socio-economic status tended to be higher in women using cleaner fuels [44]. Although several socio-economic indicators were evaluated as possible factors for adjustment, residual confounding could still have occurred. To explain the absence of associations with biomass, such confounding would have to be inverse (i.e. the under-ascertained confounder would have to be less prevalent in women who used biomass than in non-users).

The study found expected associations with several established risk factors for CHD. Thus, the odds of hypertension, angina and previous history of heart attack were all higher with older age (by 30-50% for every 10 year increase), although this was not found for definite or probable CHD on ECG. The relationship of CHD to age is well documented in the literature [45], and in women, the incidence of CHD increases rapidly after the menopause, reaching up to three times that in premenopausal women [46].

Two of the outcome measures – hypertension and previous history of heart attack – were significantly associated with affluence as measured by number of household assets. This relationship has also been observed before. In a population-based study in Pakistan, history of 'angina or heart attack' was estimated to have 3-fold higher prevalence among affluent participants than in those who were poor [47]. The direction of the association, which is the inverse of that observed in western populations, accords with a higher prevalence of diabetes, hypertension and dyslipidaemias in more educated and affluent groups, which was found in a recent study conducted in South Asian countries, including Pakistan [48].

In further support of an effect of affluence, we found that high BMI and/or WHR was associated with greater risk of hypertension, and (non-significantly) with history of heart attack. Obesity has been shown to increase the risk of hypertension in several studies [49, 50], and partly through this mechanism, also increases the risk and progression of CHD [51]. The INTERHEART study suggested that WHR (abdominal obesity) is a better marker of risk for CHD than BMI [52], but the two were correlated in our study sample, and we opted to use a combined measure.

In contrast, we found that more frequent consumption of meat and eggs was associated with reduced risk of angina. This was unexpected given the known relationship of CHD to consumption of saturated fat [53], and may have been a chance finding. It did not extend to the other outcomes investigated. However, a recent large review suggests that the relationship may be inconsistent [54].

Smoking has consistently been found to increase the risk of CHD in many studies [55]. However, in our investigation it was associated only with angina. This might be because intensity of tobacco use among female smokers in the Pakistani population is low [56].

Despite the finding of several expected associations, the failure to demonstrate more consistent relationships to known risk factors is a further indication for caution in the interpretation of our results.

Several earlier studies have indicated links between use of biomass for cooking and CHD, although the finding has not been entirely consistent [17,18]. As already discussed, one explanation for our failure to demonstrate such associations in the current study could be inaccuracies in the diagnosis of CHD. Another possibility, however, is that adverse effects of exposure to pollutants from the use of biomass persist many years after last exposure. In this survey, even among women who had not used biomass during the last 10 years, most had done so earlier, and often for a long time. Only a few participants (about 3.5% overall) had never used biomass, which was too few for meaningful risk estimates. While it would be possible to compare rural users of biomass with lifelong users of cleaner fuels in urban settings, interpretation would be complicated by other important differences between those living in rural and urban areas.

#### Conclusions

This study evaluated the association of hypertension and three measures of CHD – angina, previous history of heart attack and definite or probable CHD on ECG - with use of biomass for cooking. We found no clear associations with any of the health outcomes. However, the weak relationship of ECG abnormalities to the other two measures of CHD, and the inconsistency of their associations with well-established risk factors, suggest that this could have been because of diagnostic misclassification. Alternatively, it could be that an effect was missed because most of the women who were not currently using biomass for cooking had used it in the past, and risk remains elevated for many years after last exposure.

#### Data Availability

The data [stata.dta format] underpinning the findings of this study are available from the corresponding author upon reasonable request.

# Acknowledgments

This study reported in this paper formed part of a PhD project carried out by Dr Zafar Fatmi under the supervision of Professor David Coggon at the University of Southampton.

Mr Syed Nayab Ali Shah coordinated the data collection. Ms Shereen Jamali, Ms Fozia Jamali, Ms Iqra Memon and Ms Sana Memon administered the questionnaires at interview and recorded the ECGs. We are grateful also to Professor Keith Palmer and Professor M. Masood Kadir for their advice on various aspects of the study.

# References

- 1. Bonjour S, Adair-Rohani H, Wolf J, Bruce NG, Mehta S, Prüss-Ustün A, Lahiff M, Rehfuess EA, Mishra V, Smith KR. Solid fuel use for household cooking: country and regional estimates for 1980-2010. *Environ Health Perspect*. 2013;121:784-90.
- 2. World Health Organization. Household air pollution and health. Geneva, Switzerland. (Accessed on 4 April 2018). <u>http://www.who.int/mediacentre/factsheets/fs292/en/</u>
- 3. World Health Organization. Ambient (outdoor) air quality and health [Internet]. Geneva; 2018 [updated 2 May 2018]. Available from: <u>https://www.who.int/news-room/fact-sheets/detail/ambient-(outdoor)-air-quality-and-health</u>
- 4. Naeher LP, Brauer M, Lipsett M, Zelikoff JT, Simpson CD, Koenig JQ, et al. <u>Woodsmoke health effects: a review.</u> Inhal Toxicol. 2007;19(1):67-106. Review.
- 5. Clark ML, Peel JL, Balakrishnan K, Breysse PN, Chilrud SN, Naeher LP et al. <u>Health and household air pollution from solid fuel use: the need for improved</u> <u>exposure assessment.</u> Environ Health Perspect 2013;121:1120-8.
- 6. Smith KR, Samet JM, Romieu I, Bruce N. Indoor air pollution in developing countries and acute lower respiratory infections in children. Thorax. 2000 Jun;55(6):518-32.
- Smith KR, Mehta S, Maeusezahl-Feuz M. Indoor air pollution from household use of solid fuels: comparative quantification of health risks. In: Ezzati MLA, Rodgers A, Murray CJL, editors. Global and regional burden of disease attributable to selected major risk factors. Geneva, Switzerland: World Health Organization; 2004. pp. 1435– 1493.
- 8. Torres-Duque C, Maldonado D, Pérez-Padilla R, Ezzati M, Viegi G; Forum of International Respiratory Studies (FIRS) Task Force on Health Effects of Biomass Exposure. Biomass fuels and respiratory diseases: a review of the evidence. Proc Am Thorac Soc. 2008 Jul 15;5(5):577-90.
- 9. Liu Y, Lee K, Perez-Padilla R, Hudson NL, Mannino DM. Outdoor and indoor air pollution and COPD-related diseases in high- and low-income countries. Int J Tuberc Lung Dis. 2008;12(2):115-27.
- 10. Kurmi OP, Semple S, Simkhada P, Smith WC, Ayres JG. COPD and chronic bronchitis risk of indoor air pollution from solid feul: a systematic review and metaanalysis. Thorax. 2010; 65(3):221-8.
- 11. Liu Q, Sasco AJ, Riboli E et al. Indoor air pollution and lung cancer in Guangzhou, People's Republic of China. Am. J. Epidemiol. 1993; 137: 145–54.
- 12. Kleinerman R, Wang Z, Lubin J, Zhang S, Metayer C, Brenner A. Lung cancer and indoor air pollution in rural china. Ann Epidemiol. 2000;10(7):469.
- 13. Behera D, Balamugesh T. Indoor air pollution as a risk factor for lung cancer in women. J Assoc Physicians India. 2005; 53:190-2.
- 14. Amegah AK, Quansah R, Jaakkola JJ. Household air pollution from solid fuel use and risk of adverse pregnancy outcomes: a systematic review and meta-analysis of the empirical evidence. PloS one. 2014 Dec 2;9(12):e113920.
- 15. Lamichhane DK, Leem JH, Lee JY, Kim HC. A meta-analysis of exposure to particulate matter and adverse birth outcomes. Environ Health Toxicol. 2015 Nov 3;30:e2015011.
- 16. Calderón-Garcidueñas L, Torres-Jardón R, Kulesza RJ, Park SB, D'Angiulli A. Air pollution and detrimental effects on children's brain. The need for a multidisciplinary approach to the issue complexity and challenges. Front Hum Neurosci. 2014; 8:613.
- 17. Fatmi Z, Coggon D. Coronary heart disease and household air pollution from use of solid fuel: a systematic review. Br Med Bull. 2016 Jun;118(1):91-109.

1	
2	
3 ⊿	
4	
5	
4 5 6 7	
8	
8 9	
10	
11	
12	
13	
14	
14 15	
16	
16 17	
18	
19	
20	
20 21 22	
22	
23	
24	
24 25	
26	
27	
28 29	
29	
30	
31	
32	
33	
34 35	
35	
36 37	
3/	
38	
39 40	
40 41	
41	
42	
43	
45	
46	
47	
48	
49	
50	
51	
52	
53	
54	
55	
56	
57	
58	
59	
60	

18. Yu K, Qui G, Chan K-H, Lam K-BH, Kurmi OP, Bennett DA et al. Association of
solid fuel use with risk of cardiovascular and all-cause mortality in rural China.
JAMA 2018;319:1351-61.

- 19. Sathiakumar N. Indoor air pollution due to biomass fuel use and acute coronary syndrome among Sri Lankan women. Epidemiology 2012;23:S224.
- Fatmi Z, Coggon D, Kazi A, Naeem I, Kadir MM, Sathiakumar N. Solid fuel use is a major risk factor for acute coronary syndromes among rural women: a matched case control study. Public Health. 2014 Jan;128(1):77-82. doi: 10.1016/j.puhe.2013.09.005.
- 21. Kim C, Shu X-O, Hosgood HD, et al. Past use of coal for cooking is associated with all-cause mortality in the prospective Shanghai women's health study. Cancer Res 2014;74:Abstract nr 2184.
- 22. Lee M-S, Hang J-Q, Zhang F-Y, et al. In-home solid fuel use and cardiovascular disease: a cross-sectional analysis of the Shanghai Putuo study. Environ Health 2012;11:18.
- 23. Mitter SS, Islami F, Pourshams A, et al. Use of biomass fuels for cooking and heating is associated with increased non-communicable disease mortality: Golestan cohort study. Circulation 2012;125:AP042.
- 24. Alam DS, Chowdhury MAH, Siddiquee AT, et al. Adult cardiopulmonary mortality and indoor air pollution: a10-year retrospective cohort study in a low-income rural setting. Glob Heart 2012;7:215–21.
- 25. Baumgartner J, Schauer JJ, Ezzati M, et al. Indoor air pollution and blood pressure in adult women living in rural China. Environ Health Perspect 2011;119:1390–5.
- 26. Painschab MS, Davila-Roman VG, Gilman RH, et al. Chronic exposure to biomass fuel is associated with increased carotid artery intima-media thickness and a higher prevalence of atherosclerotic plaque. Heart 2013;99:984–91.
- 27. Burroughs Peña M, Romero KM, Velazquez EJ, et al. Relationship between daily exposure to biomass fuel smoke and blood pressure in high-altitude Peru. Hypertension 2015;65:1134–40.
- 28. Neupane M, Basnyat B, Fischer R, et al. Sustained use of biogas fuel and blood pressure among women in rural Nepal. Environ Res 2015;136: 343–51.
- 29. Ray MR, Mukherjee S, Roychoudhury S, et al. Platelet activation, upregulation of CD11b/CD18 expression on leukocytes and increase in circulating leukocyte-platelet aggregates in Indian women chronically exposed to biomass smoke. Hum Exp Toxicol 2006;25:627–35.
- 30. Dutta A, Mukherjee B, Das D, et al. Hypertension with elevated levels of oxidized low-density lipoprotein and anticardiolipin antibody in the circulation of premenopausal Indian women chronically exposed to biomass smoke during cooking. Indoor Air 2011;21: 165–76.
- 31. Dutta A, Ray MR, Banerjee A. Systemic inflammatory changes and increased oxidative stress in rural Indian women cooking with biomass fuels. Toxicol Appl Pharmacol 2012;261:255–62.
- 32. Davutoglu V, Zengin S, Sari I, et al. Chronic carbon monoxide exposure is associated with the increases in carotid intima-media thickness and C-reactive protein level. Tohoku J Exp Med 2009;219:201–6.
- 33. Clark ML, Bazemore H, Reynolds SJ, et al. A baseline evaluation of traditional cook stove smoke exposures and indicators of cardiovascular and respiratory health among Nicaraguan women. Int J Occup Environ Health 2011;17:113–21.
- 34. Rose G, McCartney P, Reid DD. Self-administration of a questionnaire on chest pain and intermittent claudication. Br J Prev Soc Med. 1977; 31:42–48.

35. Prineas RJ, Crow RS, Zhang Z-h. The Minnesota code manual of electrocardiographic findings. 2nd Edition. London. Springer London; 2010.

- 36. Christiansen TB and Lauritsen JM. (Ed.) EpiData Comprehensive Data Management and Basic Statistical Analysis System. Odense Denmark, EpiData Association, 2010-. <u>http://www.epidata.dk</u>
- 37. Stata Corp LP 2012, Stata Statistical Software: Release 12.0, College Station TX, USA.
- Jafar TH, Qadri Z, Chaturvedi N. Coronary artery disease epidemic in Pakistan: more electrocardiographic evidence of ischaemia in women than in men. Heart. 2008;94(4):408-13.
- McCracken J, Smith KR, Stone P, Diaz A, Arana B, Schwartz J. Intervention to lower household wood smoke exposure in Guatemala reduces ST-segment depression on electrocardiograms. Environ Health Perspect 2011;119:1562-8.
- 40. McCracken JP, Smith KR, Díaz A, Mittleman MA, Schwartz J. Chimney stove intervention to reduce long-term wood smoke exposure lowers blood pressure among Guatemalan women. Environ Health Perspect 2007;115:996-1001.
- 41. Alexander D, Larson T, Bolton S, Vedal S. Systolic blood pressure changes in indigenous Bolivian women associated with an improved cookstove intervention. Air Qual Atmos Health 2015;8:47-53.
- 42. Wilcosky T, Harris R, Weissfeld L. The prevalence and correlates of Rose questionnaire angina among women and men in the Lipid Research Clinics Program Prevalence Study. Am J Epidemiol. 1987;125 (3):400-409.
- 43. Jafar TH, Jafary FH, Jessani S, Chaturvedi N. Heart disease epidemic in Pakistan: women and men at equal risk. Am Heart J. 2005;150(2):221-6.
- 44. Khushk WA, Fatmi Z, White F, Kadir MM. Health and social impacts of improved stoves on rural women: a pilot intervention in Sindh, Pakistan. Indoor Air. 2005 Oct;15(5):311-6.
- 45. Castelli WP. Epidemiology of coronary heart disease: The Framingham study. American Journal of Medicine 1984, page 4.
- 46. Gordon T, Kannel WB, Hjortland MC, McNamara PM. Menopause and coronary heart disease. The Framingham Study. Ann Intern Med. 1978; 89:157–61.
- 47. Hameed K, Kadir M, Gibson T, Sultana S, Fatima Z, Syed A. The frequency of known diabetes, hypertension and ischaemic heart disease in affluent and poor urban populations of Karachi, Pakistan. Diabet Med. 1995;12(6):500-3.
- 48. Ali MK, Bhaskarapillai B, Shivashankar R, Mohan D, Fatmi Z, Pradeepa R, Masood Kadir M, Mohan V, Tandon N, Narayan KM, Prabhakaran D; CARRS investigators. Socioeconomic status and cardiovascular risk in urban South Asia: The CARRS Study. Eur J Prev Cardiol. 2016 Mar;23(4):408-19.
- 49. Hubert HB, Feinleib M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. Circulation 1983; 67:968–77.
- 50. Todd Miller M, Lavie CJ, White CJ. Impact of obesity on the pathogenesis and prognosis of coronary heart disease. J Cardiometab Syndrome 2008; 3:162–7.
- 51. Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet. 2002;360: 1903-13.
- 52. Yusuf S, Hawken S, Ounpuu S, Bautista L, Franzosi MG, Commerford P, Lang CC, Rumboldt Z, Onen CL, Lisheng L, Tanomsup S, Wangai P Jr, Razak F, Sharma AM, Anand SS; INTERHEART Study Investigators. Obesity and the risk of myocardial

1	
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	
39	
40	
41	
42	
43	
44	
45	
46	
47	
48	
49	
50	
51	
52	
53	
54	
55	
56	
57	

infarction in 27,000 participants from 52 countries: a case-control study. Lancet 2005;366(9497):1640-9.

- 53. The World Health Report 2002: reducing risks, promoting healthy life. Geneva, World Health Organization, 2002.
- 54. Chowdhury R, Warnakula S, Kunutsor S, Crowe F, Ward HA, Johnson L, Franco OH, Butterworth AS, Forouhi NG, Thompson SG, Khaw KT, Mozaffarian D, Danesh J, Di Angelantonio E. Association of dietary, circulating, and supplement fatty acids with coronary risk: a systematic review and meta-analysis. Ann Intern Med. 2014 Mar 18;160(6):398-406. doi: 10.7326/M13-1788.
- 55. Huxley RR, Woodward, M. Cigarette smoking as a risk factor for coronary heart are, ies. L. 3 Survey. J acco/surveilla. disease in women compared with men: a systematic review and meta-analysis of prospective cohort studies. Lancet. 2011;378(9799):1297-305.
- 56. Global Adult Tobacco Survey. Pakistan Fact sheet 2014.

http://www.who.int/tobacco/surveillance/survey/gats/pakfactsheet.pdf

Characteristic		All women (n=850)		Users of biomass (n=436)		Non-users of biomass (n=414)		Long-term users of biomass (n=430)		Long-term non- users of biomass (n=263)	
	N	(%)	n	(%)	n	(%)	n	(%)	n	(%)	
Age (years)											
<50	525	(61.8)	263	(60.3)	262	(63.3)	257	(59.8)	166	(63.1)	
≥50	325	(38.2)	173	(39.7)	152	(36.7)	173	(40.2)	97	(36.9)	
Educational status											
No literacy	797	(93.8)	419	(96.1)	378	(91.3)	413	(96.1)	239	(90.9)	
Any literacy	53	(6.2)	17	(3.9)	36	(8.7)	17	(4.0)	24	(9.1)	
Household income/month		6									
≤10000PKR	651	(76.6)	351	(80.5)	300	(72.5)	347	(80.7)	185	(70.3)	
>10000PKR	199	(23.4)	85	(19.5)	114	(27.5)	83	(19.3)	78	(29.7)	
Household tenure			1								
Rented	70	(8.2)	25	(5.7)	45	(10.9)	25	(5.8)	20	(7.6)	
Owned	780	(91.8)	411	(94.3)	369	(89.1)	405	(94.2)	243	(92.4)	
Construction of house				C							
Katcha/ semi-pucca	652	(76.7)	361	(82.8)	291	(70.3)	356	(82.8)	173	(65.8)	
Pucca	198	(23.3)	75	(17.2)	123	(29.7)	74	(17.2)	90	(34.2)	
Number of household assets											
Low (0-1)	268	(31.5)	140	(32.1)	128	(30.9)	139	(32.3)	84	(31.9)	
Medium (2-3)	404	(47.5)	223	(51.2)	181	(43.7)	218	(50.7)	108	(41.1)	
High (≥4)	178	(21.0)	73	(16.7)	105	(25.4)	73	(17.0)	71	(27.0)	
Father's occupation in childhood											
Non-manual	39	(4.6)	19	(4.4)	20	(4.8)	18	(4.2)	16	(6.1)	
Manual	811	(95.4)	417	(95.6)	394	(95.2)	412	(95.8)	247	(93.9)	

Table 1 Demographic and appiagenemic characteristics of participants by exposure acts

1	
2 3	
4 5	
6	
7 8	
9 10	
11	
12 13	
14 15	
16	
17 18	
19 20	
20	
22 23	
24 25	
26	
27 28	
29 30	
31	
32 33	
3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 6 7	
36	
37 38	
39 40	
41	
42 43	
44 45	
45	

46

Characteristic		Users of biomass (n=436)		Non-users of biomass (n=414)		Long-term users of biomass (n=430)		erm non-users lass )
	n	(%)	n	(%)	n	(%)	(n=263) n	(%)
Ever used biomass for cooking	436	(100)	382	(92.3)	430	(100)	231	(87.8)
Years since last used biomass for cooking								
Current user	436	(100)	-	-	430	(100)	-	-
2-9	-	-	151	(39.5)	-	-	-	-
≥10	-	-	231	(60.5)	-	-	231	(100)
Ever used wood for cooking	435	(99.8)	358	(86.5)	429	(99.8)	218	(82.9)
Ever used cow dung for cooking	422	(96.8)	358	(86.5)	416	(96.7)	216	(82.1)
Ever used kerosene for cooking	16	(3.7)	26	(6.3)	16	(3.7)	17	(6.5)
Ever used LPG/natural gas for cooking	17	(3.9)	413	(99.8)	15	(3.5)	263	(100)
Average hours per day cooked in past year								
$\leq 1$	129	(29.6)	133	(32.1)	123	(28.6)	75	(28.5)
2-3	270	(61.9)	237	(57.3)	270	(62.8)	165	(62.7)
$\geq 4$	37	(8.5)	44	(10.6)	37	(8.6)	23	(8.8)
Type of stove used for cooking								
Gas/LPG	2	(0.5)	414	(100)	2	(0.5)	263	(100)
Biomass with	166	(20, 1)			164	(20, 1)		
chimney/improved stove	166	(38.1)	-	-	164	(38.1)	-	-
Biomass with three brick open stove	267	(61.2)	-	-	263	(61.2)	-	-
Other	1	(0.2)	-	-	1	(0.2)	-	-
Type of kitchen								
Closed (four walls – linked with living	88	(20.2)	116	(28.0)	86	(20.0)	79	(30.0)
room or separate)	00	(20.2)	110	(28.0)	00	(20.0)	/ 7	(30.0)
Semi-open (fewer than four walls)	189	(43.3)	155	(37.4)	187	(43.5)	94	(35.7)
Open (no walls)	159	(36.5)	143	(34.5)	157	(36.5)	90	(34.2)
		( <b>- - - - - -</b>		(		/ - · · ·		

237 (54.4)

 Table 2. Current and past cooking arrangements according to exposure category.

 Users of biomage

Heat home with biomass

106

(25.6)

236 (54.9)

74

(28.1)

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Long-term non-users

(%)

(20.5) (59.3)

(20.2)

(46.4)

(53.6)

(45.2) (54.8)

(91.3) (8.7)

(65.8)

(34.2)

(56.7)

(34.6)

(8.7)

(33.5)

(38.0)

(28.5)

(30.0)

(38.4)

(31.2) (0.4)

of biomass (n=263)

n

54 156

53

122

141

119 144

240 23

173

90

149

91

23

88

100

75

79

101

82

1

Characteristic		piomass	Non-user (n=414)	s of biomass	Long-term users biomass (n=430)		
	n	(%)	n	(%)	n	(%)	
Birthweight							
Lower than normal	117	(26.8)	77	(18.6)	114	(26.5)	
Normal	239	(54.8)	254	(61.4)	237	(55.1)	
Higher than normal	80	(18.4)	83	(20.0)	79	(18.4)	
Ever hungry all the time during childhood because there was not enough food							
No	176	(40.4)	176	(42.5)	175	(40.7)	
Yes	260	(59.6)	238	(57.5)	255	(59.3	
Lost weight during childhood				~ /			
No	162	(37.2)	182	(44.0)	160	(37.2)	
Yes	274	(62.8)	232	(56.0)	270	(62.8	
Ever smoked regularly (any of cigarettes, bidi, huqqa)							
Never	390	(89.4)	378	(91.3)	384	(89.3	
Ever	46	(10.6)	36	(8.7)	46	(10.7	
Environmental tobacco smoke (at least one other							
household member smoked cigarettes, bidi or huqqa in							
the home)							
No	269	(61.7)	267	(64.5)	265	(61.6	
Yes	167	(38.3)	147	(35.5)	165	(38.4	
Physical activity score		× /				`	
0-2	124	(28.4)	205	(49.5)	124	(28.8	
3-4	199	(45.6)	156	(37.7)	196	(45.6	
5-6	113	(25.9)	53	(12.8)	110	(25.6	
Consumption of meat or eggs		× /		· · · /			
Do not eat either meat or eggs as much as once per week	173	(39.7)	142	(34.3)	172	(40.0	
Eat one of meat or eggs as much as once per week	176	(40.4)	163	(39.4)	173	(40.2	
Eat both meat and eggs at least once per week	87	(20.0)	109	(26.3)	85	(19.8	
Current nutrition <sup>a</sup>		\$ <i>1</i>				`	
Neither BMI nor WHR high	183	(42.0)	129	(31.2)	179	(41.6	
One of BMI or WHR high	151	(34.6)	160	(38.7)	149	(34.7	
Both BMI and WHR high	102	(23.4)	124	(30.0)	102	(23.7	
Not known	0	(0)	1	(0.2)	0	(0)	

39 40

Outcome

Users of biomass user

1

2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	
39	
40	
41	
42	
43	
44	
45	
46	
47	
48	
49 50	
50	
51	
52	
53	
54	
55	
56	
57	
58	
50	

59 60 Table 4. Associations of hypertension, angina, history of heart attack, and definite or probable CHD on ECG with current and long-term use of biomass for cooking.

Fully adjusted<sup>a</sup>

(n=850)

Fully adjusted and

0.9

(0.6-1.3)

limited to long-term users and non-users of

Adjusted only for

age (n=850)

0.8

						biomass <sup>b</sup> (n=693)		
	OR	(95%CI)	OR	(95% CI)	OR	(95% CI)		
Hypertension								
Non-users of biomass	1.0		1.0		1.0			
Users of biomass	1.2	(0.9-1.5)	1.0	(0.8-1.4)	1.1	(0.8-1.6)		
Angina								
Non-users of biomass	1.0		1.0		1.0			
Users of biomass	1.0	(0.7-1.3)	1.0	(0.8-1.4)	1.3	(0.9-1.9)		
Heart Attack								
Non-users of biomass	1.0		1.0		1.0			
Users of biomass	1.4	(0.8-2.4)	1.2	(0.7-2.2)	1.3	(0.7-2.4)		
Definite or probable CHD on								
ECG								
Non-users of biomass	1.0		1.0		1.0			

(0.6-1.2) 0.8 (0.6-1.2) <sup>a</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p < 0.1) in analyses adjusted only for age

<sup>b</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p < 0.1) in analyses adjusted only for age, but was restricted to women who were long-term users or non-users of biomass

J.ezonj

#### Supplementary Materials

**Supplementary Table 1.** Prevalence of hypertension, history of heart attack, angina and coronary heart disease in study sample.

Characteristic	n	(%)
Hypertension		
Systolic hypertension (systolic BP≥140 mmHg)	133	(15.8)
Diastolic hypertension (diastolic BP≥90 mmHg)	102	(12.1)
Regular medication for high blood pressure	198	(23.5)
Hypertension (any of the above)	297	(35.3)
Angina	227	(27.0)
History of heart attack	54	(6.4)
Definite or probable CHD on ECG <sup>a</sup>	159	(18.9)

<sup>a</sup>Based on 841 women. ECGs for 9 women were missing or could not be coded due to poor quality.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

NegativeNegative591Positive94Kappa = 0.57
Positive         94           Kappa = 0.57
Kappa = 0.57

ble CHD by two observers.

3	
4	
5	
6	
-	
/	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	
39	
40	
41	
41	
43	
44	
45	
46	
47	
48	
49	
50	
51	
52	
53	
54	
55	
56	
57	

1 2 З

Supplementary Table 3. Prevalence of definite or probable CHD changes on ECG according to history of heart attack and angina.

Other measure of CHD	Definite or probable CHD changes on ECG <sup>a</sup>						
	Yes		No				
	n	(%)	Ν	(%)			
No history of heart attack or angina	105	(18.2)	471	(81.8)			
History of angina	45	(19.8)	182	(80.2)			
History of heart attack	14	(25.9)	40	(74.1)			
History of angina or heart attack	54	(20.4)	211	(79.6)			
History of angina and heart attack #ECGs for 9 women were missing or cost	5	(31.3)	11	(68.8)			

Risk factor	Adju for a	sted only ge	Fully	adjusted <sup>a</sup>	Fully adjusted and limited to long-		
	(n=850)		( <b>n=850</b> )		term users and non-users of biomass <sup>b</sup>		
					(n=69		
	OR	(95%CI)	OR	(95%CI)	OR	(95%CI)	
Age (per 10 year increase)	1.4	(1.2-1.6)	1.4	(1.2-1.7)	1.5	(1.2-1.7)	
Educational status							
Illiterate	1.0		-		-		
Any literacy	0.6	(0.3-1.2)					
Household income/month					-		
<3000-10000PKR	1.0	(a =	-				
>10000PKR	1.0	(0.7-1.4)					
Household ownership					-		
Rented	1.0		-				
Own	0.8	(0.5-1.3)					
Construction of house					-		
Katcha/semi-pucca	1.0		-				
Pucca	0.9	(0.6-1.2)					
Number of household assets							
0-1	1.0		1.0		1.0		
2-3	1.7	(1.2-2.4)	1.6	(1.2-2.3)	1.8	(1.2-2.6)	
<u>≥</u> 4	2.4	(1.6-3.6)	2.3	(1.5-3.4)	2.7	(1.7-4.3)	
Father's occupation in woman's					-		
childhood							
Non-manual	1.0						
Manual	1.2	(0.6-2.5)					
Birthweight							
Lower than normal	1.0	(a =			-		
Normal	1.0	(0.7-1.4)	-				
Higher than normal	1.0	(0.6-1.5)					
Ever hungry during all the time					-		
during childhood because there							
was not enough food							
No	1.0		-				
Yes	0.9	(0.7-1.3)					
Lost weight during childhood	1.0				-		
No	1.0	(0.0.1.7)	-				
Yes	1.2	(0.9-1.6)					
Ever smoked regularly (any of							
cigarettes, bidi, huqqa)							
Never	1.0	(0 5 1 2)	-		-		
Ever	0.8	(0.5-1.3)					
Environmental tobacco smoke (at							
least one other household member	•						
smokes cigarettes, bidi or huqqa							
in the home)							
No	1.0		-				
Yes	0.8	(0.6-1.1)					

Do not eat either meat or eggs as	1.0		1.0		1.0	
much as once per week						
Eat one of meat or eggs as much	1.4	(1.0-1.9)	1.2	(0.9-1.7)	1.2	(0.8-1.7)
as once per week						
Eat both meat and eggs at least	1.4	(1.0-2.1)	1.2	(0.8-1.8)	1.2	(0.8-1.9)
once per week						
Current nutrition <sup>c</sup>						
Neither BMI nor WHR high	1.0		1.0		1.0	
One of BMI or WHR high	1.2	(0.9-1.7)	1.2	(0.8-1.6)	1.2	(0.8-1.8)
Both BMI and WHR high	2.0	(1.4-2.9)	1.9	(1.3-2.8)	1.8	(1.2-2.7)
Non-user of biomass	1.0		1.0			
User of biomass	1.2	(0.9-1.5)	1.0	(0.8-1.4)		
Long-term non-user of biomass	1.0				1.0	
Long-term user of biomass	1.2	(0.9-1.7)			1.1	(0.8-1.6)

<sup>a</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p<0.1) in analyses adjusted only for age

<sup>b</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p<0.1) in analyses adjusted only for age, but was restricted to women who were long-term users or non-users of biomass

°Body mass index (BMI) (kg/m²) ≥25= high; Waist-to-hip ratio (WHR) ≥0.85=high.

Supplementary Table 5	• Associations of angina with risk factors.
-----------------------	---------------------------------------------

Risk factor		sted only	Fully	adjusted <sup>a</sup>	Fully adjusted and			
	for age (n=850)		(n=8	(n=850)		limited to long- term users and non-users of biomass <sup>b</sup>		
					(n=69			
	OR	(95%CI)	OR	(95%CI)	OR	(95%CI)		
Age (per 10 year increase)	1.3	(1.1-1.6)	1.3	(1.1-1.5)	1.3	(1.1-1.5)		
Educational status								
Illiterate	1.0		-		-			
Any literacy	0.6	(0.3-1.3)						
Household income/month					-			
<3000-10000PKR	1.0		-					
>10000PKR	1.1	(0.8-1.6)						
Household ownership					-			
Rented	1.0		-					
Own	0.8	(0.5-1.3)						
Construction of house		/			-			
Katcha/semi-pucca	1.0		-					
Pucca	1.2	(0.8-1.7)						
Number of household assets	1.2	(0.0-1.7)						
0-1	1.0				-			
2-3	0.9	(0.6-1.3)	-					
2-3 >4	0.9 1.0							
—	1.0	(0.6-1.5)						
Father's occupation in woman's					-			
childhood	1.0							
Non-manual		(0,2,1,4)						
Manual	0.7	(0.3-1.4)						
Birthweight	1.0							
Lower than normal	1.0				-			
Normal	1.2	(0.8-1.8)	-					
Higher than normal	1.1	(0.7-1.8)						
Ever hungry during all the time					-			
during childhood because there								
was not enough food								
No	1.0		-					
Yes	0.8	(0.6-1.1)						
Lost weight during childhood					-			
No	1.0		-					
Yes	1.0	(0.8-1.4)						
Ever smoked regularly (any of								
cigarettes, bidi, huqqa)								
Never	1.0		1.0		1.0			
Ever	2.1	(1.3-3.3)	2.0	(1.2-3.2)	2.1	(1.3-3.6)		
Environmental tobacco smoke		/				~ /		
(at least one other household								
member smokes cigarettes, bidi								
or huqqa in the home)								
No	1.0		_					
Yes	1.0	(0.9-1.6)	-					
Consumption of meat or eggs	1.4	(0.7-1.0)						

**Consumption of meat or eggs** 

Do not eat either meat or eggs	1.0		1.0		1.0	
as much as once per week Eat one of meat or eggs as	0.6	(0.4-0.8)	0.6	(0.4-0.8)	0.7	(0.5-1.0)
much as once per week Eat both meat and eggs at least	0.4	(0.3-0.7)	0.5	(0.3-0.7)	0.5	(0.3-0.8)
once per week Current nutrition <sup>c</sup>						
Neither BMI nor WHR high	1.0					
One of BMI or WHR high	0.8	(0.5-1.1)	-			
Both BMI and WHR high	0.8	(0.5-1.2)				
Non-user of biomass	1.0					
User of biomass user	1.0	(0.7-1.3)	1.0	(0.8-1.4)		
Long-term non-user of biomass	1.0				1.0	
Long-term non-user of biomass	1.2	(0.9-1.7)			1.3	(0.9-1.9)

<sup>a</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p<0.1) in analyses adjusted only for age

<sup>b</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p<0.1) in analyses adjusted only for age, but was restricted to women who were long-term users or non-users of biomass

<sup>c</sup>Body mass index (BMI)  $(kg/m^2) \ge 25 = high$ ; Waist-to-hip ratio (WHR)  $\ge 0.85 = high$ .

Risk factor	Adjusted only for age (n=850) <sup>a</sup>		Full	y adjusted <sup>b</sup>	Fully adjusted and limited to long-term users and non-users of		
			(n=8	<b>350</b> )			
					biomass <sup>c</sup>		
					(n=6	<b>593</b> )	
	OR	(95%CI)	OR	(95%CI)	OR	(95%CI)	
Age (per 10 year increase)	1.5	(1.2-2.0)	1.5	(1.2-2.0)	1.5	(1.2-2.0)	
Educational status							
Illiterate	1.0		-		-		
Any literacy	1.5	(0.5-4.5)					
Household income/month							
<3000-10000PKR	1.0		1.0		1.0		
>10000PKR	1.6	(0.9-2.9)	1.4	(0.8-2.5)	1.6	(0.8-3.1)	
Household ownership							
Rented	1.0		-		-		
Own	1.2	(0.4-3.4)					
Construction of house	0	•			-		
Katcha/semi-pucca			-				
Pucca	1.3	(0.7-2.3)					
Number of household assets		5					
0-1	1.0		1.0		1.0		
2-3	1.4	(0.7-2.7)	1.3	(0.7-2.5)	1.8	(0.8-3.8)	
≥4	2.1	(1.0-4.3)	1.8	(0.8-3.8)	2.1	(0.9-5.1)	
Father's occupation in woman's					-		
childhood							
Non-manual	1.0		-				
Manual	1.0	(0.2-4.5)					
Birthweight							
Lower than normal	1.0				-		
Normal	1.0	(0.5-1.9)	-				
Higher than normal	0.7	(0.3-1.7)					
Ever hungry during all the time					-		
during childhood because there							
was not enough food							
No	1.0		-				
Yes	1.0	(0.6-1.7)					
Lost weight during childhood					-		
No	1.0		-				
Yes	1.1	(0.6-1.9)					
Ever smoked regularly (any of		. ,					
cigarettes, bidi, huqqa)							
Never	1.0		-				
Ever	0.9	(0.4-2.1)					
Environmental tobacco smoke (at		. /					
least one other household member							
smokes cigarettes, bidi or huqqa in							
the home)							
No	1.0		-				
Yes	0.9	(0.5-1.6)					
Consumption of meat or eggs		<u> </u>					

**Supplementary Table 6.** Associations of previous history of heart attack (diagnosed by a physician) with risk factors.

Do not eat either meat or eggs as	1.0		-				
much as once per week							
Eat one of meat or eggs as much as once per week	1.2	(0.6-2.3)					
Eat both meat and eggs at least once per week	1.8	(0.9-3.5)					
Current nutrition <sup>d</sup>							
Neither BMI nor WHR high	1.0		1.0		1.0		
One of BMI or WHR high	1.3	(0.6-2.5)	1.2	(0.6-2.5)	1.6	(0.7-3.4)	
Both BMI and WHR high	2.0	(1.0-4.0)	1.9	(0.9-3.7)	1.7	(0.8-3.6)	
Non-user of biomass	1.0		1.0		-		
Use of biomass	1.4	(0.8-2.4)	1.2	(0.7-2.2)			
Long-term non-user of biomass	1.0				1.0		
Long-term user of biomass	1.5	(0.8-2.7)			1.3	(0.7-2.4)	
<u></u>							

<sup>*a*</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p<0.1) in analyses adjusted only for age

<sup>b</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p<0.1) in analyses adjusted only for age, but was restricted to women who were long-term users or non-users of biomass

<sup>a</sup>Body mass index (BMI) (kg/m<sup>2</sup>) ≥25= high; Waist-to-hip ratio (WHR) ≥0.85=high.

Risk factor	Adjusted only for age		Fully adjusted <sup>a</sup> (n=841)		Fully adjusted and limited to long-term users and non-users		
	( <b>n=8</b> 4	41)	(11-04	1)		omass <sup>b</sup>	
					(n=68	86)	
	OR	(95%CI)	OR	(95%CI)	OR	(95%CI)	
Age (per 10 year increase)	1.1	(0.9-1.3)	1.1	(0.9-1.3)	1.0	(0.8-1.3)	
Educational status							
Illiterate	1.0		-		-		
Any literacy	0.8	(0.4-1.7)					
Household income/month		. ,					
<3000-10000PKR	1.0		1.0		1.0		
>10000PKR	1.6	(1.1-2.3)	1.6	(1.1-2.4)	1.3	(0.8-2.0)	
Household ownership		(		( 2.1)	-	(0.0 2.0)	
Rented	1.0		_				
Own	1.4	(0.7-2.9)	-				
Construction of house	1.4	(0.7-2.7)					
	10				-		
Katcha/semi-pucca	1.0	(0.7.1.5)	-				
Pucca	1.0	(0.7-1.5)					
Number of household assets							
0-1	1.0		-				
2-3	1.0	(0.7-1.5)					
<u>≥</u> 4	1.3	(0.8-2.1)					
Father's occupation in woman's					-		
childhood							
Non-manual	1.0		-				
Manual	1.0	(0.4-2.3)					
Birthweight							
Lower than normal	1.0				-		
Normal	1.1	(0.7-1.7)	-				
Higher than normal	1.1	(0.7-1.9)					
Ever hungry during all the time		()			-		
during childhood because there							
was not enough food							
No	1.0		_				
Yes	1.0	(0.8-1.6)	-				
Lost weight during childhood	1.1	(0.0-1.0)					
	1.0				-		
No	1.0	$(0 \in 1 \circ)$	-				
Yes	0.8	(0.6-1.2)					
Ever smoked regularly (any of							
cigarettes, bidi, huqqa)							
Never	1.0		-		-		
Ever	1.0	(0.6-1.8)					
Environmental tobacco smoke (at	,						
least one other household							
member smokes cigarettes, bidi							
or huqqa in the home)							
No	1.0				-		
110							

Do not eat either meat or eggs as much as once per week	s 1.0					
Eat one of meat or eggs as muc as once per week	h 0.9	(0.6-1.4)				
Eat both meat and eggs at least once per week	1.2	(0.7-1.8)				
Current nutrition <sup>c</sup>						
Neither BMI nor WHR high	1.0					
One of BMI or WHR high	0.8	(0.5-1.2)	-			
Both BMI and WHR high	1.1	(0.7-1.6)				
Non-user of biomass user	1.0		1.0			
User of biomass	0.8	(0.6-1.2)	0.8	(0.6-1.2)		
Longterm non-user of biomass	1.0				1.0	
Longterm user of biomass	0.9	(0.6-1.3)			0.9	(0.6-1.3)

<sup>a</sup>ECGs were missing for 9 women or not codable due to poor quality.

<sup>b</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p < 0.1) in analyses adjusted only for age

<sup>c</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p<0.1) in analyses adjusted only for age, but was restricted to women who were long-term users or non-users of biomass

<sup>*d*</sup>Body mass index (BMI)  $(kg/m^2) \ge 25 = high$ ; Waist-to-hip ratio (WHR)  $\ge 0.85 = high$ .

Revenues on the second se

 BMJ Open

Section/Topic	ltem #	Recommendation	Reported on page
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1-2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	3
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	3-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	3-5
Bias	9	Describe any efforts to address potential sources of bias	3-5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	5
		(b) Describe any methods used to examine subgroups and interactions	5
		(c) Explain how missing data were addressed	In relevant tables
		(d) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(e) Describe any sensitivity analyses	N/A

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	6
		confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	Not needed
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6 and Tables 1-3
		(b) Indicate number of participants with missing data for each variable of interest	Tables 1-3
Outcome data	15*	Report numbers of outcome events or summary measures	6
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence	Supplementary
		interval). Make clear which confounders were adjusted for and why they were included	Tables 4-7
		(b) Report category boundaries when continuous variables were categorized	Tables
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	8-9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10
Generalisability	21	Discuss the generalisability (external validity) of the study results	8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on	2
		which the present article is based	

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open

# **BMJ Open**

# **Coronary Heart Disease, Hypertension and Use of Biomass Fuel among Women: Comparative Cross-sectional Study.**

Journal:	BMJ Open
Manuscript ID	bmjopen-2019-030881.R3
Article Type:	Research
Date Submitted by the Author:	06-Jul-2019
Complete List of Authors:	Fatmi, Zafar; Aga Khan University, Department of Community Health Sciences Ntani, G; University of Southampton and Southampton University Hospitals NHS Trust, MRC Lifecourse Epidemiology Unit Coggon, David; University of Southampton, MRC Lifecourse Epidemiology Unit
<b>Primary Subject Heading</b> :	Global health
Secondary Subject Heading:	Epidemiology, Occupational and environmental medicine, Public health
Keywords:	Coronary heart disease < CARDIOLOGY, biomass fuel, Hypertension < CARDIOLOGY, women, EPIDEMIOLOGY, Public health < INFECTIOUS DISEASES



# **Coronary Heart Disease, Hypertension and Use of Biomass Fuel among Women: Comparative Cross-sectional Study.**

# Zafar Fatmi,<sup>1,2</sup> Georgia Ntani,<sup>2</sup> David Coggon<sup>2</sup>

<sup>1</sup>Department of Community Health Sciences, Aga Khan University, PO Box 3500, Karachi 74800, Pakistan.

<sup>2</sup>MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK.

\*Correspondence should be addressed to Zafar Fatmi; zafar.fatmi@aku.edu;

# Abstract

*Objectives:* To explore the associations of hypertension and coronary heart disease (CHD) with use of biomass fuel for cooking.

Design: Comparative cross-sectional study.

Setting: Rural villages in Sindh, Pakistan.

**Participants:** Women aged  $\geq$ 40 years who had used biomass fuel for cooking for at least the past year (n = 436), and a comparison group (n=414) who had cooked only with non-biomass fuel during the past year were recruited through door-to-door visits. None of those who were invited to take part declined.

**Primary and secondary outcome measures:** Hypertension was determined from blood pressure measurements and use of medication. CHD was assessed by three measures: history of angina (Rose angina questionnaire), previous history of 'heart attack', and definite or probable changes of CHD on electrocardiogram (ECG). Potentially confounding risk factors were ascertained by questionnaire and anthropometry. Associations of hypertension and CHD with use of biomass and other risk factors were assessed by logistic regression, and summarised by odds ratios (ORs) with 95% confidence intervals (CIs).

**Results:** After adjustment for potential confounders, there was no association of hypertension (OR: 1.0, 95% CI 0.8 – 1.4) angina (OR: 1.0, 95% CI 0.8-1.4), heart attack (OR: 1.2, 95% 0.7 – 2.2) or ECG changes of CHD (OR: 0.8, 95% CI 0.6 – 1.2) with current use of biomass for cooking. Nor were any associations apparent when analyses were restricted to long-term ( $\geq$ 10 years) users and non-users of biomass fuel.

*Conclusions:* A linked air monitoring study indicated substantially higher airborne concentrations of fine particulate matter in kitchens where biomass was used for cooking. It is possible that associations with CHD and hypertension were missed because most of the comparison group had used biomass for cooking at some time in the past, and risk remains elevated for many years after last exposure.

# Strengths and limitations of this study:

• The study was well-powered with a high response rate (93%) from those invited to take part, and large contrasts between comparison groups in recent exposure to indoor air pollution.

- Comparisons were based on recent cooking practices, but some exposures may have changed since the onset of CHD.
- Many women who did not currently use biomass for cooking, had done so in the past, and this may have obscured associations with health outcomes if effects of exposure persist long-term.
- Errors may have occurred in the assessment of outcome measures, biasing risk estimates towards the null.
- Recall of some potentially confounding factors may have been inaccurate, leading to uncontrolled residual confounding.

# **Funding Statement**

This research was supported by a fellowship from the Colt Foundation for the conduct of a PhD by Professor Zafar Fatmi. Professor David Coggon and Dr Georgia Ntani were supported by funding from the UK Medical Research Council (MRC\_MC\_UU\_12011/5).

# **Conflicts of Interest**

The authors declare that there is no conflict of interest regarding the publication of this paper.

# Authors' contributions

ZF led the design and conduct of the study, carried out the initial statistical analyses, and wrote the first draft of the manuscript.

GN oversaw and guided the statistical analysis.

DC supervised the project and amended the first draft of the manuscript.

All authors approved the final version of the manuscript.

# Introduction

Some three billion people across the globe use biomass fuel (such as wood, crop wastes, animaldung, and charcoal/coal) for cooking and heating [1]. Burning of biomass fuels in inefficient stoves or open fires causes household air pollution (HAP) and leads to an estimated 3.8 million deaths per year globally [2]. It primarily affects women and young children in low- and middle-income countries (LMICs). Such women often work for 4-5 hours per day in the kitchen, and with their young children may spend 90% of their time at home [2,3]. About 77% of households in Africa and 60% in Southeast Asia use biomass fuel [1].

The HAP from burning biomass consists of hundreds of health-damaging pollutants, but finer particles ( $<2.5\mu$ m – PM<sub>2.5</sub>) and carbon monoxide (CO) are the major emissions, and have been studied most extensively. PM<sub>2.5</sub> causes inflammation of the lungs and airways, and impairs immune responses [4]. Concentrations of PM<sub>2.5</sub> in kitchens and living rooms can be 100 times higher than the acceptable standard for ambient (outdoor) air [5]. HAP predisposes to upper and lower respiratory tract infections among children [6-8], and also causes chronic obstructive pulmonary disease [9-10] and lung cancer in adults [11-13]. It has been linked with early foetal loss, preterm delivery and low birth weight babies [14,15], and evidence is accumulating that it may also affect the physical and cognitive development of young children [16].

In addition, several studies have suggested a hazard of coronary heart disease (CHD) from HAP exposure, but evidence for this is limited and inconclusive [17, 18]. Several adverse cardiovascular outcomes have been studied, including acute coronary syndrome (myocardial infarction /unstable angina), coronary heart disease, and high blood pressure. Two small scale case-control studies found significantly high risk of acute coronary syndrome with use of solid fuel [19,20]. In addition, a cohort study found an association between myocardial infarction and domestic use of coal among women in China [21]. Lee and colleagues [22], in a large cross-sectional survey of adults in China found a positive association with CHD. On the other hand, two large cohort studies, one in Iran [23] and other in Bangladesh [24], found no association with CHD, although it is unclear how potential confounders were taken into account in those investigations. Most studies have found significant positive associations between use of solid fuel and higher blood pressure [25-28] or prevalence of hypertension [22, 29-31], but in others, no association was apparent [25,32-33].

In Pakistan, where biomass fuel is used for cooking and heating by 52% of households overall, and 75% in rural areas, an exploratory case-control study found an elevated risk of acute coronary syndrome among women using solid fuel [20].

We, therefore, carried out a cross-sectional survey to explore the association between CHD and cooking with biomass in a sample of women drawn from the general population in rural areas of Pakistan. The objective of the study was to compare the prevalence of hypertension, angina, previous history of heart attack, and electrocardiographic (ECG) changes indicative of CHD in women  $\geq$ 40 years of age who used biomass fuel for cooking with that in women of similar age who cooked using other types of fuel.

# **Materials and Methods**

# Study Setting

The survey was conducted during 2015 in villages surrounding the main urban area of Nawabshah district (recently renamed as Shaheed Benazirabad) in the province of Sindh, Pakistan. These were selected to give a mix in the fuels used for cooking within the study sample. Some of the villages had been supplied with natural gas for at least 10 years, whereas in others biomass fuel (wood and/or cow dung) was still being used.

# Recruitment of households and subjects

Within each village, trained field workers made door-to-door visits, and asked the heads of households whether their families would be willing to assist with the study, and if so, what type of fuel was used for cooking, and whether food preparation was regularly undertaken by a woman  $\geq$ 40 years of age. In this way, the study team identified quotas of the required numbers of households in each of the two categories of fuel use (biomass and other). The heads of these households were then asked to complete a consent form, and to identify and introduce the woman of the household aged  $\geq$ 40 years who had carried out the most cooking in the house over the past 10 years. The study was explained to her, and she was invited to participate and to give signed consent.

# Inclusion criteria

Women aged 40 years or older were eligible for inclusion if they gave informed consent, and had been cooking in the household for at least the past year, using only one of biomass fuel or non-biomass fuel.

# Questionnaire, examination and measurements

A standardized questionnaire was used to collect information at interview about: demographic and socio-economic characteristics, birth weight, smoking history, whether another member of the household was a regular smoker, relevant aspects of diet, physical activity, lifetime history of cooking using different types of fuel, any previous diagnosis of a 'heart attack' by a doctor, symptoms of angina (through the Rose angina questionnaire [34]), and any current use of medication for hypertension. In addition, measurements were made of height, weight, waist circumference, hip circumference and blood pressure.

Socioeconomic status was characterized by the literacy of the participant (no vs. any literacy), the type of employment of her father during her childhood (manual or non-manual), the ownership and construction of her house ('pucca' i.e. made of concrete walls and roof or 'katcha/semi-pucca' i.e. made fully or partially of thatched walls and roof), the income level of the household, and the number of household assets owned from a list of seven. Birth weight was determined from participants' recall as being 'higher than normal vs. normal vs. lower than normal'.

The questions on smoking covered use of cigarettes or *bidi* (locally made cigarettes without filters) or a hookah (pipe) regularly (at least once a week for a month or longer). The number of other people in the household who smoked provided a measure of domestic exposure to environmental tobacco smoke (ETS), which was classified according to whether at least one other household member smoked cigarettes or *bidi* or a hookah in the home.

Dietary questions covered the use of oil or ghee for cooking and eating, and weekly consumption of meat and eggs. The former was categorized to three levels: only or mostly use oil; mixed use of oil and ghee; only or mostly use ghee. Frequencies of consuming meat and eggs were each categorized to two levels: at least once per week vs. less than once per week.

Level of physical activity was assessed through questions on the frequency per week of shopping, fetching water, washing clothes, collecting wood for cooking, agricultural work on a farm and any other regular heavy physical work. Each of these activities was categorized to two levels: zero days per week or at least once per week. A composite physical activity score was then derived as the number of activities carried out at least once per week, with values ranging from 0 to 6.

Height, weight, and waist and hip circumference were measured using a stadiometer, digital weighing scale and measuring tape, following standardized methods. Body mass index (BMI) (weight in kilograms per squared height in meters) and waist-to-hip ratio (WHR) were then calculated from the

measurements. BMIs  $\geq 25$ kg/m<sup>2</sup> were considered abnormally high (overweight or obese), as were WHRs of  $\geq 0.85$ .

Categories of exposure to biomass:

Use of biomass was classed to two main categories; biomass users who currently used firewood and/or cow dung for cooking; and non-users of biomass who did not (other sorts of biomass were not used for cooking in the community studied).

In addition, two subsets of these main categories were distinguished: long-term biomass users who currently used firewood and/or cow dung for cooking and had done so for at least the past 10 years; and long-term non-users of biomass who currently did not use either firewood or cow dung for cooking and had not done so for at least the past 10 years.

Outcome measures:

Four outcome measures were specified.

Hypertension: Three measurements of blood pressure were made at five-minute intervals, using an Omron upper arm blood pressure monitor, and mean values for systolic and diastolic blood pressure were derived. Women were deemed to have hypertension if they met at least one of the three criteria: mean systolic blood pressure  $\geq$ 140 mm Hg; mean diastolic blood pressure  $\geq$ 90 mm Hg; regular use of medication for blood pressure.

Angina: Experience of angina was assessed through the Rose angina questionnaire [34], which comprises seven questions relating to chest pain, its anatomical distribution, precipitating and relieving factors, and duration. A diagnosis of angina required report of pain, pressure or discomfort in the chest centrally, or in both the left anterior chest and left arm, that occurred when walking uphill or hurrying, that caused the participant to stop or slow down when it occurred while walking, and that was then relieved within 10 minutes by standing still.

Heart attack: Previous diagnosis of 'heart attack' by a doctor was ascertained through a single question: 'In the past, have you ever been told by a health care provider that you had a 'heart attack'?'

Definite or probable CHD on ECG: A 12-lead ECG was recorded according to a standard protocol, and coded for the presence of definite or probable CHD, using the Minnesota Code Manual of Electrocardiographic Findings, second edition [35]. This corresponded to the presence of any of codes 1-1 to 1-3, 3-1, 4-1 to 4-4, 5-1 to 5-3, 7-1-1 and 9-2. In order to check the repeatability of the coding, two of us (ZF and DC) coded all of the ECGs independently. We used the same scanned ECG traces, without information about the type of cooking fuel used by the participant. Levels of agreement between the observers were assessed, using kappa statistics. Where differences occurred in the classification of an ECG trace, they were then resolved by discussion between the two observers.

#### Statistical analysis

Data were double-entered in Epidata 3.1 software [36] for validation. All discrepancies were corrected by reference to the original questionnaire or record sheet. Statistical analysis was carried out with Stata version 12.0 [37].

As a first step, several variables were reclassified or combined, based on their distribution in the full study sample, and without knowledge of participants' use of biomass fuel. Thus, a combined index was derived for frequency of consuming meat and eggs with three levels: neither meat nor eggs as much as once per week; one of meat or eggs at least once per week; both meat and eggs at least once

per week. Scores for physical activity were categorized into three levels: low (0-1 activities); medium (2-3); high (4 or more). Similarly, BMI and WHR were combined as a single variable with three categories: neither BMI nor WHR high; one of BMI or WHR high; both BMI and WHR high.

Descriptive statistics were produced for women in each of the four categories of exposure to biomass, summarizing their demographic and socioeconomic characteristics, current and past cooking arrangements, types and durations of fuel use, hours of cooking per day, types of stove and kitchen, and exposures to potentially confounding risk factors. The prevalence of the main outcomes was determined for the study sample overall, and the relationship of ECG changes to angina and history of heart attack was explored.

Logistic regression analysis was then used to assess the association of each of the four outcome variables with use of biomass fuel for cooking and other possible risk factors. First, associations with each potential risk factor were determined after adjustment for age. The main exposure of interest (user or non-user of biomass) was then carried forward into a mutually adjusted model along with all other risk factors which showed associations ( $p \le 0.1$ ) when examined individually. In addition, a second mutually adjusted model was fitted that compared long-term use and non-use of biomass for cooking.

#### Sample size

The size of the study sample was determined by a power calculation which assumed an outcome prevalence of at least 6% for definite CHD among non-users of biomass fuel, based on a previous study in Pakistan [38] (the prevalence of other outcomes was expected to be higher). This indicated that we would require at least 876 women (438 users and 438 non-users of biomass) for 80% power to detect an odds ratio of 2.0 for the use of biomass fuel with a 5% level of statistical significance.

Patient and public involvement

There was no involvement of patients or the public in development of this study.

#### Ethical approval

The study was approved by Ethics Review Committee of Aga Khan University, Karachi, Pakistan.

#### Results

A total of 24 villages were visited in order to recruit the number of households required for the survey. In 14 villages all households used biomass for cooking, while in three all used natural gas, and in the other seven, both types of fuel were used. The number of participating households per village ranged from as few as three to as many as 210. Interviews were completed with women from a total of 1073 households, 536 of which currently used biomass fuel, and 537 natural gas (including LPG). No-one declined to participate in the study, but 77 women could not be interviewed because they were not at home at the time when the survey team visited (mostly because they were engaged in agricultural work).

Among the 1073 women who completed interviews, 44 indicated that they were in fact aged less than 40 years of age, and were therefore excluded from the analysis. An additional 151 women had not made meals regularly (at least one meal per day on most days of the week) during the past year, and were also excluded. We further excluded 28 women who did not currently use firewood or cow dung for cooking, but whose time since last use of biomass was <2 years (this was done to ensure distinct exposure categories). Thus, further analysis was based on 850 women: 436 users and 414 non-users of biomass. Among them, 430 were long-term users of biomass, and 263 were long-term non- users.

#### **BMJ** Open

Table 1 summarizes the demographic and socioeconomic characteristics of the participants in the study sample overall, and according to categories of exposure to biomass fuel. In comparison with users of biomass, non-users were marginally younger (63% versus 60% <50 years), and somewhat more advantaged socioeconomically.

Table 2 describes the current and past cooking arrangements of participants, including type and duration of fuel use, intensity of cooking, and type of stove and kitchen. Even among the long-term non-users of biomass, 88% had cooked with biomass fuels at some time in their life. Among the biomass users, the large majority had used wood (93%) and cow dung (88%) for longer than 20 years. Few participants (3.7% of biomass users and 6.3% of non-users) had ever used kerosene as a cooking fuel. Most participants (approximately 60%) currently cooked for 2-3 hours per day, the average duration of cooking per day being similar in users and non-users of biomass. Where biomass was used for cooking, it was also more likely to be used to heat the home.

Table 3 shows the distribution of potentially confounding risk factors for CHD in the four categories of exposure to biomass. In comparison with non-users of biomass users, slightly higher proportions of women using biomass reported having been born with 'lower than normal' birth weight, having lost weight at some time during childhood, ever having smoked, and being exposed to environmental tobacco smoke in the home.

#### Prevalence of outcome measures

Supplementary Table 1 shows the prevalence of the main outcome measures that were investigated. In total, 297 women (35%) were classed as having hypertension, two thirds of whom were taking regular medication for blood pressure. About 27% had symptoms indicative of angina based on Rose's questionnaire. Fifty-four (6.4%) reported a previous history of 'heart attack', and 19% of women had findings of 'definite or probable CHD on ECG'.

#### Validity of ECG classification and interrelationships of outcome measures:

Supplementary Table 2 compares the classification of ECGs by the two observers. Satisfactory ECG traces were obtained for 841 (98.9%) of the participants, but four were missing from the file used to assess inter-observer agreement, and were later assessed jointly by the two observers. The overall agreement between the two observers was 85.2% (kappa = 0.57). Most disagreements were related to cases in which the exceedance of a threshold in, for example, ST elevation, ST depression or the width (duration) of a Q wave was borderline. In some cases, it was questionable whether there was a small R wave or a QS pattern. Also, there was some disagreement about whether T waves were negative or flat. Following discussion between the two observers, all of the discrepancies were reconciled, and it was finally agreed that 181 women (21.5%) showed changes indicative of 'definite or probable CHD'. However, in 22 of these cases, it appeared that the abnormality had occurred only because the ECG leads had been placed incorrectly, and those traces were reclassified as normal. Thus in further analyses, 159 (19%) of women were considered to have definite or probable CHD on ECG.

Supplementary Table 3 shows the prevalence of definite or probable CHD on ECG according to symptoms of angina and history of heart attack. It was somewhat more frequent in participants who reported an earlier heart attack (26%) than in those who did not and had no symptoms of angina (18%). However, there was no association with angina in the absence of heart attack.

#### Association of outcome measures with use of biomass and other risk factors

Associations of hypertension and the three CHD outcomes (angina, heart attack and definite or probable CHD on ECG) with potential risk factors are presented in Supplementary Tables 4 to 7, from which the risk estimates for use of biomass fuel for cooking are summarized in Table 4. The first column of each table gives odds ratios adjusted only for age, while the second column presents mutually adjusted risk estimates from a single model that included use of biomass and all of the risk factors that showed associations ( $p \le 0.1$ ) in the analyses adjusted only for age. The last column shows findings from a similar analysis but restricted to women who were long-term users or non-users of biomass.

In analyses that adjusted only for age, hypertension was associated ( $p\leq0.1$ ) with older age, a higher number of household assets, higher frequency of consuming meat and eggs, and having a high BMI or WHR (Supplementary Table 4). When these variables were carried forward to the mutually adjusted analysis, the association with consumption of meat and eggs was diminished, but the others remained. Thus, the risk of hypertension increased 40% with every 10-year increase in age, was 2.3 times higher in women with  $\geq$ 4 household assets than in those with 0 or 1, and was increased 1.9-fold in women who had both high BMI and high WHR as compared with those in whom neither BMI nor WHR were elevated. However, hypertension was not associated with use of biomass (OR 1.0 in the fully adjusted model). When analysis was restricted to long-term users and non-users of biomass, results were similar, with an OR of 1.1 for long-term use of biomass.

In analyses that adjusted only for age, the odds of angina increased with age and regular smoking, and were significantly lower with more frequent consumption of meat and eggs (Supplementary Table 5). Moreover, this pattern was maintained when risk estimates were mutually adjusted. Thus, the odds of angina increased by 30% per 10-year increase in age, and with ever having smoked regularly (OR 2.0, 95%CI 1.2-3.2), and were significantly lower in women who ate both meat and eggs at least once per week (OR 0.5, 95%CI 0.3-0.7). There was, however, no association with use of biomass (OR 1.0, 95%CI 0.8-1.4). When analysis was restricted to long-term users and non-users of biomass, results were similar except that there was a suggestion of a weak association with exposure to biomass (OR 1.3, 95%CI 0.9-1.9).

In corresponding analyses with previous history of heart attack (diagnosed by a physician) as an outcome, initial models with adjustment only for age indicated associations (p<0.1) with age, higher household income, higher number of household assets, and high BMI or WHR (Supplementary Table 6). After mutual adjustment, age remained a significant risk factor (OR 1.5, 95%CI 1.2-2.0, for each 10-year increase in age). However, the other associations, although still positive, were not significant at a 5% level. Nor was there an association with use of biomass for cooking (OR 1.2, 95%CI 0.7-2.2). In the mutually adjusted model for long-term use of biomass, results were very similar.

In analyses adjusted only for age, household income was the only variable significantly associated with definite or probable CHD on ECG, and it remained significant in the fully adjusted model (OR 1.6, 95%CI 1.1-2.4 for household income >10,000PKR) (Supplementary Table 7). However, there was no association with use of biomass for cooking, either overall or in the long-term (ORs 0.8 and 0.9).

#### Discussion

This study found no association between use of biomass fuel and any of the four outcomes studied (hypertension, angina, previous history of heart attack, and definite or probable CHD on ECG), even when comparison was with women who had not used biomass for at least the last 10 years. The strongest hint of an association was for angina in long-term users as compared with long-term non-users of biomass, but the elevation of risk was small (30%) and not statistically significant at a 5% level.

The choice of villages from which to recruit participants ensured a balance in the fuels currently used for cooking, and cooperation in the survey was good with high response rates from the households and women that were invited to take part. Inevitably, recruitment was to some extent opportunistic and limited to one province of Pakistan. However, there seems no reason to expect that the study sample would have been seriously unrepresentative in the associations of hypertension and CHD with use of biomass and other risk factors.

A linked air monitoring study found that in the kitchens of houses using biomass for cooking, the mean 24-hour  $PM_{2.5}$  concentration was 531 µg/m<sup>3</sup>, with a median of 136 µg/m<sup>3</sup> and inter-quartile

range 34-615  $\mu$ g/m<sup>3</sup> (paper in preparation). Corresponding concentrations in houses not using biomass for cooking were 69.9, 24.2, and 13.5-53.3  $\mu$ g/m<sup>3</sup>. Thus, while individual exposures may have been influenced also by time spent cooking and whether biomass was burned in a closed or open kitchen, the absence of associations with CHD and hypertension is unlikely to reflect inadequate contrasts in recent intensity of exposure.

Our aim was as far as possible to recruit households that had used the same fuel for cooking exclusively for at least past 10 years. Villages were selected with this criterion in mind, and it was covered in preliminary inquiries that were addressed to local community representatives. In practice, however, it turned out that where natural gas was available in villages, some participants had not yet switched to cleaner fuel, or had done so at a later date than others. A pragmatic decision was therefore made to include women even if they had changed their cooking fuel within the past 10 years, provided that they had used their current fuel for at least a year. This seemed reasonable since trials had suggested that interventions to reduce HAP from use of biomass for cooking can produce reductions in blood pressure and changes in ECGs over the short to medium term [39-41]. However, to check that it did not obscure associations, additional analyses were carried out with restriction to long-term users and non-users of biomass, and still no relationship was found with the health outcomes.

The sample size achieved for the study was close to that planned, and the prevalence of the four outcomes was higher than had been assumed in the power calculations. Moreover, the upper confidence limits for the odds ratios relating to use of biomass were almost all <2. Thus, the absence of associations with biomass does not reflect a lack of statistical power.

Ascertainment of current use of biomass is likely to have been highly accurate, and while there may have been some errors in recall of the times when biomass had been used in the past, it is difficult to conceive that any resultant misclassification would have obscured important associations with CHD. Generally, switches in the use of fuel were only in one direction – towards cleaner natural gas from biomass. The timing of changes was usually well recalled because in most instances the entire village received the new source of fuel in a particular year. However, the duration of using cow dung and firewood may not always have been remembered reliably, and switches between these types of fuel could also have occurred. Many women reported using cow dung and firewood for the same duration, and no attempt was made to analyse them separately.

Recall of some potentially confounding exposures may also have been inaccurate – particularly those pertaining to childhood. If so, the errors would be expected to be non-differential with respect to CHD, and therefore to bias risk estimates towards the null, possibly leading to uncontrolled residual confounding. However, the assessment of BMI and WHR used standardized methods, and should have been reasonably reliable. The interviewers were trained in how to make the measurements, and their technique was piloted in the field before the start of data collection.

A greater concern is the possibility of error in the ascertainment of outcomes. Blood pressure was objectively measured according to a standardized protocol, and was taken as the average of three readings. Moreover, most of the women who were classed as having hypertension were taking treatment for the disorder, which supports the validity of its assessment. Angina was determined through the well-established Rose questionnaire, but it is possible that symptoms in some cases arose from other pathology. Previous research has suggested that the Rose angina questionnaire may not be as reliable among women as in men [42]. Although the question to participants about history of heart attack referred specifically to diagnoses that had been given by a health professional, errors could have occurred in interpretation of the term "heart attack" (e.g. to include symptoms from dysrhythmias and acute heart failure as well as myocardial infarction). However, ascertainment of heart attack had been previously carried out by the same method in a similar population, where it was found to be reasonably accurate [43].

The diagnosis of CHD from ECGs showed only a weak relationship to history of medically diagnosed heart attack, and none at all to symptoms of angina (Supplementary Table 3). Between observer

agreement in the classification of ECGs was reasonably good (kappa = 0.57) (Supplementary Table 2), but it is notable that unlike angina and history of heart attack, CHD diagnosed from ECGs did not show the expected association with age (Supplementary Table 7).

To the extent that errors did occur in the ascertainment of outcomes, they are unlikely to have differed systematically in relation to use of biomass, and therefore would be expected to tend to obscure any true associations.

Because the study had a cross-sectional design, consideration must be given to the possibility of reverse causation. For risk factors related to childhood (e.g. birthweight, father's occupation and education), this is less of a concern. However, it is plausible that characteristics such as diet, physical activity and time spent cooking could have changed as a consequence of CHD. Depending on the circumstances, this might bias associations either upwards or downwards.

Another limitation of the study was that it did not determine when past heart attacks had occurred. Even if not as a consequence of an earlier heart attack, some of the exposures studied (e.g. BMI and WHR) may have changed in the interval since such an attack occurred. If so, this might obscure true associations.

A further possible source of error was uncontrolled residual confounding. To minimize this problem, information was collected about a range of potentially confounding variables, and as in most studies of biomass fuel, socio-economic status tended to be higher in women using cleaner fuels [44]. Although several socio-economic indicators were evaluated as possible factors for adjustment, residual confounding could still have occurred. To explain the absence of associations with biomass, such confounding would have to be inverse (i.e. the under-ascertained confounder would have to be less prevalent in women who used biomass than in non-users).

The study found expected associations with several established risk factors for CHD. Thus, the odds of hypertension, angina and previous history of heart attack were all higher with older age (by 30-50% for every 10-year increase), although this was not found for definite or probable CHD on ECG. The relationship of CHD to age is well documented in the literature [45], and in women, the incidence of CHD increases rapidly after the menopause, reaching up to three times that in premenopausal women [46].

Two of the outcome measures – hypertension and previous history of heart attack – were significantly associated with affluence as measured by number of household assets. This relationship has also been observed before. In a population-based study in Pakistan, history of 'angina or heart attack' was estimated to have 3-fold higher prevalence among affluent participants than in those who were poor [47]. The direction of the association, which is the inverse of that observed in western populations, accords with a higher prevalence of diabetes, hypertension and dyslipidaemias in more educated and affluent groups, which was found in a recent study conducted in South Asian countries, including Pakistan [48].

In further support of an effect of affluence, we found that high BMI and/or WHR was associated with greater risk of hypertension, and (non-significantly) with history of heart attack. Obesity has been shown to increase the risk of hypertension in several studies [49, 50], and partly through this mechanism, also increases the risk and progression of CHD [51]. The INTERHEART study suggested that WHR (abdominal obesity) is a better marker of risk for CHD than BMI [52], but the two were correlated in our study sample, and we opted to use a combined measure.

In contrast, we found that more frequent consumption of meat and eggs was associated with reduced risk of angina. This was unexpected given the known relationship of CHD to consumption of saturated fat [53], and may have been a chance finding. It did not extend to the other outcomes investigated. However, a recent large global review of the literature on saturated fats suggests that this relationship may be inconsistent [54].

Smoking has consistently been found to increase the risk of CHD in many studies [55]. However, in our investigation it was associated only with angina. This might be because intensity of tobacco use among female smokers in the Pakistani population is low [56].

Despite the finding of several expected associations, the failure to demonstrate more consistent relationships to known risk factors is a further indication for caution in the interpretation of our results.

Several earlier studies have indicated links between use of biomass for cooking and CHD, although the finding has not been entirely consistent [17,18]. As already discussed, one explanation for our failure to demonstrate such associations in the current study could be inaccuracies in the diagnosis of CHD. Another possibility, however, is that adverse effects of exposure to pollutants from the use of biomass persist many years after last exposure. In this survey, even among women who had not used biomass during the last 10 years, most had done so earlier, and often for a long time. Only a few participants (about 3.5% overall) had never used biomass, which was too few for meaningful risk estimates. While it would be possible to compare rural users of biomass with lifelong users of cleaner fuels in urban settings, interpretation would be complicated by other important differences between those living in rural and urban areas.

# Conclusions

This study evaluated the association of hypertension and three measures of CHD – angina, previous history of heart attack and definite or probable CHD on ECG - with use of biomass for cooking. We found no clear associations with any of the health outcomes. However, the weak relationship of ECG abnormalities to the other two measures of CHD, and the inconsistency of their associations with well-established risk factors, suggest that this could have been because of diagnostic misclassification. Alternatively, it could be that an effect was missed because most of the women who were not currently using biomass for cooking had used it in the past, and risk remains elevated for many years after last exposure.

# **Data Availability**

The data [stata.dta format] underpinning the findings of this study are available from the corresponding author upon reasonable request.

# Acknowledgments

The study reported in this paper formed part of a PhD project carried out by Dr Zafar Fatmi under the supervision of Professor David Coggon at the University of Southampton, UK.

Mr Syed Nayab Ali Shah coordinated the data collection. Ms Shereen Jamali, Ms Fozia Jamali, Ms Iqra Memon and Ms Sana Memon administered the questionnaires at interview and recorded the ECGs. We are grateful also to Professor Keith Palmer and Professor M. Masood Kadir for their advice on various aspects of the study.

## References

- 1. Bonjour S, Adair-Rohani H, Wolf J, Bruce NG, Mehta S, Prüss-Ustün A, Lahiff M, Rehfuess EA, Mishra V, Smith KR. Solid fuel use for household cooking: country and regional estimates for 1980-2010. *Environ Health Perspect*. 2013; 121:784-90.
- 2. World Health Organization. Household air pollution and health. Geneva, Switzerland. (Accessed on 4 April 2018). <u>http://www.who.int/mediacentre/factsheets/fs292/en/</u>
- 3. World Health Organization. Ambient (outdoor) air quality and health [Internet]. Geneva; 2018 [updated 2 May 2018]. Available from: <u>https://www.who.int/news-room/fact-sheets/detail/ambient-(outdoor)-air-quality-and-health</u>
- 4. Naeher LP, Brauer M, Lipsett M, Zelikoff JT, Simpson CD, Koenig JQ, et al. Woodsmoke health effects: a review. Inhal Toxicol. 2007;19(1):67-106. Review.
- 5. Clark ML, Peel JL, Balakrishnan K, Breysse PN, Chilrud SN, Naeher LP et al. Health and household air pollution from solid fuel use: the need for improved exposure assessment. Environ Health Perspect 2013; 121:1120-8.
- 6. Smith KR, Samet JM, Romieu I, Bruce N. Indoor air pollution in developing countries and acute lower respiratory infections in children. Thorax. 2000 Jun;55(6):518-32.
- Smith KR, Mehta S, Maeusezahl-Feuz M. Indoor air pollution from household use of solid fuels: comparative quantification of health risks. In: Ezzati MLA, Rodgers A, Murray CJL, editors. Global and regional burden of disease attributable to selected major risk factors. Geneva, Switzerland: World Health Organization; 2004. pp. 1435– 1493.
- 8. Torres-Duque C, Maldonado D, Pérez-Padilla R, Ezzati M, Viegi G; Forum of International Respiratory Studies (FIRS) Task Force on Health Effects of Biomass Exposure. Biomass fuels and respiratory diseases: a review of the evidence. Proc Am Thorac Soc. 2008 Jul 15;5(5):577-90.
- 9. Liu Y, Lee K, Perez-Padilla R, Hudson NL, Mannino DM. Outdoor and indoor air pollution and COPD-related diseases in high- and low-income countries. Int J Tuberc Lung Dis. 2008;12(2):115-27.
- 10. Kurmi OP, Semple S, Simkhada P, Smith WC, Ayres JG. COPD and chronic bronchitis risk of indoor air pollution from solid fuel: a systematic review and meta-analysis. Thorax. 2010; 65(3):221-8.
- 11. Liu Q, Sasco AJ, Riboli E et al. Indoor air pollution and lung cancer in Guangzhou, People's Republic of China. Am. J. Epidemiol. 1993; 137: 145–54.
- 12. Kleinerman R, Wang Z, Lubin J, Zhang S, Metayer C, Brenner A. Lung cancer and indoor air pollution in rural china. Ann Epidemiol. 2000;10(7):469.
- 13. Behera D, Balamugesh T. Indoor air pollution as a risk factor for lung cancer in women. J Assoc Physicians India. 2005; 53:190-2.
- 14. Amegah AK, Quansah R, Jaakkola JJ. Household air pollution from solid fuel use and risk of adverse pregnancy outcomes: a systematic review and meta-analysis of the empirical evidence. PloS one. 2014 Dec 2;9(12): e113920.
- 15. Lamichhane DK, Leem JH, Lee JY, Kim HC. A meta-analysis of exposure to particulate matter and adverse birth outcomes. Environ Health Toxicol. 2015 Nov 3;30: e2015011.
- 16. Calderón-Garcidueñas L, Torres-Jardón R, Kulesza RJ, Park SB, D'Angiulli A. Air pollution and detrimental effects on children's brain. The need for a multidisciplinary approach to the issue complexity and challenges. Front Hum Neurosci. 2014; 8:613.
- 17. Fatmi Z, Coggon D. Coronary heart disease and household air pollution from use of solid fuel: a systematic review. Br Med Bull. 2016 Jun;118(1):91-109.

1	
3	
4 5	
6 7	
8	
9 10	
11	
12 13	
14	
15 16	
17 18	
19	
20 21	
22	
23 24	
25	
20	
3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29	
29 30 31 32 33 34 35 36 37	
31 32	
33	
34 35	
36 37	
38	
39 40	
41	
42 43	
44 45	
46	
47 48	
49	
50 51	
52	
53 54	
55 56	
57	
58 59	
59	

18. Yu K, Qui G, Chan K-H, Lam K-BH, Kurmi OP, Bennett DA et al. Association of
solid fuel use with risk of cardiovascular and all-cause mortality in rural China.
JAMA 2018; 319:1351-61.

- 19. Sathiakumar N. Indoor air pollution due to biomass fuel use and acute coronary syndrome among Sri Lankan women. Epidemiology 2012;23: S224.
- Fatmi Z, Coggon D, Kazi A, Naeem I, Kadir MM, Sathiakumar N. Solid fuel use is a major risk factor for acute coronary syndromes among rural women: a matched case control study. Public Health. 2014 Jan;128(1):77-82. doi: 10.1016/j.puhe.2013.09.005.
- 21. Kim C, Shu X-O, Hosgood HD, et al. Past use of coal for cooking is associated with all-cause mortality in the prospective Shanghai women's health study. Cancer Res 2014;74:Abstract nr 2184.
- 22. Lee M-S, Hang J-Q, Zhang F-Y, et al. In-home solid fuel use and cardiovascular disease: a cross-sectional analysis of the Shanghai Putuo study. Environ Health 2012;11:18.
- 23. Mitter SS, Islami F, Pourshams A, et al. Use of biomass fuels for cooking and heating is associated with increased non-communicable disease mortality: Golestan cohort study. Circulation 2012;125: AP042.
- 24. Alam DS, Chowdhury MAH, Siddique AT, et al. Adult cardiopulmonary mortality and indoor air pollution: a10-year retrospective cohort study in a low-income rural setting. Glob Heart 2012; 7:215–21.
- 25. Baumgartner J, Schauer JJ, Ezzati M, et al. Indoor air pollution and blood pressure in adult women living in rural China. Environ Health Perspect 2011; 119:1390–5.
- 26. Painschab MS, Davila-Roman VG, Gilman RH, et al. Chronic exposure to biomass fuel is associated with increased carotid artery intima-media thickness and a higher prevalence of atherosclerotic plaque. Heart 2013; 99:984–91.
- 27. Burroughs Peña M, Romero KM, Velazquez EJ, et al. Relationship between daily exposure to biomass fuel smoke and blood pressure in high-altitude Peru. Hypertension 2015; 65:1134–40.
- 28. Neupane M, Basnyat B, Fischer R, et al. Sustained use of biogas fuel and blood pressure among women in rural Nepal. Environ Res 2015;136: 343–51.
- 29. Ray MR, Mukherjee S, Roychoudhury S, et al. Platelet activation, upregulation of CD11b/CD18 expression on leukocytes and increase in circulating leukocyte-platelet aggregates in Indian women chronically exposed to biomass smoke. Hum Exp Toxicol 2006; 25:627–35.
- 30. Dutta A, Mukherjee B, Das D, et al. Hypertension with elevated levels of oxidized low-density lipoprotein and anticardiolipin antibody in the circulation of premenopausal Indian women chronically exposed to biomass smoke during cooking. Indoor Air 2011;21: 165–76.
- 31. Dutta A, Ray MR, Banerjee A. Systemic inflammatory changes and increased oxidative stress in rural Indian women cooking with biomass fuels. Toxicol Appl Pharmacol 2012; 261:255–62.
- 32. Davutoglu V, Zengin S, Sari I, et al. Chronic carbon monoxide exposure is associated with the increases in carotid intima-media thickness and C-reactive protein level. Tohoku J Exp Med 2009; 219:201–6.
- 33. Clark ML, Bazemore H, Reynolds SJ, et al. A baseline evaluation of traditional cook stove smoke exposures and indicators of cardiovascular and respiratory health among Nicaraguan women. Int J Occup Environ Health 2011; 17:113–21.
- 34. Rose G, McCartney P, Reid DD. Self-administration of a questionnaire on chest pain and intermittent claudication. Br J Prev Soc Med. 1977; 31:42–48.

35. Prineas RJ, Crow RS, Zhang Z-h. The Minnesota code manual of electrocardiographic findings. 2nd Edition. London. Springer London; 2010.

- 36. Christiansen TB and Lauritsen JM. (Ed.) EpiData Comprehensive Data Management and Basic Statistical Analysis System. Odense Denmark, EpiData Association, 2010-. <u>http://www.epidata.dk</u>
- 37. Stata Corp LP 2012, Stata Statistical Software: Release 12.0, College Station TX, USA.
- Jafar TH, Qadri Z, Chaturvedi N. Coronary artery disease epidemic in Pakistan: more electrocardiographic evidence of ischaemia in women than in men. Heart. 2008;94(4):408-13.
- McCracken J, Smith KR, Stone P, Diaz A, Arana B, Schwartz J. Intervention to lower household wood smoke exposure in Guatemala reduces ST-segment depression on electrocardiograms. Environ Health Perspect 2011;119:1562-8.
- 40. McCracken JP, Smith KR, Díaz A, Mittleman MA, Schwartz J. Chimney stove intervention to reduce long-term wood smoke exposure lowers blood pressure among Guatemalan women. Environ Health Perspect 2007; 115:996-1001.
- 41. Alexander D, Larson T, Bolton S, Vedal S. Systolic blood pressure changes in indigenous Bolivian women associated with an improved cookstove intervention. Air Qual Atmos Health 2015; 8:47-53.
- 42. Wilcosky T, Harris R, Weissfeld L. The prevalence and correlates of Rose questionnaire angina among women and men in the Lipid Research Clinics Program Prevalence Study. Am J Epidemiol. 1987;125 (3):400-409.
- 43. Jafar TH, Jafary FH, Jessani S, Chaturvedi N. Heart disease epidemic in Pakistan: women and men at equal risk. Am Heart J. 2005;150(2):221-6.
- 44. Khushk WA, Fatmi Z, White F, Kadir MM. Health and social impacts of improved stoves on rural women: a pilot intervention in Sindh, Pakistan. Indoor Air. 2005 Oct;15(5):311-6.
- 45. Castelli WP. Epidemiology of coronary heart disease: The Framingham study. American Journal of Medicine 1984, page 4.
- 46. Gordon T, Kannel WB, Hjortland MC, McNamara PM. Menopause and coronary heart disease. The Framingham Study. Ann Intern Med. 1978; 89:157–61.
- 47. Hameed K, Kadir M, Gibson T, Sultana S, Fatima Z, Syed A. The frequency of known diabetes, hypertension and ischaemic heart disease in affluent and poor urban populations of Karachi, Pakistan. Diabet Med. 1995;12(6):500-3.
- 48. Ali MK, Bhaskarapillai B, Shivashankar R, Mohan D, Fatmi Z, Pradeepa R, Masood Kadir M, Mohan V, Tandon N, Narayan KM, Prabhakaran D; CARRS investigators. Socioeconomic status and cardiovascular risk in urban South Asia: The CARRS Study. Eur J Prev Cardiol. 2016 Mar;23(4):408-19.
- 49. Hubert HB, Feinleib M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. Circulation 1983; 67:968–77.
- 50. Todd Miller M, Lavie CJ, White CJ. Impact of obesity on the pathogenesis and prognosis of coronary heart disease. J Cardiometab Syndrome 2008; 3:162–7.
- 51. Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet. 2002;360: 1903-13.
- 52. Yusuf S, Hawken S, Ounpuu S, Bautista L, Franzosi MG, Commerford P, Lang CC, Rumboldt Z, Onen CL, Lisheng L, Tanomsup S, Wangai P Jr, Razak F, Sharma AM, Anand SS; INTERHEART Study Investigators. Obesity and the risk of myocardial

infarction in 27,000 participants from 52 countries: a case-control study. Lancet 2005;366(9497):1640-9.

- 53. The World Health Report 2002: reducing risks, promoting healthy life. Geneva, World Health Organization, 2002.
- 54. Chowdhury R, Warnakula S, Kunutsor S, Crowe F, Ward HA, Johnson L, Franco OH, Butterworth AS, Forouhi NG, Thompson SG, Khaw KT, Mozaffarian D, Danesh J, Di Angelantonio E. Association of dietary, circulating, and supplement fatty acids with coronary risk: a systematic review and meta-analysis. Ann Intern Med. 2014 Mar 18;160(6):398-406. doi: 10.7326/M13-1788.
- 55. Huxley RR, Woodward, M. Cigarette smoking as a risk factor for coronary heart disease in women compared with men: a systematic review and meta-analysis of prospective cohort studies. Lancet. 2011;378(9799):1297-305.
- 56. Global Adult Tobacco Survey. Pakistan Fact sheet 2014. http://www.who.int/tobacco/surveillance/survey/gats/pakfactsheet.pdf

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Characteristics		All women (n=850)		Users of biomass (n=436)		Non-users of biomass (n=414)		Long-term users of biomass (n=430)		Long-term non- users of biomass (n=263)	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	
Age (years)											
<50	525	(61.8)	263	(60.3)	262	(63.3)	257	(59.8)	166	(63.1)	
≥50	325	(38.2)	173	(39.7)	152	(36.7)	173	(40.2)	97	(36.9)	
Educational status											
No literacy	797	(93.8)	419	(96.1)	378	(91.3)	413	(96.1)	239	(90.9)	
Any literacy	53	(6.2)	17	(3.9)	36	(8.7)	17	(4.0)	24	(9.1)	
Household income/month		6		. ,		· · · ·					
≤10000PKR	651	(76.6)	351	(80.5)	300	(72.5)	347	(80.7)	185	(70.3)	
>10000PKR	199	(23.4)	85	(19.5)	114	(27.5)	83	(19.3)	78	(29.7)	
Household tenure			1								
Rented	70	(8.2)	25	(5.7)	45	(10.9)	25	(5.8)	20	(7.6)	
Owned	780	(91.8)	411	(94.3)	369	(89.1)	405	(94.2)	243	(92.4)	
Construction of house											
Katcha/ semi-pucca	652	(76.7)	361	(82.8)	291	(70.3)	356	(82.8)	173	(65.8)	
Pucca	198	(23.3)	75	(17.2)	123	(29.7)	74	(17.2)	90	(34.2)	
Number of household assets											
Low (0-1)	268	(31.5)	140	(32.1)	128	(30.9)	139	(32.3)	84	(31.9)	
Medium (2-3)	404	(47.5)	223	(51.2)	181	(43.7)	218	(50.7)	108	(41.1)	
High (≥4)	178	(21.0)	73	(16.7)	105	(25.4)	73	(17.0)	71	(27.0)	
Father's occupation in childhood											
Non-manual	39	(4.6)	19	(4.4)	20	(4.8)	18	(4.2)	16	(6.1)	
Manual	811	(95.4)	417	(95.6)	394	(95.2)	412	(95.8)	247	(93.9)	

Table 1. Demographic and socio-conomic characteristics of participants by exposure extremely

Characteristics	User (n=4	s of biomass 36)	Non-users biomass (n=414)	s of		g-term users omass 30)	Long-ter of bioma (n=263)	rm non-users ass
	n	(%)	n	(%)	n	(%)	n	(%)
Ever used biomass for cooking	436	(100)	382	(92.3)	430	(100)	231	(87.8)
Years since last used biomass for cooking								
Current user	436	(100)	-	-	430	(100)	-	-
2-9	-	-	151	(39.5)	-	-	-	-
≥10	-	-	231	(60.5)	-	-	231	(100)
Ever used wood for cooking	435	(99.8)	358	(86.5)	429	(99.8)	218	(82.9)
Ever used cow dung for cooking	422	(96.8)	358	(86.5)	416	(96.7)	216	(82.1)
Ever used kerosene for cooking	16	(3.7)	26	(6.3)	16	(3.7)	17	(6.5)
Ever used LPG/natural gas for cooking	17	(3.9)	413	(99.8)	15	(3.5)	263	(100)
Average hours per day cooked in past year								
≤1	129	(29.6)	133	(32.1)	123	(28.6)	75	(28.5)
2-3	270	(61.9)	237	(57.3)	270	(62.8)	165	(62.7)
$\geq 4$	37	(8.5)	44	(10.6)	37	(8.6)	23	(8.8)
Type of stove used for cooking								
Gas/LPG	2	(0.5)	414	(100)	2	(0.5)	263	(100)
Biomass with chimney/improved stove	166	(38.1)	-	. 1	164	(38.1)	-	-
Biomass with three brick open stove	267	(61.2)	-	-	263	(61.2)	-	-
Other	1	(0.2)	-	-	1	(0.2)	-	-
Type of kitchen		· · ·						
Closed (four walls – linked with living room or separate)	88	(20.2)	116	(28.0)	86	(20.0)	79	(30.0)
Semi-open (fewer than four walls)	189	(43.3)	155	(37.4)	187	(43.5)	94	(35.7)
Open (no walls)	159	(36.5)	143	(34.5)	157	(36.5)	90	(34.2)
Heat home with biomass	237	(54.4)	106	(25.6)	236	(54.9)	74	(28.1)

 Table 2. Current and past cooking arrangements according to exposure category.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Long-term non-users of biomass (n=263)

(%)

(20.5) (59.3) (20.2)

(46.4) (53.6)

(45.2) (54.8)

(91.3) (8.7)

(65.8) (34.2)

(56.7) (34.6) (8.7)

(33.5)

(38.0) (28.5)

(30.0) (38.4)

(31.2) (0.4)

n

54 156 53

122 141

119 144

240 23

173

90

149 91 23

88

100 75

79 101

Characteristics	Users of t (n=436)	piomass	Non-users (n=414)	of biomass		term users o ss (n=430)
	n	(%)	n	(%)	n	(%)
Birthweight						
Lower than normal	117	(26.8)	77	(18.6)	114	(26.5)
Normal	239	(54.8)	254	(61.4)	237	(55.1)
Higher than normal	80	(18.4)	83	(20.0)	79	(18.4)
Ever hungry all the time during childhood because there	,					
was not enough food						
No	176	(40.4)	176	(42.5)	175	(40.7)
Yes	260	(59.6)	238	(57.5)	255	(59.3)
Lost weight during childhood						
No	162	(37.2)	182	(44.0)	160	(37.2)
Yes	274	(62.8)	232	(56.0)	270	(62.8)
Ever smoked regularly (any of cigarettes, bidi, huqqa)						
Never	390	(89.4)	378	(91.3)	384	(89.3)
Ever	46	(10.6)	36	(8.7)	46	(10.7)
Environmental tobacco smoke (at least one other						
household member smoked cigarettes, bidi or huqqa in						
the home)						
No	269	(61.7)	267	(64.5)	265	(61.6)
Yes	167	(38.3)	147	(35.5)	165	(38.4)
Physical activity score		· · · · · ·				
0-2	124	(28.4)	205	(49.5)	124	(28.8)
3-4	199	(45.6)	156	(37.7)	196	(45.6)
5-6	113	(25.9)	53	(12.8)	110	(25.6)
Consumption of meat or eggs		· · · · · ·		· · · · · ·		
Do not eat either meat or eggs as much as once per week	173	(39.7)	142	(34.3)	172	(40.0)
Eat one of meat or eggs as much as once per week	176	(40.4)	163	(39.4)	173	(40.2)
Eat both meat and eggs at least once per week	87	(20.0)	109	(26.3)	85	(19.8)
Current nutrition <sup>a</sup>						
Neither BMI nor WHR high	183	(42.0)	129	(31.2)	179	(41.6)
One of BMI or WHR high	151	(34.6)	160	(38.7)	149	(34.7)
Both BMI and WHR high	102	(23.4)	124	(30.0)	102	(23.7)
Not known	0	(0)	1	(0.2)	0	(0)

Outcome

**Hypertension** 

Angina

ECG

Users of biomass

Users of biomass

Users of biomass

**Heart Attack** 

Non-users of biomass

Non-users of biomass

Non-users of biomass

Non-users of biomass

Users of biomass user

Definite or probable CHD on

1

2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
23 24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	
39	
40	
41	
42	
43	
44	
45	
46	
47	
48	
49	
50	
51	
52	
53	
54	
55	
56	
57	
58	
20	

59 60 **Table 4.** Associations of hypertension, angina, history of heart attack, and definite or probable CHD on ECG with current and long-term use of biomass for cooking.

(95%CI)

(0.9-1.5)

(0.7-1.3)

(0.8-2.4)

(0.6-1.2)

<sup>a</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all

<sup>b</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p<0.1) in analyses adjusted only for age, but was restricted to women

Fully adjusted<sup>a</sup>

(95% CI)

(0.8-1.4)

(0.8-1.4)

(0.7-2.2)

(0.6-1.2)

(n=850)

OR

1.0

1.0

1.0

1.0

1.0

1.2

1.0

0.8

Fully adjusted and

biomass<sup>b</sup> (n=693)

OR

1.0

1.1

1.0

1.3

1.0

1.3

1.0

0.9

limited to long-term users and non-users of

(95% CI)

(0.8-1.6)

(0.9-1.9)

(0.7-2.4)

(0.6-1.3)

Adjusted only for

age (n=850)

OR

1.0

1.2

1.0

1.0

1.0

1.4

1.0

0.8

who were long-term users or non-users of biomass

of the variables that were significant (p < 0.1) in analyses adjusted only for age

	19
For peer review only - http:/	//bmjopen.bmj.com/site/about/guidelines.xhtml

## Supplementary Materials

**Supplementary Table 1.** Prevalence of hypertension, history of heart attack, angina and coronary heart disease in study sample.

Characteristic	n	(%)
Hypertension		
Systolic hypertension (systolic BP≥140 mmHg)	133	(15.8)
Diastolic hypertension (diastolic BP≥90 mmHg)	102	(12.1)
Regular medication for high blood pressure	198	(23.5)
Hypertension (any of the above)	297	(35.3)
Angina	227	(27.0)
History of heart attack	54	(6.4)
Definite or probable CHD on ECG <sup>a</sup>	159	(18.9)

<sup>a</sup>Based on 841 women. ECGs for 9 women were missing or could not be coded due to poor quality.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

NegativeNegative591Positive94Kappa = 0.57
Positive         94           Kappa = 0.57
Kappa = 0.57

ble CHD by two observers.

3	
4	
5	
6	
-	
/	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	
39	
40	
41	
41	
43	
44	
45	
46	
47	
48	
49	
50	
51	
52	
53	
54	
55	
56	
57	

1 2 З

Supplementary Table 3. Prevalence of definite or probable CHD changes on ECG according to history of heart attack and angina.

Other measure of CHD	Definite or	probable CHD	changes on	ECG <sup>a</sup>
	Yes		No	
	n	(%)	Ν	(%)
No history of heart attack or angina	105	(18.2)	471	(81.8)
History of angina	45	(19.8)	182	(80.2)
History of heart attack	14	(25.9)	40	(74.1)
History of angina or heart attack	54	(20.4)	211	(79.6)
History of angina and heart attack #ECGs for 9 women were missing or cost	5	(31.3)	11	(68.8)

Risk factor	Adju for a	sted only ge	Fully	adjusted <sup>a</sup>	Fully adjusted and limited to long-		
	(n=850)		(n=850)		term users and non-users of biomass <sup>b</sup>		
					(n=69		
	OR	(95%CI)	OR	(95%CI)	OR	(95%CI)	
Age (per 10 year increase)	1.4	(1.2-1.6)	1.4	(1.2-1.7)	1.5	(1.2-1.7)	
Educational status							
Illiterate	1.0		-		-		
Any literacy	0.6	(0.3-1.2)					
Household income/month					-		
<3000-10000PKR	1.0	(a =	-				
>10000PKR	1.0	(0.7-1.4)					
Household ownership					-		
Rented	1.0		-				
Own	0.8	(0.5-1.3)					
Construction of house					-		
Katcha/semi-pucca	1.0		-				
Pucca	0.9	(0.6-1.2)					
Number of household assets							
0-1	1.0		1.0		1.0		
2-3	1.7	(1.2-2.4)	1.6	(1.2-2.3)	1.8	(1.2-2.6)	
<u>≥</u> 4	2.4	(1.6-3.6)	2.3	(1.5-3.4)	2.7	(1.7-4.3)	
Father's occupation in woman's					-		
childhood							
Non-manual	1.0						
Manual	1.2	(0.6-2.5)					
Birthweight							
Lower than normal	1.0				-		
Normal	1.0	(0.7-1.4)	-				
Higher than normal	1.0	(0.6-1.5)					
Ever hungry during all the time					-		
during childhood because there							
was not enough food							
No	1.0		-				
Yes	0.9	(0.7-1.3)					
Lost weight during childhood	1.0				-		
No	1.0	(0.0.1.7)	-				
Yes	1.2	(0.9-1.6)					
Ever smoked regularly (any of							
cigarettes, bidi, huqqa)	1.0						
Never	1.0	(0 5 1 2)	-		-		
Ever	0.8	(0.5-1.3)					
Environmental tobacco smoke (at							
least one other household member	•						
smokes cigarettes, bidi or huqqa							
in the home)							
No	1.0		-				
Yes	0.8	(0.6-1.1)					

Do not eat either meat or eggs as	1.0		1.0		1.0	
much as once per week						
Eat one of meat or eggs as much	1.4	(1.0-1.9)	1.2	(0.9-1.7)	1.2	(0.8-1.7)
as once per week						
Eat both meat and eggs at least	1.4	(1.0-2.1)	1.2	(0.8-1.8)	1.2	(0.8-1.9)
once per week						
Current nutrition <sup>c</sup>						
Neither BMI nor WHR high	1.0		1.0		1.0	
One of BMI or WHR high	1.2	(0.9-1.7)	1.2	(0.8-1.6)	1.2	(0.8-1.8)
Both BMI and WHR high	2.0	(1.4-2.9)	1.9	(1.3-2.8)	1.8	(1.2-2.7)
Non-user of biomass	1.0		1.0			
User of biomass	1.2	(0.9-1.5)	1.0	(0.8-1.4)		
Long-term non-user of biomass	1.0				1.0	
Long-term user of biomass	1.2	(0.9-1.7)			1.1	(0.8-1.6)

<sup>a</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p<0.1) in analyses adjusted only for age

<sup>b</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p<0.1) in analyses adjusted only for age, but was restricted to women who were long-term users or non-users of biomass

°Body mass index (BMI) (kg/m²) ≥25= high; Waist-to-hip ratio (WHR) ≥0.85=high.

Supplementary Table 5	• Associations of angina with risk factors.
-----------------------	---------------------------------------------

Risk factor	Adju for a	sted only ge	Fully	adjusted <sup>a</sup>	Fully adjusted and limited to long-		
	(n=850)		(n=8	50)	term users and non-users of biomass <sup>b</sup>		
					(n=69		
	OR	(95%CI)	OR	(95%CI)	OR	(95%CI)	
Age (per 10 year increase)	1.3	(1.1-1.6)	1.3	(1.1-1.5)	1.3	(1.1-1.5)	
Educational status							
Illiterate	1.0		-		-		
Any literacy	0.6	(0.3-1.3)					
Household income/month					-		
<3000-10000PKR	1.0		-				
>10000PKR	1.1	(0.8-1.6)					
Household ownership		*			-		
Rented	1.0		-				
Own	0.8	(0.5-1.3)					
Construction of house					-		
Katcha/semi-pucca	1.0		_				
Pucca	1.2	(0.8-1.7)					
Number of household assets	1.2	(0.0 1.7)			_		
0-1	1.0		_		_		
2-3	0.9	(0.6-1.3)	-				
2-3 ≥4	1.0	(0.6-1.5)					
Eather's occupation in woman's	1.0	(0.0-1.3)					
childhood					-		
Non-manual	1.0						
	0.7	(0,2,1,4)					
Manual	0.7	(0.3-1.4)					
Birthweight	1.0						
Lower than normal	1.0	(0,0,1,0)			-		
Normal	1.2	(0.8-1.8)	-				
Higher than normal	1.1	(0.7-1.8)		$\mathbf{O}$			
Ever hungry during all the time					-		
during childhood because there							
was not enough food	1.0						
No	1.0	(0 < 1 1)	-				
Yes	0.8	(0.6-1.1)					
Lost weight during childhood	1.0				-		
No	1.0		-				
Yes	1.0	(0.8-1.4)					
Ever smoked regularly (any of							
cigarettes, bidi, huqqa)							
Never	1.0		1.0		1.0		
Ever	2.1	(1.3-3.3)	2.0	(1.2-3.2)	2.1	(1.3-3.6)	
Environmental tobacco smoke							
(at least one other household							
member smokes cigarettes, bidi							
or huqqa in the home)							
No	1.0		-				

**Consumption of meat or eggs** 

Do not eat either meat or eggs	1.0		1.0		1.0	
as much as once per week Eat one of meat or eggs as	0.6	(0.4-0.8)	0.6	(0.4-0.8)	0.7	(0.5-1.0)
much as once per week Eat both meat and eggs at least once per week	0.4	(0.3-0.7)	0.5	(0.3-0.7)	0.5	(0.3-0.8)
Current nutrition <sup>c</sup>						
Neither BMI nor WHR high	1.0					
One of BMI or WHR high	0.8	(0.5-1.1)	-			
Both BMI and WHR high	0.8	(0.5-1.2)				
Non-user of biomass	1.0					
User of biomass user	1.0	(0.7-1.3)	1.0	(0.8-1.4)		
Long-term non-user of biomass	1.0				1.0	
Long-term non-user of biomass	1.2	(0.9-1.7)			1.3	(0.9-1.9)

<sup>a</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p<0.1) in analyses adjusted only for age

<sup>b</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p<0.1) in analyses adjusted only for age, but was restricted to women who were long-term users or non-users of biomass

<sup>c</sup>Body mass index (BMI)  $(kg/m^2) \ge 25 = high$ ; Waist-to-hip ratio (WHR)  $\ge 0.85 = high$ .

Risk factor	Adju for a	sted only ge	Full	y adjusted <sup>b</sup>	Fully adjusted and limited to long-term			
	c	2	(n=8	<b>350</b> )	users and non-users of			
	(n=85	50) <sup>a</sup>			biomass <sup>c</sup>			
					(n=6	<b>(93</b> )		
	OR	(95%CI)	OR	(95%CI)	OR	(95%CI)		
Age (per 10 year increase)	1.5	(1.2-2.0)	1.5	(1.2-2.0)	1.5	(1.2-2.0)		
Educational status								
Illiterate	1.0		-		-			
Any literacy	1.5	(0.5-4.5)						
Household income/month								
<3000-10000PKR	1.0		1.0		1.0			
>10000PKR	1.6	(0.9-2.9)	1.4	(0.8-2.5)	1.6	(0.8-3.1)		
Household ownership								
Rented	1.0		-		-			
Own	1.2	(0.4-3.4)						
Construction of house					-			
Katcha/semi-pucca			-					
Pucca	1.3	(0.7-2.3)						
Number of household assets		5			-			
0-1	1.0		1.0		1.0			
2-3	1.4	(0.7-2.7)	1.3	(0.7-2.5)	1.8	(0.8-3.8)		
≥4	2.1	(1.0-4.3)	1.8	(0.8-3.8)	2.1	(0.9-5.1)		
Father's occupation in woman's					-	·		
childhood								
Non-manual	1.0		-					
Manual	1.0	(0.2-4.5)						
Birthweight		. ,						
Lower than normal	1.0				-			
Normal	1.0	(0.5-1.9)	-					
Higher than normal	0.7	(0.3-1.7)						
Ever hungry during all the time		. ,			-			
during childhood because there								
was not enough food								
No	1.0		-					
Yes	1.0	(0.6-1.7)						
Lost weight during childhood		. /			-			
No	1.0		-					
Yes	1.1	(0.6-1.9)						
Ever smoked regularly (any of		()						
cigarettes, bidi, huqqa)								
Never	1.0		-					
Ever	0.9	(0.4-2.1)						
Environmental tobacco smoke (at		()						
least one other household member								
smokes cigarettes, bidi or huqqa in								
the home)								
No	1.0		_					
Yes	0.9	(0.5-1.6)	_					
Consumption of meat or eggs	0.7	(0.5-1.0)						

**Supplementary Table 6.** Associations of previous history of heart attack (diagnosed by a physician) with risk factors.

Do not eat either meat or eggs as	1.0		-				
much as once per week							
Eat one of meat or eggs as much as once per week	1.2	(0.6-2.3)					
Eat both meat and eggs at least once per week	1.8	(0.9-3.5)					
Current nutrition <sup>d</sup>							
Neither BMI nor WHR high	1.0		1.0		1.0		
One of BMI or WHR high	1.3	(0.6-2.5)	1.2	(0.6-2.5)	1.6	(0.7-3.4)	
Both BMI and WHR high	2.0	(1.0-4.0)	1.9	(0.9-3.7)	1.7	(0.8-3.6)	
Non-user of biomass	1.0	· · ·	1.0		-		
Use of biomass	1.4	(0.8-2.4)	1.2	(0.7-2.2)			
Long-term non-user of biomass	1.0				1.0		
Long-term user of biomass	1.5	(0.8-2.7)			1.3	(0.7-2.4)	
							-

<sup>*a*</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p<0.1) in analyses adjusted only for age

<sup>b</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p<0.1) in analyses adjusted only for age, but was restricted to women who were long-term users or non-users of biomass

<sup>a</sup>Body mass index (BMI) (kg/m<sup>2</sup>) ≥25= high; Waist-to-hip ratio (WHR) ≥0.85=high.

Risk factor	Adju age	sted only for	Fully adjusted <sup>a</sup> (n=841)		Fully adjusted and limited to long-term users and non-users		
	(n=841)		(11–04	1)		omass <sup>b</sup>	
					(n=68	86)	
	OR	(95%CI)	OR	(95%CI)	OR	(95%CI)	
Age (per 10 year increase)	1.1	(0.9-1.3)	1.1	(0.9-1.3)	1.0	(0.8-1.3)	
Educational status							
Illiterate	1.0		-		-		
Any literacy	0.8	(0.4-1.7)					
Household income/month							
<3000-10000PKR	1.0		1.0		1.0		
>10000PKR	1.6	(1.1-2.3)	1.6	(1.1-2.4)	1.3	(0.8-2.0)	
Household ownership		(1.1 2.0)		( 2)	-	(0.0 2.0)	
Rented	1.0		_				
Own	1.4	(0.7-2.9)	-				
Construction of house	1.4	(0.7-2.7)					
	10				-		
Katcha/semi-pucca	1.0	(0.7.1.5)	-				
Pucca	1.0	(0.7-1.5)					
Number of household assets							
0-1	1.0		-				
2-3	1.0	(0.7-1.5)					
<u>≥</u> 4	1.3	(0.8-2.1)					
Father's occupation in woman's					-		
childhood							
Non-manual	1.0		-				
Manual	1.0	(0.4-2.3)					
Birthweight							
Lower than normal	1.0				-		
Normal	1.1	(0.7-1.7)	-				
Higher than normal	1.1	(0.7-1.9)					
Ever hungry during all the time		(			-		
during childhood because there							
was not enough food							
No	1.0		_				
Yes	1.0	(0.8-1.6)	-				
Lost weight during childhood	1.1	(0.0-1.0)					
	1.0				-		
No	1.0	$(0 \in 1 \circ)$	-				
Yes	0.8	(0.6-1.2)					
Ever smoked regularly (any of							
cigarettes, bidi, huqqa)							
Never	1.0		-		-		
Ever	1.0	(0.6-1.8)					
Environmental tobacco smoke (at							
least one other household							
member smokes cigarettes, bidi							
or huqqa in the home)							
No	1.0				_		
110	1.0						

Do not eat either meat or eggs as much as once per week	s 1.0					
Eat one of meat or eggs as muc as once per week	h 0.9	(0.6-1.4)				
Eat both meat and eggs at least once per week	1.2	(0.7-1.8)				
Current nutrition <sup>c</sup>						
Neither BMI nor WHR high	1.0					
One of BMI or WHR high	0.8	(0.5-1.2)	-			
Both BMI and WHR high	1.1	(0.7-1.6)				
Non-user of biomass user	1.0		1.0			
User of biomass	0.8	(0.6-1.2)	0.8	(0.6-1.2)		
Longterm non-user of biomass	1.0				1.0	
Longterm user of biomass	0.9	(0.6-1.3)			0.9	(0.6-1.3)

<sup>a</sup>ECGs were missing for 9 women or not codable due to poor quality.

<sup>b</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p < 0.1) in analyses adjusted only for age

<sup>c</sup>Mutually adjusted risk estimates derived from a single regression model that included use of biomass and all of the variables that were significant (p<0.1) in analyses adjusted only for age, but was restricted to women who were long-term users or non-users of biomass

<sup>*d*</sup>Body mass index (BMI)  $(kg/m^2) \ge 25 = high$ ; Waist-to-hip ratio (WHR)  $\ge 0.85 = high$ .

reziez onz

 BMJ Open

Section/Topic	ltem #	Recommendation	Reported on page
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1-2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	3
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	3-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	3-5
Bias	9	Describe any efforts to address potential sources of bias	3-5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	5
		(b) Describe any methods used to examine subgroups and interactions	5
		(c) Explain how missing data were addressed	In relevant tables
		(d) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(e) Describe any sensitivity analyses	N/A

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	6
		confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	Not needed
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6 and Tables 1-3
		(b) Indicate number of participants with missing data for each variable of interest	Tables 1-3
Outcome data	15*	Report numbers of outcome events or summary measures	6
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence	Supplementary
		interval). Make clear which confounders were adjusted for and why they were included	Tables 4-7
		(b) Report category boundaries when continuous variables were categorized	Tables
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	8-9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10
Generalisability	21	Discuss the generalisability (external validity) of the study results	8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on	2
		which the present article is based	

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml