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ORIGINAL ARTICLE

# Acute coronary syndrome and use of biomass fuel among women in rural Pakistan: a case–control study

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## Abstract

**Objectives** Three billion people use biomass fuel for cooking and heating globally. We assessed the association between acute coronary syndromes (ACS) and use of biomass fuel for cooking.

**Methods** We conducted a case–control study among women living in defined areas that were served by two tertiary care hospitals. A total of 364 women admitted to cardiac care units with ACS were compared with 727 controls, individually matched for age, who were inpatients at the same hospitals with a miscellany of diagnoses. Exposure to biomass fuel and other risk factors was ascertained through a questionnaire and assessed by conditional logistic regression.

**Results** After adjustment, risk of ACS was elevated in women who had ever used biomass for cooking. In comparison with never users, the odds ratio for those who currently cooked with biomass was 4.8 (95% confidence interval 1.7, 13.8). However, among those who had ever used biomass, there was no decline in risk with time since last exposure.

**Conclusions** The study found increased risk of ACS from use of biomass for cooking. However, full benefits from interventions may not accrue in short term.

**Keywords** Acute coronary syndrome · Biomass fuel · Women · Case–control study · Pakistan

## Introduction

Globally, some 40% of households cook with solid fuels (wood, charcoal, dung, crop waste and coal) in open fires or simple traditional stoves (Bonjour et al. 2013), exposing 3 billion people to high levels of indoor air pollution (IAP) by fine particulate matter, carbon monoxide and other toxic chemicals (generated by incomplete combustion) and causing an estimated 4.3 million premature deaths per year (WHO 2018). A major impact on respiratory disease in women and young children is well established (Torres-Duque et al. 2008), but there is concern that risk of coronary heart disease (CHD) may also be increased. Such an effect would be consistent with the known hazard of CHD from particulate pollution in outdoor air (Brook et al. 2004; Franklin et al. 2015) and might be mediated through inflammatory responses to fine particles taken up from the lungs (Banerjee et al. 2012). To date, however, its relationship to IAP has been explored in only a few, relatively small studies. A recent systematic review concluded that the balance of epidemiological evidence supported a hazard of CHD from IAP generated by the use of solid fuel, and especially biomass (wood, charcoal, dung and crop

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waste), for cooking and heating, but identified a need for further, confirmatory studies (Fatmi and Coggon 2016).

In Pakistan, where biomass fuel is widely used for cooking in rural communities (National Institute of Population Studies (Pakistan) and ICF International 2013) and rates of CHD are high. A population-based survey of adults aged $\geq$ 40 years indicated a prevalence of 25–30% of CHD (Jafar et al. 2005). Moreover, women were at somewhat higher risk than men, despite smoking less. The highest exposures to IAP from use of biomass fuels will also tend to occur in women, since it is normally they who carry out the cooking for their household.

We therefore carried out a case–control study among Pakistani women in rural areas of Sindh province, to assess the risk of myocardial infarction and unstable angina [collectively termed acute coronary syndrome (ACS)] from use of biomass fuels. This built on an earlier pilot investigation in the same population (Fatmi et al. 2014).

## Methods

### Study setting

The study population comprised women resident in defined parts of the catchment areas of two public sector hospitals in Mirpurkhas and Nawabshah (recently renamed Shaheed Benazirabad). Mirpurkhas (population 1.5 million) is a rural district in southern Sindh, while Nawabshah (population 1.6 million) is in the central part of the province. The two hospitals received cardiac patients from the districts in which they are located and from adjacent villages. Cases and controls were eligible for study if they came from Mirpurkhas, Nawabshah, Badin, Jamshoro, Khairpur, Matiari, Nausheroferoze, Sanghar, Tando Allahyar, Tharparkar or Umerkot districts, areas in which there was mixed use of biomass fuel and natural gas for cooking. Both hospitals provided tertiary care with well-established cardiology units delivering outpatient, inpatient and 24-h emergency services. They also offered services in all other major medical specialties.

### Case definition

Cases of ACS were defined according to criteria published by Mendis et al. (2011), which were followed by clinicians in the participating hospitals, but with some simplification to reflect what was affordable and practical in a developing country. A patient was deemed to have ACS if she met any of the following criteria:

1. ECG changes of myocardial infarction (ST segment elevation or pathological Q waves) plus at least one value above the upper reference limit for a cardiac biomarker (creatine kinase-MB (CK-MB), troponin I or troponin T).
2. Pain or discomfort in the chest, jaw, left arm or epigastric area in combination with at least one value above the upper reference limit for a cardiac biomarker (CK-MB, troponin I or troponin T), but with no ST segment elevation or pathological Q waves on ECG.
3. Pain or discomfort in the chest, jaw, left arm or epigastric area in combination with ST segment elevation or pathological Q waves on ECG, but with no value above the upper reference limit for any cardiac biomarker (CK-MB, troponin I or troponin T)—classed as unstable angina.

### Recruitment of cases and controls

Women were eligible for inclusion as cases if they lived in the defined study area and were admitted to the cardiac care unit at one of the two study hospitals with a new episode of ACS (no previous occurrence in the past 28 days) during February 2014–January 2016. Admissions were arranged, and diagnoses made as part of routine care by the cardiologists and physicians of the hospital. The study team visited the cardiac ward each day, and potential cases who were considered sufficiently well by their nursing team were told about the study and invited to take part. Those who were too unwell on the day of admission were followed for up to 3 days and approached if their condition improved. If a patient was still not sufficiently well to be interviewed after 3 days or declined to participate, she was excluded from the study.

For each case that was recruited, we used a prescribed algorithm to select two matched controls of the same age to within 5 years, who had been admitted to the medical wards of the same hospital for reasons other than ACS. We first considered women admitted on the same day as the case, and if that did not give the two controls needed, we next tried to recruit from women admitted on the following day, then on the previous day, then 2 days later, then 2 days earlier, etc. If more than the required number of eligible controls was available from a given day, we chose the patient(s) whose age matched that of the case most closely. Those who were selected and who were considered sufficiently well by their clinical team were told about the study and invited to take part. Controls who could not take part, or declined to do so, were replaced according to the same algorithm.

## Data collection

With written informed consent, participating cases and controls were interviewed in the ward by trained members of the research team, as soon as possible after they were identified. A standardized questionnaire (Online Resource), similar to that employed in an earlier pilot study (Fatmi et al. 2014), was used to elicit information on: socio-demographic characteristics; recent and past medical history; aspects of nutrition in early life, measures of current affluence, active and passive smoking; key aspects of diet; parental history of heart attack; lifetime use of different fuels for cooking; and type of kitchen. In addition, permission was sought to access the patient's medical record to abstract diagnostic information, including ECG recordings and cardiac biomarker measurements in cases (where ECGs had not been placed in the medical record, or the record was missing because the patient had been referred for further treatment elsewhere after completing their interview, diagnoses were accepted if they had been made by the physicians and senior nurses in the cardiac units, since the case definition for the study corresponded to their standard diagnostic criteria). Subsequently, measurements of height, weight and waist and hip circumference were made by the interviewers using a stadiometer, digital scales and a tape measure, once the patient was stable and her physician had given permission.

## Statistical analysis

Statistical analysis was carried out with Stata version v.12.1 software (Stata Corp LP 2012, Stata Statistical Software: Release 12.1, College Station TX, USA). The distributions of variables from the questionnaire were explored in the study sample as a whole, and collinearity of risk factors was assessed by cross-tabulation. Several of the variables were then reclassified or combined. This was done without knowledge of their distribution by case–control status.

Use of biomass for cooking was classified as follows: never used biomass (firewood and/or cow dung) for cooking; last use of biomass for cooking $> 10$ years ago; last use of biomass $\leq 10$ years ago, but no current use; household currently uses biomass, but participant cooks for $\leq 1$ h per day on average; household currently uses biomass, and participant cooks for $> 1$ h per day on average.

Other potentially confounding risk factors for ACS were specified as in Table 1. Hunger during childhood was defined by a positive response to the question 'During your childhood, did you ever feel hungry all the time because there was not enough food?' The classification of house construction distinguished properties that were 'pucca' (concrete roof and walls) from those that were 'katcha/semi-pucca' (totally or partially made of thatch/wood). A total of seven household assets were considered (tractor, car, motor cycle, cycle, television, refrigerator and telephone/cell phone). Exposure to environmental tobacco smoke was defined according to whether anyone in the participant's household (other than her) currently smoked in the home. In characterizing the current nutritional status, we used our measurements of weight and height to determine body mass index (BMI) in $kg/m^2$ and our measurements of waist and hip circumference to calculate waist-to-hip ratio (WHR). BMI was classed as high if it was $\geq 25$ $kg/m^2$ and otherwise as normal. WHR was considered high if it was $\geq 0.85$ and otherwise normal.

Associations of ACS with use of biomass fuel and other risk factors were assessed by conditional logistic regression and summarized by odds ratios (ORs) with associated 95% confidence intervals (CIs).

## Results

During the 2 years of data collection, we interviewed a total of 381 cases and 762 controls (see Fig. 1). Further 40 cases could not be recruited because they were too unwell during the first 3 days after admission (25, including 7 who died), were transferred to other hospitals (12), or the interviewers were absent for personal reasons (3). Also lost to study were 65 potential controls, who were judged by their physician to be unfit for interview (24) or declined to take part (41). Among the women who were interviewed, four cases and 10 controls were subsequently excluded because their interviews were incomplete, along with 11 cases who had a history of ACS during the past 28 days. It was then necessary to exclude a further two cases and 25 controls because they were no longer matched. This left 364 matched sets that were suitable for analysis, 363 with two controls and one with a single control.

The remaining 364 cases included 91 (25%) with ST elevation and/or pathological Q waves on ECG as well as raised levels of a biomarker, 140 (38%) with raised biomarkers but no ST elevation or pathological Q wave and 63 (17%) with unstable angina. The other 70 (19%) were diagnosed as ACS by the cardiologist who was caring for them, but their clinical records could not subsequently be accessed (e.g. because they had been transferred elsewhere for further treatment). Among the 727 controls, the most common reasons for admission were non-tuberculous respiratory disease (30%), hepatitis or chronic liver disease (16%), other gastrointestinal disease (20%), fever from various causes (10%) and anaemia (5%).

**Table 1** Associations of acute coronary syndrome with use of biomass fuel and other risk factors among women in Sindh, Pakistan (2014–2016)

| Risk factor[a] | Cases (*n* = 364) | | Controls (*n* = 727) | | Unadjusted risk estimate | | Adjusted risk estimate[c] | |
|---|---|---|---|---|---|---|---|---|
| | *N* | (%) | *N* | (%) | OR | (95% CI)[b] | OR | (95% CI)[b] |
| Ethnicity | | | | | | | | |
| Non-Sindhi | 208 | (57.1) | 439 | (60.4) | 1 | | 1 | |
| Sindhi | 156 | (42.9) | 288 | (39.6) | 1.2 | (0.9, 1.5) | 1.5 | (1.1, 2.2) |
| Birthweight | | | | | | | | |
| High or normal | 307 | (84.3) | 665 | (91.5) | 1 | | 1 | |
| Lower than normal | 40 | (11.0) | 38 | (5.2) | 2.5 | (1.5, 4.1) | 2.7 | (1.4, 4.9) |
| Not known | 17 | (4.7) | 24 | (3.3) | | | | |
| Hungry during childhood | | | | | | | | |
| No | 231 | (63.5) | 523 | (71.9) | 1 | | 1 | |
| Yes | 130 | (35.7) | 185 | (25.5) | 2.3 | (1.6, 3.4) | 1.9 | (1.1, 3.3) |
| Not known | 3 | (0.8) | 19 | (2.6) | | | | |
| Lost weight at some time during childhood | | | | | | | | |
| No | 246 | (67.6) | 569 | (78.3) | 1 | | 1 | |
| Yes | 99 | (27.2) | 132 | (18.2) | 2.4 | (1.6, 3.6) | 1.5 | (0.8, 2.8) |
| Not known | 19 | (5.2) | 26 | (3.6) | | | | |
| Household income/month | | | | | | | | |
| < 10,000 PKR[e*] | 176 | (48.3) | 334 | (45.9) | 1 | | 1 | |
| ≥ 10,000 PKR | 152 | (41.8) | 356 | (49.0) | 0.8 | (0.6, 1.0) | 0.5 | (0.3, 0.7) |
| Not known/not answered | 36 | (9.9) | 37 | (5.1) | | | | |
| Construction of house | | | | | | | | |
| Katcha/semi-pucca[d] | 244 | (67.0) | 572 | (78.7) | 1 | | 1 | |
| Pucca | 120 | (33.0) | 155 | (21.3) | 1.9 | (1.4, 2.5) | 1.3 | (0.8, 1.9) |
| Number of household assets | | | | | | | | |
| Low (0–1) | 91 | (25.0) | 369 | (50.8) | 1 | | 1 | |
| Medium (2–3) | 159 | (43.7) | 262 | (36.0) | 2.8 | (2.0, 3.8) | 2.9 | (1.9, 4.2) |
| High (≥ 4) | 114 | (31.3) | 96 | (13.2) | 5.3 | (3.6, 7.8) | 6.4 | (3.8, 10.9) |
| Overall exposure from smoking | | | | | | | | |
| None | 165 | (45.3) | 331 | (45.5) | 1 | | 1 | |
| Environmental but never active smoker | 128 | (35.2) | 268 | (36.9) | 1.0 | (0.7, 1.3) | 1.1 | (0.8, 1.6) |
| Ever active smoker not environmental | 24 | (6.6) | 63 | (8.7) | 0.8 | (0.5, 1.3) | 0.8 | (0.4, 1.5) |
| Ever active smoker and environmental | 47 | (12.9) | 65 | (8.9) | 1.4 | (0.9, 2.2) | 1.6 | (0.9, 2.8) |
| Use of oil or ghee for cooking in household | | | | | | | | |
| Only or mostly oil | 182 | (50.0) | 219 | (30.1) | 1 | | 1 | |
| Half oil and half ghee | 58 | (15.9) | 129 | (17.7) | 0.5 | (0.4, 0.8) | 0.6 | (0.4, 0.9) |
| Only or mostly ghee | 122 | (33.5) | 377 | (51.9) | 0.4 | (0.3, 0.5) | 0.5 | (0.3, 0.8) |
| Not known | 2 | (0.6) | 2 | (0.3) | | | | |
| Consumption of meat and eggs | | | | | | | | |
| Do not eat either as much as once per week | 207 | (56.9) | 478 | (65.8) | 1 | | 1 | |
| Eat only one of meat or eggs as much as once per week | 84 | (23.1) | 137 | (18.8) | 1.7 | (1.2, 2.4) | 1.0 | (0.6, 1.5) |
| Eat both meat and eggs at least once per week | 73 | (20.0) | 111 | (15.3) | 1.9 | (1.3, 2.9) | 1.1 | (0.6, 1.9) |
| Not known | | | 1 | (0.1) | | | | |
| Current nutritional status[e] | | | | | | | | |
| BMI and WHR both normal | 32 | (8.8) | 120 | (16.5) | 1 | | 1 | |
| One of BMI or WHR high | 210 | (57.7) | 494 | (68.0) | 1.6 | (1.0, 2.5) | 1.6 | (1.0, 2.7) |
| Both BMI and WHR high | 119 | (32.7) | 106 | (14.5) | 4.9 | (3.0, 8.1) | 6.1 | (3.3, 11.3) |
| Not known | 3 | (0.8) | 7 | (1.0) | | | | |

**Table 1** (continued)

| Risk factor[a] | Cases (*n* = 364) | | Controls (*n* = 727) | | Unadjusted risk estimate | | Adjusted risk estimate[c] | |
|---|---|---|---|---|---|---|---|---|
| | *N* | (%) | *N* | (%) | OR | (95% CI)[b] | OR | (95% CI)[b] |
| Biomass exposure | | | | | | | | |
| Never used biomass | 8 | (2.2) | 29 | (4.0) | 1 | | 1 | |
| Last biomass use > 10 years ago | 103 | (28.3) | 136 | (18.7) | 3.1 | (1.3, 7.2) | 6.7 | (2.4, 18.7) |
| Last biomass use ≤ 10 years ago | 102 | (28.0) | 232 | (31.9) | 1.7 | (0.8, 3.8) | 3.4 | (1.2, 9.1) |
| Current biomass use but cook ≤ 1 h/day | 61 | (16.8) | 125 | (17.2) | 1.7 | (0.7, 4.1) | 3.6 | (1.2, 10.4) |
| Current biomass use and currently cook > 1 h/day | 85 | (23.4) | 189 | (26.0) | 1.5 | (0.7, 3.6) | 4.8 | (1.7, 13.8) |
| Not known | 5 | (1.4) | 16 | (2.2) | | | | |

[a]For further information on the specification of risk factors, see text

[b]Odds ratio with 95% confidence interval

[c]Mutually adjusted risk estimates derived from a single conditional regression model including all of the risk factors in the table

[d]Katcha/semi-pucca refers to totally or partially made of thatch/wood, while puccas refers to concrete roof and walls

[e]PKR = Pakistani rupees; BMI = body mass index; WHR = waist–hip ratio

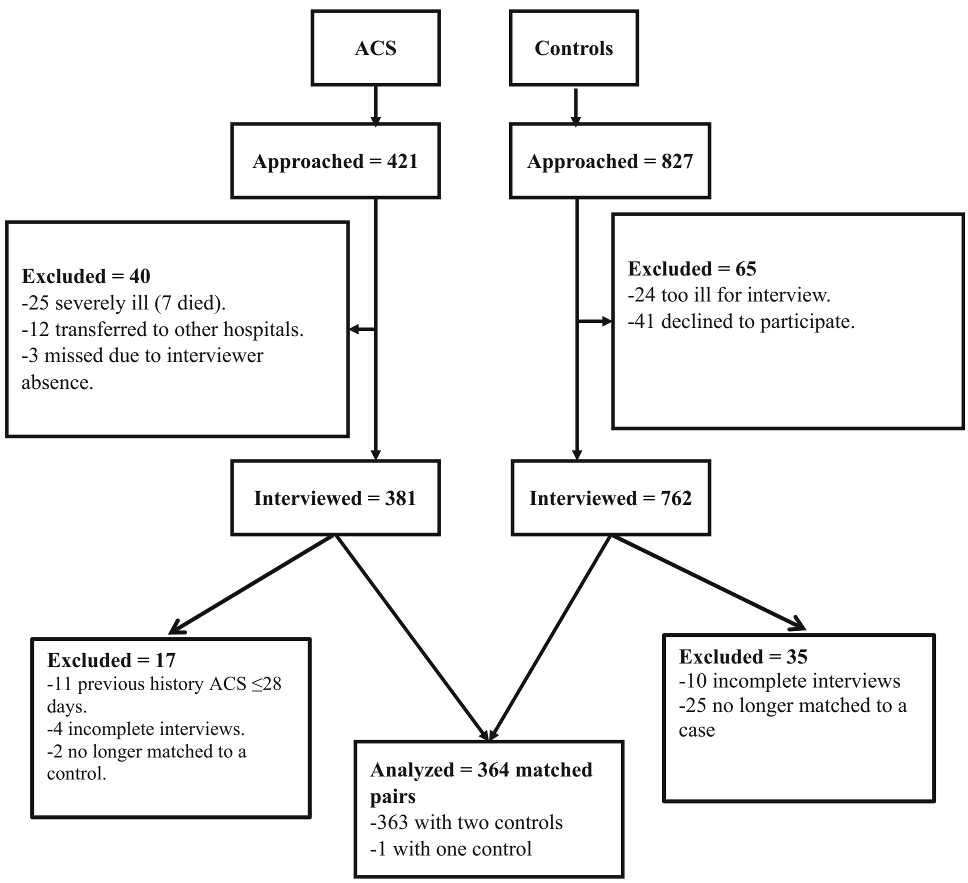


**Fig. 1** Flow chart summarizing recruitment of cases and controls from Sindh, Pakistan (2014–2016)

As expected from the matching, the ages of the cases (mean 59.1 years, median 60.3 and range 23–91) and controls (mean 58.3 years, median 60.3 and range 21–96) were similar. The numbers recruited at the two hospitals were fairly similar (58% at Mirpurkhas).

Table 1 summarizes the relationship of ACS to the risk factors that were examined. In unadjusted conditional logistic regression analyses, associations were observed with several measures of poor nutrition in early life (low birthweight, hunger during childhood and weight loss during childhood), higher current nutrition and two indices of current affluence (living in a pucca house and having more household assets). There was, however, no increased risk with higher household income, and the association with smoking was only weak. Associations with dietary measures were inconsistent, risk being higher in regular consumers of meat or eggs, but lower in women who used ghee rather than oil for cooking. Risk was also higher in women who had ever used biomass for cooking.

When risk estimates were mutually adjusted in a single conditional logistic regression model, the associations with hunger and weight loss during childhood were somewhat attenuated, but that with report of low birthweight remained strong (OR 2.7, 95% CI 1.4, 4.9). Moreover, the relationship to current nutrition was strengthened (OR 6.1, 95% CI 3.3, 11.3, for both vs. neither of BMI and WHR being high). The association with having more household assets persisted (OR 6.4, 95% CI 3.8, 10.9, for $\geq$ 4 vs. 0–1 assets), but was to some extent offset by an inverse association with higher household income (OR 0.5, 95% CI 0.3, 0.7). The relationship to smoking became a little stronger (OR 1.6, 95% CI 0.9, 2.8, for the combination of active smoking and exposure to environmental tobacco smoke), and there was still a reduced risk in women who used only or mostly ghee rather than oil for cooking (OR 0.5, 95%CI 0.3, 0.8). Associations with use of biomass fuel were strengthened, with significantly elevated odds ratios for all categories of use relative to never use (ORs 3.4–6.7). However, there was no clear gradient of risk according to time since last exposure, the highest odds ratio being in women who last used biomass more than 10 years earlier (OR 6.7, 95% CI 2.4, 18.7). In women who currently cooked using biomass for > 1 h per day, the odds ratio in comparison with never users was 4.8 (95%C I 1.7, 13.8). Information about type of kitchen was missing for three of the women who currently cooked for > 1 h per day with biomass (all cases). However, among the remainder, there was no clear difference in risk according to whether the kitchen was open or closed (adjusted ORs relative to never used biomass 4.0, 95% CI 1.4, 11.8 and 4.2, 95%CI 1.4, 12.6, respectively).

In a sensitivity analysis that adjusted also for previous diagnoses of hypertension and diabetes and parental history of heart attack, risk estimates for other variables, including exposure to biomass, were little altered (Supplementary Table 1) (Online Resource).

## Discussion

This case–control investigation found an elevated risk of ACS among women from households that used biomass fuels for cooking. Expected associations were also observed with low birthweight, indicators of undernutrition during childhood and of higher current nutrition, current affluence and (to a lesser extent) exposure to tobacco smoke. After adjustment for these potentially confounding factors, risk estimates for use of biomass increased, but among those who had used such fuel, there was no clear decline in risk with longer time since last exposure.

The study had the advantage of a larger sample size than earlier similar investigations (Sathiakumar 2012; Fatmi et al. 2014) and was conducted in a population with good heterogeneity of relevant exposures. Moreover, the hospitals from which participants were recruited had the largest public sector cardiac care units in the region, and most women in the study population with ACS would have been admitted to one of the two facilities. It is possible that a few could afford to be treated privately and therefore did not get recruited, while conversely some may have been too poor even to cover the cost of entering a public sector hospital and therefore resorted to treatment at home. However, the same would have applied to potential controls, and therefore at most, only minimal bias would be expected from such selection.

We applied a clear case definition and were able to study almost all of the potential cases that were identified. Patients at the participating hospitals were not charged for their medical consultation or accommodation, but diagnostic tests and medicines were not uniformly free of charge. No payment was required for ECGs and measurements of CK-MB, but measurement of troponin T and troponin I was provided only by a nearby private laboratory and was charged to the patient. Where this occurred, the test result was considered to be the patient's property and was not always placed in the hospital records. Also, some patients were referred for further treatment elsewhere after their interviews had been completed and took with them with their diagnostic records. In these circumstances, diagnoses were accepted if they had been made by the physicians and senior nurses in the cardiac units, since the case definition for the study accorded with their standard diagnostic criteria. A further limitation was that most biochemical assays were performed by laboratories which did not participate in formal accreditation schemes. However, any diagnostic misclassification of cases, either because of unidentified variations in clinical practice or from errors in the assay of biomarkers, should have been non-differential with respect to use of biomass for cooking and therefore would tend, if anything, to bias risk estimates towards the null.

The participation rate among controls was also high. As often happens with hospital controls, there was a possibility that their exposures might be systematically unrepresentative of those in the population at risk of becoming cases, in particular if the risk factors of interest were in some way associated with the diseases that led to their admission. However, they had a broad mix of diagnoses, making it less likely that serious bias would have arisen in this way. The most frequent reason for admission in the controls was non-tuberculous respiratory disease (including bronchitis and chronic obstructive pulmonary disease), some of which may have been caused or exacerbated by IAP. However, if anything, that would be expected to reduce rather than inflate the observed associations of IAP with ACS.

A small number of cases (40) and potential controls (24) were excluded from the study because their clinical team judged that they were too unwell to participate. However, there is no reason to expect that clinicians' decisions on this would be in any way related to the type of fuel used for cooking, and any effect on risk estimates should have been minimal.

Most exposures were assessed by questionnaire. The current use of biomass should have been readily distinguished from that of other cleaner fuels, and switching to cleaner fuel is generally a major event that would be recalled reliably. However, there is a possibility of error in participants' recall of times since last exposure to different types of cooking fuel, which if non-differential with respect to current diagnosis, could have obscured trends in risk. We did not analyse total years of using biomass since that information could not be derived reliably from the questionnaire. Errors may have occurred in subjects' recall of hunger and weight loss during childhood, but again there is no reason to expect that they would be differential with respect to case/control status. The likely effect, therefore, would be to bias risk estimates for the variables concerned towards the null and to underestimate their negative confounding of associations with use of biomass fuel for cooking.

Anthropometric measurements were taken, while the patient was still in hospital, provided that she was sufficiently well. Field workers could not be blinded to participants' case/control status, but the measurement of BMI and WHR should not have been affected importantly by this. Nor should values have been affected much by the illness of the cases, which was recent in onset. However, some controls (e.g. those with cancer) may have lost weight because of their disease. If so, risk estimates for current nutrition would have been biased upwards.

Where exposure variables needed to be reclassified or combined, that was based on their distribution in the total study sample and was done without knowledge of the distribution in cases and controls separately.

Our finding of increased risk with poor nutrition in early life and with over-nutrition in adulthood accords with the previous research (Barker and Osmond 1986; Barker et al. 1993). It has been hypothesized that the associations reflect 'metabolic programming', whereby poor nutrition early in life induces permanent changes in metabolic function, which then predisposes to cardiac and other disease in adulthood if the individual is later exposed to better nutrition (Harding 2001).

The associations that we found with specific aspects of current diet were less clear. Higher risk in women who consumed meat and eggs at least once per week disappeared after adjustment for other factors, and use mainly of ghee for cooking carried a significantly lower risk than use mainly of oil (which would be expected to contain less saturated fat). Most previous research has suggested an increased risk of CHD with higher consumption of saturated fat (World Health Organization 2002), although recently, a large systematic review and meta-analysis have called this into question (Chowdhury et al. 2014). As diet was not the main focus of our study, and its assessment was only limited, the association that we observed with use of ghee should not be given undue weight in the context of the much wider body of evidence that is available from elsewhere.

Smoking (both active and passive) is a well-established risk factor for ACS (Yusuf et al. 2004; Teo et al. 2006), but the effect of smoking was not clearly apparent in our study. Risk was increased in women who were exposed to the combination of active smoking (ever) and environmental tobacco smoke in the home (currently), but the finding was not statistically significant, and there was no association with active smoking in the absence of exposure also to environmental tobacco smoke. A clearer effect may have been missed through random sampling variation (the upper 95% confidence limits for the odds ratios in active smokers were 1.5 and 2.8). Also, we did not assess intensity of smoking, and it is possible that among the women under study, smoking was relatively light.

Risk was markedly elevated in women with a larger number of household assets, but significantly lower among those with higher household income. This divergent pattern of risk applied even in unadjusted analyses, suggesting that it did not simply reflect inter-confounding. About 10% of cases declined to report their household income, as compared with only 5% of controls (Table 1). Thus, there may have been some bias from incomplete reporting of income. Furthermore, most people in the study area did not earn regular fixed salaries, their economy being based on seasonal crops, and this may have made it more difficult to estimate monthly incomes, especially for women who generally were not themselves employed earners. For these reasons, the questions about household assets may have provided a more reliable measure of affluence. An association with affluence would be consistent with an earlier pilot study (Fatmi et al. 2014) and another study in South Asia (Ali et al. 2016).

After adjustment for other risk factors, ACS was strongly associated with ever having used biomass for cooking. Associations were stronger after adjustment for other risk factors, indicating negative confounding by higher current nutrition and other risk factors associated with current affluence. Women who had never used biomass fuel tended to be more affluent. Similar negative confounding occurred in an earlier pilot study in the same community (Fatmi et al. 2014).

There was no indication; however, that risk declined when women stopped using biomass. Thus, the highest odds ratio (relative to never users) was in those who had last used biomass for cooking more than 10 years earlier. Little evidence is available from elsewhere with which to compare this finding. One cross-sectional survey in China of 13,438 adults randomly selected from census records found no dose–response relationship between risk of CHD and duration of using solid fuel for cooking (Lee et al. 2012). Relative to never users, those who had used solid fuel for more than 25 years had somewhat lower risk (OR 1.5, 95% CI 1.0, 2.2) than those who had used it for 10–25 years (OR 2.0, 95% CI 1.3, 2.9). An intervention study aimed at reducing exposures to IAP from use of biomass did show some reduction in blood pressure in the short term (McCracken et al. 2007), but the incidence of ACS was not assessed. Studies of ambient air pollution indicate that short-term increases in concentrations of fine particulate matter are associated with higher rates of hospital admission for ischaemic heart disease (Dominici et al. 2006; Pope et al. 2006), but that does not preclude there also being longer-term persistent effects. Our findings suggest that air pollution from use of biomass causes persistent pathology, and that when substantial exposure has occurred, risk remains elevated for a long time. If so, the benefits from interventions to reduce exposures may not be fully realized in the short term.

In our main analysis, we did not adjust for the previous diagnosis of hypertension or diabetes because we were concerned that these might, at least in part, mediate rather than confound effects of biomass on risk of ACS. Nor did we include parental history of heart attack since it was possible that such disease could to some extent be caused by use of biomass in the family home. However, in a sensitivity analysis that adjusted additionally for these variables, risk estimates for exposure to biomass were virtually unchanged (Supplementary Table 1).

## Conclusion

Our findings add to the weight of evidence for an importantly increased risk of ACS from use of biomass for cooking and are a further encouragement to initiatives aimed at reducing exposures to the household air pollution that it produces. However, they suggest that the full benefits from better design of stoves or switching to other fuels may not accrue until many years after such changes are introduced.

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## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** This research protocol was reviewed and approved by Ethics Review Committee of Aga Khan University.

**Informed consent** Written informed consent was taken which was signed by each study participant.

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