

Solid fuel use and risks of respiratory diseases: a cohort study of 280,000 Chinese never-smokers

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ZC, RP, LY, and YC contributed to the overall design and oversaw the conduct and long-term follow-up of the China Kadoorie Biobank study. KHC, OPK, DAB, KBHL, and ZC conceived the present study. KHC reviewed the literature, analyzed the data and wrote the first draft of the report, supervised by OPK, DAB, KBHL, and ZC. All

31 authors contributed to the interpretation and development of the report, and approved
32 the final version.

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50 **At a glance commentary**

51 **Scientific Knowledge on the Subject:**

52 Although previous cross-sectional and case-control studies has suggested an
53 association between household air pollution (HAP) from solid fuel use and excess
54 risk of COPD, the magnitude of the risk estimates varied greatly across different
55 studies, with several recent larger studies reporting null associations. There is only

56 limited evidence about the effects on respiratory diseases other than COPD in adults,
57 with the only two published cohort studies on HAP reporting inconclusive findings on
58 respiratory deaths and acute lower respiratory infections in adults. There is also a
59 lack of information from large-scale population-based cohort studies on the
60 respiratory health impact of switching from solid to clean fuels or use of ventilation in
61 adults, both of which have been associated with significantly lower exposure.

62 **What This Study Adds to the Field:**

63 In this cohort study of 280,000 never-smoking Chinese adults, long-term solid fuel
64 use for cooking was associated with significant excess risks of hospitalization and
65 death from both acute and chronic respiratory diseases, including chronic lower
66 respiratory disease and acute lower respiratory tract infection. The excess risk was
67 greater among persistent wood than coal users, but smaller among those who
68 switched from solid to clean fuels or used ventilated cookstoves with solid fuels. An
69 association between solid fuel use and COPD admissions and death was found, but
70 was far weaker than estimates from meta-analysis of cross-sectional studies for
71 airflow obstruction.. This study also provides suggestive evidence that improved
72 ventilation or switching to clean fuels may alleviate the excess respiratory risks
73 associated with solid fuel use.

74

75 This article has an online data supplement, which is accessible from this issue's table
76 of content online at www.atsjournals.org

77 **ABSTRACT**

78 **Rationale:** Little evidence from large-scale cohort study exists about the relationship
79 of solid fuel use with hospitalization and mortality from major respiratory diseases.

80 **Objectives:** To examine the associations of solid fuel use and risks of acute and
81 chronic respiratory diseases.

82 **Methods:** A cohort study of 277,838 Chinese never-smokers with no prior major
83 chronic diseases at baseline. During 9-years follow-up, 19,823 first hospitalization
84 episodes or deaths from major respiratory diseases, including 10,553 chronic lower
85 respiratory disease (CLRD), 4,398 chronic obstructive pulmonary disease (COPD),
86 and 7,324 acute lower respiratory infection (ALRI) were recorded. Cox regression
87 yielded adjusted hazard ratios (HRs) for disease risks associated with self-reported
88 primary cooking fuel use.

89 **Measurements and main results:** Overall 91% of participants reported regular
90 cooking, with 52% using solid fuels. Compared with clean fuels users, solid fuel users
91 had adjusted HR of 1.36 (95%CI 1.32-1.40) for major respiratory diseases, whereas
92 those who switched from solid to clean fuels had weaker HR (1.14, 1.10-1.17). The
93 HRs were higher in wood (1.37, 1.33-1.41) than coal users (1.22, 1.15-1.29) and in
94 those with prolonged use (≥ 40 years: 1.54, 1.48-1.60; < 20 years: 1.32, 1.26-1.39),
95 but lower among those who used ventilated than non-ventilated cookstoves (1.22,
96 1.19-1.25 versus 1.29, 1.24-1.35). For CLRD, COPD and ALRI, the HRs associated
97 with solid fuel use were 1.47 (1.41-1.52), 1.10 (1.03-1.18) and 1.16 (1.09-1.23),
98 respectively.

99 **Conclusions:** Among Chinese adults, solid fuel use for cooking was associated with
100 higher risks of major respiratory disease admissions and death and switching to
101 clean fuels or use of ventilated cookstoves had lower risk than those who were not.

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104 **INTRODUCTION**

105 Household air pollution (HAP), arising mainly from domestic burning of solid fuels
106 (e.g. coal and biomass) for cooking, is a leading cause of premature death and
107 disease burden worldwide.(1) Currently, over 2.7 billion individuals, mainly those
108 from rural areas in low- and middle-income countries (LMICs), are regularly exposed
109 to high levels of HAP.(2)

110 Despite the biological plausibility (due to its resemblance to smoking), that
111 solid fuel use is associated with higher risk of chronic obstructive pulmonary disease
112 (COPD) in adults does not have a strong evidence base, as conclusions drawn from
113 previous meta-analyses of studies with relatively small sample sizes were limited by
114 high levels of heterogeneity and publication bias.(3-6) In contrast, three out of the
115 four more recent, larger studies have found no evidence of a significant association
116 with airflow obstruction.(7-10) There has also been little reliable evidence on the
117 relationship between HAP and hospitalization or death from COPD, which is relevant
118 to the understanding of the public health burden in LMICs like China, where COPD is
119 often diagnosed based on symptoms (chronic bronchitis) or radiological evidence
120 (emphysema) rather than airflow obstruction as spirometry is not routinely
121 performed.(8, 11) Few studies have investigated the effects of HAP on respiratory
122 diseases other than COPD such as acute lower respiratory infection (ALRI) in
123 adults.(12, 13) We report findings on the use of solid fuels for cooking and its
124 association with hospitalization and death from acute and chronic respiratory
125 diseases in about 280,000 never-smoking Chinese adults from the China Kadoorie
126 Biobank (CKB) study.

127 **METHODS**

128 **Study design**

129 Detailed methods of the CKB study have been described previously.(14-16) Between
130 2004 and 2008, 512,000 adults aged 30-79 years were recruited from ten areas
131 across China (**Figure E1**) and undertook a computer-assisted interview and physical
132 measurements (including spirometry) by trained health workers following
133 standardized procedures.(14, 15) The laptop-based questionnaire incorporated
134 stringent logic and error checks to avoid coding errors, and the quality of data
135 collection was closely monitored, with regular feedback and further training provided
136 to health workers.(14, 15) Spirometry was performed according to the American
137 Thoracic Society guidelines as described previously,(10) but no bronchodilator was
138 administered. Approval was obtained from the ethical review committee of the
139 Chinese Center for Disease Control and Prevention (Beijing, China) and the Oxford
140 Tropical Research Ethics Committee, University of Oxford (UK). Written informed
141 consent was obtained from all participants.

142 **Assessment of solid fuel use**

143 At baseline, each participant was asked to recall, for up to their three most-recent
144 residences, how many years they had lived there, cooking frequency (no cooking
145 facility/ never/ rarely, monthly, weekly, daily), and ownership of ventilated
146 cookstoves.(17) Participants who cooked at least monthly, in each of their respective
147 residences, were asked about the primary fuel type used (electricity, gas, coal, wood
148 or charcoal, other unspecified). If two or more fuel types were used at a residence,
149 the one used most frequently and for the longest duration was recorded. Clean fuels
150 included electricity or gas, whilst solid fuels comprised coal or wood (including
151 charcoal because of their compositional and emission similarities(12)). Participants

152 cooking weekly or daily were considered as cooking regularly (90% of whom cooked
153 daily at baseline), and their HAP exposure at each residence was classified
154 according to the primary fuel type. Long-term exposure was assessed by grouping
155 participants who used the same primary fuel type throughout their three residences
156 and those who had switched from solid to clean fuels before baseline separately.
157 Long-term solid fuel users were further categorized into three groups (always coal,
158 always wood, a mixture of coal and wood), along with the estimated duration of
159 continuous exposure to solid fuels for cooking during the recall period (<20, 20-39,
160 ≥40 years). To explore the potential impact of ventilated cookstove use, a three-
161 category composite exposure was derived (clean fuels, solid fuels with ventilated
162 cookstoves, and solid fuels without ventilated cookstoves). Further details on
163 exposure assessment are available online (**Supplementary methods 1**).

164 **Follow-up for mortality and morbidity**

165 All participants were followed-up through electronic linkage, using unique personal
166 identification numbers, to established death and morbidity registries and to a
167 nationwide health insurance system (~99% coverage in the study areas), which
168 provided coded fatal and non-fatal events (International Classification of Diseases,
169 10th Revision; ICD-10).(15) The endpoints investigated in this study include the first
170 hospitalization event (during the follow-up period) or death of major respiratory
171 diseases (including chronic lower respiratory disease [CLRD; ICD-10 J40-J47, where
172 J41-J44 were considered as COPD], acute lower respiratory infection [ALRI; J12-J18,
173 J20-J22], acute upper respiratory infection [AURI; J00-J06], other upper respiratory
174 disease [J30-J39]) and death from any respiratory diseases (excluding those due to
175 external agents: J00-J47, J80-J94, J96-J99). Participants without the above events
176 were censored upon death, loss to follow-up, or January 1 2016. To verify the validity

177 of COPD diagnoses, a random sample of ~1000 COPD cases (~10%) between 2004
178 and 2013 was adjudicated by respiratory physicians independently.(18) Only 14% of
179 the COPD cases had pre-bronchodilator spirometry performed. However, most (85%)
180 COPD diagnoses were considered to be adequately supported by different sources
181 of evidence based on clinical symptoms, risk exposure, radiological examinations, or
182 spirometry in accordance to the existing clinical guidelines.(18)

183 **Statistical analysis**

184 Our analyses were restricted to never-smokers (n = 317,614), defined as those that
185 had either never smoked or had smoked <100 cigarettes or equivalent during their
186 lifetime. We excluded participants with unreliable recall information on residence
187 duration (n = 1,573) and those with self-reported doctor-diagnosed major chronic
188 diseases (chronic bronchitis, emphysema, tuberculosis, asthma, any cancer, stroke,
189 transient ischemic attack or coronary heart disease) prior to the baseline survey (n =
190 26,095). Participants who used other unspecified fuels at any residence (n = 2,527),
191 those who switched from clean to solid fuels (n = 655), or had cooked previously but
192 stopped at baseline (n = 8,926) were also excluded, leaving 277,838 participants in
193 the final study population.

194 Direct standardization yielded age, sex, and study-area-adjusted percentages
195 or means of baseline characteristics for long-term cooking fuel exposure categories.
196 We used Cox regression to estimate hazard ratios (HRs) and 95% confidence
197 intervals (CIs) for first hospitalization or death from respiratory disease in association
198 with long-term solid fuel use for cooking (referred to as risk of respiratory disease in
199 the subsequent text), stratifying for age-at-risk (five-year intervals), sex, and study
200 area (10 areas), and adjusted for education (no formal school, primary school, middle

201 school, high school/college/ university), household income (<10,000, 10,000-19,999,
202 20,000-34,999, ≥35,000), occupation (agricultural worker, factory worker, non-manual
203 worker, others), alcohol consumption (never/rarely, occasional, ex-drinker or
204 reduced-intake, weekly regular), body mass index (BMI; continuous), environmental
205 tobacco smoke (ETS) exposure (<1 day/week, 1-5 days/week, daily or almost every
206 day), cookstove ventilation (all stoves, some stoves, none), primary heating fuel
207 exposure (always clean fuels, solid to clean fuel, always solid fuels, others), and
208 length of recall period (continuous), where appropriate. Fuller details of the selection
209 process used for confounders for adjustment are provided online (**Supplementary**
210 **methods 2**). The proportional hazard assumption was confirmed to be upheld by
211 using standard methods.(19) For exposure measures with more than two categories,
212 a group-specific CI of HR was calculated from the variance of the log hazard in each
213 category (including the reference category) as described previously(16, 20) and more
214 details are provided online (**Supplementary methods 3**). The cumulative probability
215 of being hospitalized or dying from each specific cause during follow-up are
216 presented using Kaplan-Meier plots.

217 We conducted subgroup analyses by baseline characteristics (birth year, age,
218 sex, education, ETS, alcohol consumption, BMI, leg length, years of having a
219 refrigerator at home [the latter two are proxies for the early life environment]). We
220 carried out further sensitivity analyses to reduce the potential impact of reverse
221 causation and residual confounding by excluding i) participants with <20 years of
222 recall period (“frequent movers”, n = 26,742), ii) participants with poor self-reported
223 health at baseline (n = 26,551), iii) participants who cooked weekly at baseline (n =
224 25,466), and iv) individuals with spirometry-defined airflow obstruction (n = 15,879) or
225 chronic respiratory symptoms (n = 4,842) at baseline, respectively. Details of the

226 assessment and definitions of airflow obstruction and chronic respiratory symptoms
227 are available online (**Supplementary methods 4**). All analyses were conducted
228 using SAS software version 9.3.

229 **RESULTS**

230 Among the 277,838 never-smoking participants, the mean (SD) age was 50.3 (10.3)
231 years and 91% were female. The mean total duration of the three most-recent
232 residences was 39.7 (14.5) years, with 91% participants having had at least 20 years
233 of residence covered. Among 91% who reported regular cooking during the recall
234 period, 52% used solid fuel throughout. Compared to long-term clean fuel users,
235 solid fuel users were older, less educated, had lower income, more likely to live in
236 rural areas, to report poor general health status, and were less likely to use ventilated
237 cookstoves. There was no major difference in exposure to ETS or BMI between the
238 two groups (**Table 1**).

239 During 2.6 million person-years of follow-up (mean 9.1 [1.4] years), 19,823
240 first hospitalization events and deaths from major respiratory diseases were recorded,
241 including 10,553 CLRD, 4,398 COPD, 7,324 ALRI, and 3,011 AURI. **Figure 1**
242 presents the Kaplan-Meier probability of hospitalization or death from each cause-
243 specific outcome across the three main exposure categories (always clean, solid to
244 clean, always solid). Compared with long-term clean fuel use, long-term solid fuel
245 use for cooking was associated with higher risks of several major respiratory
246 diseases, with adjusted HRs of 1.36 (group-specific 95% CI 1.32-1.40; rate difference
247 [RD] 291/ 100,000 person-years) for all major respiratory diseases, 1.47 (1.41-1.52;
248 248) for CLRD, 1.10 (1.03-1.18; 30) for COPD, 1.16 (1.09-1.23; -16) for ALRI, 1.59
249 (1.48-1.71; 86) for AURI, 1.56 (1.40-1.73; 35) for other upper respiratory disease,

250 and 1.56 (1.28-1.89; 21) for respiratory death. The HRs were significantly weaker in
251 participants who switched from solid to clean fuels than those who used solid fuels
252 persistently (for major respiratory disease: 1.14 [1.10-1.17] versus 1.36 [1.32-1.40])
253 (**Table 2**). For major respiratory diseases, the corresponding HR was similar in men
254 and women (1.46 [1.30-1.63] versus 1.37 [1.32-1.41]), and across a range of
255 baseline characteristics (**Table E1**).

256 Compared with participants who had always used clean fuels for cooking, the
257 risk of major respiratory diseases increased with duration of persistent solid fuel use,
258 with HRs of 1.32 (1.26-1.39; RD 232/ 100,000 person-years), 1.41 (1.37-1.45; 304),
259 and 1.54 (1.48-1.60; 293) in those who used solid fuels for <20, 20-39, and ≥40 years,
260 respectively ($P_{\text{trend}} < 0.0001$). Similar relationships were observed for each specific
261 respiratory disease ($P_{\text{trend}} \leq 0.003$ for all comparisons) (**Figure 2**). Amongst long-term
262 solid fuel users for cooking, those who used wood had higher HRs for major
263 respiratory diseases than those who used coal (1.37 [1.33-1.41] versus 1.22 [1.15-
264 1.29]), and those who switched between wood and coal had an intermediate risk
265 (1.25 [1.19-1.31]). Similar patterns of association were observed for CLRD, COPD,
266 ALRI, and respiratory death but not for other respiratory disease outcomes (**Figure 3**).
267 Excess risk of major respiratory diseases amongst the solid fuel users with ventilated
268 cookstoves were significantly lower compared to those who used unventilated
269 cookstoves (1.22 [1.19-1.25] versus 1.29 [1.24-1.35]). Similar associations were
270 observed for CLRD, AURI, other upper respiratory disease, and respiratory death
271 (**Figure 4**).

272 The strength of observed associations between solid fuel use for cooking and
273 most respiratory diseases did not change substantially after excluding frequent
274 movers, participants with poor self-reported health, those who cooked weekly, or

275 those who had signs of airflow obstruction or chronic respiratory symptoms at
276 baseline (**Table E2**).

277 **DISCUSSION**

278 In this large study of 280,000 never-smoking Chinese adults who had no known prior
279 history of major chronic diseases at baseline, long-term use of solid fuels for cooking
280 was associated with significant elevated risks of hospitalization or death from both
281 acute and chronic respiratory diseases, with consistent results in men and women
282 and across a range of population subgroups. The excess risks appeared to be
283 greater among those who used wood compared to coal. Switching from solid to clean
284 fuels or use of ventilated cookstoves was associated with relatively smaller excess
285 risks.

286 Most previous epidemiological studies on solid fuel use and respiratory
287 diseases focused on COPD in adults, with the majority of them being cross-sectional
288 or case-control studies examining airflow obstruction as the outcome.(3-6, 9, 21, 22)
289 Earlier pooled-analyses of these studies, often with small sample sizes, reported
290 large excess risks (summary odds ratios from 1.94 to 2.80),(3-6) but strong evidence
291 of publication bias ($p < 0.007$) and high levels of heterogeneity ($I^2 = 85\%$) has been
292 found.(5) Four larger and more recent population-based cross-sectional studies
293 involving 13,000 to 67,000 participants, including two conducted in China, reported
294 much weaker associations (from no association to ~40% excess risk) with airflow
295 obstruction.(7-9, 22) In contrast, the present study of 280,000 Chinese never-
296 smokers found that long-term use of solid fuel for cooking was associated with about
297 10% excess risk of COPD hospitalization or death. The cohort design of this study
298 enabled us to take account of the influence of reverse causation, by excluding those

299 with prior history of major respiratory diseases, signs of airflow obstruction, or chronic
300 respiratory symptoms, and by examining prospectively recorded hospitalizations or
301 deaths. Furthermore, our analyses were restricted to never-smokers, so the residual
302 confounding from smoking, a leading cause of COPD, should be minimized.

303 Many previous studies on COPD, including a previous cross-sectional analysis
304 of CKB,(10) examined spirometry-defined airflow obstruction, the hallmark of COPD,
305 as the outcome. In the present study we focused on hospitalization and death as
306 there has been little information on the risk of respiratory hospitalizations and deaths
307 associated with long-term HAP. Indeed, the low utility of spirometry for diagnosing
308 COPD in China (7-10%) (8, 23) means many asymptomatic and mild airflow
309 obstruction cases not requiring medical attention were less likely to have been
310 identified, diagnosed, and captured in our records as COPD. Under-diagnosis of
311 COPD is disproportionately higher in rural China,(8) where solid fuel use is more
312 prominent. The higher likelihood of undiagnosed cases in the exposed group means
313 that the observed risks for COPD may well be diluted. In this regard, we observed a
314 stronger association between long-term solid fuel use for cooking and CLRD
315 (HR=1.47 [95% CI 1.41-1.52]), which included all COPD cases plus mostly
316 unspecified bronchitis (ICD-10 J40; n=7,471). It is possible that many of these
317 unspecified bronchitis cases (but not acute bronchitis as included within ALRI) could
318 be mild, early stages COPD or acute exacerbations of pre-existing, but previously
319 undetected COPD, given that spirometry is rarely used for diagnosis in China.
320 Nevertheless, this may also suggest that solid fuel use is more strongly associated
321 with chronic bronchitis (or mucus hypersecretion in general) than with emphysema or
322 other COPD phenotypes, which has been suggested in previous studies.(6, 9, 24)

323 For non-COPD respiratory diseases, previous evidence has been more limited.
324 Two small cohort studies on respiratory death (with 155 cases) and ALRI (with 229
325 participants, no case numbers were given) reported inconclusive findings.(25, 26) A
326 recent systematic review(13) of eight relevant studies on ALRI, most of which
327 involved less than 1,000 disease events, found no consistent evidence. Our study
328 included much larger numbers of events than all previous studies combined (about
329 7,300 ALRI; 3,000 AURI). We found strong evidence that long-term solid fuel use is
330 associated with significantly elevated risk of hospitalizations or deaths from ALRI and
331 AURI in adults. This highlights the potential need of considering adult ALRI when
332 assessing the disease burden related to HAP exposure. It is worth noting that ALRI
333 and AURI are acute recurring conditions. The observed associations reflect an
334 overall shorter time to the first documented infection during the follow-up in solid fuel
335 users, which may indirectly imply a higher rate of recurrent infection among them
336 Future analysis focusing on recurrent events (including acute exacerbations of COPD)
337 should be able to clarify this.

338 Most previous studies on COPD have examined biomass (mostly wood) only,
339 while we analyzed both coal and wood (combined as “solid fuels” and separately),
340 the latter of which has been linked to higher levels of particulate pollution and
341 possibly higher risk of COPD.(6, 12) Consistently, the risks of CLRD, COPD, and
342 ALRI in our study were higher amongst those that persistently used wood compared
343 with those using coal. However, an earlier cross-sectional analysis of CKB on the
344 prevalence of airflow obstruction found seemingly protective effects of wood burning
345 (OR = 0.91 [95% CI 0.86-0.98]) and a deleterious effect of coal use (1.10 [1.02-1.20])
346 at baseline in women.(10) The two studies differ importantly by the disease outcome
347 examined (prevalence of spirometry-detected airflow obstruction(10) versus rate of

348 clinical episodes of COPD), as well as inclusion criteria, exposure classification, and
349 analysis strategy. In the current study participants with any prior chronic diseases
350 were excluded. We classified individuals who cooked weekly or daily as regular users
351 of fuels (clean or solid), whereas the previous analysis included also less frequent
352 (monthly) cooks (who were more likely to be men, factory workers, and clean fuel
353 users compared to the more frequent cooks). Furthermore, the current study has
354 additionally adjusted for other important confounders that were not taken into account
355 in the previous study (e.g. ETS, occupation, BMI). For upper respiratory disease, the
356 excess risks appeared to be broadly similar in the long-term wood and coal users for
357 reasons that are not fully understood. It is possible that the etiology or mechanisms
358 between chronic respiratory disease and respiratory infections in relation to air
359 pollutants generated by burning of different fuel types may differ. Further
360 investigation including direct measurement of HAP and characterization of smoke
361 constituents are planned and should help to clarify our findings.

362 It has been reported in both observational and intervention studies that HAP
363 exposure and acute respiratory symptoms in adults may be reduced through
364 adequately maintained cookstove ventilation.(27) However, there has been no clear
365 evidence on the long-term respiratory benefits of improved cookstove ventilation in
366 adults.(27) A retrospective cohort study involving 42,000 Chinese adults reported
367 significantly lower risks of pneumonia mortality (225 cases) and self-reported
368 physician diagnosis of COPD (1,487 cases) in lifelong coal users for cooking who
369 adopted ventilated cookstove compared to those who did not.(28, 29) In contrast,
370 another cohort study of 600 Chinese adults (74 cases) found no significant effect of
371 improved ventilation on the risk of airflow obstruction.(30) In our study, solid fuel
372 users who used ventilated cookstoves had lower risks of CLRD and upper respiratory

373 diseases, but not ALRI, COPD or respiratory death, compared with those who used
374 unventilated cookstoves. This is in agreement with existing evidence that improved
375 ventilation generally may have more prominent benefits on mild, acute conditions but
376 not on more severe diseases such as COPD or ALRI, possibly because the HAP
377 levels after improvement remain substantially above the recommended threshold.(27,
378 31) The discrepancy in the results on CLRD and COPD, as discussed above, may be
379 related to the unspecified bronchitis (ICD-10: J40) which could be acute exacerbation
380 of early stages of COPD. Future large-scale randomized controlled trials with long
381 follow-up and appropriately designed interventions are needed to assess the effect of
382 using ventilated cookstoves on major respiratory conditions such as ALRI or COPD
383 in adults.

384 Compared to the long-term persistent solid fuel users, participants who had
385 switched their primary cooking fuel from solid to clean fuels prior to the baseline
386 survey had smaller excess risks of all respiratory diseases studied. Although limited,
387 there is consistent trial evidence that switching from solid to clean fuels is associated
388 with markedly greater HAP reduction than adopting improved ventilation.(32) Our
389 findings offer supportive evidence that clean fuel adoption may be beneficial for the
390 prevention of acute and chronic respiratory conditions. While this might seem intuitive,
391 it highlights that the elevated risks associated with historical solid fuel use may still be
392 attenuated by switching to clean fuels later in life, a phenomenon similar to that of
393 smoking cessation.(16) This should encourage greater efforts to facilitate universal
394 access to clean energy especially in LMICs, as promoted in the United Nations
395 Sustainable Development Goal Seven.(33)

396 The key strengths of this study lie in the large number of never-smokers,
397 comprehensive investigation of prospectively documented hospitalization and death

398 of a range of respiratory diseases, and the high consistency of exposure-outcome
399 relationships across these diseases and across different population subgroups.
400 Moreover, two common limitations of previous research on this topic, namely reverse
401 causality and residual confounding from smoking, were carefully dealt with in this
402 study. However, our study has several limitations that need to be taken into
403 consideration. First, our outcome was based on linkages to hospitalization records
404 and death certificates. Misclassification due to misdiagnosis is possible, especially for
405 COPD due to the low utility of spirometry in China. Although we have excluded
406 participants with pre-existing chronic diseases, admissions for COPD were unlikely to
407 represent new onset “incident” cases as COPD has a prolonged development period
408 with risk factors that could trace back to pre-conception, meaning that it is difficult to
409 establish temporality accurately. Nevertheless, the aim of this study was to
410 investigate whether HAP may be associated with respiratory admissions and deaths,
411 rather than the development of incident cases. We have also excluded those with
412 signs of airflow obstruction at baseline or poor self-reported health in the sensitivity
413 analyses and the results persisted. Second, HAP exposure was estimated by self-
414 reports of the main type of fuel used as many other previous studies. It is possible
415 that historical or concurrent exposure to solid fuel emission from secondary or
416 neighborhood fuels could have elevated the background risks of clean fuel users, but
417 we lack data on these or from direct exposure measurement in order to more
418 accurately assess exposure-response relationships. Third, instead of prospectively
419 monitoring lifetime exposure, we were only able to estimate long-term exposure
420 based on recall information on the three most-recent residences of our participants.
421 This might have resulted in misclassification, especially among clean fuel users who
422 might have used solid fuels in their early life. However, the recall period covered was

423 on average 40 years ($\geq 70\%$ of the adulthood in 80% participants) and the exclusion
424 of participants with < 20 years of recall information provided gave similar findings with
425 all participants included. Fourth, residual confounding from early-life exposure and
426 ETS is possible, due to the lack of direct early-life exposure data and the relatively
427 crude adjustment on ETS (based on self-reported frequency of exposure).
428 Nonetheless, the associations observed were consistent across subgroups defined
429 by proxies of early-life exposures (leg length, education level, years of having a
430 refrigerator at home), and additional adjustment for duration of exposure to ETS did
431 not alter the relationship of interest (data not shown). Finally, our study sample has
432 an imbalanced gender ratio (9:1) and one may argue that the findings may not be
433 generalizable to men. However, in the gender-specific analyses (with $> 26,000$ men),
434 we found no evidence of heterogeneity.

435 In conclusion, in Chinese adults, solid fuel use for cooking was associated
436 with higher risks of admissions and death for both acute and chronic respiratory
437 diseases, with the excess risk seemingly greater for wood than coal users, especially
438 for CLRD, and in those with more prolonged use. A much weaker association with
439 COPD was observed as compared to the earlier meta-analysis estimates used in
440 global disease burden estimation. Moreover, use of ventilated cookstoves and
441 switching to clean fuels were associated with smaller excess risks of some
442 respiratory diseases associated with solid fuel use, reinforcing the need for
443 strengthening the existing global initiatives to improve access to clean energy and to
444 distribute improved cookstoves in communities where a complete switch to cleaner
445 fuels is not yet feasible.

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Table 1. Baseline characteristics of never-smoking participants by long-term primary cooking fuel exposure. *

Characteristic	Always clean	Solid to clean	Always solid	Never cooked regularly	All participants
N	53,130	66,115	131,270	27,323	277,838
Age, years (SD)	45.3 (9.5)	50.9 (9.8)	53.0 (10.2)	45.6 (11.2)	50.3 (10.3)
Female sex, %	86.8	97.0	95.5	40.7	90.9
Urban residence, %	88.0	79.2	8.5	49.8	44.3
No formal education, %	14.5	18.8	28.7	20.0	23.6
Household income <10,000 yuan/yr, %	18.3	20.4	37.8	22.6	28.6
Occupation					
Agricultural worker	19.7	26.6	48.4	31.0	41.3
Factory worker	13.1	12.1	11.1	15.9	12.0
Non-manual worker	17.9	13.9	6.6	16.2	9.9
Others †	49.3	47.4	34.0	36.8	36.9
Current drinker in males, %	21.3	21.5	18.5	19.6	19.1
Current drinker in females, %	2.0	1.7	1.5	2.0	1.6
Environmental tobacco smoke, %					
<1 day/ week	44.9	39.6	39.4	41.9	40.5
1-5 days/ week	17.8	19.1	18.8	17.3	19.0
Daily or almost everyday	37.3	41.4	41.8	40.8	40.4
Cookstove ventilation, %					
All stoves	61.1	55.8	22.8	47.9	44.7
Some stoves	19.7	24.4	46.5	28.3	31.9
None	19.2	19.9	30.7	23.8	23.5
Body-mass index, kg/m² (SD)	23.8 (3.3)	24.2 (3.4)	23.6 (3.4)	23.7 (3.2)	23.8 (3.4)
Systolic blood pressure, mmHg (SD)	127.9 (19.9)	128.7 (21.4)	130.2 (22.2)	128.4 (20.3)	129.7 (21.6)
Self-reported poor health, %	8.3	8.2	10.4	9.7	9.1

* Means and percentages were adjusted for age, sex and study area when appropriate. Participants who switched from clean to solid fuels, used unspecified fuels or cooked regularly but stopped were excluded from analysis (n=12,108).

† "Others" in occupation include housewife/ husband, retired, self-employed, unemployed or other unspecified.

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Table 2. Incidence rates and adjusted HRs for hospitalization or death from major respiratory diseases by long-term cooking fuel exposure

	Number of events	Rate (/100,000 person-years) *	HR (95% CI) †
Major respiratory diseases‡			
Always clean	2,576	797	1.00 (0.96-1.04)
Solid to clean	4,575	891	1.14 (1.10-1.17)
Always solid	12,672	1,088	1.36 (1.32-1.40)
Chronic lower respiratory disease§			
Always clean	1,093	371	1.00 (0.94-1.07)
Solid to clean	2,271	444	1.20 (1.15-1.26)
Always solid	7,189	619	1.47 (1.41-1.52)
Chronic obstructive pulmonary disease 			
Always clean	357	192	1.00 (0.89-1.12)
Solid to clean	778	167	0.96 (0.89-1.03)
Always solid	3,263	222	1.10 (1.03-1.18)
Acute lower respiratory infection¶			
Always clean	1,037	344	1.00 (0.93-1.07)
Solid to clean	1,871	308	1.08 (1.02-1.13)
Always solid	4,416	328	1.16 (1.09-1.23)
Acute upper respiratory infection**			
Always clean	444	108	1.00 (0.90-1.11)
Solid to clean	584	149	1.13 (1.04-1.23)
Always solid	1,983	194	1.59 (1.48-1.71)
Other upper respiratory disease††			
Always clean	327	75	1.00 (0.89-1.13)
Solid to clean	424	70	1.10 (0.99-1.22)
Always solid	984	113	1.56 (1.40-1.73)
Respiratory death‡‡			
Always clean	51	17	1.00 (0.75-1.33)
Solid to clean	126	14	0.96 (0.78-1.19)
Always solid	457	38	1.56 (1.28-1.89)

* Event rates were adjusted for age, sex and study area structure of the China Kadoorie Biobank study population.

† Hazard ratios were stratified for age-at-risk, sex and study area and adjusted for education, household income, occupation, alcohol consumption, body-mass index, environmental tobacco smoke, cookstove ventilation, heating fuel, and length of recall period.

‡ ICD-10 code J00-J06, J12-J18, J30-J22, J30-J39, J40-J47.

§ ICD-10 code J40-47.

|| ICD-10 code J41-44.

¶ ICD-10 code J12-J18, J20-J22.

** ICD-10 code J00-J06.

†† ICD-10 code J30-J39.

‡‡ ICD-10 code J00-J47, J80-J94, J96-J99.

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629

630 **Figure legend**

631 **Figure 1. Kaplan Meier probability of developing specific respiratory disease**
632 **during follow-up**

633 **Figure 2. Adjusted HRs for major respiratory diseases by duration of**
634 **continuous exposure to solid cooking fuel in never-smokers**

635 Hazard ratios were stratified by age-at-risk (in 5 year groups), sex and study area
636 and adjusted for education, household income, occupation, alcohol consumption,
637 body mass index, environmental tobacco smoke, cookstove ventilation, primary
638 heating fuel exposure and length of recall period. The black boxes represent hazard
639 ratios, with the size inversely proportional to the variance of the logarithm of the
640 hazard ratio, and the horizontal lines represent 95% confidence intervals (CI).

641 **Figure 3. Adjusted HRs for major respiratory diseases by type of primary**
642 **cooking fuel used in never-smokers**

643 Conventions as in figure 1.

644 **Figure 4. Adjusted HRs of major respiratory diseases associated with primary**
645 **cooking fuel and use of ventilated cookstoves at baseline**

646 Conventions as in figure 1 except that the HRs were not adjusted for cookstove
647 ventilation and length of recall period.

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