The establishment of the Household Air Pollution Consortium (HAPCO)

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Abstract

Household air pollution (HAP) is of public health concern with ~3 billion people worldwide (including >15 million in the US) exposed. HAP from coal use is a human lung carcinogen, yet the epidemiological evidence on carcinogenicity of HAP from biomass use, primarily wood, is not conclusive. To robustly assess biomass's carcinogenic potential, prospective studies of individuals experiencing a variety of HAP exposures are needed. We have built a global consortium of 13 prospective cohorts (HAPCO: Household Air Pollution Consortium) that have site- and disease-specific mortality and solid fuel use data, for a combined sample size of 587,257 participants and 57,483 deaths. HAPCO provides a novel opportunity to assess the association of HAP with lung cancer death while controlling for important confounders such as tobacco and outdoor air pollution exposures. HAPCO is also uniquely positioned to determine the risks associated with cancers other than lung as well as non-malignant respiratory and cardiometabolic outcomes, for which prospective epidemiologic research is limited. HAPCO will facilitate research to address public health concerns associated with HAP-attributed exposures by enabling investigators to evaluate sex-specific and smoking status-specific effects under various exposure scenarios.

Keywords

1. Introduction

Exposure to household air pollution (HAP), created by the combustion of coal, wood, and other forms of biomass for heating and cooking, is experienced by approximately 3 billion people worldwide [1] and causes over 3.5 million deaths per year [2,3]. In addition, one of its major components, polycyclic aromatic hydrocarbons (PAHs), is a known carcinogen [4]. Some of the strongest evidence on lung cancer caused by HAP is based on studies in Xuanwei, China. Xuanwei is ideal to study HAP-attributed lung cancer due to its high incidence rate of female lung cancer (~120 per 100,000 women)[5] combined with the fact that most women are never-smokers with substantial HAP exposures [6,7]. In Xuanwei, coal burning is associated with increased lung cancer risk [8] and improving stoves to mitigate HAP exposure is associated with significant reductions in lung cancer risk and lung cancer mortality [6,7]. A meta-analysis (>10,000 cases; >10,000 controls) of studies from Asia, Africa, Europe, and North America confirmed that significant increased risk of incident lung cancer was observed not only for coal burning in Southwestern China, which includes Xuanwei, but in areas throughout the world (OR=2.15; 95%CI=1.61–2.89; n=25), particularly in Asia (OR=2.27; 95%CI= 1.65–3.12; n=20) [9].

The International Agency for Research on Cancer (IARC) has classified HAP from indoor emissions from household coal combustion as a Group 1 human lung carcinogen [10]. However, due to limited epidemiologic evidence, IARC has classified HAP from biomass, primarily wood, as a probable human carcinogen (Group 2A) [11]. In an analysis pooling 7 case-control studies [12], it was suggested that individuals using wood to heat their homes experienced a higher risk of lung cancer than individuals who used non-solid fuels to heat their homes. With over 2.5 billion people exposed to wood smoke [1,10], and its increasing use for home heating in the US (over 15 million citizens currently exposed) [13], studies investigating the link between household wood smoke exposure and lung cancer are of tremendous importance.

Beyond the question of the pulmonary carcinogenicity of biomass, research priorities include elucidating the associations between HAP and cancer at other anatomical sites [14]. Retrospective studies have suggested that risk of cancers of the upper aero-digestive tract may be associated with exposures attributed to HAP. A review of 18 published studies evaluating the associations between HAP and cancers other than the lung found that HAP was associated with cervical, oral, nasopharyngeal, pharyngeal, and laryngeal cancers [15]. The observed associations between HAP and upper aero-digestive tract cancers remained significantly elevated when analyses were restricted to studies that controlled for smoking. In addition, a case-control study published subsequent to the meta-analysis found an association between HAP and breast cancer [16]. These associations, however, are considered preliminary as most studies had limited sample size, and all were retrospective in design. Moreover, additional research is needed to robustly assess the non-malignant health outcomes that have been reported in the literature to be associated with the use of solid fuel for heating and cooking in the home. Several systematic reviews have assessed the association between HAP exposures and chronic diseases other than cancer, including respiratory and cardiovascular diseases[17–21]. Similar to systematic reviews of the existing cancer literature, these reviews observed inconclusive findings and that the literature is limited in scope with regards to prospective studies, as well as a variety of exposure scenarios.

There is a need for large-scale prospective data that can assess the relationship between HAP and health outcomes, while adjusting for important demographic and clinical factors. However, most prospective studies are limited in the number of ascertained disease outcomes. A consortium effort that brings together multiple prospective studies may lead to a sufficient number of cases of malignant and non-malignant diseases to assess many of the previously mentioned HAP-disease relationships that have been inconclusive in the literature to date.

2. Materials and Methods

Prospective longitudinal cohort studies provide an excellent opportunity to assess the impact of HAP on chronic disease. To accurately quantify the relative and absolute risks of carcinogenic and cardiometabolic diseases associated with HAP exposure, particularly biomass-derived, we have established the Household Air Pollution Consortium (HAPCO). To date, 13 cohorts have agreed to participate (Table 1). These cohorts include: Three

Prefecture Cohort Study Aichi (Aichi) [22], British Columbia Generations Project (BCGP) [23], CARTaGENE (CaG) [24], Golestan Cohort (GCS) [25], Health Effects of Arsenic Longitudinal Study (HEALS) [26], Korea Multi-center Cancer Cohort (KMCC) [27], Three Prefecture Cohort Study Miyagi (Miyagi) [22], Mexican Teachers Cohort (MTC) [28], RERF life-span study (RERF) [29], Sister Study (SIS) [30], Shanghai Men's Health Study (SMHS) [31], Shanghai Women's Health Study (SWHS) [32], and Xuanwei Cohort Study (XW) [6]. Almost all cohorts have accrued more than 5 years of follow-up data (with many having accrued 10–20 years) and all cohorts have more than 15,000 participants. In all cohorts, participants filled out baseline questionnaires that collected information about, among many other things, their fuel use for heating and/or cooking.

Given that no direct HAP exposure air monitoring measurements are available beyond the questionnaires, the baseline questionnaires were used to initially categorize individuals from each cohort into ever/never solid fuel users for heating or cooking in the home. Eight studies directly asked each participant if they have ever used solid fuels in their homes for heating or cooking. This variable was used to classify participants as ever/never users in these studies. In the remaining studies, individuals with high exposure levels were classified as ever exposed and individuals with low exposure levels were classified as never exposed. For 2 studies, those with any years of coal or wood use were classified as ever users, while those with zero years of use were classified as never users. For 3 studies, the ever users were those who used solid fuel in a stove without a chimney, and the never users were those who used a stove with a chimney. As described below, future aims of HAPCO include refining these harmonized exposure variables, and possibly correlating questionnaire data with quantified biomarkers of HAP exposure (i.e., urinary PAH levels).

3. Results

In total, there are data from 587,257 participants (348,146 participants in cohorts conducted in Asia; 239,111 participants in cohorts conducted in North America), of whom 73.5% are females (220,903 females in cohorts conducted in Asia; 210,472 females in cohorts conducted in North America) and 62.0% are never-smokers (214,520 never-smokers in cohorts conducted in Asia; 149,610 never-smokers in cohorts conducted in North America) (Table 1). Overall, the mean age at baseline among all cohorts tended to be in the mid-50's, except for HEALS, XW, and MTC, which were slightly younger. The average BMI at baseline tended to be lower among the cohorts conducted in Asia compared to those conducted in North America. Given the maturity of many of these cohorts, there has been a large number of deaths (n = 57,483). To date, there have been a total of 8,347 lung cancer deaths, as well as 306 oral and nasopharyngeal, 852 esophageal, and 154 laryngeal cancer deaths (Table 2). There have also been a total of 25,465 cardiovascular deaths.

About a third of all subjects experienced HAP attributed to solid fuel use (Table 3). The prevalence of biomass (wood) use was 18.6% in all cohorts (25.3% in cohorts conducted in Asia, 8.8% in cohorts conducted in North America) and coal use was 13.4% (26.2% in cohorts conducted in Asia, 2.1% in cohorts conducted in North America). Regarding additional data available for harmonization, the number of years of use for each fuel type is

available for 73% of subjects, and data related to the presence of ventilation in the vicinity of the fuel use and the type of stove used are available for 70% of subjects (Table 4).

The original, baseline questionnaire data from the cohorts will be harmonized to allowing for pooling the HAP exposures in terms of the intensity and duration of exposure. Each HAPCO cohort has the covariate data for our analyses (Table 4), such as age, gender, active tobacco smoking, education, and BMI. These variables will be harmonized to ensure comparability across cohorts. For example, active tobacco smoking will be first classified granularly (ever, never), where never smoking is defined has not having smoked more than 100 cigarettes in their lifetime. Smoking will also be assessed by years of smoking and pack-years smoked. Finally, years since quitting smoking will also be harmonized, which will also allow for classification of individuals as current, former, and never smokers. In addition to these covariates, OAP exposures will be estimated by GIS-based methods that link geocoded residential addresses to exposure databases. Air pollution estimates will be available for all cohorts either through local models and/or via the global air pollution maps for $PM_{2.5}$ and NO_2. The CaG and BCGP cohorts are covered by air pollution exposure surfaces as generated and collated within the CANUE project[33]. The SIS cohort has already estimated $PM_{2.5}$ and NO_2 concentration through national, satellite-based models[34]. $PM_{2.5}$ and NO_2 concentrations for the other cohorts are currently being derived using satellite-based estimates as well as from available ground-level monitoring data. Once data harmonization is complete, the mortality rates of each disease outcome of interest will be assessed overall, by sex, and by smoking status. Next, the associations between HAP exposure and mortality from lung, esophageal, oral, pharyngeal, and laryngeal cancers, by smoking status and sex, will be assessed.

4. Conclusions

HAPCO currently involves 13 cohorts from 8 countries on 2 continents. Major strengths of HAPCO include the use of prospectively designed studies that substantially mitigate recall and temporal biases, as well as the large sample size lending itself to high statistical power. A collaborative data harmonization procedure for exposures, potential confounders, and outcomes will be developed for accurate estimation of magnitude and type of HAP exposure. By providing this platform, HAPCO will facilitate research by investigators to address public health concerns associated with HAP-attributed exposures. A robust assessment of exposures may serve to better predict risk of cancer and/or cardiovascular disease, which may impact future local, region, and national policies. Future aims of HAPCO are to (1) identify additional cohort studies to join the consortium, particularly cohorts conducted in Africa and South America where solid fuel use remains prevalent, and (2) quantitatively assess potential biomarkers for HAP exposure. HAPCO also welcomes additional project proposals from interested researchers. Such proposals will be reviewed by, and individually approved by, each cohort before access to the respective cohort data can be facilitated by HAPCO. These studies will have the potential to inform future interventions to reduce disease burden in global populations.

Acknowledgments

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Table 1.

Characteristics of Cohorts Participating in HAPCO (Household Air Pollution Consortium).

Cohort (Abbreviation)	Country	Enrollment Dates	Total Subject	Males		Females		Never Smokers		Ever Smokers		Age at Baseline		BMI at Baseline (kg/m²)	
				N	%	N	%	N	%	N	%	Mean	Range	Mean	Range
Cohorts conducted in Asia															
Golestan Cohort (GCS)	Iran	2004–2008	50045	21221	42.4%	28824	57.6%	39035	78.0%	11010	22.0%	52.1	40.0–75.0	26.7	11.8–62.2
Health Effects of Arsenic Longitudinal Study (HEALS)	Bangladesh	2000–2002	16386	0	0.0%	16386	100.0%	13928	85.0%	2458	15.0%	37.1	17.0–75.0	19.8	9.7–51.8
Korea Multi-center Cancer Cohort (KMCC)	Korea	1993–2004	20636	8235	39.9%	12401	60.1%	12819	62.1%	7471	36.2%	54.1	15.0–99.0	23.1	9.7–51.8
RERF life-span study (RERF)	Japan	1963–1993	52883	20390	38.6%	32493	61.4%	28408	53.7%	22102	41.8%	52.2	19.3–98.7	21.7	10.4–74.0
Shanghai Men's Health Study (SMHS)	China	2002–2006	25958	25958	100.0%	0	0.0%	9046	34.8%	16912	65.2%	59.3	40.1–75.0	23.9	11.6–40.3
Shangai Women's Health Study (SWHS)	China	1996–2000	74942	0	0.0%	74942	100.0%	72829	97.2%	2113	2.8%	52.6	40.0–71.0	24.0	12.7–49.0
Three Prefecture Cohort Study Aichi (Aichi)	Japan	1985	33529	15746	47.0%	17783	53.0%	15285	45.6%	15723	46.9%	56.4	40.0–103.0	22.1	10.6–57.0
Three Prefecture Cohort Study Miyagi (Miyagi)	Japan	1984	31345	13992	44.6%	17353	55.4%	12704	40.5%	18641	59.5%	57.3	40.0–98.0	23.2	7.2–64.9
Xuanwei Cohort Study (XW)	China	1992–1996	42422	21701	512%	20721	48.8%	22351	52.7%	20071	47.3%	39.5	25.0–59.0	not available	
Sub-Totals for Cohorts in Asia			**348146**	**127243**	**36.5%**	**220903**	**63.5%**	**214520**	**61.6%**	**97773**	**28.1%**				
Cohorts conducted in North America															
British Columbia Generations Project (BCGP)	Canada	2008–2016	29852	9345	313%	20462	68.5%	15321	51.3%	13412	44.9%	56.4	31.0–74.0	26.4	10.3–62.1
CARTaGENE (CaG)	Canada	2009–2016	43061	19249	44.7%	23812	55.3%	17259	40.1%	23434	54.4%	53.6	38.3–73.1	27.6	11.3–125.1
Mexican Teachers Cohort (MTC)	Mexico	2006–2008	115314	0	0.0%	115314	100.0%	90061	78.1%	25254	21.9%	43.0	20.0–84.0	27.4	10.2–57.8

Cohort (Abbreviation)	Country	Enrollment Dates	Total Subject	Males		Females		Never Smokers		Ever Smokers		Age at Baseline		BMI at Baseline (kg/m²)	
				N	%	N	%	N	%	N	%	Mean	Range	Mean	Range
Sister Study (SIS)	United States	2003–2009	50884	0	0.0%	50884	100.0%	26969	53.0%	23915	47.0%	55.6	35.0–76.5	27.8	11.5–72.1
Sub-Totals for Cohorts in North America			**239111**	**28594**	**12.0%**	**210472**	**88.0%**	**149610**	**62.6%**	**86015**	**36.0%**				
Totals for all Cohort Contributing Data			**587257**	**155837**	**26.5%**	**431375**	**73.5%**	**364130**	**62.0%**	**183788**	**31.3%**				

Table 2.

Number of selected cancer-related deaths in HAPCO (Household Air Pollution Consortium).

	Lung			Oral and nasopharyngeal	Esophageal	Laryngeal
	Men	Women	All	All	All	All
Cohorts conducted in Asia	4694	3478	8172	293	832	147
Cohorts conducted in North America	113	62	175	13	20	7
All Cohorts	**4807**	**3540**	**8347**	**306**	**852**	**154**

Table 3.

Prevalence of household air pollution exposures in HAPCO (Household Air Pollution Consortium).

	All subjects	Clean Fuel[†] Users		Coal Users		Biomass[¥] Users		Solid Fuel[¶] Users	
	n	n	%	n	%	n	%	n	%
Cohorts conducted in Asia	348146	162963	46.8%	91067	26.2%	88134	25.3%	178965	51.4%
Cohorts conducted in North America	239111	226870	94.9%	4942	2.1%	21045	8.8%	25987	10.9%
All Cohorts	**587257**	**381129**	**64.9%**	**78755**	**13.4%**	**109179**	**18.6%**	**187698**	**32.0%**

[†] includes all non-solid fuels (i.e., electric, gas)

[¥] includes wood and other biomass sources such as dung cakes and charcoal briquettes

[¶] includes coal and biomass users, which are not mutually exclusive (i.e., some individuals use both coal and biomass)

Table 4.

Data available in each HAPCO (Household Air Pollution Consortium) cohort.

	HEALS	SWHS	GCS	KMCC	Aichi	Miyagi	RERF	XW	CaG	BCGP	MTC	SIS	SMHS
Age at Baseline (years)													
BMI at Baseline (kg/m2)													
Educational Attainment													
Tobacco Smoking Status (ever/never)													
Pack-years smoked													
Solid Fuel Use													
Fuel Type													
Stove Type													
Use of Ventilation													
Years of HAP Exposure													
OAP (NO2, PM2.5)	¥	¥	¥	¥	¥	¥	¥	¥			¥		¥

¥
Currently being derived