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Addressing Disease Burdens Attributable to Ambient and Household Air Pollution in India: A Review to Scope Future Research Priorities for Carcinogenicity of Air Toxics

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SUMMARY

Air pollution ranks among the leading risk factors contributing to the burden of disease in South Asia with household and ambient air pollution accounting for 6 percent and 3 percent respectively of the total national burden of disease in India. Both urban and rural communities bear this burden in terms of premature mortality and disability adjusted life years, resulting from excess risks of communicable and non-communicable diseases. We review the information pertaining to exposures to fine particulate matter and air toxics together with the attributable disease burden estimates. We also provide a summary of the results from recent assessments on carcinogenicity of ambient and household air pollution conducted by The International Agency for Research on Cancer. We conclude with a list of specific priorities for action related to air toxics and cancer in India.

Keywords: Ambient air pollution, Household air pollution, Particulate matter, Air toxics, Disease burden, Carcinogenicity, Air quality actions.

1. INTRODUCTION

Air pollution ranks among the leading risk factors contributing to the burden of disease in South Asia (WHO, 2004). In the Comparative Risk Assessment (CRA), conducted as part of the Global Burden of Disease (GBD-CRA) 2010 Project (Lim *et al*. 2012) in India, approximately 1.04 million premature deaths and 31.4 million Disability Adjusted Life Years (DALYs) were attributable to household air pollution (HAP) resulting from solid cook-fuels while 627,000 premature deaths and 17.8 million DALYs were attributable to ambient air pollution (AAP), in the form of fine particles (measured as $PM_{2.5}$) annually. Household and ambient air pollution account for 6% and 3% of the total national burden of disease (IHME 2013), respectively, and together exceed the burden from any of the other risk factors examined in the GBD-CRA in 2010. The total attributable disease burden estimates for AAP and HAP in India in 2010 are also

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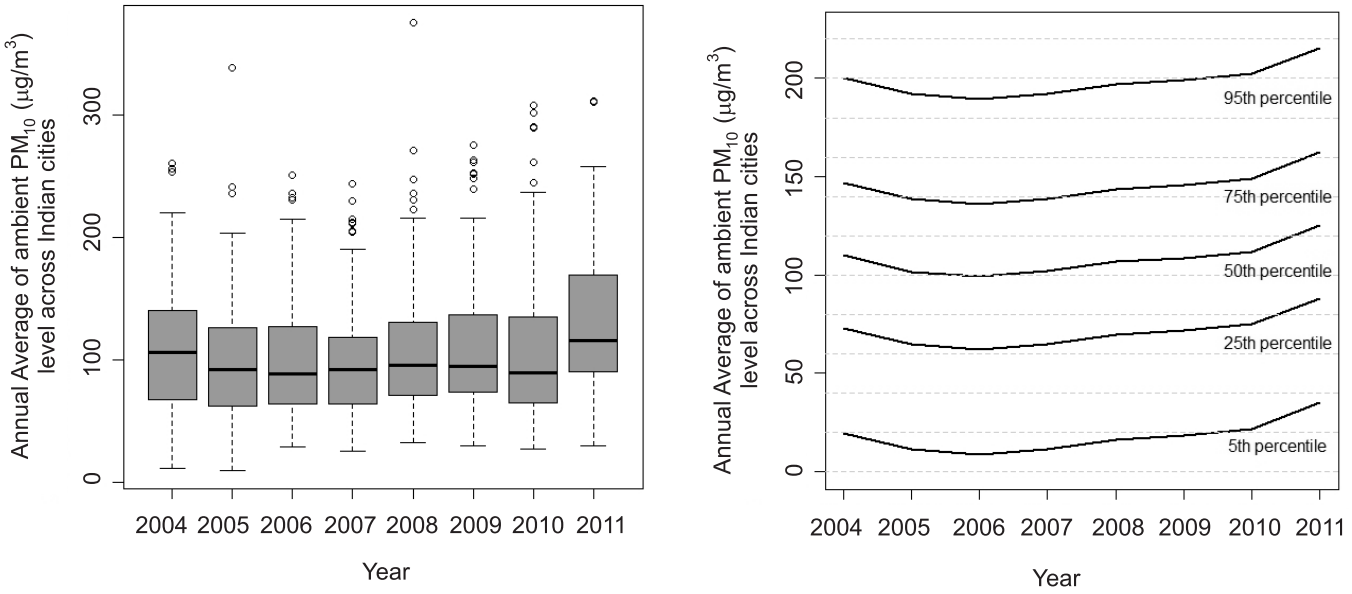

Fig. 1. Distribution of 24-hr ambient concentrations of PM_{10} across Indian cities covered by the National Ambient Air Quality Monitoring Programme (Based on data from The Environmental Data Bank, Central Pollution Control Board (CPCB 2012)).

considerably higher than the previous estimates for these risk factors in GBD-2000 (WHO 2004). The large and steadily increasing burden that now straddles both rural and urban settings in India and thus warrants a closer examination of the nature of the exposure and associated disease profiles. While several previous reviews have focused on exposures to criteria air pollutants and cardio-respiratory health effects, exposures to air toxics and the implications for cancer disease burdens in particular remain poorly described. In this review, we consolidate information from recent publications on ambient and household air pollution exposures, the associated disease burdens and the carcinogenicity of air pollution and to identify priorities for research and policy in India. We also identify specific opportunities for statistical applications to close some key data gaps in this area.

2. AMBIENT AIR POLLUTION EXPOSURES

Ambient air quality information in India is collected primarily by the National Air quality Monitoring Programme (NAMP) administered by the Central Pollution Control Board (CPCB), Ministry of Environment and Forests, Government of India (GoI). Particulate matter (PM) in the air includes particles of less than 10 micrometers in aerodynamic diameter (measured as PM_{10}) which are small enough to enter the human lungs, with the potential of causing serious health problems. Even smaller "fine" particles ($PM_{2.5}$) of less than 2.5 micrometers in diameter can be due to combustion such as in motor vehicles, power plants, residential wood burning, forest fires, agricultural burning, and some industrial processes. Criteria air pollutants monitored under the NAMP include PM_{10} SO_2 and NO_2. However, $PM_{2.5}$ and select air toxics such Benzo (a) Pyrene (BaP) and metals such as arsenic and nickel have only recently been included in the revised National Ambient Air Quality Standards (NAAQS) (CPCB 2009a) and are slowly being added to the routine monitoring being performed under the NAMP. Analysis of routinely collected ambient air quality data that are available in the Environmental Data Bank maintained by CPCB (CPCB 2012) indicates annual average PM_{10} concentrations to exceed the NAAQS at more than half of the 503 locations monitored across the country between 2004 to 2011 (Fig. 1).

The newly revised Indian national standards (CPCB 2009a) for annual average PM_{10} of 60 µg/m^3 are comparable to the Interim Target 1 (IT-1) guideline values for air quality as recommended by WHO (WHO 2006), but are still much higher than the recommended WHO-guideline (WHO-AQG) value of 20 µg/m^3 indicating that residual health impacts may persist even if the national standards were met. Given that the levels not only exceed the national standards but are also reported to be critically high (defined as > 90 µg/m^3 by CPCB, GoI) across most locations, these results from routine monitoring clearly provide unequivocal evidence for substantial health impacts from PM and its constituents in Indian urban locations.

While limited data are available on PM composition within the NAMP data, the reported mass concentrations are likely indicators for exposures to complex mixtures that include air toxics, as suggested by the available information on major sources (Fig. 2).

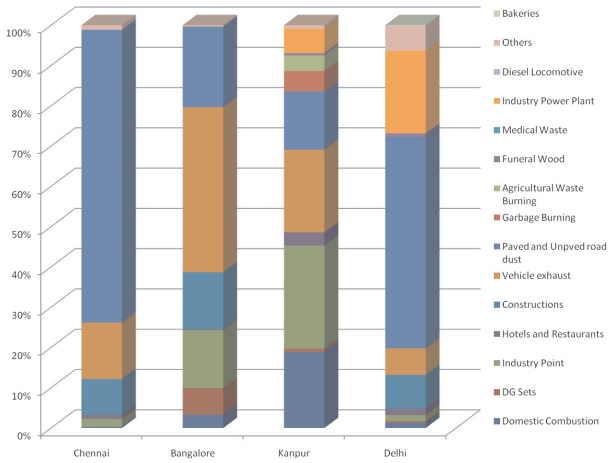

Fig. 2. Sample results for percent source contributions to ambient PM_{10} concentrations from the National Source Apportionment Study conducted by CPCB indicating exposures to complex mixtures. Adapted from (CPCB 2011).

Vehicle exhaust, road and soil dust, secondary particulates, construction activities, oil burning (*e.g.* diesel or heavy oil), biomass burning, coal combustion, kerosene combustion and industries have been identified as dominant sources for criteria air pollutants in a representative set of major cities in a national source apportionment exercise concluded recently (CPCB 2011). High Elemental Carbon (EC) to Organic Carbon (OC) ratio (EC/OC) obtained from samples across cities also indicates significant contributions from vehicular emissions. Further, within the transport sector, the maximum contributions were estimated to come from heavy duty diesel vehicles (40 – 59% of PM_{10} and 43 – 75% of NO_2). Diesel exhaust was labelled as a confirmed human carcinogen (Group I) in a recent assessment by The International Agency for Research on Cancer (IARC 2012a). Given the nature of sources including many that involve diesel combustion, the levels of PM in urban locations are of special concern for health endpoints related to carcinogenicity.

Yet another indication of the extent of air toxics exposures is available through a recent initiative undertaken by the CPCB to identify industrial hotspots using risk assessment criteria defined in terms of the Comprehensive Environmental Pollution Index (CEPI). The CEPI weights the toxicity of the agents, the volume of emissions, the scale of population exposed and the exposure pathways involved. Of special relevance to carcinogenicity is the fact that unlike criteria air pollutant data provided by the NAMP, the CEPI includes weighted contributions from a range of compounds that includes probable carcinogens (USEPA Class 2 and 3 or substances with some systemic toxicity, such as VOC's, PAHs, PCBs), as well as known carcinogens or chemicals with significant systemic or organ system toxicity (such as vinyl chloride, benzene, lead, radionuclide, hexavalent chromium, cadmium, and organophosphates). A CEPI score of 70 is deemed to indicate significant toxic impacts. Thus far 43 industrial clusters across the country have been identified to be critically polluted with primary contributions from chemical industries.

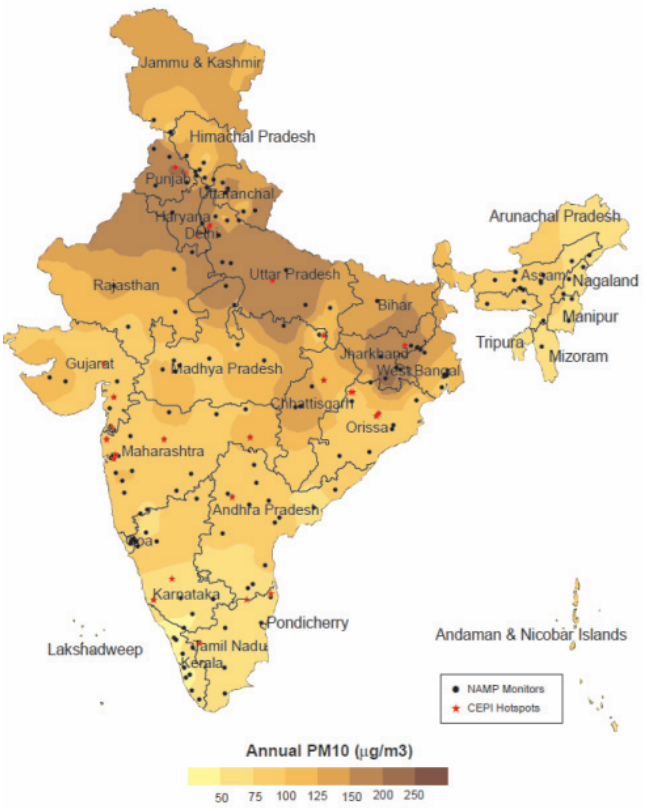

Fig. 3. Inverse distance weighted averages of annual concentrations (as shown by color intensities on the map) of annual PM_{10} recorded across NAMP monitors between 2004-2011 in relation to monitor locations and CEPI hotspots (based on data from The Environmental Data Bank (CPCB 2012) and the CEPI Report (CPCB 2009b)).

Table 1. Reported range concentrations of air toxics in studies conducted across Indian cities.

Reference	Study Area City (State)	Period of monitoring	Pollutant	Averaging Period; Units	Range	Mean
(Rajput and Lakhani 2010)	Agra (Uttar Pradesh)	2005- 2006	Total PAHs bound to PM_{10}	24-30 hrs; ng/m^3	15-392	119
(NEERI 2006)	Delhi (Delhi)	1991-2005	Total PAHs bound to Total Suspended Particulate Matter (TSPM)	24 hrs; ng/m^3		850
	Chennai (Tamil Nadu)					679
	Kanpur (Uttar Pradesh)					660
	Mumbai (Maharashtra)					581
	Kolkata (West Bengal)					969
(Sharma H *et al*. 2008)	Delhi (industrial)	2003	Total PAHs bound to TSPM	24 hrs; ng/m^3		2098
	Delhi (traffic)					1511
	Delhi (residential)					1108
(Sharma *et al*. 2003)	Delhi	2001-2002	Total PAHs bound to TSPM	24 hrs; ng/m^3	35-116	
(Gupta *et al*. 2006); (Vaishali *et al.* 1997)	Nagpur	2005-2006	Total PAHs bound to TSPM	24 hrs; ng/m^3		106
(Kulkarni and Venkataraman 2000)	Mumbai	1996	Total PAHs bound to TSPM	72 hrs; ng/m^3	24.5-38.8	
(Raiyani *et al.* 1993)	Ahmedabad	1993	Total PAHs bound to TSPM	24 hrs; ng/m^3	90-195	
(Herlekar *et al*. 2012)	Mumbai (industrial)	2007-2008	Total PAHs bound to PM_{10}	24 hrs; ng/m^3		247.70 ± 163.19
	Mumbai (residential)					47.84 ± 14.07
(CPCB 2011)	Bangalore	2007	NHMC	24 hrs ppm	8-12	11
	Chennai				0.02-0.18	0.06
	Delhi				0.2-1.7	0.9
	Kanpur				0.06-0.25	0.14
	Mumbai				0.1-24.6	2.3
	Pune				1.3-3.8	2.5
	Bangalore	2007	Benzene	24 hrs μg/m^3	7-237	119
	Chennai				4-17	10
	Delhi				2-11	5
	Kanpur				5-68	27
	Mumbai				-	
	Pune				28-96	57
	Bangalore	2007	1,3, Butadiene	24 hrs ppb	0.5-3.7	2.18
	Chennai				0.5-1.8	1.1
	Delhi				0.2-1.6	0.78
	Kanpur				-	-
	Mumbai				-	-
	Pune				0.4-2.5	1.2
(Chattopadhyay *et al*. 2007)	Kolkata	2004-2005	Benzene	4 hrs, μg/m^3	15.2-40.7	
(Majumdar *et al*. 2011)	Kolkata	2005	BTEX	4 hrs, μg/m^3	Benzene (ind-out): 18.7-58.1, 17.3-47.2	BTEX 42, 69.3, 22.8, 52.1, 21.6
(Masih *et al*. 2012)	Agra, Uttar Pradesh	2006-2007	Total PAHs	24 hrs, ng/m^3	2.29-113.56	
(Singh *et al.* 2013)	Coastal refinery zone, India	2009	BTEX	8 hrs, μg/m^3,	3.69-56.67	

Although the details of ambient concentrations of air toxics may not available in the publications reporting CEPI scores, the description of the procedure used to compute the CEPI score suggests significant emissions and exposures to compounds known to be associated with carcinogenic endpoints at these sites. The annual average concentration recorded across the NAMP monitors and the locations of the CEPI hotspots are illustrated in Fig. 3.

A limited number of ambient air pollution related research studies also report quantitative exposure information pertaining to air toxics. Table 1 provides a description of the range of concentrations/exposures reported in select studies.

3. HOUSEHOLD AIR POLLUTION EXPOSURES

Use of solid fuels (such as biomass and coal) for household energy needs including cooking and heating has been well recognized as a major contributor to air pollution exposures in populations of developing countries (WHO 2006). An estimated 2.8 billion people globally (Bonjour *et al*. 2013) and nearly 74% of India's population continue to rely on such solid fuels (Census 2011). The incomplete combustion of these solid fuels in inefficient cookstoves results in much of the fuel energy to be emitted as potentially toxic pollutants, including particles of varying sizes, CO, NO_2, volatile and semi-volatile organic compounds such as formaldehyde and benzo(a)pyrene (BaP), methylene chloride, and dioxins (Naeher *et al*. 2007). Well over 200 studies that have measured air pollution levels in developing country households, across all WHO regions (Saksena *et al*. 2003), including numerous studies in India, have provided unequivocal evidence of extreme exposures in households using solid cook-fuels, often many fold higher than recommended WHO Air Quality Guidelines (AQGs) (WHO 2006). These studies have also shown the distribution of exposures to be heterogeneous and complex with multiple determinants (such as fuel/stove type, kitchen area ventilation, fuel quantity, age, gender and time-activity profiles influencing spatial and temporal patterns within and between households/individuals across world regions. In communities that heavily rely on solid cookfuels, household emission of pollutants can also be a significant contributor to ambient air pollution. As a result, these communities often suffer from elevated indoor and outdoor air pollution. Table 2 provides a summary of select studies in India that reported results from measurements of household air pollution. These measurements have been largely focused on PM or CO measurements with limited information available on concentrations of air toxics. However, biomass smoke has been shown to contain 17 pollutants designated as priority pollutants by the USEPA because of their toxicity in animal studies, up to 14 carcinogenic compounds, 6 cilia-toxic and mucous coagulating agents, and 4 co-carcinogenic or cancer promoting agents (Naeher *et al*. 2007). Carcinogenic PAHs, methylated PAHs, and nitrogen-containing heterocyclic aromatic compounds have also been reported in the particles emitted from bituminous (smoky) coal combustion (Mumford *et al*. 1987). The PM exposure profiles reported in solid fuel settings thus indicate exposures to a range of air toxics with significant implications for carcinogenicity related health impacts.

Previous global burden of disease (GBD) (WHO 2004) estimates for household air pollution (HAP) from solid cook-fuel use were based on simple indicators of exposure such as type of cook-fuel used, as few epidemiological studies could perform quantitative measurements. Recent progress in GBD methodologies that use integrated–exposure–response (IER) curves (described later), for combustion particles required the development of models to estimate quantitative HAP exposures experienced by large populations. GBD 2010 used results from one of first such modeling exercises that estimated state and national average household concentrations of $PM_{2.5}$ from solid cookfuel use for India, on the basis of quantitative air pollution measurements and information on household level variables from multiple states available through the National Family Health Surveys (Balakrishnan *et al*. 2013). The state and national average $PM_{2.5}$ concentrations related to solid fuel use, estimated using such models are shown in Fig. 4.

Table 2. Reported range of household air pollution concentrations in studies conducted across solid fuel using households of rural/urban districts in India

Reference, Location	Fuel	Stove type	Sampling duration	Levels of pollutants reported
(Aggarwal *et al.* 1982); Gujarat (Urban)	Wood/Dung/ Charcoal	Traditional	Half-an-hour during cooking	TSP: 7203-26147 ($\mu g/m^3$); PAH (BaP): 1270-8248 (ng/m^3)
(Smith *et al*. 1983) Gujarat (Rural)	Wood	Traditional	Meal duration	TSP: 6400 ($\mu g/m^3$); BaP: 4100 (ng/m^3)
		Improved	Meal duration	TSP: 4600 (g/m^3); BaP: 2400 (ng/m^3)
(Ramakrishna 1988) Kerala, Karnataka, Haryana (Rural)	Wood	Traditional	Meal duration	TSP: 3200-3300 (g/m^3) CO: 7-19 (mg/m^3)
		Improved	Meal duration	TSP: 1700-2900 (g/m^3) CO: 5.7-8.9 (mg/m^3)
(Menon 1988) Andhra Pradesh (Rural)	Wood	Traditional	Not specified	TSP: 2000-5000 (g/m^3) CO: 30.9-74.4 (mg/m^3)
(Norboo *et al.* 1991) Jammu & Kashmir State (Rural)	Wood	Traditional	Meal duration	CO: 12-29.8 (mg/m^3)
(Saksena *et al.* 1992) Uttar Pradesh (Rural)	Wood	Traditional	Meal duration	TSP: 5600 ($\mu g/m^3$) ; CO: 21 (mg/m^3)
(Raiyani *et al.* 1993) Gujarat (Urban)	Wood/Dung/ Charcoal	Traditional	Meal duration	TSP: 1190-3470 ($\mu g/m^3$) BaP: 38-410 (ng/m^3)
(Smith *et al*. 1994) Maharashtra (Urban)	Crop Residues/ Wood	Traditional	Meal duration	PM_{10}: 900-1100 ($\mu g/m^3$)
(TERI 1995) Uttar Pradesh (Rural)	Wood	Traditional	Meal duration	PM_5: 850-1460 ($\mu g/m^3$)
(Mandal *et al.* 1996) Delhi (Urban)	Wood	Traditional	4 hours	TSP: 646 ($\mu g/m^3$)
(Balakrishnan *et al.* 2002) Tamil Nadu (Rural)	Wood/Crop residues/ Wood Chips	Traditional	1-2 hours during cooking/24 hours	PM_4: 1307-1535 ($\mu g/m^3$) PM_4: 847-1327 ($\mu g/m^3$)
(Saksena *et al.* 2003) New Delhi (Urban)	Wood	Traditional	Meal duration	PM_5: 1204 ($\mu g/m^3$) CO: 13.7 (mg/m^3)
(Balakrishnan *et al.* 2004) Andhra Pradesh (Rural)	Wood/Dung/ Crop residues	Traditional	22-24 hours	PM_4 (Wood): 431-467 ($\mu g/m^3$) PM_4 (Dung): 297-666 ($\mu g/m^3$) PM_4 (Crop Residues): 215-357 ($\mu g/m^3$)

(Bhargava *et al*. 2004) Uttar Pradesh (Rural)	Wood/Dung	Traditional	1-hour during cooking	BaP: 0.5-1.86 (%)
(Sinha *et al.* 2006) Gujarat (Rural)	Wood/Dung	Not Specified	45 min to 1-hour during cooking	Benzene: 45-114.3 ($\mu g/m^3$) Toluene: 2-8.5 ($\mu g/m^3$)
(Smith *et al*. 2007) Maharashtra, Madhya Pradesh (Rural/Peri-urban)	Wood	Traditional	48 hours	$PM_{2.5}$: 520-1250 ($\mu g/m^3$) CO: 9.02-12.4 (mg/m^3)
	Wood	Improved	48 hours	$PM_{2.5}$: 330-940 ($\mu g/m^3$) CO: 6.17-7.6 (mg/m^3)
(Massey *et al*. 2009) Uttar Pradesh (Peri-urban)	Wood	Traditional	24 hours	$PM_{2.5}$: 173-178 ($\mu g/m^3$) PM_1: 133-153 ($\mu g/m^3$) $PM_{0.5}$: 73-96 ($\mu g/m^3$) $PM_{0.25}$: 6-8 ($\mu g/m^3$)
(Balakrishnan *et al*. 2013) Tamil Nadu, Madhya Pradesh, Uttaranchal, West Bengal (Rural)	Wood/Dung	Traditional	22-24 hours	$PM_{2.5}$: 157-741 ($\mu g/m^3$)

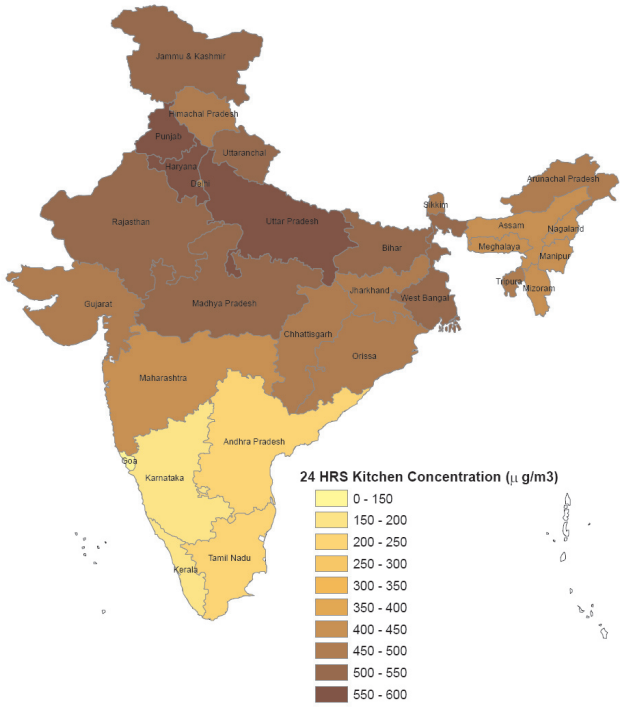

Fig. 4. State level household concentrations of $PM_{2.5}$ from solid fuel use, as shown by color intensities on the map (Adapted from Balakrishnan *et al.* 2013).

4. DISEASE BURDEN PROFILES IN RELATION TO AMBIENT AND HOUSEHOLD AIR POLLUTION

The basic approach used in burden of disease assessments and the comparative risk assessment has been to calculate the proportion of deaths or disease burden due to specific risk factors (*e.g.* hypertension caused by increased salt intake) while holding other independent factors unchanged, and determine the total burden from that contributed by each risk factor. In the Comparative Risk Assessment (CRA) done as part of the Global Burden of Disease Project (GBD-2010), the global and regional burdens were estimated for more than 60 other risk factors (Lim *et al*. 2012). As described in Lim *et al.* (2012) this involved (1) selection of risk–outcome pairs to be included in the analysis based on criteria about causal associations; (2) estimation of distributions of exposure to each risk factor in the population; (3) estimation of etiological effect sizes, often relative risk per unit of exposure for each risk–outcome pair; (4) choice of an alternative (counterfactual) exposure distribution to which the current exposure distribution is compared, also termed the theoretical-minimum-risk exposure distribution (TMRED) and (5) computation of burden attributable to each risk factor, including uncertainty from all sources.

Since for many disease endpoints, exposure – response information has been available mostly in relation to ambient $PM_{2.5}$ exposures and/or smoking studies in developed countries (with only a few studies populating the evidence base for household air pollution), the CRA-GBD 2010 project relied on the use of Integrated Exposure-Response functions (IERs) to

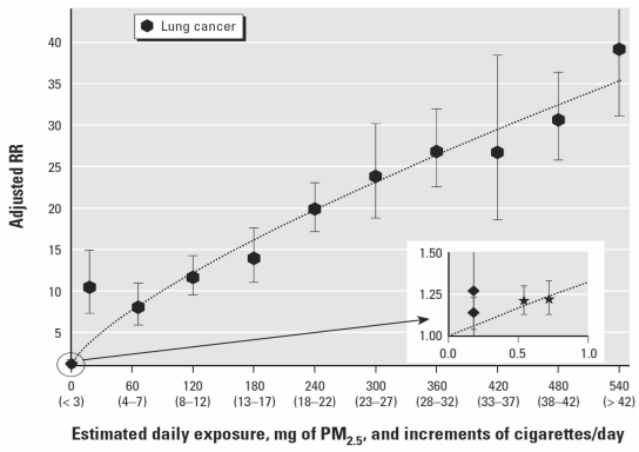

Fig. 5. An Integrated Exposure-Response (IER) Curve (reproduced with permission from Environmental Health Perspectives – figure from (Pope *et al.* 2011). It shows that exposure-response functions for lung cancer with adjusted RRs (with 95% confidence intervals) of lung cancer mortality plotted over estimated daily exposure of $PM_{2.5}$ (milligrams) and increments of cigarette smoking relative to never smokers). Diamonds represent risk estimates for $PM_{2.5}$ from air pollution; stars represent comparable pooled RR estimates associated with second hand smoke (SHS). The dotted lines represent the nonlinear power function fit through the origin and the estimates (including active smoking, SHS, ambient $PM_{2.5}$). The fitted function, $RR = 1 + 0.3195(dose)^{0.7433}$, represents a monotonic, nearly linear exposure–response relationship with fairly constant marginal increases in RR with increasing exposure. Estimated doses from different increments of active smoking are dramatically larger than estimated doses from ambient air pollution or SHS; therefore, associations at lower exposure levels (due to ambient air pollution and SHS) are shown as inset with a magnified scale.

generate consistent risk estimates across the four major categories of combustion particle exposures. This included, household air pollution (HAP), ambient air pollution (AAP), active tobacco smoking (ATS) and second hand tobacco smoke (SHS) and IERs were generated for disease endpoints concerning ischaemic heart disease (IHD), stroke, lung cancer, and child acute lower respiratory infections (ALRI) (Burnett *et al*. 2014; Smith *et al*. 2014). The IERS were based on an exponential decay model with a power of concentration (that did not constrain the relationship to be linear) and allowed the evidence from epidemiological studies concerning any of the categories of combustion particles to be pooled using the daily dose of $PM_{2.5}$ as the primary exposure metric, thereby straddling across some 3 orders of magnitude in exposure levels. It also allowed the HAP risk estimates to be made for diseases known to be caused by ATS, SHS, and AAP, but for which there are no or minimal HAP studies by interpolating between ATS results at higher exposures and SHS/AAP results at lower exposures. The IER for lung cancer used in GBD-CRA 2010 has recently become available (Burnett *et al*. 2014; Smith *et al*. 2014). Fig. 5, as reproduced from an earlier publication (Pope *et al*. 2011), which provided the basis for the GBD-CRA 2010 IERs, illustrates the form of IERs across combustion particle sources for lung cancer. The HAP exposure model used in GBD 2010 (based on measurements and modeling results from India), estimated daily average $PM_{2.5}$ exposures of 285 µg/m^3, 337 µg/m^3 and 204 µg/m^3 for children, women and men respectively (Balakrishnan *et al*. 2013), (Smith *et al*. 2014 (forthcoming)). The global model used for AAP exposures (that for the first time included ambient air quality of rural areas) estimated a 2010 population-weighted annual mean $PM_{2.5}$ of 27.2 µg/m^3 in India, up 6% from 1990, with a distribution that includes much higher levels in urban and some rural areas (Brauer *et al*. 2012).

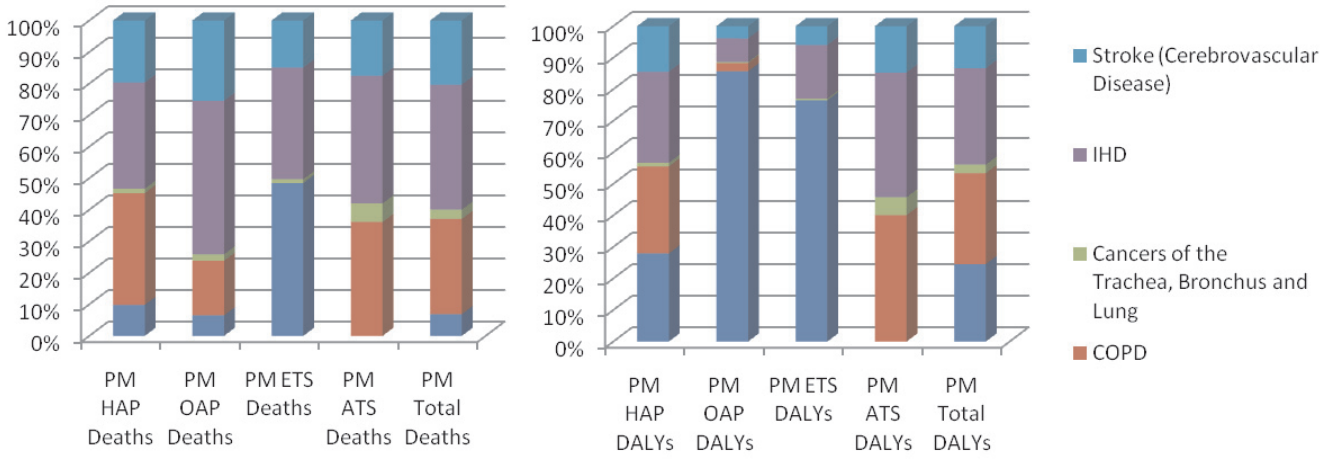

Fig. 6. Percent contributions to burden of disease (Deaths and DALYs) from major categories of particulate matter in India (Based on data from (IHME 2013)).

Table 3. Results from GBD 2010 for disease burden attributable to particulate matter in India (based on data from (IHME 2013)). PM-Particulate Matter; DALYs-Disability adjusted Life Years; HAP-Household Air Pollution; AAP-Ambient Air Pollution; ETS-Environmental Tobacco Smoke; ATS-Active Tobacco Smoking.

Deaths	**PM HAP Deaths**	**PM AAP Deaths**	**PM ETS Deaths**	**PM ATS Deaths**	**PM Total Deaths**
Lower Respiratory Infections <5	100383	40732	30048	0	171163
COPD	362429	108792	0	282860	754080
Cancers of the Trachea, Bronchus and Lung	14506	12729	757	46356	74347
IHD	343664	305266	21910	317011	987851
Stroke (Cerebrovascular Disease)	201276	159954	9270	137234	507734
Total	1022258	627473	61985	783461	**2495175**
DALYs	**PM HAP DALYs**	**PM AAP DALYs**	**PM ETS DALYs**	**PM ATS DALYs**	**PM Total DALYs**
Lower Respiratory Infections < 5	8638607	3503152	2586490	0	14728249
COPD	8560004	108792	0	8635069	17303866
Cancers of the Trachea, Bronchus and Lung	367265	12729	17034	1226224	1623251
IHD	8930148	305266	573688	8503157	18312259
Stroke (Cerebrovascular Disease)	4485358	159954	203001	3171893	8020206
Total	30981382	4089893	3380213	21536343	**59987831**

With the availability of quantitative exposure estimates and IERs, the HAP and AAP working groups were able to use the same TMRED (counterfactual) of approximately ~7 μg/m^3 annual mean $PM_{2.5}$ across both the risk factors to estimate the total risk range for burden calculations. This counterfactual chosen by the AAP CRA working group in GBD 2010 represents approximate levels in the cleanest cities and is roughly equivalent to what can be achieved by vented cooking with gas fuels. Estimates of burden of disease in terms of deaths and DALYs in India attributable to major sources of combustion particles and major categories of disease end points are summarized in Table 3 and Fig. 6. These estimates underscore the inter-related contribution from HAP and AAP exposures to the burden of disease in India.

5. SUMMARIES OF IARC ASSESSMENTS ON CARCINOGENICITY OF AMBIENT AND HOUSEHOLD AIR POLLUTION

In October 2006, the Expert Working Group for International Agency for Research on Cancer (IARC) Monograph Vol. 95 (IARC 2010) evaluated the carcinogenicity of the household use of solid fuels and high-temperature frying. The report was updated with information on indoor emissions from household combustion of coal in 2012 (IARC 2012b). The evaluation concluded with indoor emissions from household combustion of coal classified as a known human carcinogen (Group 1) and emissions from the combustion of biomass fuels as a probable human carcinogen (Group 2A) (IARC 2010). Cancers that have been associated with IAP include cancers of the lung, upper aero-digestive tract, and cervix, among which lung cancers have been the most well studied and well characterized (IARC 2010). Although, coal accounts for less than 5% of total solid fuel use and is limited to a few north-eastern states in India, it may still pose risks for populations in specific districts and hence we summarise the information pertaining to both coal and biomass in relation to carcinogenicity.

IARC based its determination that household exposure to coal combustion by-products causes lung cancer in humans principally on strong epidemiological studies conducted in China that were able to adequately address tobacco use and other relevant factors as

confounders. The concentration of polycyclic aromatic hydrocarbons (PAHs) in emissions from indoor coal combustion were found to be associated with lung cancer, and both the cytochrome P450 and aldo-keto-reductase pathways, as well as polymorphisms in DNA repair and phase II pathways, have been shown to modify the association (IARC 2010). Signaling pathways implicated in tumor growth and metastasis such as those involving expression of the toll-like receptor (TLR) and receptors for advanced glycation end-products (RAGE) were found to be influenced by air pollution (Shoenfelt *et al.* 2009) (Reynolds *et al.* 2011).

In experiments with animals, inhalation of emissions from coal, burned under conditions similar to those in epidemiological studies, increased the incidence of various types of malignant lung tumours, squamous-cell carcinomas and adenocarcinomas in male and female Kunming mice and Wistar rats. Based on consistent evidence of carcinogenicity in human and experimental animal studies and strong evidence of mutagenicity, IAP from combustion of coal was thus classified as a confirmed human carcinogen (Group1).

In the same assessment, significantly fewer studies of lung cancer in association with the combustion of biomass were found available and the available studies did not evaluate associations according to the specific type of fuel used, thus making comparisons difficult. Although, exposure to 1,3-butadiene, benzene, formaldehyde, PAHs, and acetaldehyde as measured from air samples was highly correlated with exposure to indoor wood burning for heating homes (these agents themselves being individually known to be mutagenic) and changes in expression and phosphorylation of P53 in lung cancer patients who were exposed to wood smoke were noted, because of limited evidence from human and experimental animal studies, IAP from biomass combustion was labeled as a possible carcinogen (Group 2A).

In 2013, The IARC Working Group (Monograph Volume 109) unanimously classified outdoor air pollution and particulate matter from outdoor air pollution as carcinogenic to humans (IARC Group 1), based on sufficient evidence of carcinogenicity in humans and experimental animals and strong mechanistic evidence. An increased risk of lung cancer was consistently observed in cohort and case-control studies including millions of people and many thousands of lung cancer cases from Europe, North America, and Asia with many studies adjusting for confounding by smoking. Evidence regarding the carcinogenicity of outdoor air pollution in experimental animals came from prior work concerning diesel engine exhaust and of emissions from the combustion of coal and wood (IARC 2010, 2012a). All of these agents that can be present in outdoor air were shown previously to cause benign and malignant lung tumors in mice or rats. Several studies in which animals were exposed to traffic related air pollution or were injected subcutaneously with organic solvent extracted material from particles collected from outdoor air pollution, showed increased incidence of injection-site tumors, including fibrosarcomas, and pulmonary adenoma or adenocarcinoma. In particular, association between traffic pollution and leukemias has been studied at length. Recently, weak associations were found to exist between early exposure to traffic pollution and several childhood cancers (Heck *et al*. 2014). Finally, exposure to polluted outdoor air in occupational settings or urban and industrial areas was also associated with changes in the expression of genes involved in DNA damage and repair, inflammation, immune and oxidative stress response, as well as altered telomere length and epigenetic effects such as DNA methylation. Thus, based on strong evidence of carcinogenicity from human and experimental animal studies and mutagenicity, ambient air pollution was classified as a confirmed human carcinogen (Loomis *et al*. 2013).

Several recent studies documenting cyto-pathological changes in response to exposure to ambient and household air pollution are now becoming available to add to the evidence base for carcinogenicity of air pollution in India. Traffic policemen and street hawkers of the city occupationally exposed to vehicular emission reported elevated levels of neutrophils and eosinophils in the sputum samples (Lahiri *et al*. 2006). These findings suggest persistent inflammation in response to air pollution-induced oxidative stress. Cooking with biomass has also been reported to alter sputum cytology (increasing counts of neutrophils, lymphocytes, eosinophils and alveolar macrophages (AM)) increase airway inflammation (higher sputum levels of IL–6, –8 and TNF–α) and oxidative stress (enhanced ROS generation and depletion of SOD activity) that might result in further amplification of the tissue damaging cascade in women chronically exposed to biomass smoke (Banerjee *et al*. 2012; Dutta *et al*. 2013). Prevalence of mucus plugs, goblet cell hyperplasia, and nuclear anomaly of columnar epithelial cells was found to be higher in urban subjects exposed to high levels of urban air pollution in Kolkata as

compared to controls drawn from relatively cleaner peri-urban zones (Ray and Lahiri 2010). However, as compared to these controls, Papanicolau-stained sputum samples of biomass users showed 3-times higher prevalence of metaplasia and 7-times higher prevalence of dysplasia in airway epithelial cells (AEC) (Roychoudhury *et al*. 2012). Siderophages (iron-containing macrophages in sputum indicative of either past intrathoracic bleeding or extravasations of red blood cells into the alveoli due to a sluggish blood flow) were abundant in sputum of the residents of Delhi and Kolkata implying microscopic hemorrhage in the lungs (Roy *et al*. 2001). Elastin is a fibrous protein present in the elastic tissues of lung. Elevated levels of elastase (a proteolytic enzyme found in the lysosomes of neutrophils and alveolar macrophages capable of destroying elastin and causing alveolar degradation) were reported in urban populations of Delhi and Kolkata with some of the highest levels recorded in automobile service station workers, traffic policemen and roadside hawkers (Basu *et al*. 2001). Cumulative exposure to biomass smoke has also been shown to increase oxidative stress-mediated activation of Akt signal transduction potentially increasing the risk of lung cancer (Roychoudhury *et al*. 2012). Currently, the biological evidence of activated carcinogenic mechanisms associated with air pollution is substantial and growing, and is corroborated by studies conducted in the Indian context.

6. PRIORITIES FOR ACTION

As may be seen from the preceding account describing the magnitude and extent of air pollution exposures across rural and urban environments in India, the recent evidence on the burden of disease attributable to air pollution exposures and the comprehensive evidence of carcinogenicity (provided by the IARC assessments), it is clear that there is an imminent need to identify certain priorities for action. We describe below some key areas for such prioritization efforts.

6.1 Generating Nationally Representative and Systematic Data on Exposure Profiles for Air Toxics Across Urban and Rural Populations

The data on criteria air pollutants in the country are quite robust as nationally representative datasets become more widely available. However, information on air toxics is still too sparse and is not collected across a representative range of settings to allow estimation of exposures to air toxics. Without a critical mass of such data, to conduct precise modeling exercises is difficult. Further, given that the air toxics are an important part of both vehicular and solid fuel emissions and multiple agents in these emissions, and since the mixtures themselves have been evaluated to be carcinogenic, detailed information on the composition and concentration of air toxics is critical for assessment of risks in exposed populations. Wider availability of sampling and analysis infra-structure and broader validation of field protocols across typical rural/urban settings is critical for generation of such data. A network of accredited laboratories would need to be engaged routinely to allow the generation of such information in the near-term with adequate sampling and design strategies for country-wide coverage. Adequate attention must be paid for development of human resources in the form of more trained personnel in areas of Statistics, Epidemiology, Computer Science and Big Data Analytics with specialization in emerging topics such as environmental pollution, urban planning, energy and waste management, etc.

6.2 Augmenting Efforts to Estimate Emission/ Exposure Profiles for Diesel Exhausts

There is currently a large fleet of existing diesel vehicles with complex engine-fuel mixes in operation that has compounded the problem of expanding vehicular fleets in India. With the recent evaluation by IARC on the carcinogenicity of diesel exhaust, there is an imminent need for profiling population exposures specifically to diesel exhaust. Detailed source apportionment and/or emissions inventory exercises would also allow refinements in the existing modeling methods that rely on chemical transport (such as the WRF-Chem) used now to generate long-range exposure profiles for air toxics.

6.3 Creating Geo-coded Datasets from Available Cancer Registries

An increasing base of information is becoming available through the cancer case registries maintained by individual tertiary care facilities in addition to records available through National Cancer Institutes and The National Cancer Registry (maintained by the Indian Council of Medical Research). While city or district level estimates of incidence are available across many locations, detailed geo-coding of residences reporting cancer cases has not been attempted. Such spatial

mapping combined with temporal surveillance data would be much more powerful for analysis of exposures in terms of source contributions. A modest level of seed grants to schools could enable institutions maintaining such registries to efficiently generate such data through student efforts. Once routine geo-coding is enabled, integration with air quality datasets can be relatively easily accomplished on GIS platforms. Specific training and capacity building efforts on GIS for college level graduates would allow the mapping to be undertaken routinely and also motivate them to conduct research on such problems.

6.4 Initiating the Conduct of a Co-ordinated Set of Case-control Studies on Air Pollution and Cancer across Rural and Urban Populations in India

The available base of epidemiological studies on air pollution and cancer in India is rather small with most studies plagued by inadequate adjustment for confounding or exposure misclassification. The lack of routinely accessible cancer registry information has been a major impediment to be able to design observational studies that can use routinely collected data. Given the challenges of mounting cohort studies or randomized control trials, on account of the low prevalence and long latency, a co-ordinated set of case-control studies that straddle across rural and urban exposure situations would be enormously helpful in identifying exposure and impact hotspots. Wherever feasible, air pollution exposures can be added as an additional variable in on-going long term studies concerning cancer surveillance, prevalence or management.

Adding to the evidence base from epidemiological studies concerning air toxics and cancer in India can be valuable in closing the gap between risk estimates from ambient and household air pollution exposures. As may be seen in Fig. 5, there is considerable uncertainty for lung cancer risk estimates in the range < 0.5 mg/m^3 of daily dose of $PM_{2.5}$ (*i.e*. 500 μg/m^3), the range of relevance for ambient and household air pollution in India. There is limited evidence from epidemiological studies on cancers for many other organ systems and thus substantial information from a range of exposure settings are needed to establish accurate modeling of the exposure-response relationships on firmer grounds. Indeed, given the new strength of evidence from IERs for comparability of smoking and air pollution related endpoints, it may be strategic to look for smoking related cancers as the target list. Recent consolidation of the evidence (Smith *et al*. 2014) suggests that cervical, naso-pharyngeal cancers and leukemia may be ripe to attempt such an analysis in the near term.

Further, given the complexity of conducting epidemiological studies on cancer, evidence for mutagenicity can be efficiently collected by standardizing in-vitro protocols for testing concentrated air pollutant mixtures from urban or rural hotspots. This would allow recognition of signatures for carcinogenicity as populations face risk from complex mixtures of unknown composition from new sources of emissions in their specific communities. Focusing on biomarker studies concerning exposure, early detection of biological effects and susceptibility would afford an improved understanding of the range of health impacts. With infra-structure for genome-wide omic studies becoming more widely available in the country, the creation of a network of necessary bio-repositories and systematic analysis may allow a detailed understanding of disease (cancer) susceptibility, and thus afford opportunities for targeted intervention. Unprecedented rates of industrialization and development, in conjunction with rapid urbanization, migration and changing lifestyles, may need appropriate designs for spatio-temporal, longitudinal or prospective investigation of potential health outcomes of different forms of air pollution exposures, for instance, *in utero* and in early childhood. Further insights can be derived from multisectoral data resources such as the national census – *e.g*., occupation, socio-economic disparities, etc., which may either affect or be affected by the health outcomes of air pollution. Finally, studies in the emerging field of epigenetic epidemiology could shed light on both harmful as well as protective mechanisms in exposed populations brought about by possible gene-environment and gene-diet interactions due to exposures that are specific to different geographic and socio-economic contexts present in India, which may lead to further research on remedial strategies.

6.5 Including Air Toxics Exposure and Cancer Surveillance as Part of Future Air Pollution Intervention Programs

Numerous efforts are underway to design and implement air quality interventions in the urban and rural settings. Newer emissions control norms for vehicles and industries, more stringent auto-fuel

policies, zoning restrictions, construction of green landscapes, and new electricity-run metro-railways are expected to change exposure profiles across cities as well as over time. Similarly a major effort to provide cleaner cook-stoves and or cleaner fuels is being proposed under initiatives by the Ministry of New and Renewable Energy to reduce health, environment and quality of life impacts associated with solid fuel use among rural populations. Maintaining national-scale databases that capture changes associated with such environmental experiments would afford a unique opportunity to test shifts in disease profiles in response to exposure reductions. Such observations would strengthen both the scientific evidence as well as add more evidence for policy based actions. Creation of effective templates and infra-structure for routine surveillance using newer developments in bio-markers of exposure and early biological effect would play a key role to take advantage of such opportunities.

6.6 Harnessing Big Data in Environmental Studies

While large datasets on air pollution are being generated continuously, sophisticated statistical methodology, such as hierarchical Bayesian models, can be useful for combining evidence across multiple locations while quantifying sources of heterogeneity and identifying effect modification. In addition, new methodologies and collaborations may be developed for Big Data research for fusion and mining of high-volume multi-sectoral datasets including pollution monitoring and related data streams, public health and hospital event records, satellite and remote sensor data, geo-referenced dynamic data on traffic and other sources of emissions, crowd-sourced real-time data (such as using mobile phones and specialized smart phone apps), the increasingly resourceful social networks, etc., for timely discovery, as well as prediction, of the emerging, inter-connected patterns of health and disease.

7. CONCLUSION

Air pollution continues to be a major public health concern in India with burdens from both communicable and non-communicable diseases including cancer, affecting all age groups in our communities. While focusing on criteria air pollutants and acute respiratory end points in major metropolitan cities may provide some insights on the extent of the health impacts of air pollution, this may be just reflect the proverbial "tip of the iceberg". There is a tremendous need for better understanding of the landscape of exposure and attributable disease distributions both in India and elsewhere, and accurate statistical modeling and analysis of data will play a key role here. Our review has provided a detailed justification of the need for a multi-disciplinary understanding of the challenges from air toxics and carcinogenicity of air pollution. It is hoped that some of the latest information provided here will serve to add impetus to on-going as well as forthcoming efforts directed at reducing the massive public health burden from air pollution in rural and urban India.

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REFERENCES

Aggarwal, A.L., Raiyani, C.V., Patel, P.D., Shah, P.G. and Chatterjee, S.K. (1982). Assessment of exposure to benzo(a)pyrene in air for various population groups in Ahmedabad. *Atmos. Environ.,* **16,** 867-870.

Balakrishnan, K., Sankar, S., Parikh, J., Padmavathi, R., Srividya, K. and Venugopal, V., *et al*. (2002). Daily average exposures to respirable particulate matter from combustion of biomass fuels in rural households of southern India. *Environ. Health Perspect.,* **110,** 1069-1075.

Balakrishnan, K., Sambandam, S., Ramaswamy, P., Mehta, S. and Smith, K.R. (2004). Exposure assessment for respirable particulates associated with household fuel use in rural districts of Andhra Pradesh, India. *J. Exposure Sci. Environ. Epidem.,* **14,** S14-S25.

Balakrishnan, K., Ghosh, S., Ganguli, B., Sambandam, S., Bruce, N. and Barnes, D.F. *et al*. (2013). State and national household concentrations of $pm_{2.5}$ from solid cookfuel use: Results from measurements and modeling in India for estimation of the global burden of disease. *Environ. Health,* **12,** 77.

Banerjee, A., Mondal, N., Das, D. and Ray, M. (2012). Neutrophilic inflammatory response and oxidative stress in premenopausal women chronically exposed to indoor air pollution from biomass burning. *Inflammation,* **35**, 671-683.

Basu, C., Ray, M. and Lahiri, T. (2001). Traffic-related air pollution in calcutta associated with increased respiratory symptoms and impaired alveolar macrophage activity. *J. Environ. Poll.,* **8**, 187-195.

Bhargava, A., Khanna, R.N., Bhargava, S.K. and Kumar, S. (2004). Exposure risk to carcinogenic pahs in indoor-air during biomass combustion whilst cooking in rural India. *Atmos. Environ.,* **38,** 4761-4767.

Bonjour, S, Adair-Rohani, H, Wolf, J, Bruce, N.G., Mehta, S. and Pruss-Ustun, A. *et al*. (2013). Solid fuel use for household cooking: Country and regional estimates for 1980-2010. *Environ. Health Perspect.,* **121,** 784-790.

Brauer, M., Amann, M., Burnett, R.T., Cohen, A., Dentener, F. and Ezzati, M. *et al*. (2012). Exposure assessment for estimation of the global burden of disease attributable to outdoor air pollution. *Environ. Sci. Tech.,* **46,** 652-660.

Burnett, R.T., Pope, C.A., 3rd, Ezzati, M., Olives, C., Lim, S.S. and Mehta, S. *et al*. (2014). An integrated risk function for estimating the global burden of disease attributable to ambient fine particulate matter exposure. *Environ. Health Perspect.,* **122,** 397-403.

Chattopadhyay, B.P., Mukherjee, A., Mukherjee, K. and Roy Chowdhury, A.L. (2007). Exposure to vehicular pollution and assessment of respiratory function in urban inhabitants. *Lung,* **185,** 263.

C.P.C.B. (2009a). National ambient air quality standards. New Delhi.

C.P.C.B. (2009b). Comprehensive environmental assessment of industrial clusters. (Ecological Impact Assessment Series). Central Pollution Control Board, New Delhi.

C.P.C.B. (2011). Air quality monitoring, emission inventory and source apportionment study for Indian cities. New Delhi , India.

C.P.C.B. (2012). National ambient air quality staus and trends in India 2010 New Delhi, India.

Dutta, A., Roychoudhury, S., Chowdhury, S. and Ray, M. (2013). Changes in sputum cytology, airway inflammation and oxidative stress due to chronic inhalation of biomass smoke during cooking in premenopausal rural Indian women. *Int. J. Hyg. Environ. Health,* **216,** 301-308.

Gupta, D., Nag, S., Mukhopadhyay, U.K. (2006). Characterisation of pm 10, pm 2.5 and benzene soluble organic fraction of particulate matter in an urban area of Kolkata, India. *Environ. Monit. Assess.*, **115,** 205-222.

Herlekar, M., Elizabeth, J.A., Kumar, R., Gupta, I. (2102). Chemical speciation and source assignment of particulate (pm_{10}) phase molecular markers in Mumbai. *Aerosol. Air Quality Res.,* **12,** 1247-1260.

I.A.R.C. (2010). Household use of solid fuels and high-temperature frying. International Agency for Research on Cancer, World Health Organisation, Lyon, France.

I.A.R.C. (2012a). Diesel and gasoline engine exhausts and some nitroarenes. International Agency for Research On Cancer, World Health Organisation, Lyon, France.

I.A.R.C. (2012b). A review of human carcinogens: Personal habits and indoor combustions. International Agency for Research on Cancer, Lyon.

I.H.M.E. (2013). The global burden of disease: Generating evidence, guiding policy-South Asia regional edition. Institute for Health Metrics and Evaluation.

Kulkarni, P. and Venkataraman, C. (2000). Atmospheric polycyclic aromatic hydrocarbons in Mumbai, India. *Atmos. Environ.,* **34,** 2785-2790.

Lahiri, T, Ray, M. and Lahiri, P. (2006). Health effects of air pollution in Delhi. Central Pollution Control Board, New Delhi.

Lim, S.S., Vos, T., Flaxman, A.D., Danaei, G., Shibuya, K. and Adair-Rohani, H. *et al.* (2012). A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: A systematic analysis for the global burden of disease study 2010. Lancet 380, 2224-2260.

Loomis, D., Grosse, Y., Lauby-Secretan, B., Ghissassi, F.E., Bouvard, V. and Benbrahim-Tallaa, L. *et al*. (2013). The carcinogenicity of outdoor air pollution. *The Lancet Oncology*, **14,** 1262-1263.

Majumdar, D., Mukherjeea, A. and Sen, S. (2011). Btex in ambient air of a metropolitan city. *J. Environ. Protect.,* **2,** 11-20.

Mandal, A.K., Kishore, J. and Rangesamy, S. (1996). Pah concentration in Indian kitchen and its relation to breast carcinoma. *Proceedings of the Proceedings of the 7th International Conference on Indoor Air Quality and Climate, Nagoya, Japan,* **2,** 349-351.

Masih, J., Singhvi, R., Kumar, K., Jain, V.K. and Taneja, A. (2012). Seasonal variation and sources of polycyclic aromatic hydrocarbons (pahs) in indoor and outdoor air in a semi arid tract of northern India. *Aerosol. Air Qual. Res.,* **12,** 515-525.

Massey, D., Masih, J., Kulshrestha, A., Habil, M. and Taneja, A. (2009). Indoor/outdoor relationship of fine particles less than 2.5 mm ($pm_{2.5}$) in residential homes locations in central Indian region. *Build. Environ.,* **44,** 2037-2045.

Menon, P. (1988). Indoor spatial monitoring of combustion generated pollutants by Indian cookstoves. University of Hawaii, Honolulu, USA.

Mumford, J.L., He, X.Z., Chapman, R.S., Cao, S.R., Harris, D.B. and Li, X.M. *et al*. (1987). Lung cancer and indoor air pollution in Xuan Wei, China. *Science*, **235,** 217-220.

Naeher, L.P., Brauer, M., Lipsett, M., Zelikoff, J.T., Simpson, C.D. and Koenig, J.Q. *et al*. (2007). Woodsmoke health effects: A review. *Inhal. Toxicol.,* **19,** 67-106.

N.E.E.R.I. (2006). Ambient air quality status for ten cities of India (1991-2005). National Environmental Engineering Research Institute, Nagpur.

Norboo, T., Yahya, M., Bruce, N.G., Heady, J.A., Ball, K.P. (1991). Domestic pollution and respiratory illness in a himalayan village. *Int. J. Epidemiol.,* **20,** 749-757.

Pope, C.A., 3rd, Burnett, R.T., Turner, M.C., Cohen, A., Krewski, D. and Jerrett, M. *et al*. (2011). Lung cancer and cardiovascular disease mortality associated with ambient air pollution and cigarette smoke: Shape of the exposure-response relationships. *Environ. Health Perspect.,* **119,** 1616-1621.

Raiyani, C.V., Jani, J.P., Desai, N.M., Shaha, J.A. and Kashyap, S.K. (1993). Levels of polycyclic aromatic hydrocarbons in ambient environment of Ahmedabad. *Ind. J. Environ. Protect.,* **13,** 206-216.

Rajput, A. and Lakhani, N. (2010). Measurements of polycyclic aromatic hydrocarbons in an urban atmosphere of Agra, India. *Atmosfera,* **23**, 165-183.

Ramakrishna, J. (1988). Patterns of domestic air pollution in rural India. University of Hawaii, Honolulu, USA.

Ray, M. and Lahiri, T. (2010). *Air Pollution: Health and Environmental Impacts*. CRC Press, Taylor and Francis Group, 165-201.

Roy, S., Roy, M., Basu, C., Lahiri, P. and Lahiri, T. (2001). Abundance of siderophages in sputum. Indicator of an adverse lung reaction to air pollution. *Acta. Cytol.,* **45,** 958-964.

Roychoudhury, S., Mondal, N., Mukherjee, S., Dutta, A., Siddique, S. and Ray, M. (2012). Activation of protein kinase b (pkb/akt) and risk of lung cancer among rural women in India who cook with biomass fuel. *Toxicol. Appl. Pharmacol.*, **259,** 45-53.

Saksena, S., Prasad, R., Pal, R.C. and Joshi, V. (1992). Pattern of daily exposure to tsp and co in the Garhwal Himalaya. *Atmos. Environ.*, **26A,** 2125-2134.

Saksena S, Singh PB, Prasad RK, Prasad R, Malhotra P, Joshi V, *et al*. 2003. Exposure of infants to outdoor and indoor air pollution in low-income urban areas - a case study of Delhi. *J. Expo. Anal. Environ. Epidemiol.,* **13,** 219-230.

Saksena S, Thompson L, Smith KR. 2003. The indoor air pollution and exposure database: Household pollution levels in developing countries. Part 7/1/2003. The World Health Organisation, University of California, Berkeley.

Sharma, H., Jain, V. and Khan, Z. (2008). Atmospheric polycyclic aromatic hydrocarbons in urban air of Delhi during 2003. *Environ. MonitAssess.,* **147,** 43-55.

Sharma, N., Sawant, A., Uma, R. and Cocker, D. (2003). Preliminary chemical characterization of particle-phase organic compounds in New Delhi, India. **37,** 4317-4323.

Singh, R.K., Ramteke, D.S., Juneja, H.D. and Pandya, G.H. (2013). Ambient air quality monitoring in terms of volatile organic compounds (vocs) occupational health exposure at petroleum refinery. *Intt. J. Environ. Protect.,* **3,** 22-32.

Sinha, S.N., Kulkarni, P.K., Shah, S.H., Desai, N.M., Patel, G.M. and Mansuri, M.M. *et al*. (2006). Environmental monitoring of benzene and toluene produced in indoor air due to combustion of solid biomass fuels. *Sci. Total Environ.,* **357,** 280-287.

Smith, K.R., Aggarwal, A.L. and Dave, R.M. (1983). Air pollution and rural biomass fuels in developing countries: A pilot village study in India and implications for research and policy. *Atmos. Environ.,* **17,** 2343-2362.

Smith, K.R., Apte, M.G., Ma, Y., Wongsekiarttirat, W. and Kulkarni, A. (1994). Air pollution and the energy ladder in asian cities. *Energy,* **19,** 587-600.

Smith, K.R., Dutta, K., Chengappa, C., Gusain, P., Masera, O. and Berrueta, V. (2007). Monitoring and evaluation of improved biomass cookstove programs for indoor air quality and stove performance: Conclusions from household energy and health project. *Energy for Sustainable Dev.,* **11,** 5-18.

Smith, K.R., Bruce, N., Balakrishnan, K., Adair-Rohani, H., Balmes, J. and Chafe, Z. *et al*. (2014). Millions dead: How do we know and what does it mean? Methods used in the comparative risk assessment of household air pollution. *Ann. Rev. Inc*., **35**, 185-206.

Smith, K.R., Bruce, N., Balakrishnan, K., Adair-Rohani, H., Balmes, J. and Chafe, Z. *et al*. (2014). (forthcoming). Millions dead: How do we know and what does it mean? Methods used in the comparative risk assessment of household air pollution. *Ann. Rev. Public Health,* 35.

T.E.R.I. (1995). Biomass fuels, indoor air pollution and health: A multi-disciplinary, multi-centre study. The Energy Research Institute, New Delhi.

Vaishali, R., Phadke, K.M., Thakre, R. and Hasan, M. (1997). Pahs in respirable particulate matter in Nagpur city. *J. Ind. Assoc. Environ. Manage.,* **24,** 11-16.

WHO. (2004). Comparative quantification of health risks: Global and regional burden of disease due to selected major risk factors, Geneva.

WHO. (2006). WHO air quality guidelines for particulate matter, ozone, nitrogen dioxide and sulfur dioxide; global update 2005; summary of risk assessment, Geneva.