### Lung Cancer and Indoor Air Pollution in Xuan Wei, China: Exposure Assessment, Etiology, and Intervention

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### **Indoor Air Pollution to Solid Fuels**

- Half of the world's population is exposed to smoke from cooking or heating with solid fuels
- Indoor air pollution from solid fuel use → the eighth largest risk factor for global disease (2<sup>nd</sup> environmental factor)



### National Household Solid Fuel Use, 2000



#### Xuan Wei; A special case of solid fuel exposure





### Lung Cancer Mortality Rates in Xuanwei are among the Highest in China



County-specific lung cancer mortality rates (per 100,000, 1973-75)



## Xuanwei



# Risk estimates of lung cancer associated with household coal use



Hosgood et al., 2011



### What is special about Xuan Wei?

- Type of coal?
- Type of stoves?
- Population?





## Lung cancer mortality in XW

- Associated with "smoky coal"
  - Bituminous coal
  - So-called for the smoke released upon combustion
- Formed at permiantriassic boundary
  - Permian extinction event
- Smokeless coal
  - Anthracite coal

Deaths from lung cancer among individuals ages less than 70 years in Xuanwei cohort 1976-96, stratified by type of coal used, sex, and smoking habit (Baron-Adesi et.al 2012)

	Smoky Coal	Smokeless Coal
Sex and smoking status	Mortality (95% CI)*	Mortality (95% CI)*
Men		
Never smoked	450 (355 to 545)	NA
Ever smoked	488 (459 to 518)	13.1 (5.7 to 21.1)
Women		
Never smoked	527 (496 to 558)	4.7 (1.0 to 9.4)
Ever smoked	NA	NA
*Age standardised morta group of smokeless coa	ality per 100 000 person years. Th I users (n=9962) was used as the	ne age structure of the standard population.

### Variation within smoky coal users





## What is special about XuanWei?

X

- Type of coal
- Type of stoves?
- Population?



## Primary hypotheses regarding lung cancer

- PAH hypothesis
  - Multiple recognized carcinogens
  - High personal exposure observed among smoky coal users
- Quartz hypothesis
  - Recognized carcinogen
  - Identified in coal samples
  - Personal exposure unknown
- Interaction between individual components?



#### Downward et al., 2014

## **Coal Analyses**

- Coal samples collected directly from the homes of participants
- 116 smoky
  - 63 Xuanwei
  - 51 Fuyuan
- 29 smokeless
  - 7 Xuanwei
  - 22 Fuyuan





## Hydrocarbon release of Coal

- Clear difference between smoky and smokeless coals
- Base differences in hydrocarbon material as would be expected when comparing bituminous to anthracite coal

Major Coal Type	N	S1 (mgHC/g coal)	S2 (mgHC/g coal)	Tmax (°C)
Smoky	116	2.2*	71. 5*	460*
Smokeless	29	0.3	8.4	581



### **Hydrocarbon release of Smoky Coal**

County	Coal Sup-type	Coal Mine	N	S1 (mgHC/g <u>coal</u> )	S2 ) (mgHC/g co <u>al)</u>	Tmax (°C)
Xuanwei			65	2.35	73.24	462
	Coking Coal		63	2.34*	73.24*	462*
	-	Azhi	15	2.52	75.62	462
		Baoshan	5	2.24	61.59	463
		Laibin	14	2.23	76.14	460
		TangTang	22	1.62	61.98	464
		Yangchang	7	4.03	138.69	443
Euvuan			E 1	1 05		4521
гиуиап	Colving Cool			1.95	00.00+	452+
	Coking Coal	Daning	12	1.09	43.90	407 150 5
		Enhong	4	2.34	20.9 40.53	450.5
		Haidan	4	1.75	40.33	409.5
		Zude	1	4 21	61 02	408
		2000	-	1121	01102	17.5
	1/3 Coking		8	1.98	52.35	459*
		Bagong	5	1.7	47.19	465
		Dahe	3	3.08	80.18	445
	Gas Fat		23	1.97	131.87	433
		Housuo	20	2.03	138.44	433.5
		Qingyun	3	1.62	110.4	431
		-				
	Meagre Lean	Gumu	1	3.83	53.43	469

## Quartz contents coal

- SEM reveals elevated quartz in smoky coal compared to smokeless coal
- Including quartz of size <9.6µm (respirable fraction)</li>

Coal Type	N	Total Quartz (% of coal)	Respirable Quartz (% of coal)
Smoky	19	4.58*	1.92*
Smokeless	6	2.24	0.6





## PAH exposure in air (ng/m<sup>3</sup>)

	Smoky coal		Smokeless coal		Wood			Plant				
	AM	GM	GSD	AM	GM	GSD	AM	GM	GSD	AM	GM	GSD
Smoky Coal	74.4	44.8	2.7	15.1	10.5*	2.5	66.6	58.2	1.7	95.6	83.8	1.9
Ventilated Stove	50.2	38.1	2.1	5.6	5.5	1.3	73.4	61.2	1.9	-	-	-
Unventilated Stove	224.5	160.3	2.4	13.8	9.3*	2.7	-	-	-	116.1	116.1	-
Portable Stove	41.5	31.5	2.2	19.3	14.2	2.4	78.4	70.1	1.7	39.5	39.5	-
Firepit	186.4	151.5†	2.0	-	-	-	50.2	47.7	1.4	67.3	67.3	-
Mixed Ventilation	85.7	48.9	3.1	10.6	10.6	-	-	-	-	159.5	159.5	-
Unknown	13.2	7.7	3.0	-	-	-	-	-	-	-	-	-



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Downward et al., Submitted

## Quartz in indoor air

Fuel Type	% Detects(n)	% Non-detects(n)	Total n
Smoky Coal	14% (11)	86% (69)	80
Smokeless Coal	0% (0)	100% (17)	17
Other Coal	12% (2)	88% (15)	17
Wood	11% (1)	89% (8)	9
Plant	20% (1)	80% (4)	5
Other Fuel	10% (3)	90% (27)	30

LOD  $0.2\mu g/m^3$ 

 Quartz in the coal ends up in the nonrespirable fraction of the ash



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Downward et al., submitted

## Key Pathways in B(a)P Metabolism



### **GSTM1** Null Genotype

 GSTM1 null genotype → lack of GSTM1 enzyme activity

 Results in decreased detoxification of PAH metabolites



### **GSTM1** Genotype and Lung Cancer Risk

GSTM1	Case N (%)	Control N (%)	OR <sup>a</sup> (95%CI)
Positive	40(32.8)	62(49.2)	1.0
Null	82(67.2)	60(50.8)	2.3 (1.3-4.2)

a ORs and 95% CIs adjusted for total smoky coal use without ventilation, pack -years, COPD, and family history of lung cancer by multiple conditional logistic regression.



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Lan et al., 2000 CEBP

### Aldo-keto Reductase Family 1, Member C3 (AKR1C3 Gln5His)

AKR1C3-GIn5His polymorphism (Exon 1)

- Produces a change from glutamine  $\rightarrow$  histidine
- A shift from a neutral to a basic amino acid



### AKR1C3-GIn5His Polymorphism and Lung Cancer Risk

Genotype	Case N (%)	Controls N (%)	OR (95%CI)
His/His + His/Gln	22 (19)	33 (29)	1.0
Gln/Gln	94 (81)	79 (71)	1.8 (1.0-3.5)

#### Lan et al., 2004 Carcinogenesis



### **OGG1 (Oxoguanine glycosylase 1)** Ser326Cys polymorphism

- OGG1 repairs 8-oxo-7,8-dihydroguanine (8oxoG)
- OGG1 Ser326Cys polymorphism (Exon 6)
- Repair activity of OGG1-Ser326 has been shown to be > OGG1-Cys326



### OGG1 Ser326Cys Polymorphism and Lung Cancer Risk

<i>OGG1</i> Genotype	Case N (%)	Control N (%)	OR (95%CI)	
Ser/Ser	37 (31)	51 (47)	1.0	
Ser/Cys +Cys/Cys	81 (69)	58 (53)	1.9 (1.1-3.3)	

ORs and 95%CIs obtained by logistic regression analysis adjusted for age, sex, pack-year of smoking.



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Lan et al., 2004 Carcinogenesis

## Primary hypotheses regarding lung cancer

- PAH hypothesis
  - Multiple recognized carcinogens
  - High personal exposure observed among smoky coal users
  - Gene-environment interaction with key genes in BaP metabolism
- Exposures however not high enough to explain the high excess risks?
  - Armstrong and Gibbs derived a ERC curve for BaP exposure and lung cancer among coke oven workers, which predicted a relative risk of 2.68 at 100 µg/m3 BaP years using a power risk-curve -> RR ~ 8



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Vermeulen, R.; Rothman, N.; Lan, Q. Coal combustion and lung cancer risk in XuanWei: a possible role of silica? Med Lav 102:362-7; 2011.

## **Open questions**

- Causative agent: organic fraction of smoky coal
- Agent/Agent interactions?
- Timing of exposure?



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Age at starting cooking (years)

### **Engineering Interventions to Reduce Health Burden from Household Solid Fuel Use**

#### Ventilation changes

- Chimneys on stoves
- Placement of stoves outside
- Improved home ventilation

#### Stoves changes

- Using existing biomass fuels, e.g., "gasifier" stoves
- Using processed biomass, e.g., pellet stoves
- Improve efficiency
- Fuel Changes





### **Stove improvement programs**

• Stove improvement programs were implemented in the mid-eighties

#### Fire pit



#### Portable stove



#### Vented stoves







### **Reduction in IAP exposure**

	Smoky coal			Sm	okeless	coal
	AM	GM	GSD	AM	GM	GSD
Smoky Coal	74.4	44.8	2.7	15.1	10.5*	2.5
Ventilated Stove	50.2	38.1	2.1	5.6	5.5	1.3
Unventilated Stove	224.5	160.3	2.4	13.8	9.3*	2.7
Portable Stove	41.5	31.5	2.2	19.3	14.2	2.4
Firepit	186.4	151.5†	2.0	-	-	-
Mixed Ventilation	85.7	48.9	3.1	10.6	10.6	-
Unknown	13.2	7.7	3.0	-	-	_



#### **Stove Improvement and Lung Cancer in Xuanwei, China Product-limit survival plot – Probability of not having lung cancer**



### Initiation of a New Hospital-Based Case-Control of Lung Cancer among Nonsmoking Women (2006-2008)

- Enroll 1000 newly diagnosed non-smoking female cases and 1000 female controls
- Biological sample collection: collect blood, sputum, buccal cells
- Questionnaire collects extensive information on lifetime exposure to smoky coal and potential confounders
  Hospitals for the new case-controls study
- Detailed exposure assessment in 140 households (36 villages)
  - Personal
  - Stationary



















## Collaborators

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