Does carbon black cause heart disease?

Robert J. McCunney, MD, MPH

Mass General Brigham Hospital

Pulmonary Division Harvard Medical School Boston, MA USA

## Major Causes of Death in USA \* \* CDC 2019

- 1. Heart Disease: 659,000
- 2. Cancer: 600,000
- 3. Accidents: 173,000
- 4. COPD: 160,000
- 5. Stroke: 150,000
- 6. Alzheimers: 121,000
- 7. Diabetes: 88,000
- 8. Kidney Disease: 51,000

# Risk Factors of Heart Disease

- Smoking
- Hypertension
- High Cholesterol
- Diabetes
- Family History
- Obesity

# Background

Epidemiological studies of exposure to airborne environmental particulates have reported associations with a variety of cardiovascular effects including myocardial infarction (MI) and ischemic heart disease (IHD). These effects were first reported among North American and European populations, and a recent study of four Chinese cities generated similar findings.

# Background

- In light of the potential for environmental particles to increase the risk of heart disease (HD), <u>the American Heart</u> <u>Association (AHA)</u> published a position paper on <u>particulate</u> <u>matter</u> and HD, noting:
- "It is the opinion of the writing group that the overall evidence is consistent with a causal relationship between PM<sub>2.5</sub> exposure and cardiovascular morbidity and mortality"

# Background

- <u>The European Society of Cardiology:</u> "There is abundant evidence that air pollution contributes to the risk of cardiovascular disease.
- Further research should explore optimal methods of air pollution reduction and document the effects on the incidence of cardiovascular disease and related mortality to motivate policy makers to intensify legislative efforts on air pollution reduction.

Does carbon black cause heart disease?

What is Carbon Black ? Essentially pure (98-99%) carbon

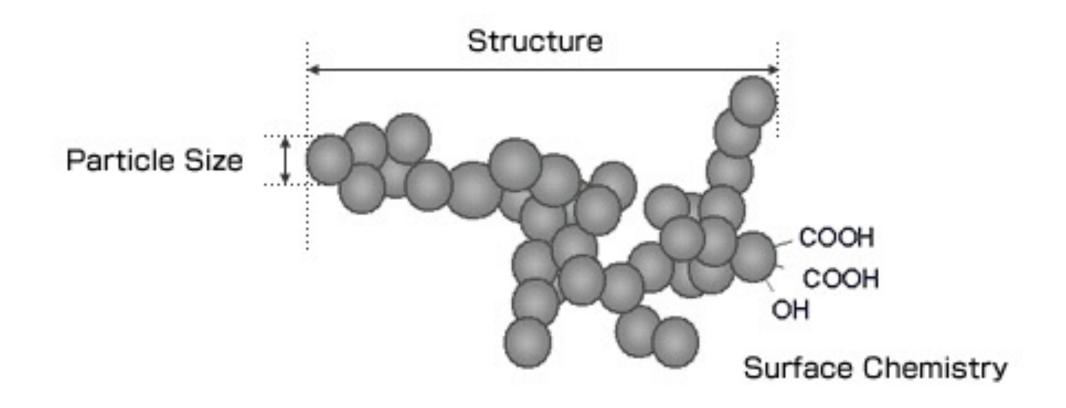
May contain traces of polycyclic aromatic hydrocarbons (PAHs) adsorbed and tightly bound on the surface of the particle.

# Carbon Black

Powder Form (Particle size < 1 micron)



# Carbon Black Structure



# <u>CB Cohort</u> <u>Mortality</u> <u>Studies</u>

Three cohort mortality studies in UK, USA and Germany have evaluated links between carbon black exposure and deaths from various diseases, including heart disease

Carbon Black Mortality Studies



#### Largest study published; 6634 workers

Includes workers back to the 1930s

Cumulative inhalable carbon black assessed by individual life time exposure in mg/m<sup>3</sup>-years.

98.5 % ascertainment of vital status

<u>USA Carbon</u> <u>Black</u> <u>Mortality</u> <u>Study</u> Full Cohort: 6634 workers; Inception Cohort: 3890 workers

#### **Diseases of the Heart:**

Full Cohort: Observed Deaths: 616; Expected: 790

SMR: 0.78 (95% CI: 0.72-0.84)

Inception Cohort: Observed Deaths: 332; Expected: 394

SMR: 0.84 (95% CI: 0.75-0.94)

**Ischemic Heart Disease:** 

Full Cohort: Observed Deaths: 511; Expected: 622

SMR: 0.82 (95% CI:0.75 - 0.90)

Inception Cohort: Observed Deaths: 272; Expected: 309

SMR: 0.88 (95% CI: 0.78 - 0.99)

# UK Mortality Study

### 1,147 workers, 5 plants, 1951-1996

### Diseases of the circulatory system ICD-9 390-458

SMR = 1.00 (Deaths: 157, 95% Cl 0.85 – 1.17)

# German Mortality Study

One plant evaluated (Wellmam et al, 2006; Morfeld and McCunney 2007; 2009)

1535 workers

# Carbon Black Cardiovascular Epidemiology:German Cohort

1,535 workers; reference population: West Germany heart diseases ICD-9: 410-429 full cohort: SMR = 1.29 (obs 103; 95% CI 1.05 – 1.57) inception cohort: SMR = 1.39 (obs 60 ; 95% CI 1.06 – 1.79)

#### ischemic heart disease ICD-9: 410-414 full cohort: SMR = 1.30 (obs 75 ; **95% Cl 1.02 – 1.63**) inception cohort: SMR = 1.36 (obs 43 ; **95% Cl 0.98 – 1.83**)

other heart diseases ICD-9: 415-429full cohort:SMR = 1.28 (obs 28 ; 95% CI 0.85 - 1.85)inception cohort:SMR = 1.47 (obs 17 ; 95% CI 0.86 - 2.35)

### German cohort



 1,535 workers, 1 plant;
 reference population: Northrhine Westphalia

 heart diseases ICD-9 410-429

 full cohort:
 SMR = 1.17 (obs 103; 95% CI 0.96 - 1.42)

 inception cohort:
 SMR = 1.28 (obs 60; 95% CI 0.98 - 1.65)

ischemic heart disease ICD-9 410-414 full cohort: SMR = 1.19 (obs 75 ; **95% Cl 0.94 – 1.49**) inception cohort: SMR = 1.27 (obs 43 ; **95% Cl 0.92 – 1.71**)

other heart diseases ICD-9 415-429full cohort:SMR = 1.13 (obs 28; 95% CI 0.75 - 1.63)inception cohort:SMR = 1.31 (obs 17; 95% CI 0.76 - 2.10)

# Carbon Black Epidemiology Summary

Studies of over 9000 workers in the carbon black industry in USA, UK and Germany.

- UK and US cohorts: no excess detected
- German cohort: excess detected of borderline significance in comparison to national rates but not state rates (NRW)

Carbon Black Exposure and potential cardiovascular diseases

#### Purpose:

- Address whether there is an elevated risk of cardiac disease
   <u>Plan:</u>
- Develop harmonized study with more power and from different populations

Based on "Meta-Analysis of Cardiac Mortality in Three Cohorts of Carbon Black Production Workers"

Morfeld, Sorahan, Mundt, McCunney, Int. J. Environ. Res. Public Health 2016, 13, 302

Funded by International Carbon Black Association

## Methods

- Combine standardized mortality ratio (SMR) and Cox Proportional Hazards results from US, UK and German CB production workers.
- Analyze mortality for
- 1. Heart disease (HD),
- 2. Ischemic heart disease (IHD) and
- 3. Acute myocardial infarction (AMI).
- Fit Fixed random effects metaregression models for employment duration, and overall cumulative and recent (lugged by 5 and 10 years) quantitative CB exposure estimates.

## Methods

Endpoints studied

NOTE: Different ICD Codes used in the US, UK and German mortality studies

#### Heart disease:

• ICD-10, I20-I52; ICD-9, 410-429; ICD-8, 410-429

Ischemic heart disease (IHD):

• ICD-10, I20-I25; ICD-9, 410-414; ICD-8, 410-414

Acute myocardial infarction (AMI):

• ICD-10, I21; ICD-9, 410; ICD-8, 410.

# Methods

1. <u>Calculate SMRs</u> for the following ICD-9 groups in each cohort:

- heart diseases (ICD-9 410-429)
- ischemic heart disease (ICD-9 410-414)
- acute myocardial infarction (ICD-9 410)
- 2. <u>Stratify SMRs</u> for all endpoints by time since first exposure tsfe (<5,5-9,10-14, ...) and cessation of exposure.

NOTE: Analyses performed on the <u>full cohorts</u> and inception cohorts

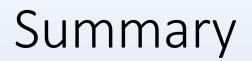
### Results

#### Full cohort meta-SMRs:

1.01 (95% CI: 0.79–1.29) for Heart Disease;

1.02 (95% CI: 0.80–1.30) for Ischemic Heart Disease,

1.08 (95% CI 0.74–1.59) for Acute Myocardial Infarction mortality.



- This study included all cohort studies of CB manufacturing workers published to date, and therefore has the greatest potential to identify cardiovascular disease mortality risks.
- We combined SMR and Cox Proportional Hazards results from cohort studies of US, UK and German CB production workers, particularly for IHD and AMI.
- Meta-analysis procedures used to combine cohort-specific results derived enhanced statistical power, thus improving the ability to identify even small associations.
- Availability of reasonably detailed employment histories and exposure assessment in the three cohorts allowed quantitative evaluation of risk of cardiovascular mortality by standardized individual CB exposure estimates.
- Meta-SMRs were unexceptional. Meta-Cox coefficients showed no association with lugged or unlugged duration of exposure.

## Conclusion

- Results do not demonstrate that CB exposure increases cardiac disease mortality.
- Based on the evolving body of evidence regarding inhalable particles and cardiovascular disease risks more attention should be paid to the combination of physical and chemical properties of particulate air pollutants, as well as the context in which people are exposed.