Epidemiological Study of U.S. Carbon Nanotube Workers

John D. Beard, MPH, PhD
Brigham Young University

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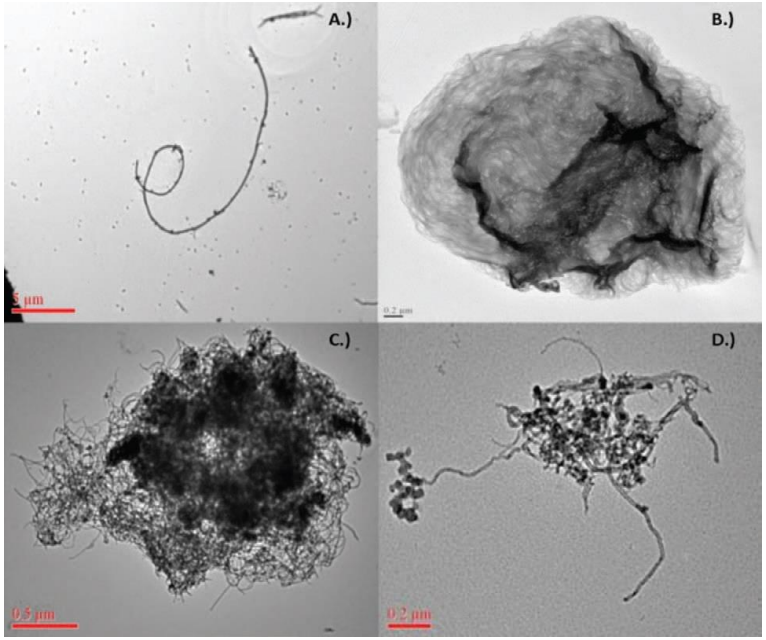
Study Objective

- Estimate associations between occupational carbon nanotube and nanofiber (CNT/F) exposure and early human health effects

- Study conducted by the National Institute for Occupational Safety and Health

Study Design

- Industrywide cross-sectional study
- 12 sites across the U.S.
  - Primary producers
  - Secondary users
  - Hybrid
- 108 CNT/F workers
  - 75% of recruited workers



From Dahm et al. (2015)

Exposure Assessment

- Personal breathing zone, filter-based air sampling
  - Background-corrected elemental carbon (EC) concentrations (2 variables)
  - CNT/F structure count concentrations (6 variables)

Exposure Assessment

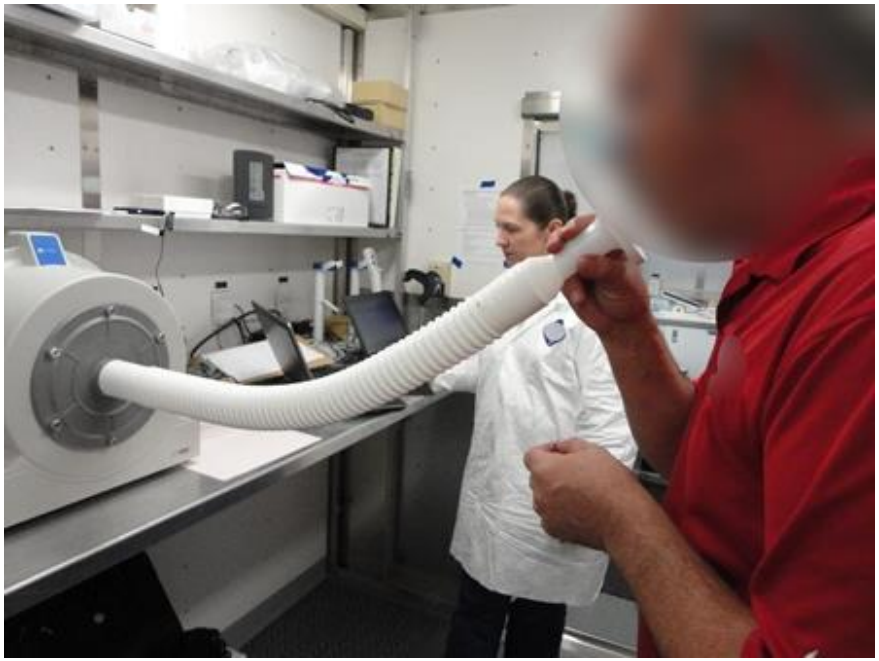
- Direct-reading instruments
  - Fine and ultrafine particulate matter mass and count concentrations (3 variables)
- Other (4 variables)

Outcome Assessment

- 36 sputum biomarkers
- 37 blood biomarkers
- Chest symptoms and respiratory allergies since start of CNT/F work

Outcome Assessment

- Lung function
- Resting blood pressure (RBP)
- Resting heart rate (RHR)
- Complete blood count (CBC) components



Sputum Biomarker Factor Loadings

78% of variance explained

Colored loadings have largest magnitudes for each biomarker

Biomarker	Factor 1	Factor 2	Factor 3
Cancer/Fibrosis			
MUC-1/KL-6	0.16	**0.84**	0.08
MMP-2	**0.77**	0.44	0.15
MMP-7	0.09	**0.88**	0.16
TIMP-1	**0.65**	0.54	0.25
Inflammation			
α-2-M	**0.93**	0.07	0.07
Apo-AI	**0.93**	0.18	0.16
Apo-AII	**0.91**	0.24	0.02
IL-1 β	**0.66**	0.28	0.55
IL-6R-β	0.43	**0.65**	0.27
IL-8	0.59	**0.66**	0.31
IL-18	0.07	0.19	**0.88**
Oxidative Stress			
8-OHdG	**0.45**	0.38	-0.36
MPO	0.48	0.31	**0.69**
Cardiovascular/Coagulation			
Fibrinogen	**0.71**	0.23	0.36
PAI-1	**0.58**	0.53	0.27
VCAM-1	**0.87**	0.28	0.19

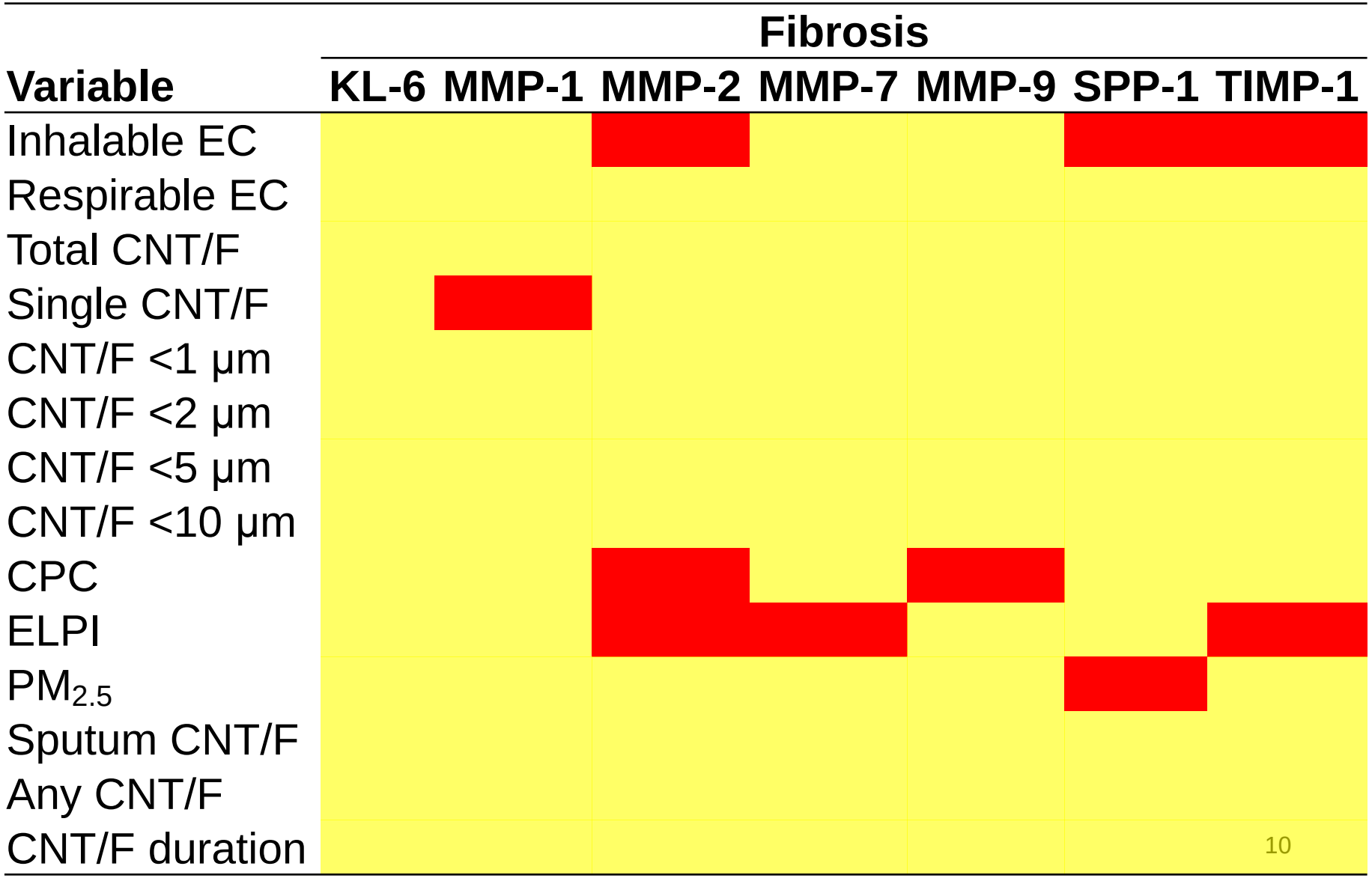
CNT/F and Sputum Biomarker Factors

Key

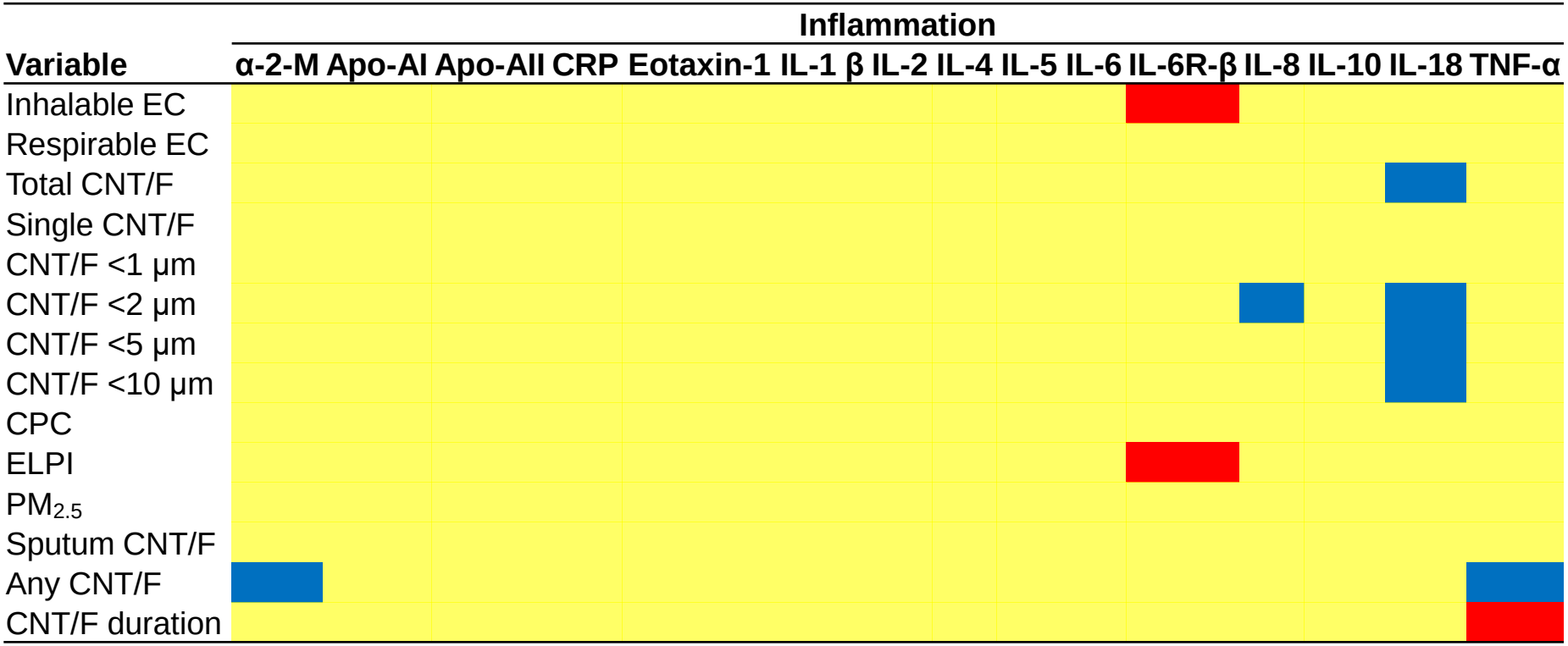
- Positive association p-value < 0.05
- p-value ≥ 0.05
- Inverse association p-value < 0.05

Variable	Factor 1	2	3
Inhalable EC			
Respirable EC			
Total CNT/F			
Single CNT/F			
CNT/F <1 µm			
CNT/F <2 µm			
CNT/F <5 µm			
CNT/F <10 µm			
CPC			
ELPI			
$PM_{2.5}$			
Sputum CNT/F			
Any CNT/F			
CNT/F duration			

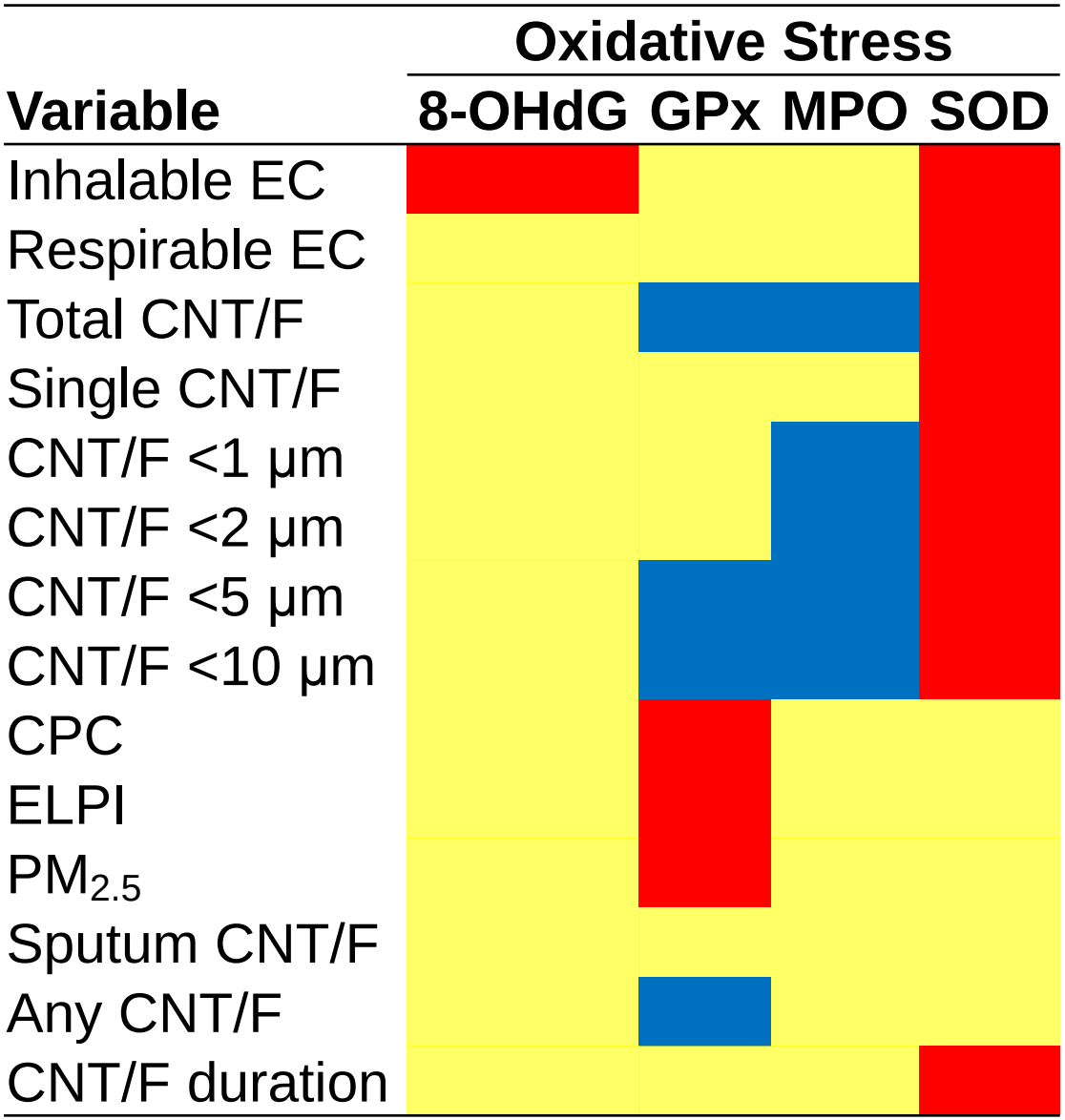
CNT/F and Sputum Biomarkers



CNT/F and Sputum Biomarkers



CNT/F and Sputum Biomarkers



CNT/F and Sputum Biomarkers

	Cardiovascular					
Variable	**Fibrinogen**	**ICAM-1**	**PAI-1**	**t-PA**	**VCAM-1**	**vWF**
Inhalable EC						
Respirable EC						
Total CNT/F						
Single CNT/F						
CNT/F <1 µm						
CNT/F <2 µm						
CNT/F <5 µm						
CNT/F <10 µm						
CPC						
ELPI						
$PM_{2.5}$						
Sputum CNT/F						
Any CNT/F						
CNT/F duration						

Blood Biomarker Factor Loadings

67% of variance explained

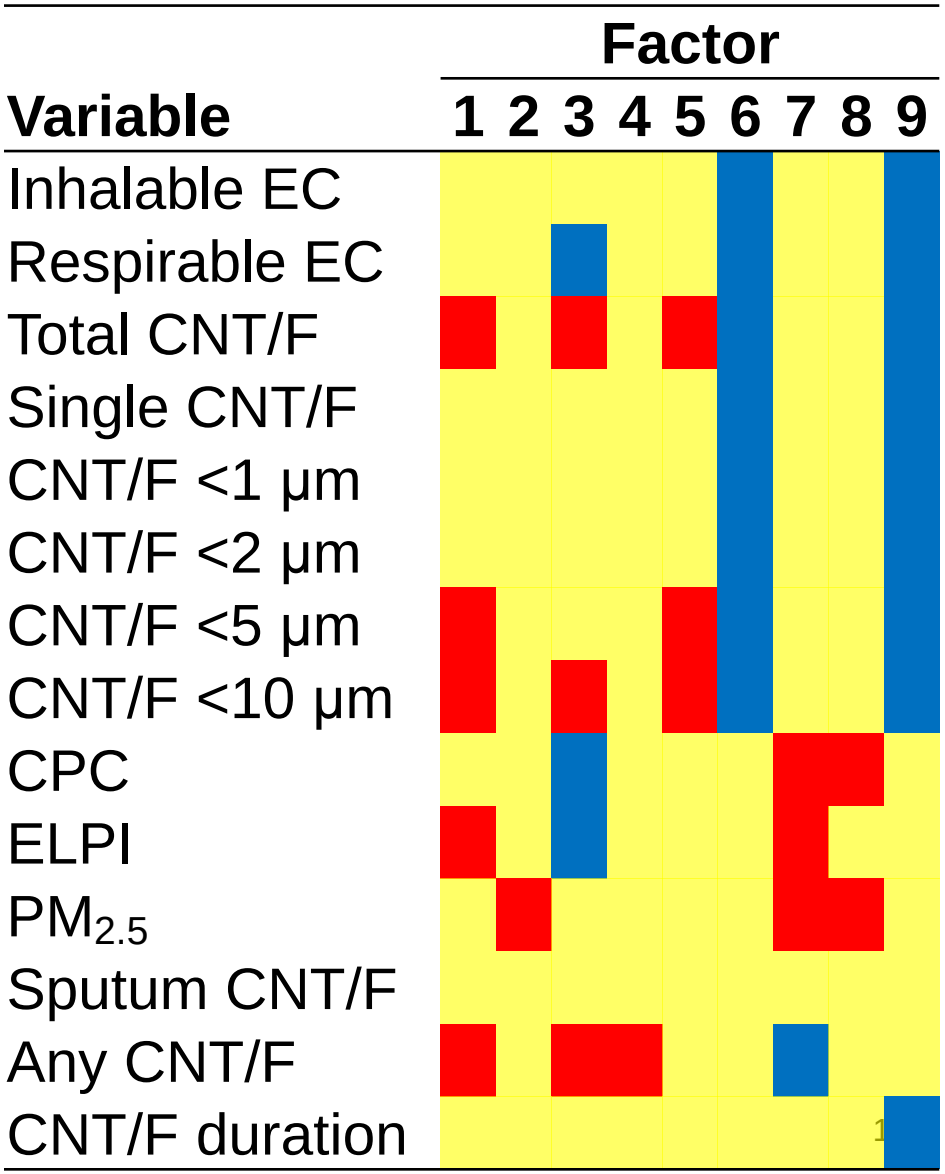
Colored loadings have largest magnitudes for each biomarker

Biomarker	Factor 1	2	3	4	5	6	7	8	9
Cancer/Fibrosis									
MUC-1/KL-6	-0.04	0.20	**-0.77**	-0.02	0.04	0.05	0.18	-0.09	-0.03
MMP-2	-0.29	0.29	-0.10	0.27	-0.12	0.20	**0.45**	0.40	0.00
MMP-7	0.07	0.27	-0.19	-0.10	**0.70**	0.06	0.24	0.11	-0.13
MMP-9	0.14	-0.02	-0.03	0.03	0.53	-0.04	-0.06	**0.54**	0.18
SPP-1	-0.08	-0.07	0.00	**0.61**	-0.11	-0.05	-0.16	0.24	0.37
TIMP-1	0.20	0.30	0.02	**0.56**	0.20	0.32	0.12	-0.15	-0.22
Inflammation									
α-2-M	-0.09	**-0.54**	-0.38	-0.12	0.03	-0.02	0.23	0.09	0.48
Apo-AI	-0.07	-0.24	0.17	0.04	0.19	0.11	**0.75**	-0.20	0.26
Apo-AII	-0.01	0.28	**0.75**	0.12	-0.02	0.13	0.13	-0.30	0.02
CRP	**0.73**	0.12	0.21	-0.15	0.03	0.34	-0.01	-0.06	-0.15
C3	**0.65**	0.14	0.25	-0.08	0.19	0.16	0.10	0.19	0.07
IL-1 β	0.32	-0.02	-0.15	-0.01	0.37	0.00	0.29	-0.08	**0.38**
IL-6R-β	0.11	0.29	0.19	**0.60**	0.00	-0.28	0.24	0.09	0.15
IL-8	0.23	0.13	0.04	0.07	**0.71**	0.14	-0.04	0.01	0.02
IL-18	**0.62**	0.27	0.00	0.27	0.03	-0.15	-0.02	-0.03	0.00
MDC	-0.08	**0.59**	0.10	-0.12	0.21	0.18	-0.27	-0.01	0.23
Oxidative Stress									
8-OHdG	0.05	0.09	**0.75**	0.08	-0.05	0.19	-0.01	-0.02	-0.18
GPx	0.14	0.01	-0.27	-0.22	-0.03	-0.17	**0.63**	0.17	-0.03
MPO	-0.06	0.06	-0.08	0.24	0.05	-0.03	0.03	**0.82**	-0.13
SOD	-0.07	0.13	-0.04	0.03	-0.02	0.02	0.07	-0.06	**0.78**
Cardiovascular/Coagulation									
EDN1	-0.09	0.02	0.06	**0.45**	0.42	-0.18	-0.28	-0.04	-0.01
Fibrinogen	0.46	0.09	0.08	0.00	0.14	**0.71**	0.17	0.26	0.10
ICAM-1	**0.65**	0.03	-0.20	0.11	0.15	-0.11	-0.03	-0.09	-0.06
PAI-1	0.25	**0.72**	0.07	0.13	0.19	0.11	0.13	0.20	0.08
t-PA	0.29	**0.76**	-0.09	0.03	0.08	0.10	-0.03	-0.04	-0.03
VCAM-1	0.09	-0.09	0.09	**0.75**	-0.01	0.17	-0.08	0.19	-0.14
vWF	-0.12	0.27	0.22	0.06	0.05	**0.79**	-0.12	-0.17	-0.01

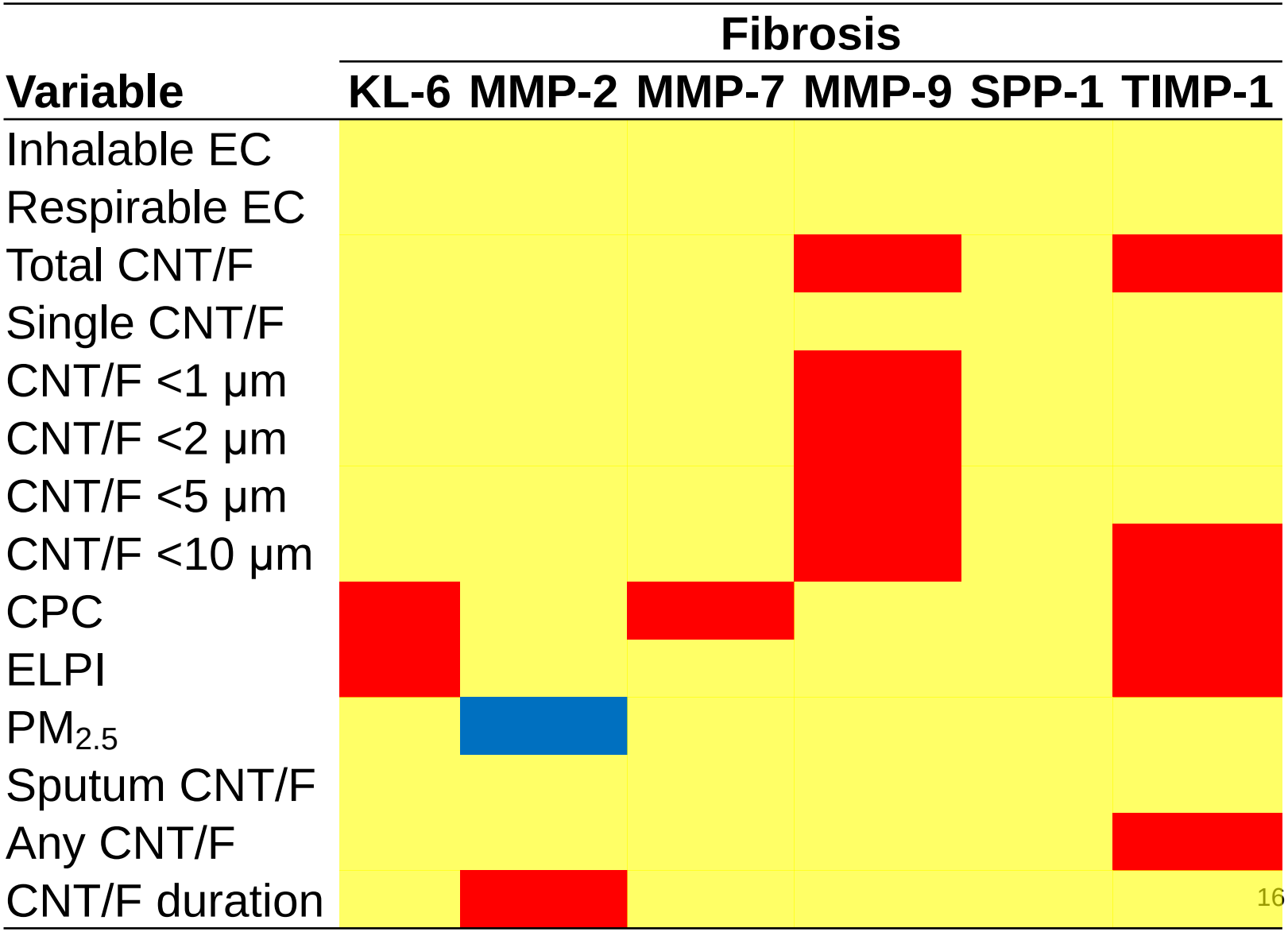
CNT/F and Blood Biomarker Factors

Key

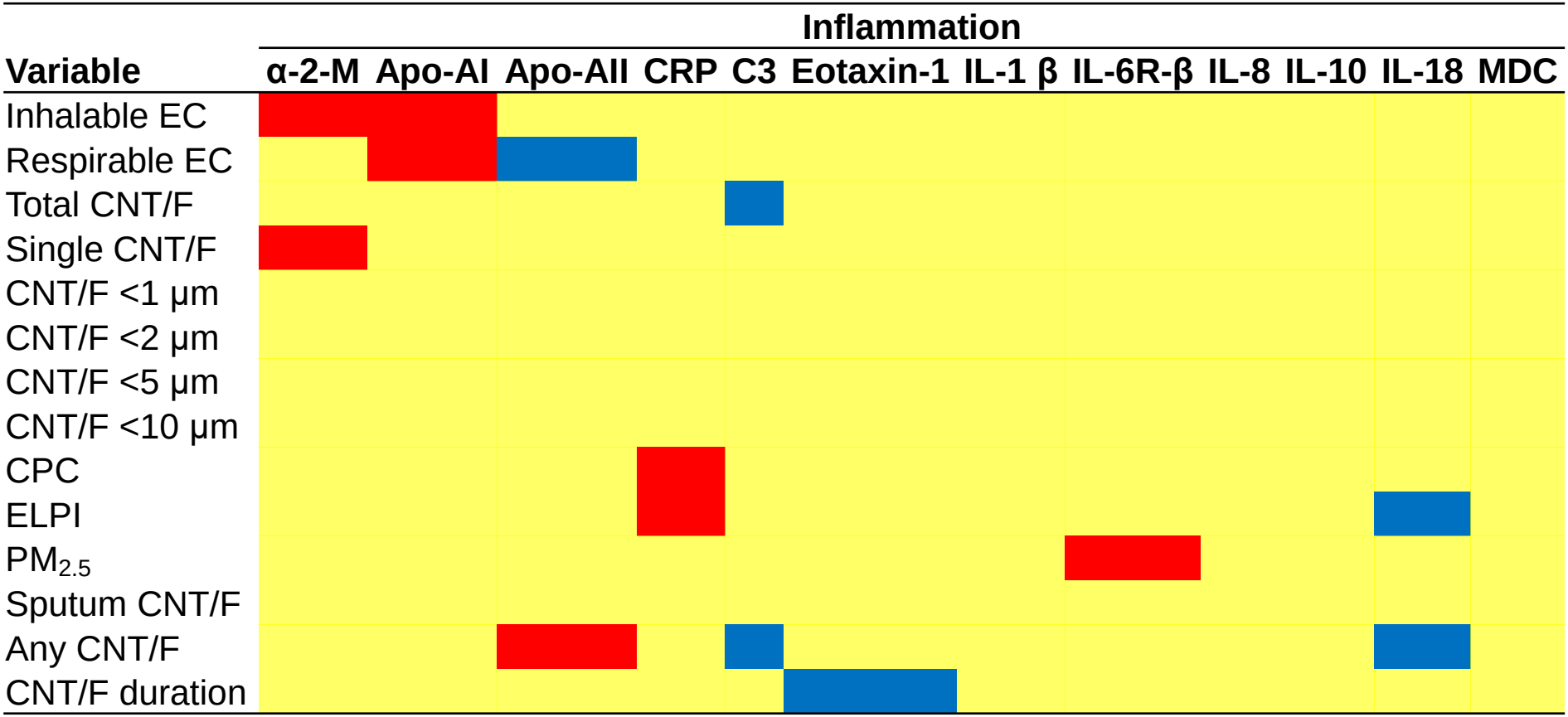
- Positive association p-value < 0.05
- p-value ≥ 0.05
- Inverse association p-value < 0.05



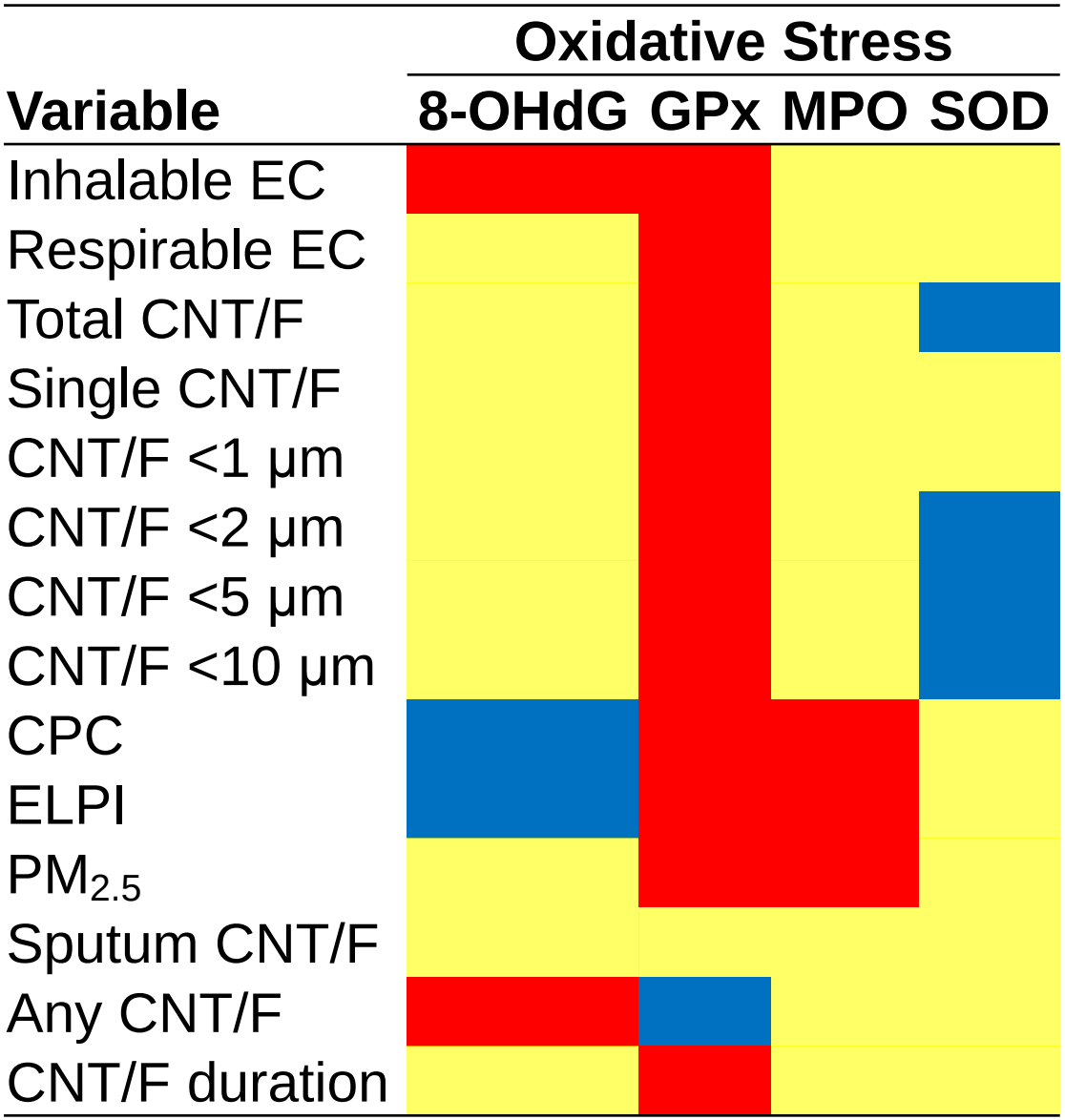
CNT/F and Blood Biomarkers



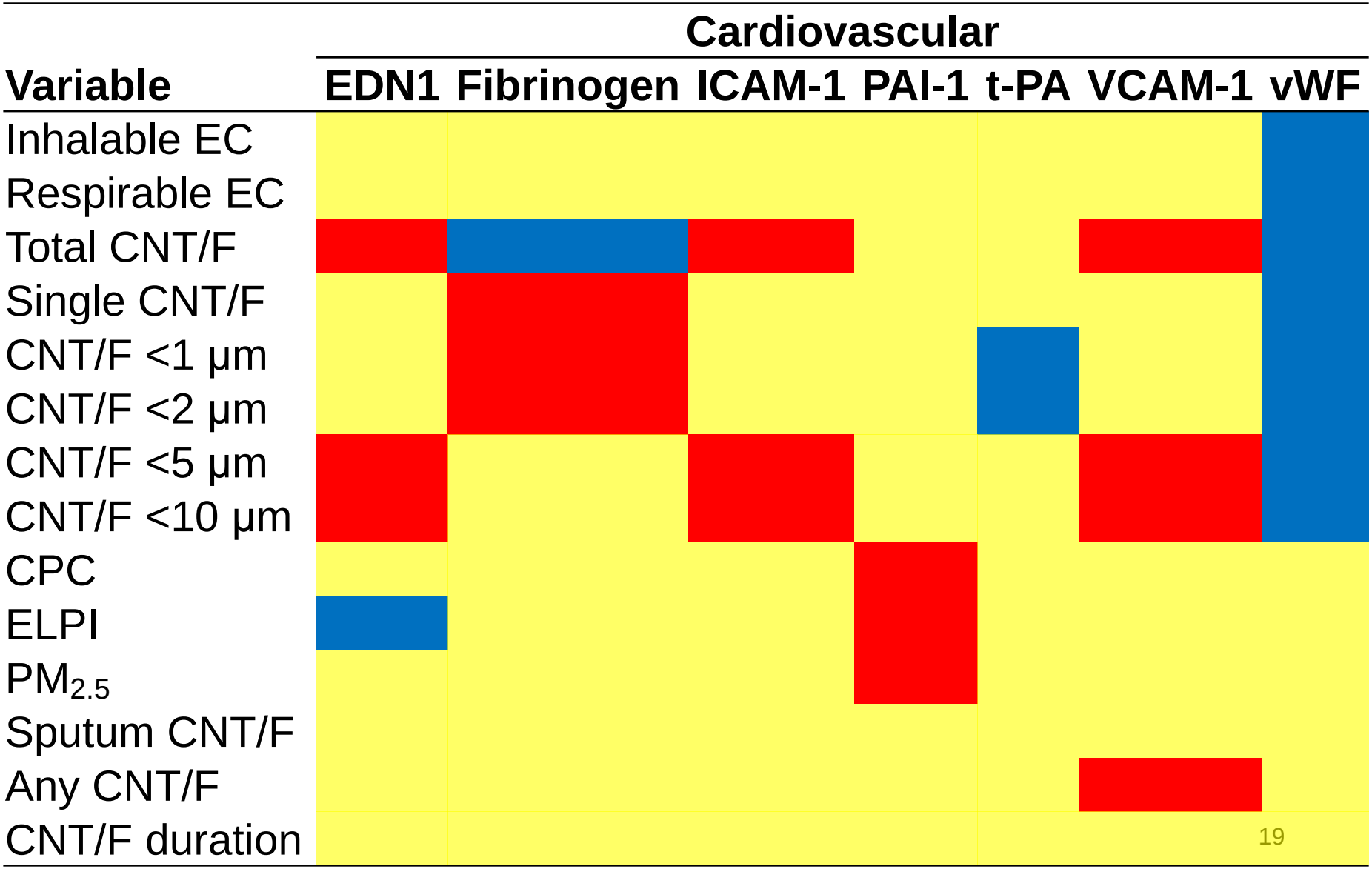
CNT/F and Blood Biomarkers



CNT/F and Blood Biomarkers



CNT/F and Blood Biomarkers



CNT/F and Chest Symptoms

Variable	Chest Symptoms	Respiratory Allergy
Inhalable EC		
Respirable EC		
Total CNT/F		
CPC		
ELPI		
$PM_{2.5}$		
Sputum CNT/F		
CNT/F duration		

CNT/F and Lung Function

Variable	FVC	FEV1/FVC	FEF25-75	PEF
Inhalable EC				
Respirable EC				
Total CNT/F				
Sputum CNT/F				
CNT/F duration				

CNT/F and RBP and RHR

Variable	Systolic BP	Diastolic BP	Heart Rate
Inhalable EC			
Respirable EC			
Total CNT/F			
Sputum CNT/F			
CNT/F duration			

CNT/F and CBC Components

Variable	Leukocytes	Neutrophils	Lymphocytes
Inhalable EC			
Respirable EC			
Total CNT/F			
Sputum CNT/F			
CNT/F duration			

Variable	Monocytes	Platelets	Hemoglobin	Hematocrit
Inhalable EC				
Respirable EC				
Total CNT/F				
Sputum CNT/F				
CNT/F duration				

Conclusions

- Findings support associations between occupational CNT/F exposure and early human health effects
- Results need to be confirmed in other exposed populations
- Consider recommended exposure limits based on inhalable CNT/F

Acknowledgements

Field Studies	Measurement Methods	Toxicology
Mary Schubauer-Berigan	Eileen Birch	Aaron Erdely
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