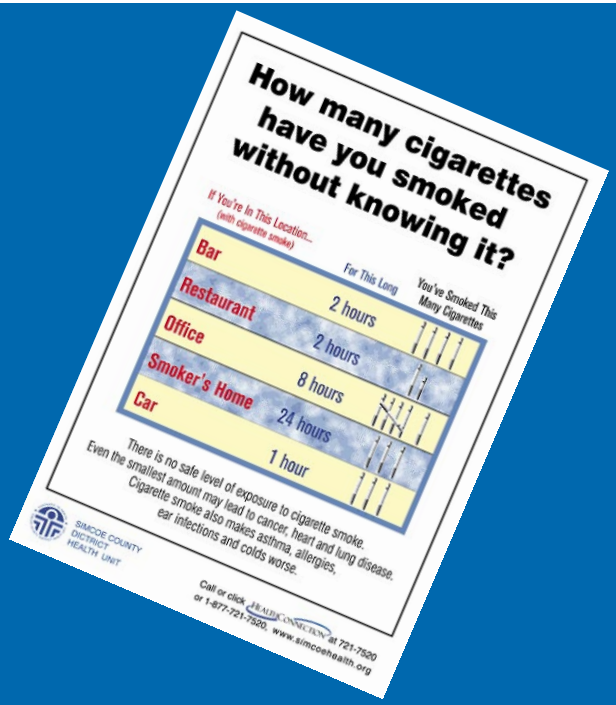
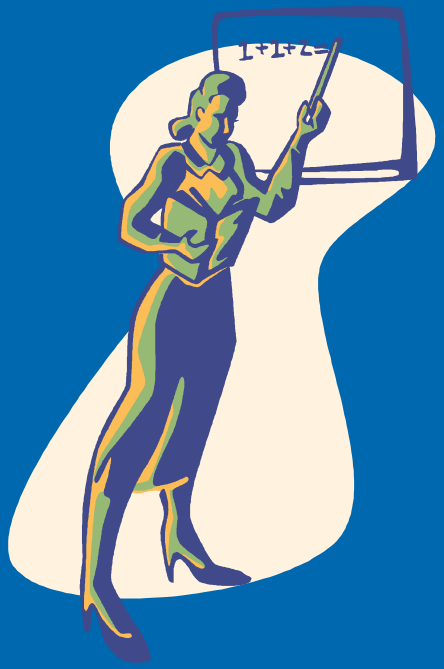


Human Exposure to Environmental Tobacco Smoke: Chemistry and Exposure

Roger A. Jenkins, Ph.D.

Presented at the LSRO Individual Exposure Assessment Committee meeting in Bethesda, MD

December 13, 2005



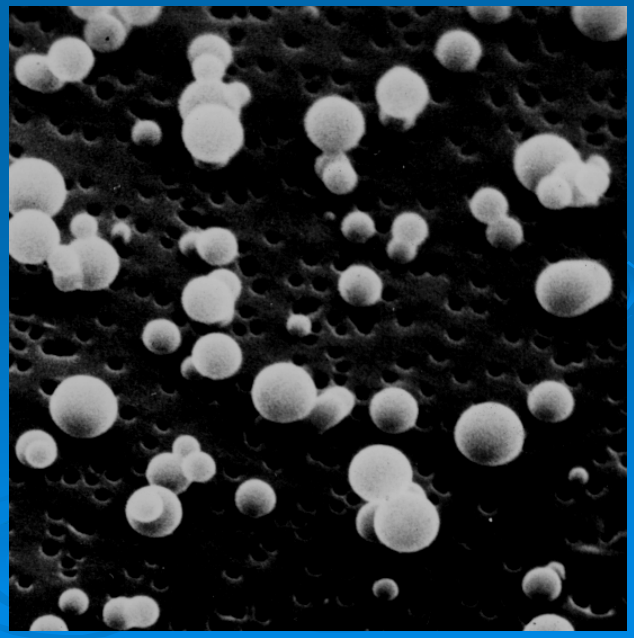
Environmental Tobacco Smoke 101

Three Kinds of Tobacco Smoke

- Mainstream: the material inhaled when a cigaetted is puffed on.
- Sidestream: The smoke that curls off the firecone of the cigarette when it is smoldering.
- ETS: A combination of highly diluted and aged sidestream and exhaled mainstream smoke.

The Two Phases of Tobacco Smoke

- **Particle Phase**, made up of liquid droplets which are comprised of higher MW hydrocarbons.
  - ***This is the smoke that is visible, because the tiny droplets scatter light***.
- **Vapor Phase**, made up of volatile organic chemicals and permanent gases, such as carbon dioxide, carbon monoxide, methane, ammonia.
  - ***The vapor phase is not visible to the human eye.***



Environmental Tobacco Smoke: What Is It?

Highly diluted mixture of sidestream (70 - 90%)
and
exhaled mainstream (10 - 30%) tobacco smoke

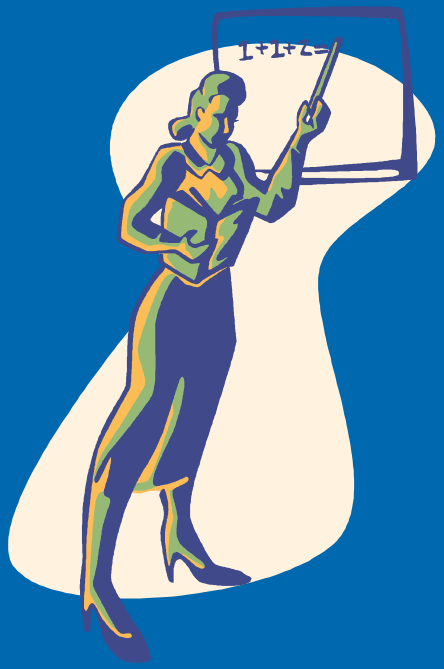
Sidestream Tobacco Smoke

+

Exhaled Mainstream Tobacco Smoke

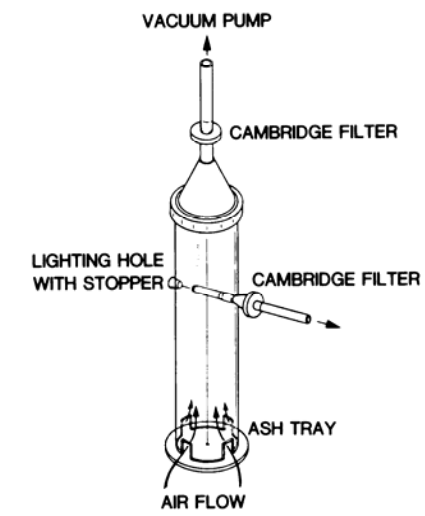
Environmental Tobacco Smoke: What Is It? (continued)

- Mainstream, sidestream, and ETS are NOT the same material.
- The term "*second hand smoke*" is probably misleading, since most ETS is derived from smoke which is emitted by the smoldering firecone of the cigarette.
- Differences between ETS and mainstream smoke are primarily due to differences in combustion mechanisms between sidestream and mainstream tobacco smoke.
- Differences between ETS and sidestream smoke are mostly due to the interactions of various components with the surrounding environment.

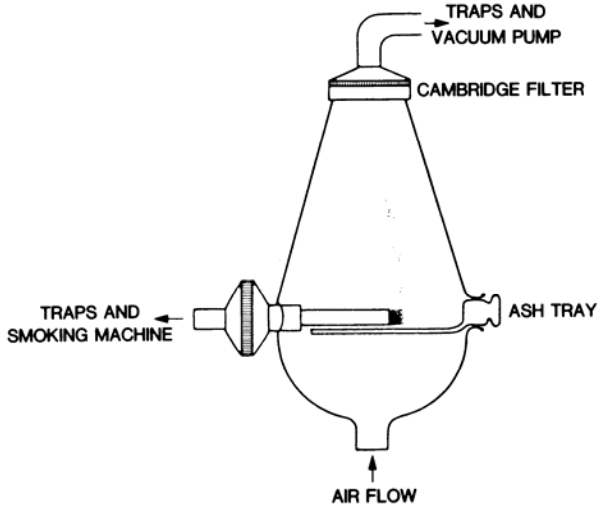


Environmental Tobacco Smoke 201

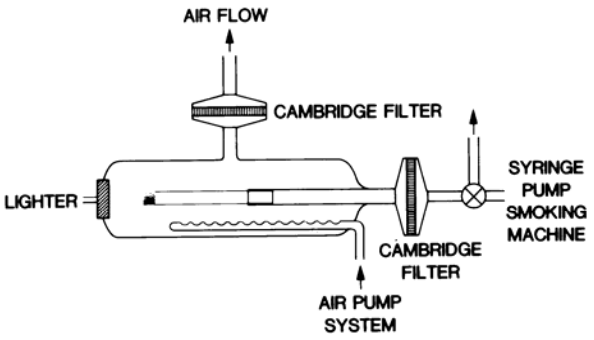
Early Sidestream Smoke Generators



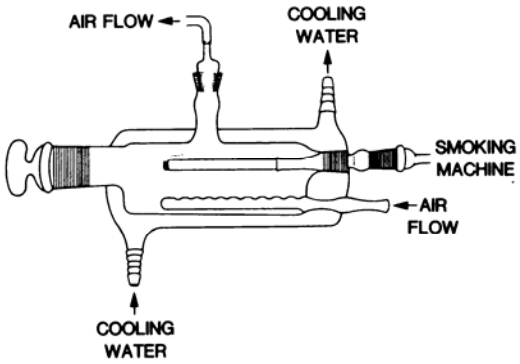
BROWNE, et. al., 1980
JOHNSON, et. al., 1973



SAKUMA, et. al., 1983

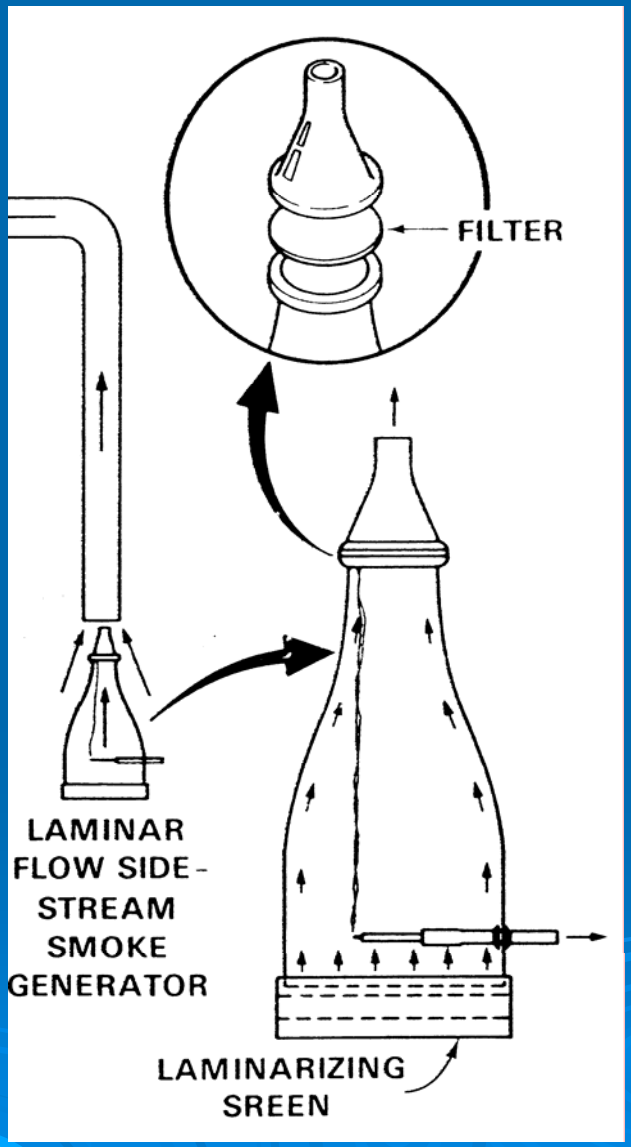


NORMAN, et. al., 1983



BRUNNEMANN AND HOFFMANN, 1974

ORNL Laminar Flow "Milk Bottle" Chamber



Comparison of ETS to Mainstream and Sidestream Cigarette Smoke

	Mainstream Tobacco Smoke	Sidestream Tobacco smoke	Environmental Tobacco Smoke
Particle Concentration	1,000,000 - 100,000,000 ug/m^3	1,000,000 - 5,000,000 ug.m^3	20 - 200 ug/m^3
Where is the nicotine?	~ 100% is in the particle phase ~0 % is in the vapor phase	Distributed between particle and vapor phase	~3% is in the particle phase ~97% is in the vapor phase
Composition	Water and many volatile organic compounds in the particle phase	Water and many volatile compounds distributed between particle and vapor phase	Water and most volatile organic compounds in the vapor phase
Temperature of formation	1475^o F. - 1750^o F	1100^o F.	"75^o F"
pH	lower than neutral (more acidic)	higher than neutral (more alkaline)	higher than neutral (more alkaline)

Use of Controlled Atmosphere Chambers to Assess Smoking Product Emissions

1R4F SS Composition: Fishtail vs. Room Size Chamber

	1R4F SS Fishtail Chamber (Borgerding)	1R4F SS Room Size Chamber (Daisey)
"Tar", mg/cigt	25	7.7
Formaldehyde, ug/cigt	900	1330
Acetaldehyde, ug/cigt	1900	2200
Phenol, ug/cigt	275	238
m+p Cresol, ug/cigt	88	68

Cigarette Emissions (μg/cigt): Simulated or Actual ETS

Constituent	Daisey et al, 1998 (6 US Commercial Cigarettes)	Martin, et al, 1997 Weighted Market Share Average of 50 Brand Styles
Acetaldehyde	2150 ± 477	2496 ± 34
Benzene	406 ± 71	280 ± 5
Formaldehyde	1310 ± 348	1333 ± 34
Pyridine	428 ± 122	278 ± 7
Styrene	147 ± 24	94 ± 2
Toluene	656 ± 107	498 ± 11
o-Xylene	67 ± 16	59 ± 2
Nicotine	919 ± 240	1585 ± 42
PM2.5/RSP	8100 ± 2000	13674 ± 411

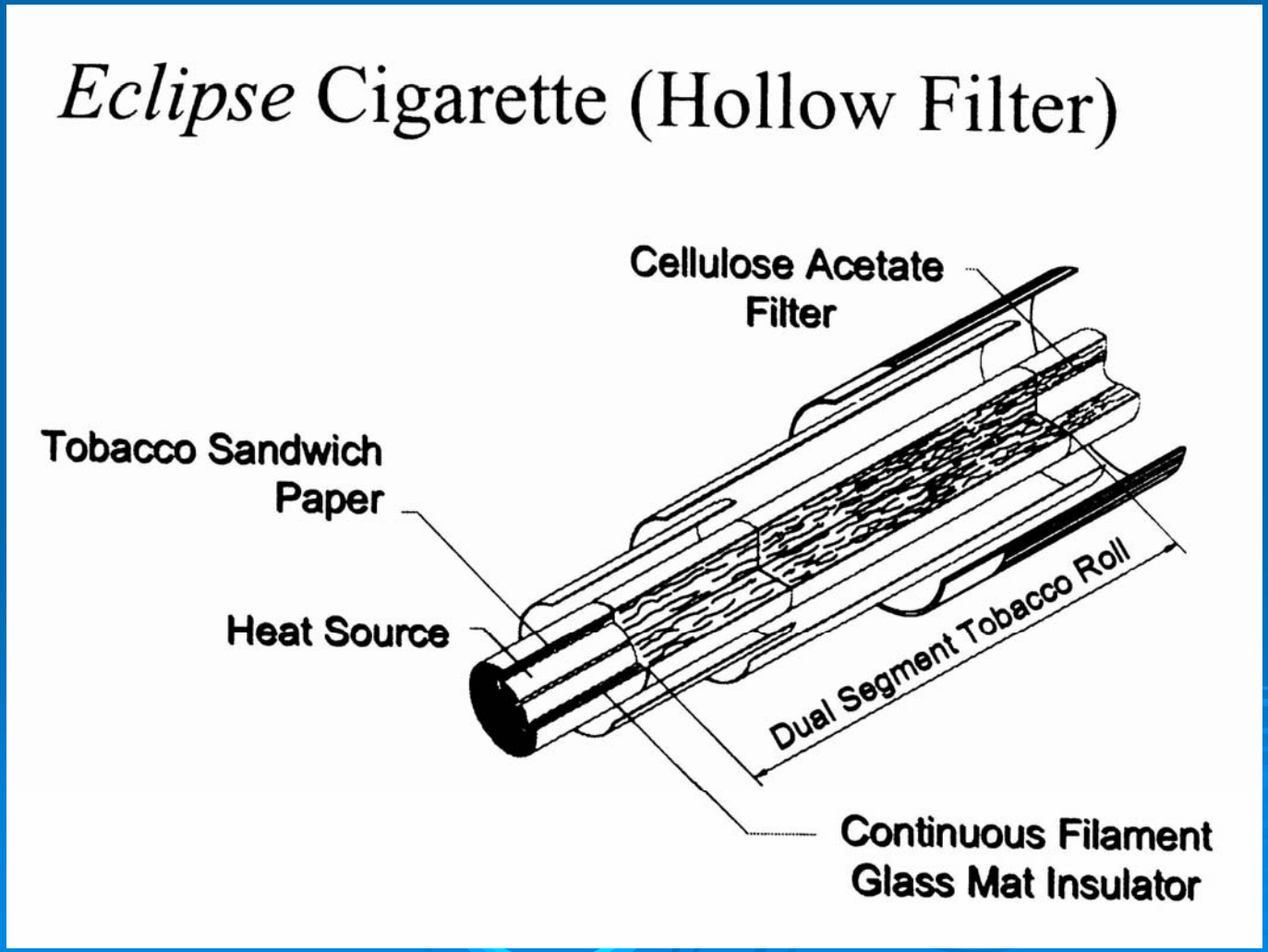
Some Vapor Phase Components of ETS

- Nicotine
- CO, CO2
- methane
- 3-vinyl pyridine (3-EP)
- dimethyl nitrosamine
- benzene
- formaldehyde
- neophytadiene
- limonene
- toluene
- pyridine
- Acetone
- Acetaldehyde
- 2-picoline
- Styrene
- Benzaldehyde
- Methylethyl ketone
- 2,5- dimethyl furan
- Dimethyl benzenes
- Butanone
- 1,3-butadiene

Some Particle Phase Components of ETS

- Solanesol
- Scopoletin
- Benzo(a)pyrene
- Anthracene
- Cholesterol
- Nonacosane
- 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)
- Phenanthrene
- Cadmium
- Nickel
- Zinc
- Selenium
- Stigmasterol

Low Sidestream Emission Cigarettes :
Cigarettes that Heat, but Don't burn Tobacco

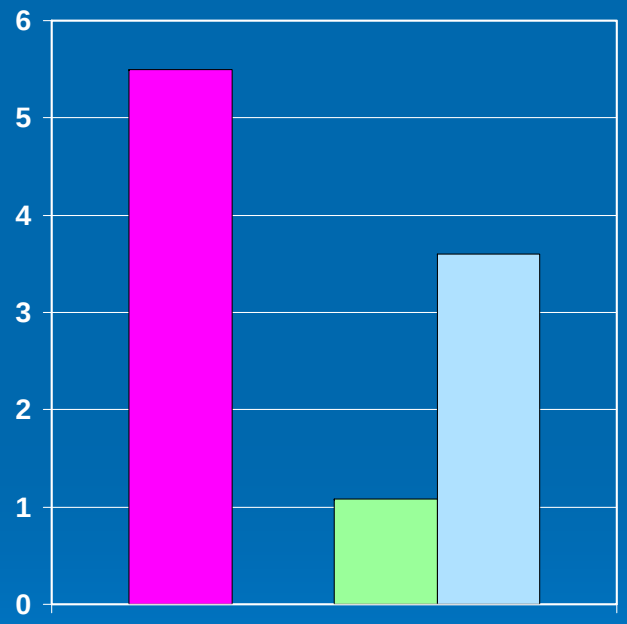


SS Emission Reduction for Eclipse

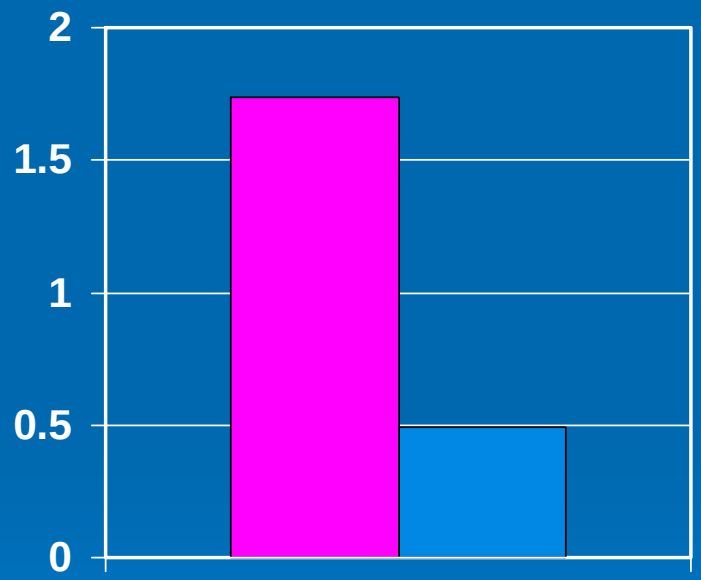
Constituent	% Reduction Relative to 1R5F	Constituent	% Reduction Relative to 1R5F
SS “Tar”	-99+	Catechol	-97
Formaldehyde	-81	Phenol	-97
Acetaldehyde	-95	m+p Cresol	-97
Hydroquinone	-97	B(a)P	-98

Sidestream Smoke is Not Equivalent to ETS #1

NDMA:CO Ratio



Acrolein:Formaldehyde Ratio



Sidestream smoke

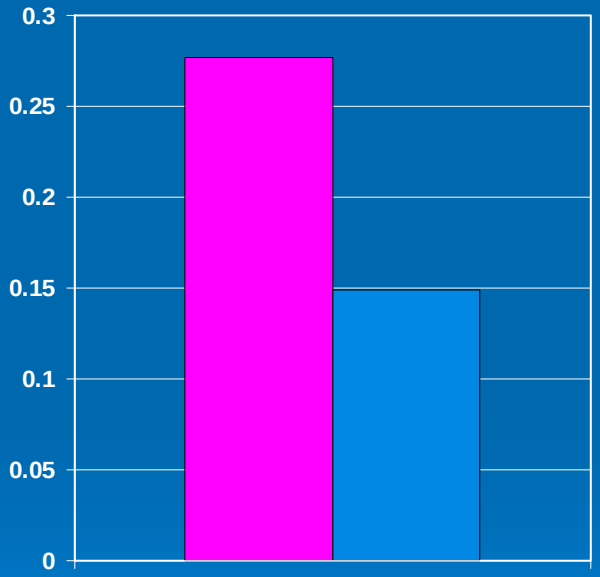
Chamber ETS

Office #1 ETS

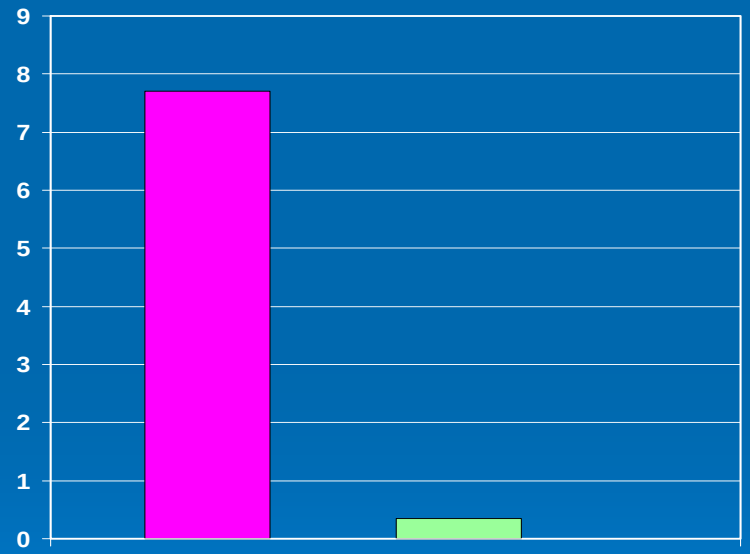
Office #2 ETS

Sidestream Smoke is Not Equivalent to ETS #2

Ammonia:CO Molar Ratio



NNK:CO Ratio



Sidestream smoke

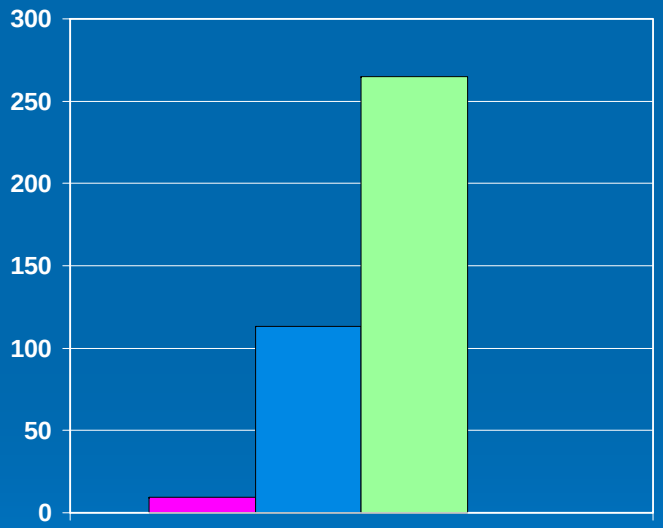
Chamber ETS

Office #1 ETS

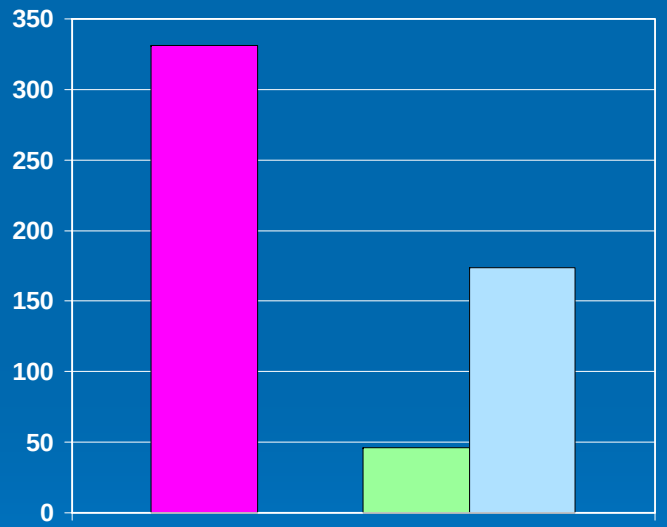
Office #2 ETS

Sidestream Smoke is Not Equivalent to ETS, #3

CO:Nicotine Ratio



NDMA:NOx Ratio



Sidestream smoke

Chamber ETS

Office #1 ETS

Office #2 ETS

How Do We Determine Human Exposure to ETS?

Area vs Personal Monitoring

Personal Exposure Determinations

Advantages

- Measures (through sample collection or real time analysis) the integrated concentration of airborne species actually in the breathing zone of the subject.
- Directly reflects human activity patterns.

Disadvantages

- Number or size of systems which can be worn by the subject without seriously affecting activity is limited.
- Knowledgable subjects may alter their behavior patterns

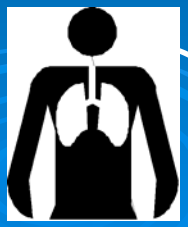
What is “Exposure”?

- Exposure is defined as the product of the average concentration of airborne material during a given time period and the duration of that time period.
- Often reported in microgram-hours per cubic meter (ug-hr/m^3)

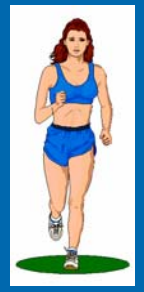
Exposure = Concentration  **x** Time 

What is Potential Inhaled Quantity of Environmental Tobacco Smoke (ETS)?

- The PIQ is the **product** of the concentration of ETS in the air, the time spent in that environment, and the breathing rate.
- Breathing rate is dependent on how fast you are moving or how hard you are working.

PIQ = Concentration  **X** Time  **X** Breathing Rate 

Breathing Rate is Dependent on How Hard You Work or How Fast You Move

Activity	Sleeping	Resting or Sitting	Walking 1 - 3 mph	Walking > 3 mph or slow jogging	Very vigorous exercise
		 		 	
Estimated Breathing Rate*, cubic meters per hour (m3/hr)	0.4	0.5	1.1	1.7	2.8

* from 1996 EPA Exposures Factor Handbook, DRAFT

Cleaning

Cooking

Indoor Air Pollution Can Be Derived From a Variety of Non-Tobacco Sources

Consumer Products

Wood Burning

All Incomplete Combustion Processes Produce Smoke Comprised of Thousands of Constituents

Many components are toxic at some level, and all smokes are likely to contain a few "signature" components

Desirable Characteristics of Marker Compounds

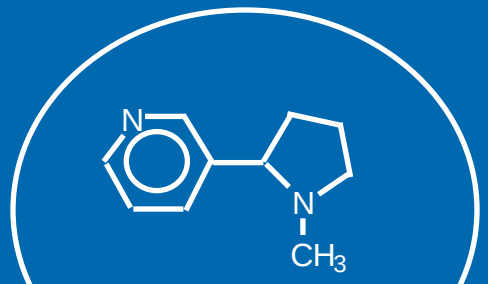
(Taken from the National Academy of Sciences Report on ETS)

- Useful for describing the concentration of complex materials.
- Unique to the substance in question.
- Behaves like the material or phase of the substance that is being assessed.
- Present in measurable quantities even at low substance concentrations

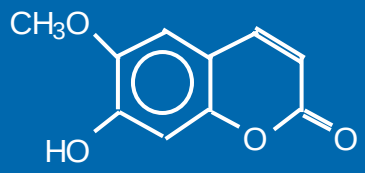
Potential ETS Markers

- Respirable suspended particulate matter (RSP)
- Ultraviolet absorbing and fluorescing particulate matter (UVPM & FPM)
- Solanesol
- Carbon Monoxide (CO)
- Nicotine
- 3-ethenyl pyridine (3-EP)
- Hi MW straight chain hydrocarbons (n-C_{27} - n-C_{31})
- Isoalkanes and ante-isoalkanes

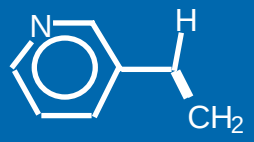
Environmental Tobacco Smoke Markers in Common Use



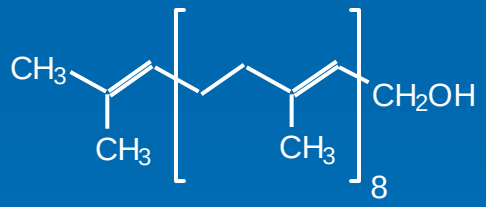
Nicotine



Scopoletin



3-ethenyl pyridine



Solanesol

Myosmine

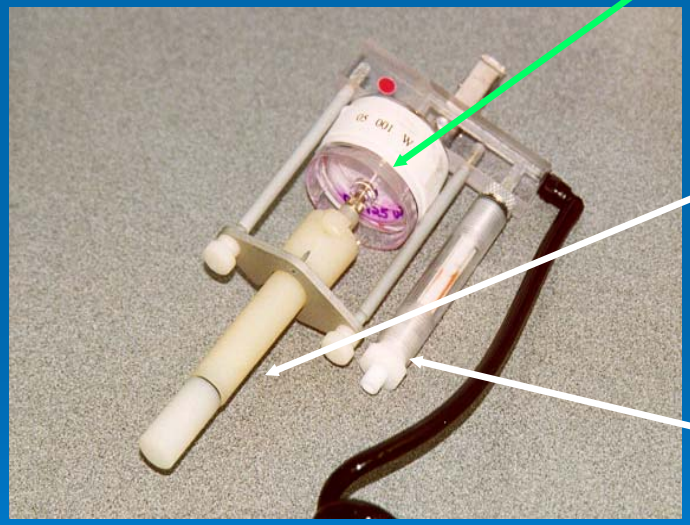
Most Widely Used

Sample Collection in the Workplace

Sampling Head

Sampling Pump

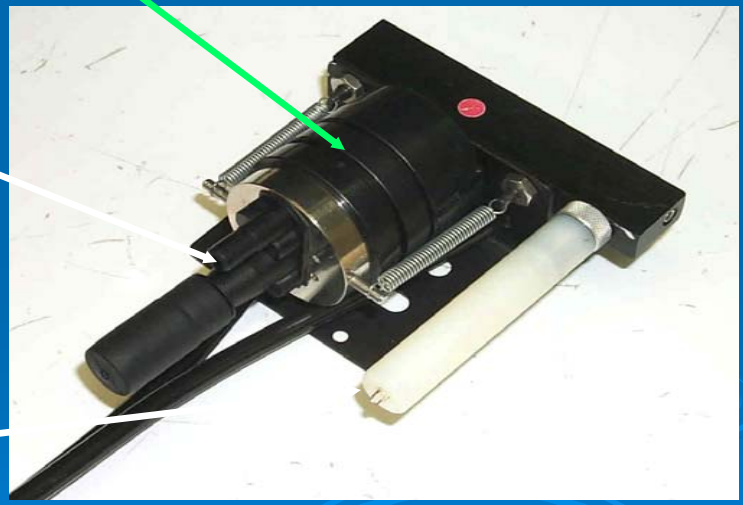
Technology is Always Improving: Opaque Filter Holders May Mitigate Post-Collection Degradation of Solanesol



Filter Holder

Cyclone Separator

XAD-4 Vapor Collection Cartridge

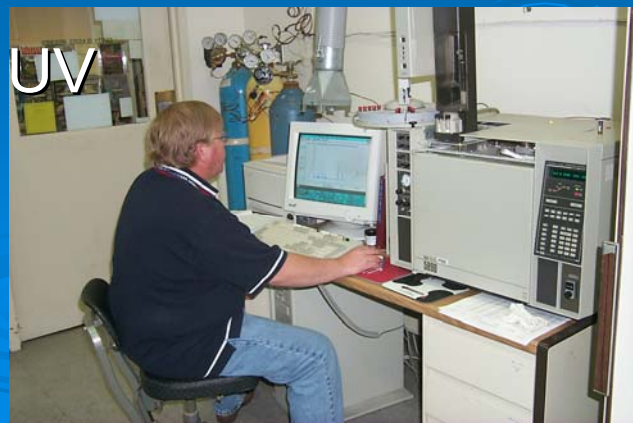


Clear plastic filter holder used in 16 Cities Study (1993-94)

Opaque plastic filter holder used from 1997 on

60,000 Foot View of the Analytical Chemistry

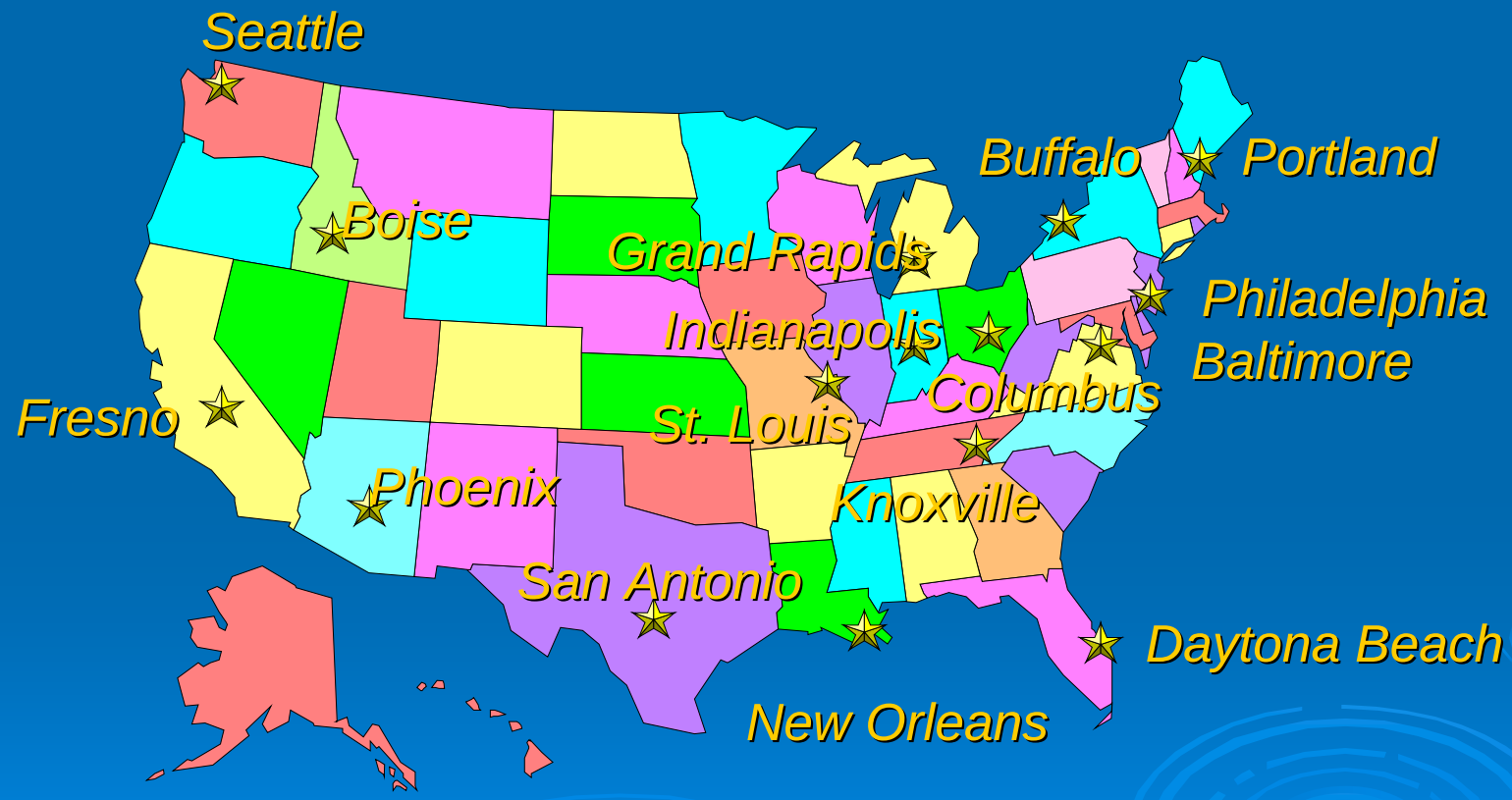
- Analysis of sub-ppb concentrations of airborne pollutants still ain't all that easy.
- Nicotine and 3-EP: collection on XAD-4 resin, extraction with ethyl acetate spiked with an adsorption blocker, and analyzed via GC-NPD.
- Solanesol: extraction with methanol, reverse phase HPLC with UV absorption detection at 205 nm.
- UV-PM/FPM: Column-less HPLC with UV and fluorescence detection.



ORNL ETS Personal Exposure Studies

- Restaurant patron study part of airborne nicotine method development
  - 32 venues, published in 1989
- Area vs Personal Monitoring
  - Variety of venues (ca. 25) included restaurants, laundromats, bowling alleys, etc. Reported in 1990
- 16 Cities Personal Exposure Monitoring
  - ca. 1600 subjects geographically dispersed Published in 1996
- Waiters/waitresses/bartenders
  - ca. 160 subjects, area & personal monitoring. Published in 2000
- Demographically representative study
  - Personal exposure monitoring of ca. 240 subjects. Reported in 2000
- Unrestricted smoking workplace
  - 25 subjects in one facility: area vs personal monitoring. Published in 2001
- ETS Exposure Variability:
  - 67 Subjects in smoking homes or workplaces for four consecutive days. Just finished Final Report. Presented at ISEA Tucson, Oct 2005

16 Cities Study:
Urban Areas Distributed Geographically



Phillips et al Personal Exposure Studies in Europe

Bremen

UK

Paris

Barcelona

Lisbon

Stockholm

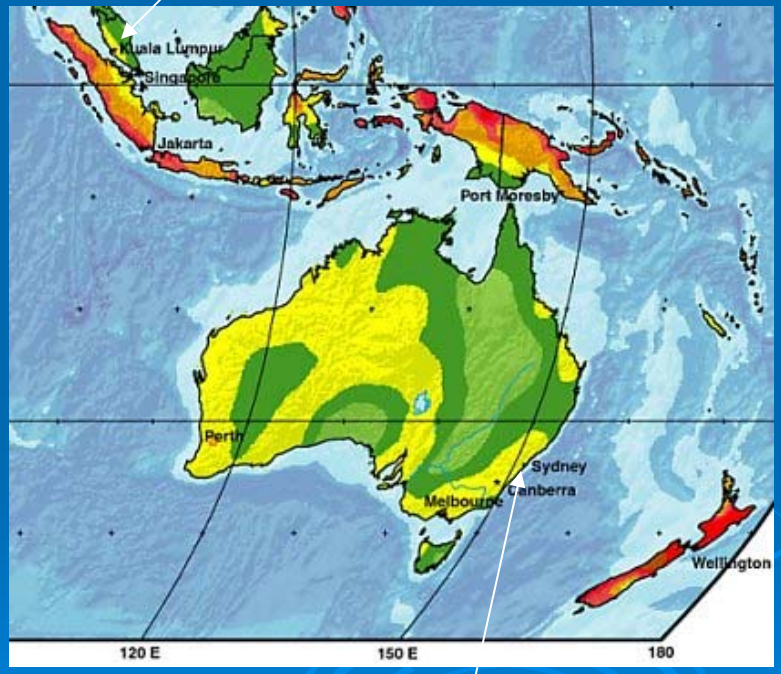
Prague

Basel

Turin

Phillips et al Personal Exposure Studies in South Asia/Australia

Kuala Lumpur



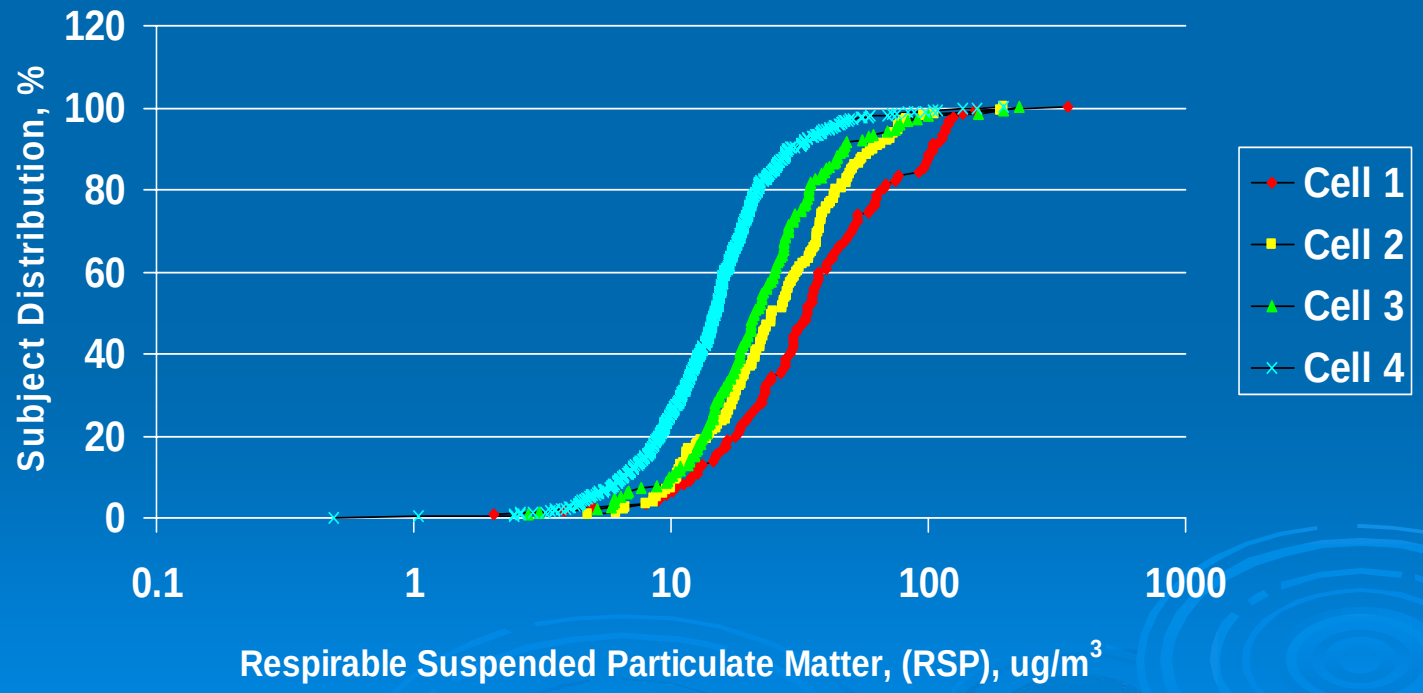
Sidney

Other Notable Personal exposure Studies

- Eisner, et al 2001 (50 asthmatic adults)
- Heavner, Morgan, and Ogden, 1995 (ETS and VOCs in 49 homes
- Proctor et al, 1991(52 working and nonworking females in smoking and non-smoking homes in UK)
- Ogden, 1996 (105 non-smokers and 105 smoking spouses)
- Baek and Jenkins, 2001 (60 subjects in Daegu, Korea)
- Crouse and Oldaker, 1990 (subjects in 21 restaurants)
- Johnsson et al, 2003 (23 Finnish hospitality workers)

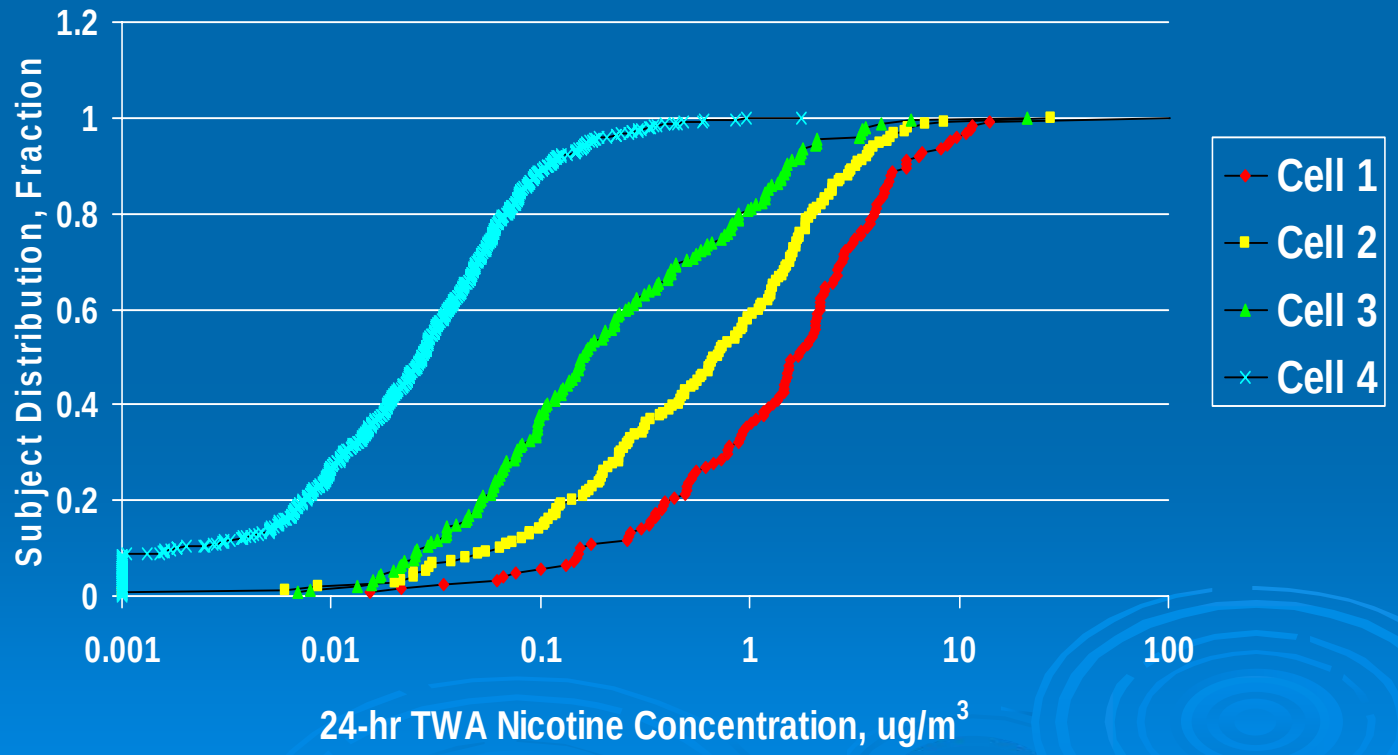
Distribution of 24-hour TWA RSP Levels

Subject Segregation by Self-Reported Home and Workplace Smoking Status Confirmed by Diary Observations (All Subjects with Avg. Cotinine <15 ng/mL)



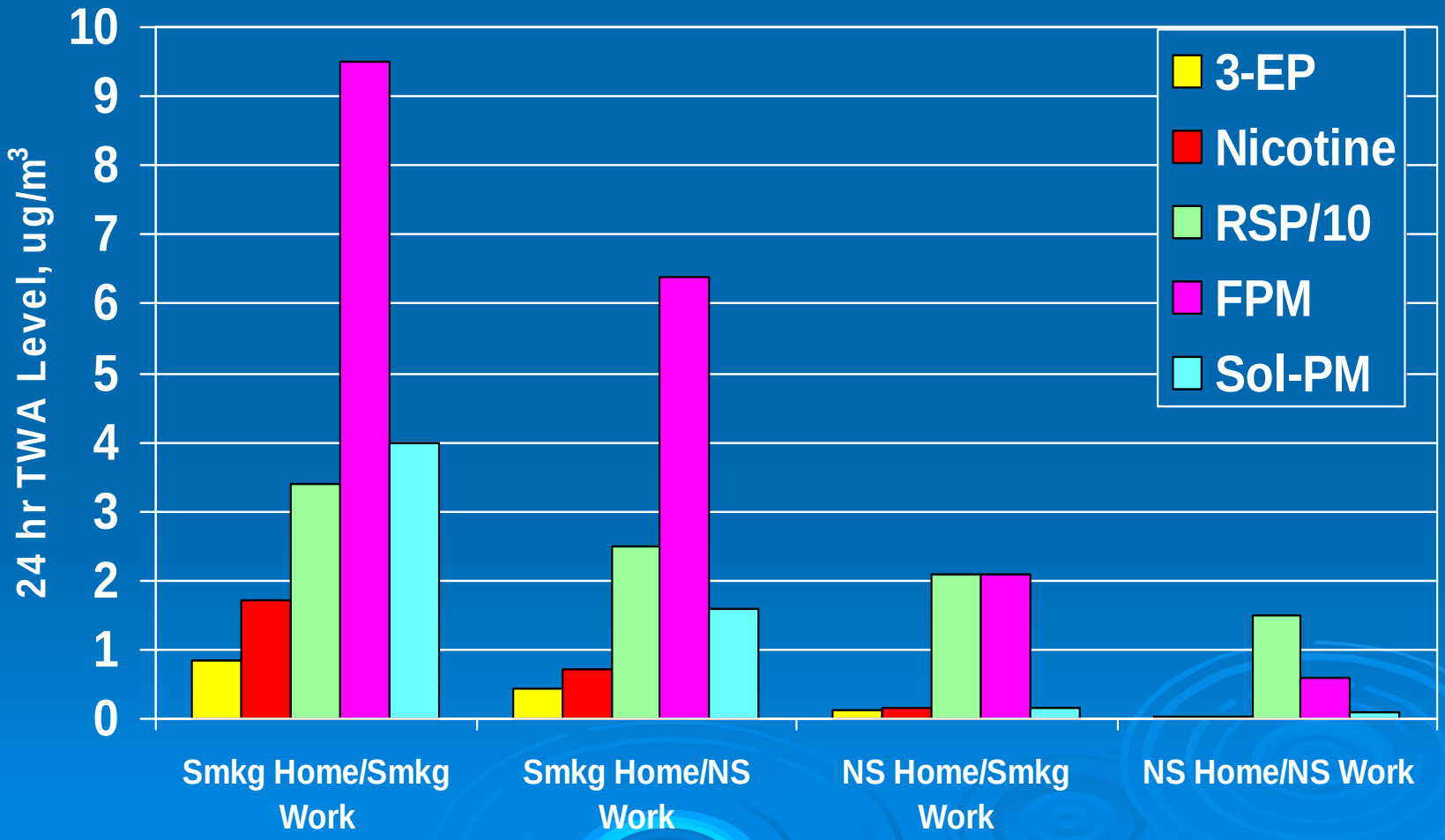
Distribution of 24-hour TWA Nicotine Levels

Subject Segregation by Self-Reported Home and Workplace Smoking Status Confirmed by Diary Observations (All Subjects with Avg. Cotinine <15 ng/mL)



Concentrations of Selected ETS Markers 16 Cities Study: Confirmed Smoking/Non-Smoking Locations

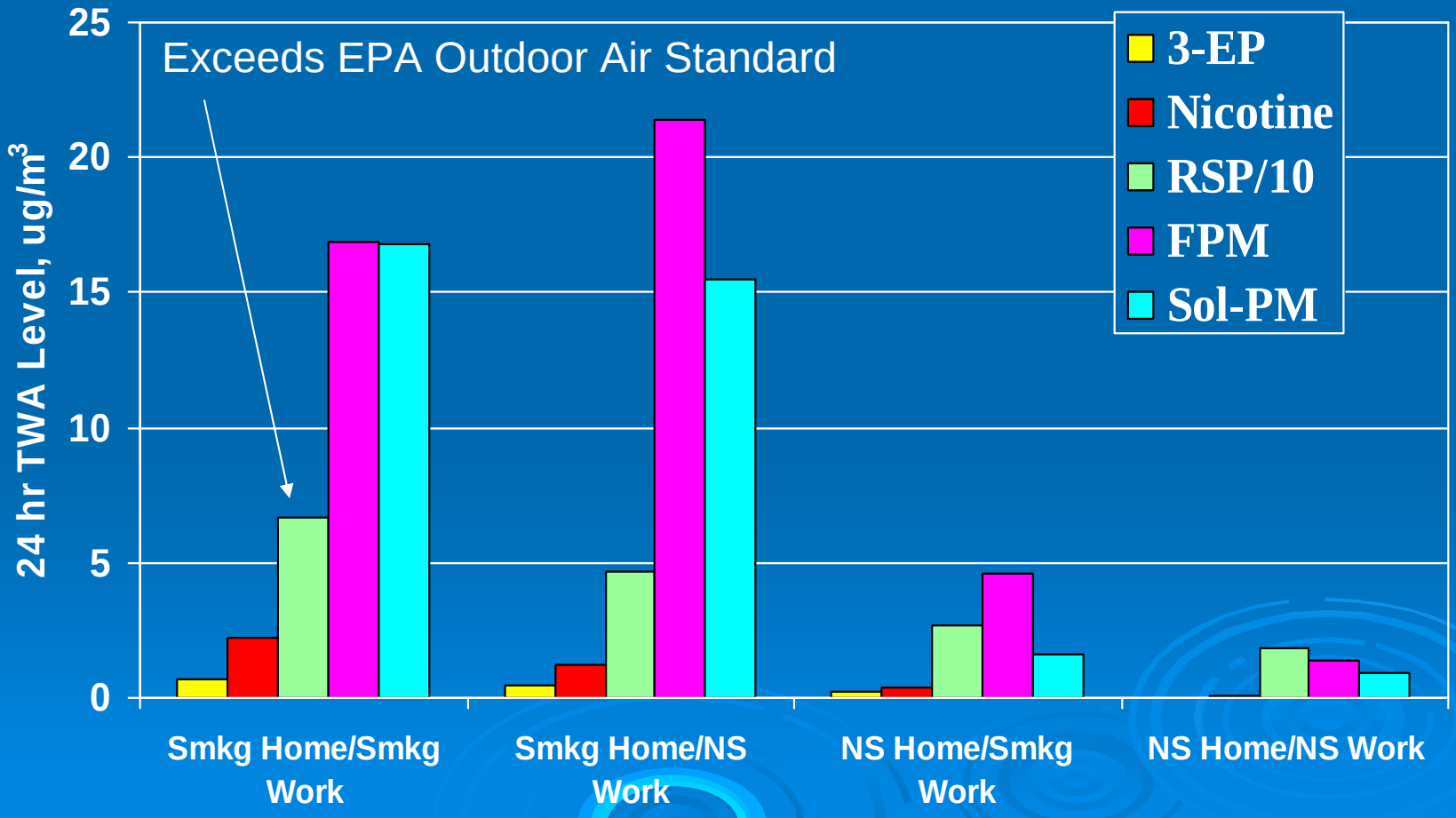
Median 24-hr TWA Levels, ug/m^3



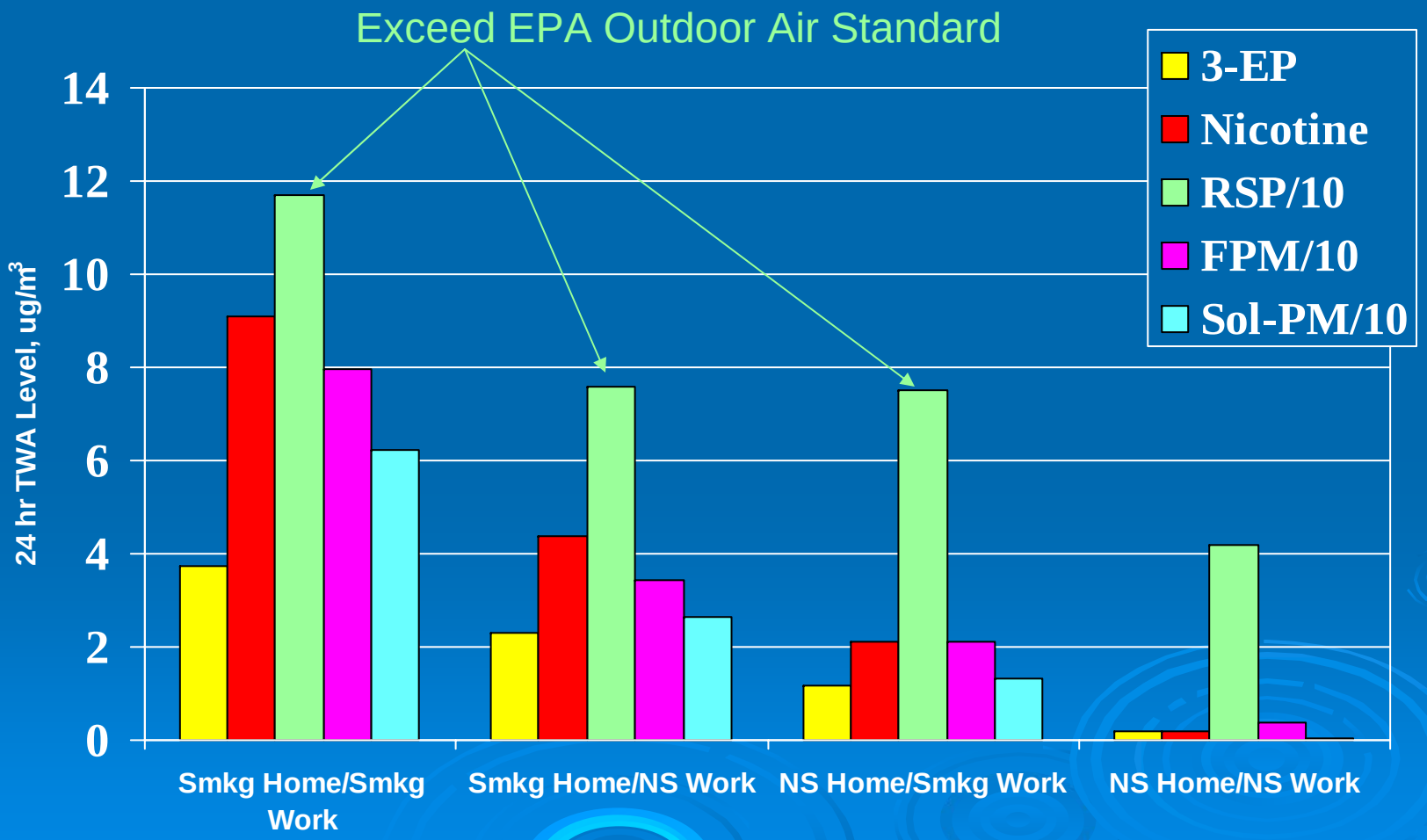
Concentrations of Selected ETS Markers: Confirmed Smoking/Non-Smoking Locations

Demographically Representative Study: Knoxville SMSA, TN

Median 24-hr TWA Levels, ug/m^3

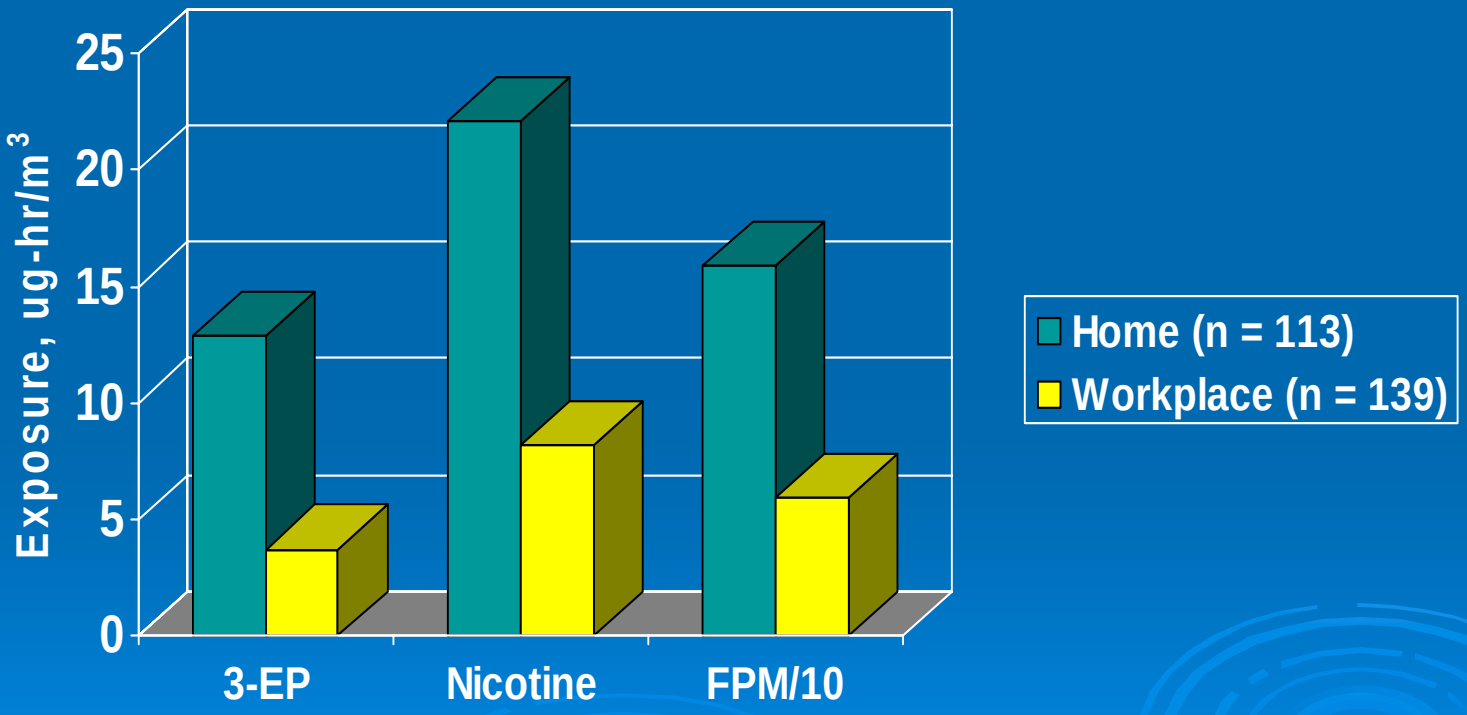


Concentrations of Selected ETS Markers
16 Cities Study
Confirmed Smoking/Non-Smoking Locations
95th Percentile 24-hr TWA Levels, ug/m³



Median ETS Exposures* in Environments Where Smoking is Unrestricted 16 Cities Study

Exposure = Concentration x Time

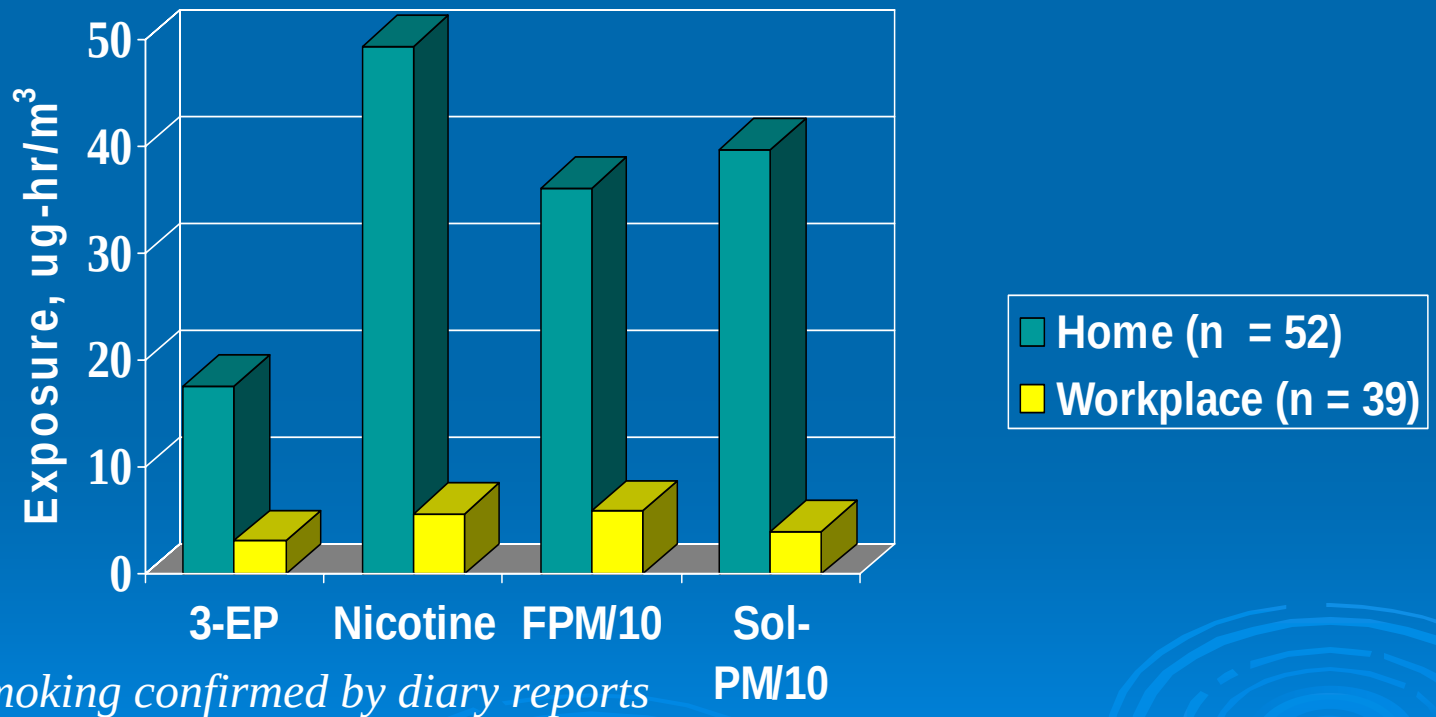


* *Smoking confirmed by diary reports*

Median ETS Exposures* in Environments Where Smoking is Unrestricted

Demographically Representative Study: Knoxville SMSA, TN

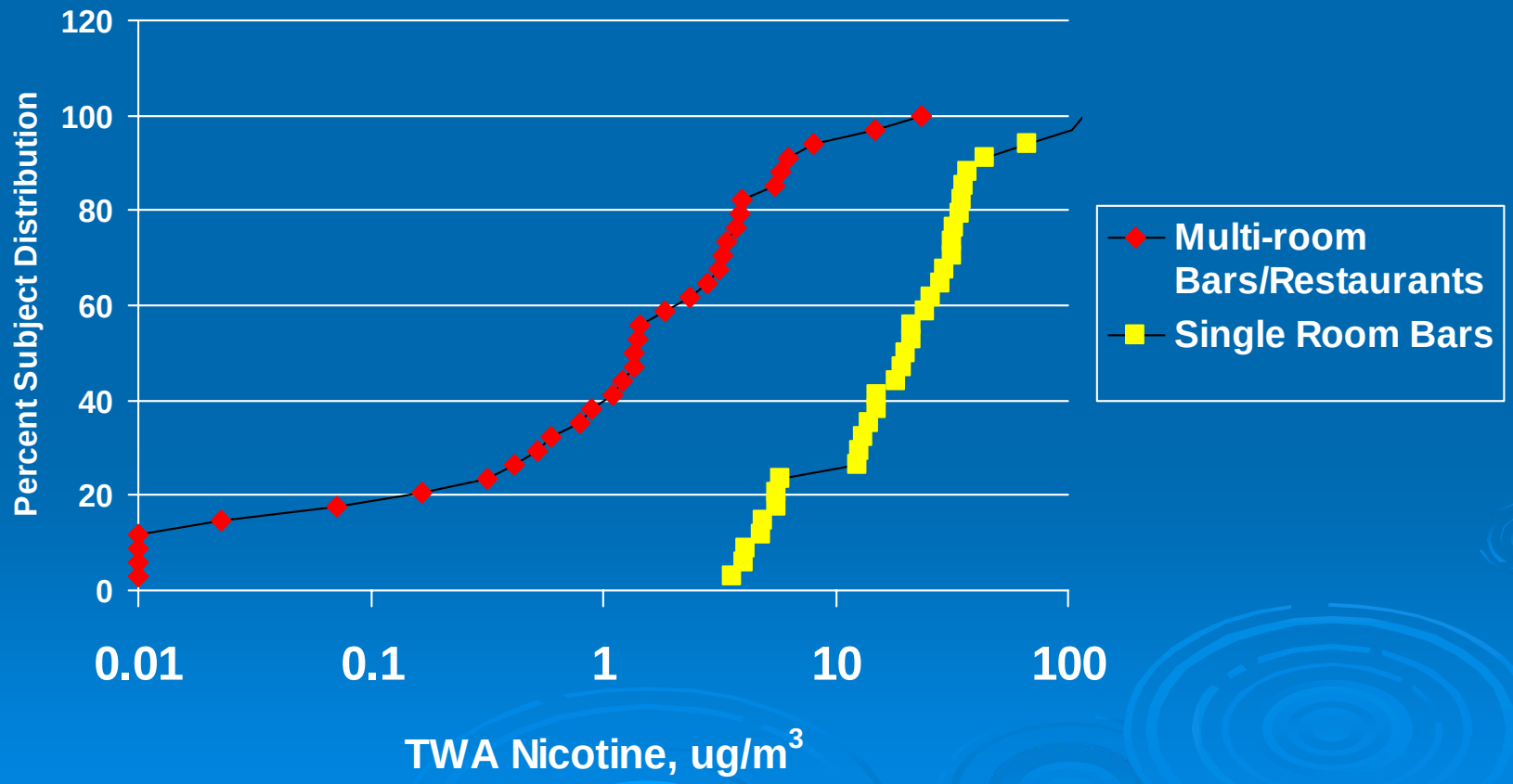
Exposure = Concentration x Time



* *Smoking confirmed by diary reports*

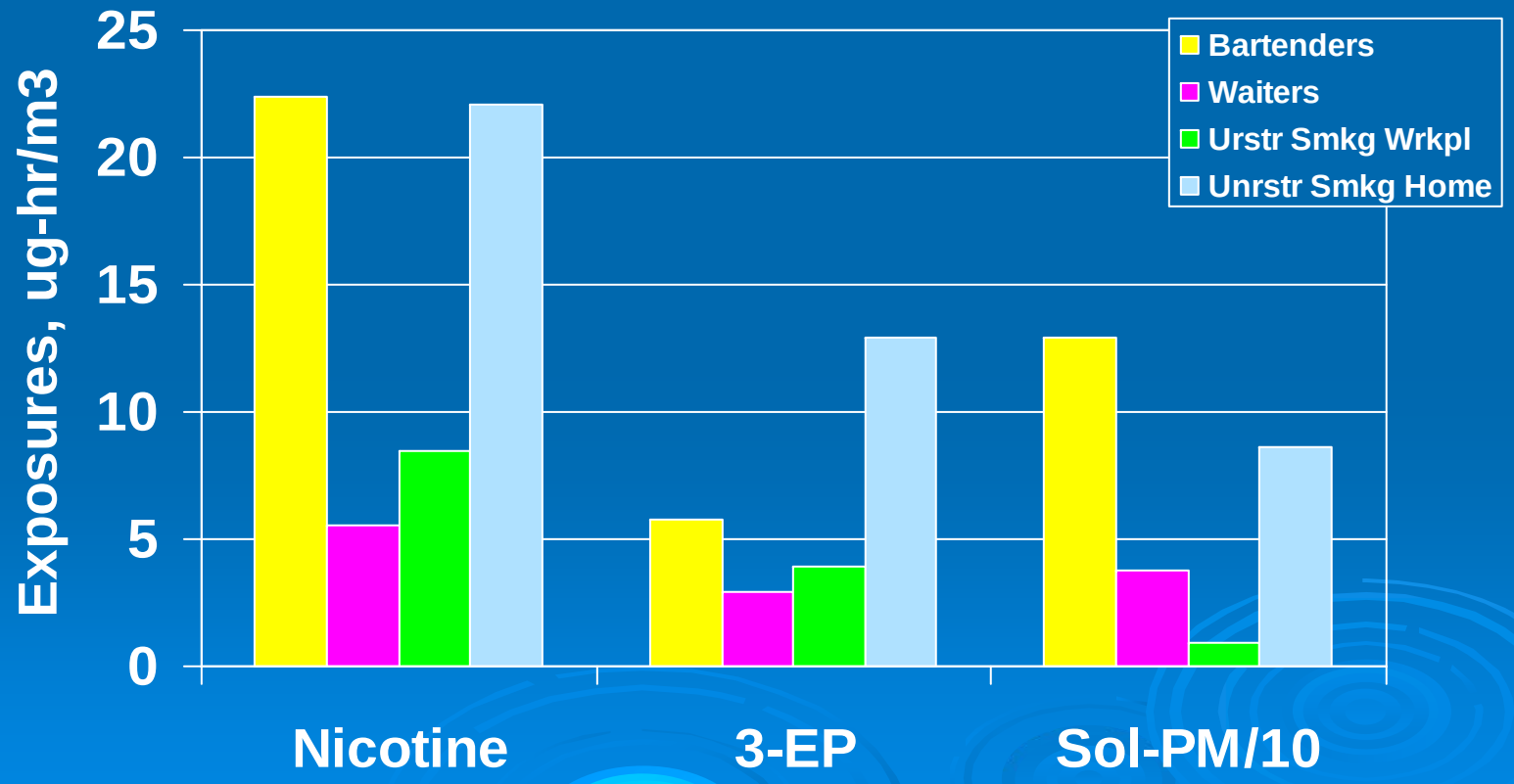
Distributions of Bartender TWA Nicotine Levels:

Multi-Room Bar/Restaurants vs. Single Room Bars

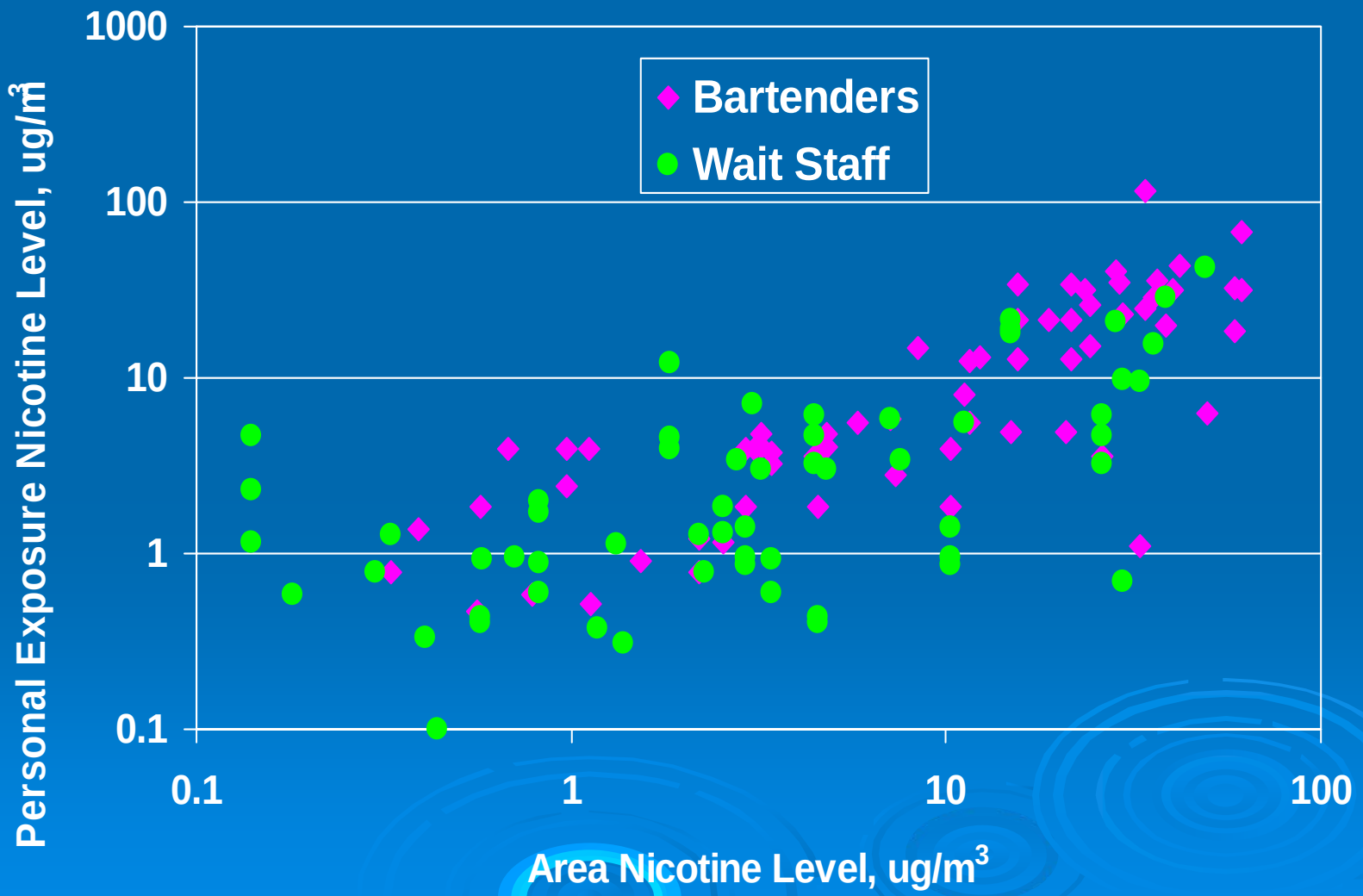


Exposures of Wait Staff and Bartenders vs. Subjects in Unrestricted Smoking Workplaces and Homes (16 Cities Study)

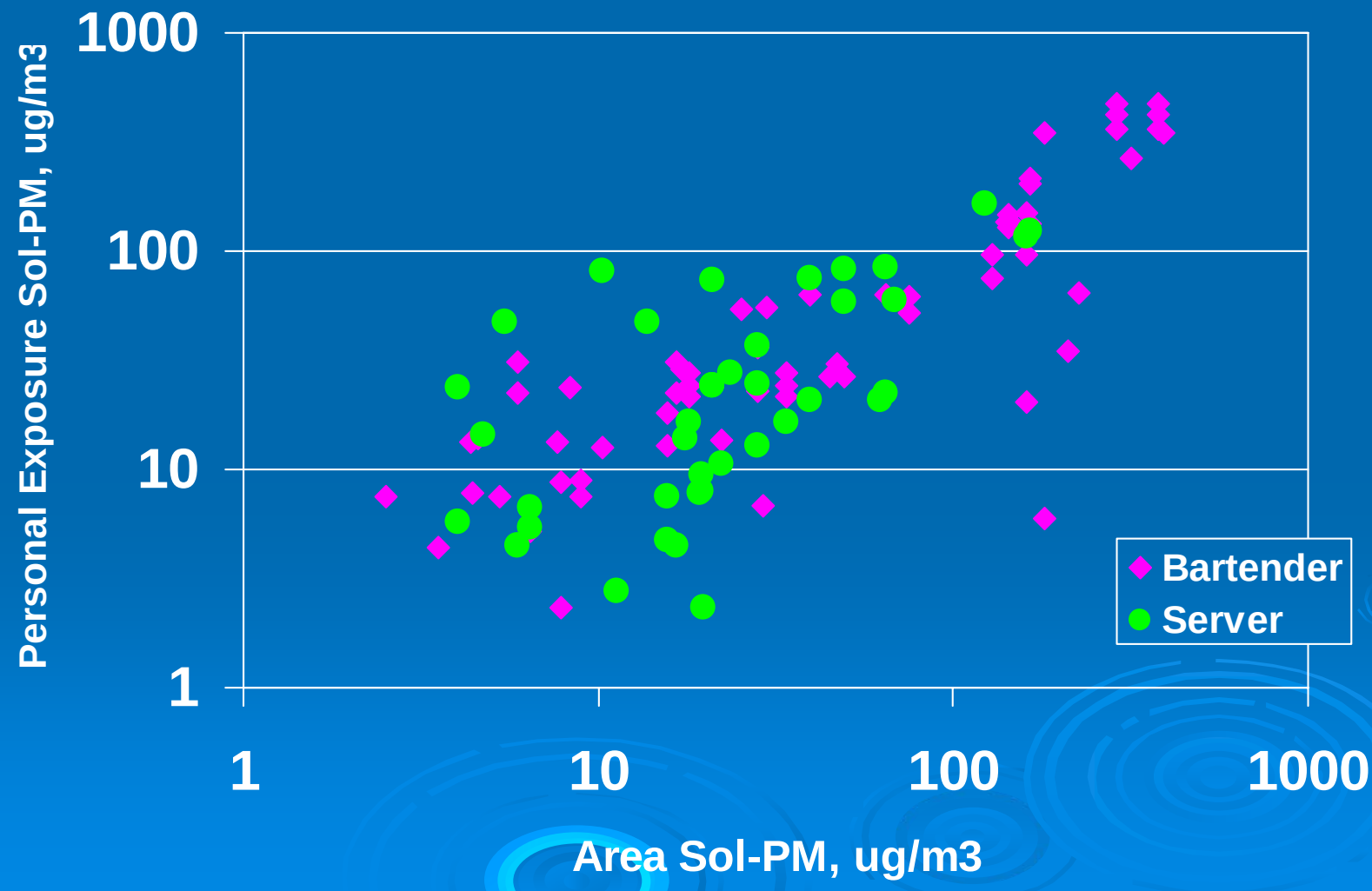
Exposures in μg-hr/m^3



Comparison of Area and Personal Monitoring from Restaurant & Tavern Servers: **Nicotine**

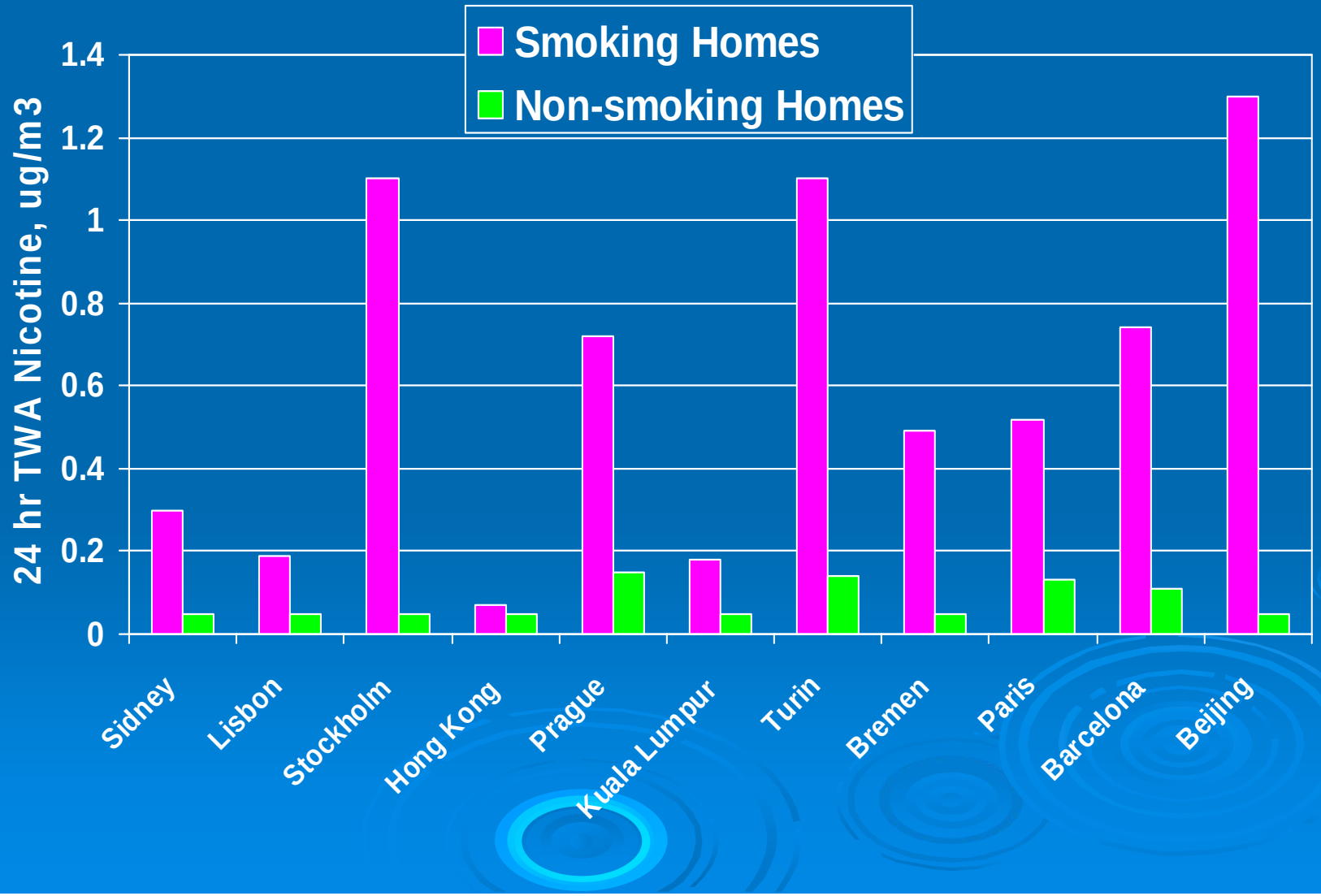


Comparison of Area and Personal Monitoring from Restaurant & Tavern Servers: **Sol-PM**

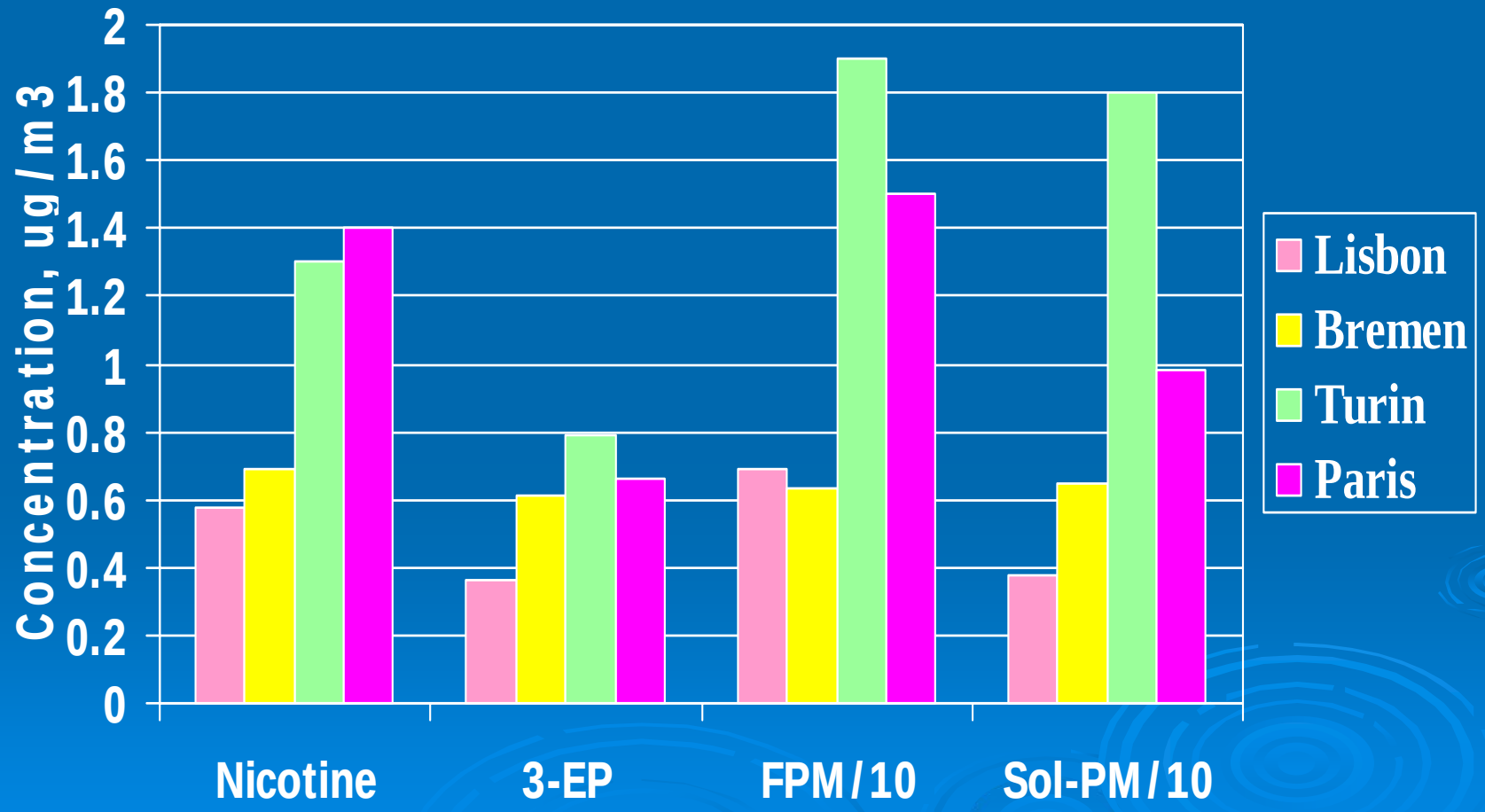


24 hr TWA Nicotine Levels

House-persons Living in Smoking vs Non-Smoking Homes
From Phillips et al

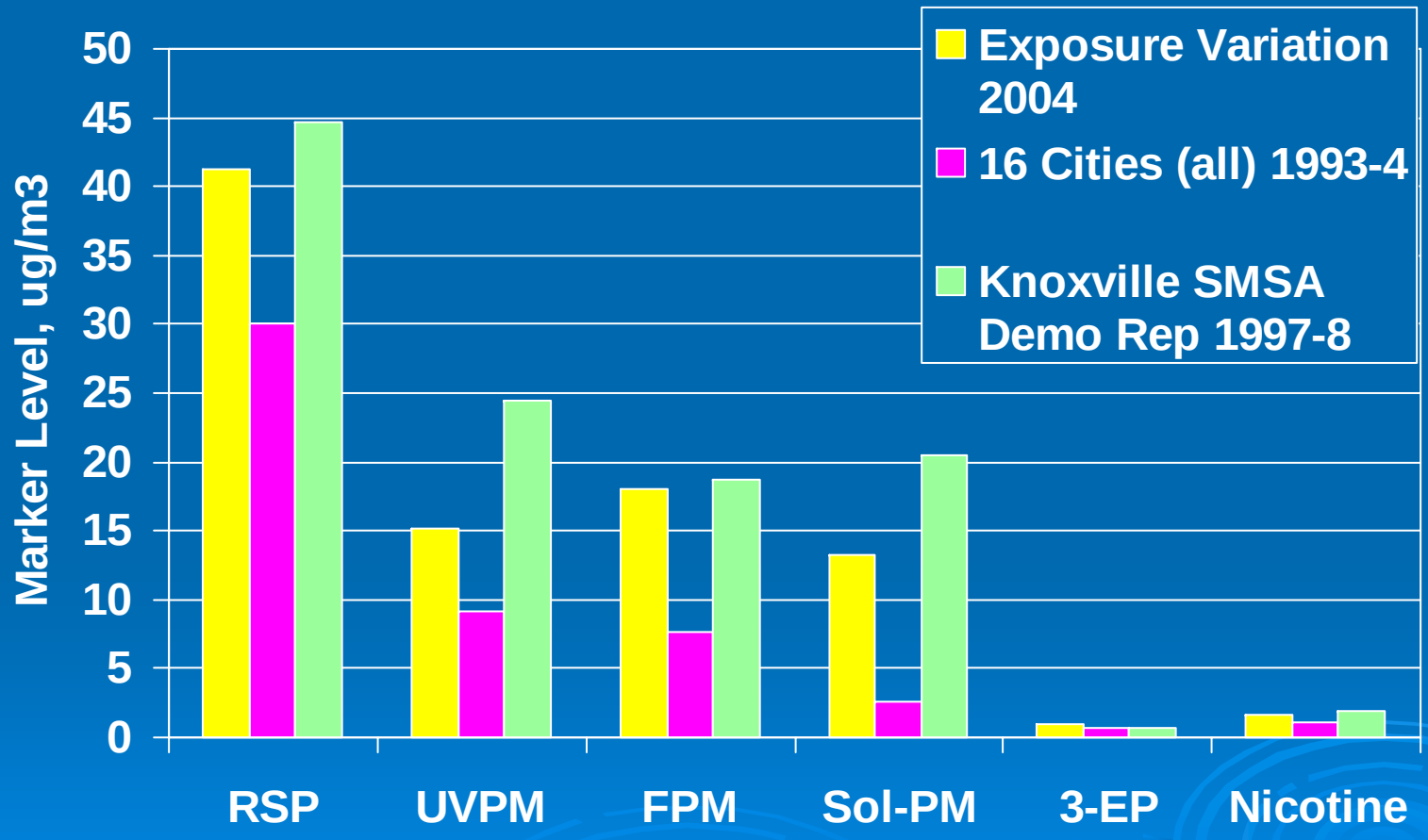


Median 24-hour TWA Levels for Subjects in Smoking Homes/Smoking Workplaces Selected European Cities (Phillips et al)



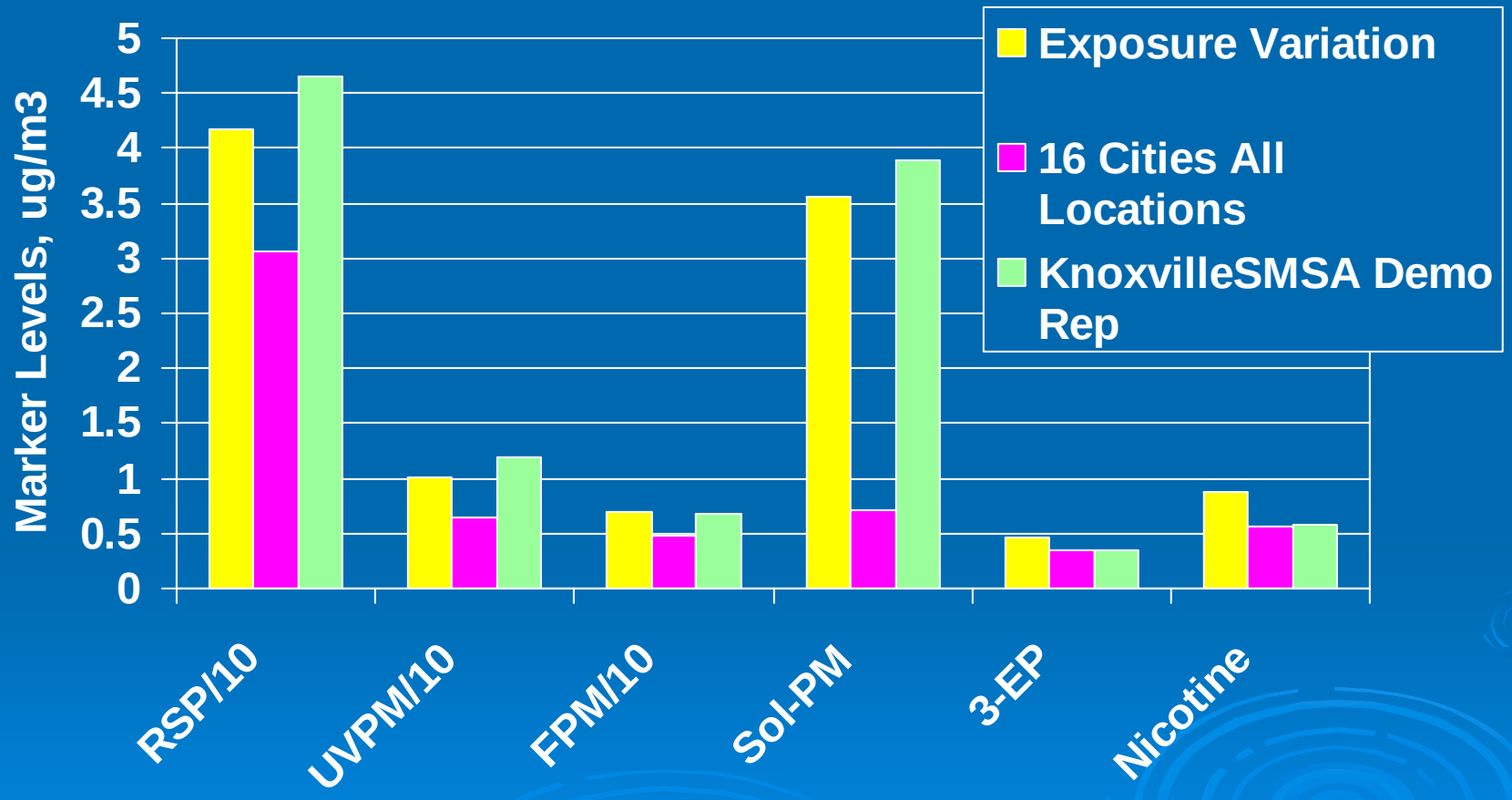
Comparison of Similar Studies

Median Levels: Away from Work for Confirmed Smoking Homes



Comparison of Similar Studies

Median Levels: Confirmed Smoking Workplaces



Typically Encountered Concentrations of ETS in High Exposure Venues Are Still Pretty Low

- Highest encountered level of respirable suspended particulates (RSP) in our wait staff/bartenders study was about 1/7th of OSHA Permissible Exposure Limit (PEL).
- Median area concentration of nicotine was 0.9 parts per billion.

How Does Living with a Smoker Compare to Being a Smoker?

??

- Typical smoker will inhale 480 mg/day of smoke particles, and 32 mg per day of nicotine.
- In a home where smoking is unrestricted, the typical non-smoker will inhale the equivalent of 0.45 mg of smoke particles and 0.028 mg of nicotine.

If you "Do the Math":
The difference is about a factor of 1100

Exposure Concentration Equivalent to 10 g/m³ Nicotine

Note: This is greater than 95th %ile 24-hr TWA from 16 Cities Study

Constituent	Concentration, g/m³	Constituent	Concentration, g/m³
1,3-butadiene	4.4	Formaldehyde	15.7
Acetone	14.3	Ammonia	49.9
Benzene	3.3	Catechol	0.1
Acetonitrile	13.0	Carbon Monoxide	644
Toluene	6.0	Oxides of Nitrogen	21.5
Pyridine	2.6	Styrene	1.1

*From Martin, et al, 1997

Breathing ETS Will Expose You to Toxins, but Not Like Breathing Urban Air

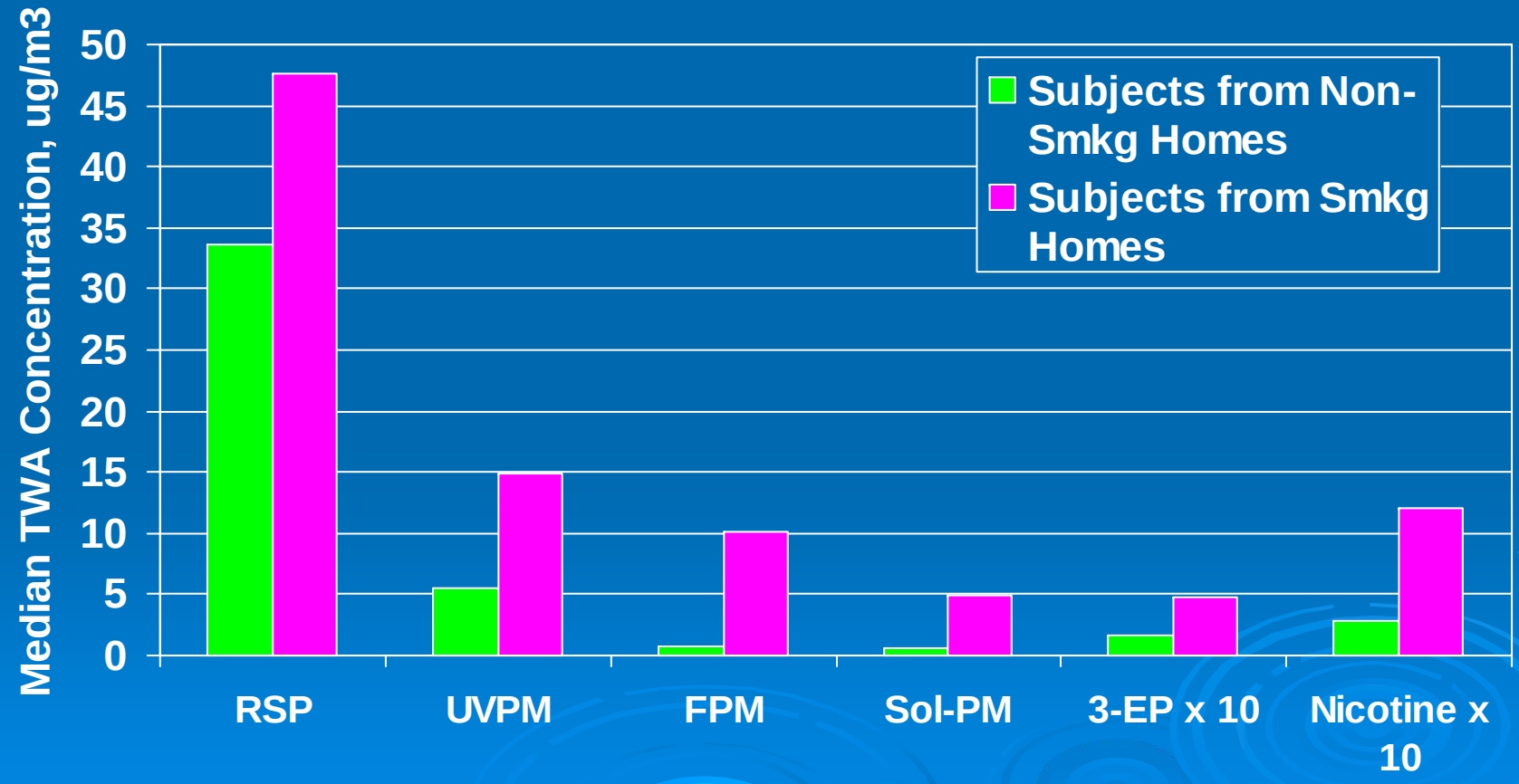
Volatile Compound	Mean Daily Exposure Estimate Based on Living with a Smoker, μg/day*	Confirmed Exposures of Teenagers in Urban Environments from Non-Smoking Homes, μg/day**
Benzene	14	94
Acetaldehyde	126	260
Formaldehyde	66	230

* Estimate based on 16 Cities exposures to nicotine and Baek/Jenkins chamber study, Atm. Env, 38, 6583 (2004)

** Estimate based on Kinney et al, Env. Hlth. Persp. 110/S4, 539 (2002)

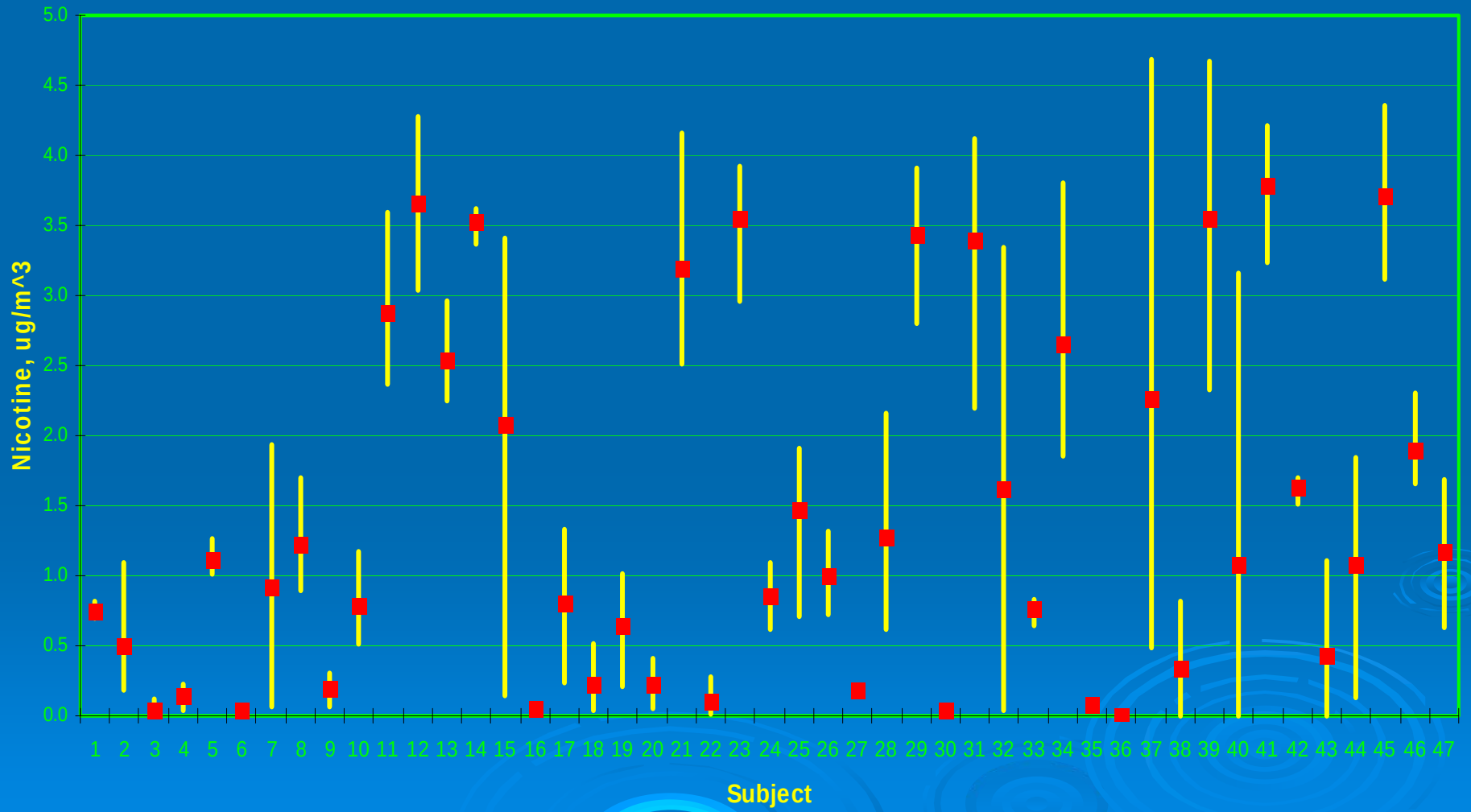
Could Avoidance In Smoking Workplaces Be Occurring?

Are subjects who live in non-smoking homes exposed to lower ETS levels in smoking workplaces?



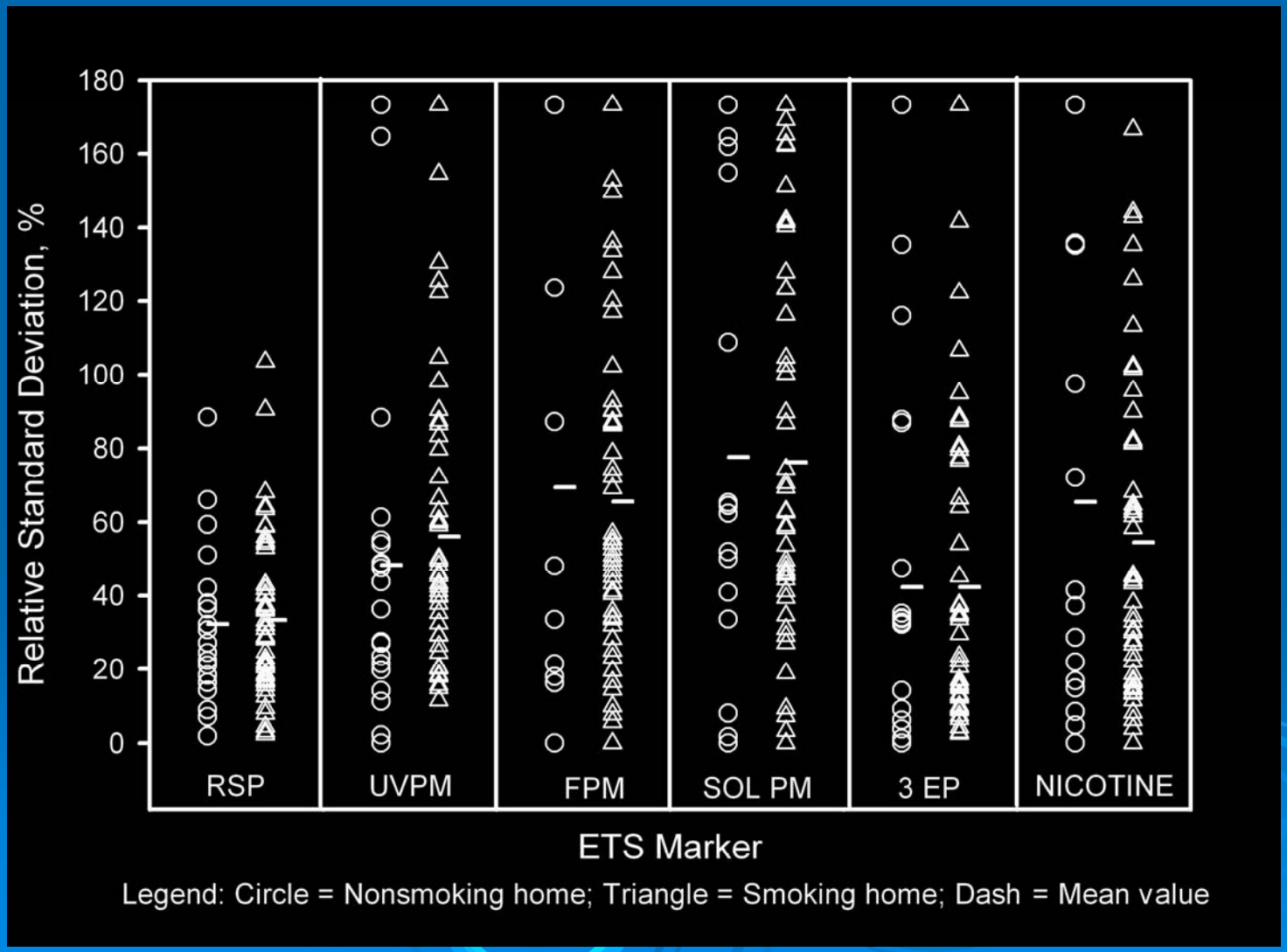
All differences are significant at 95% level, except for solanesol

Variation of 16 hr TWA Nicotine Concentrations, Subjects Residing in Smoking Homes 2004 Exposure Study

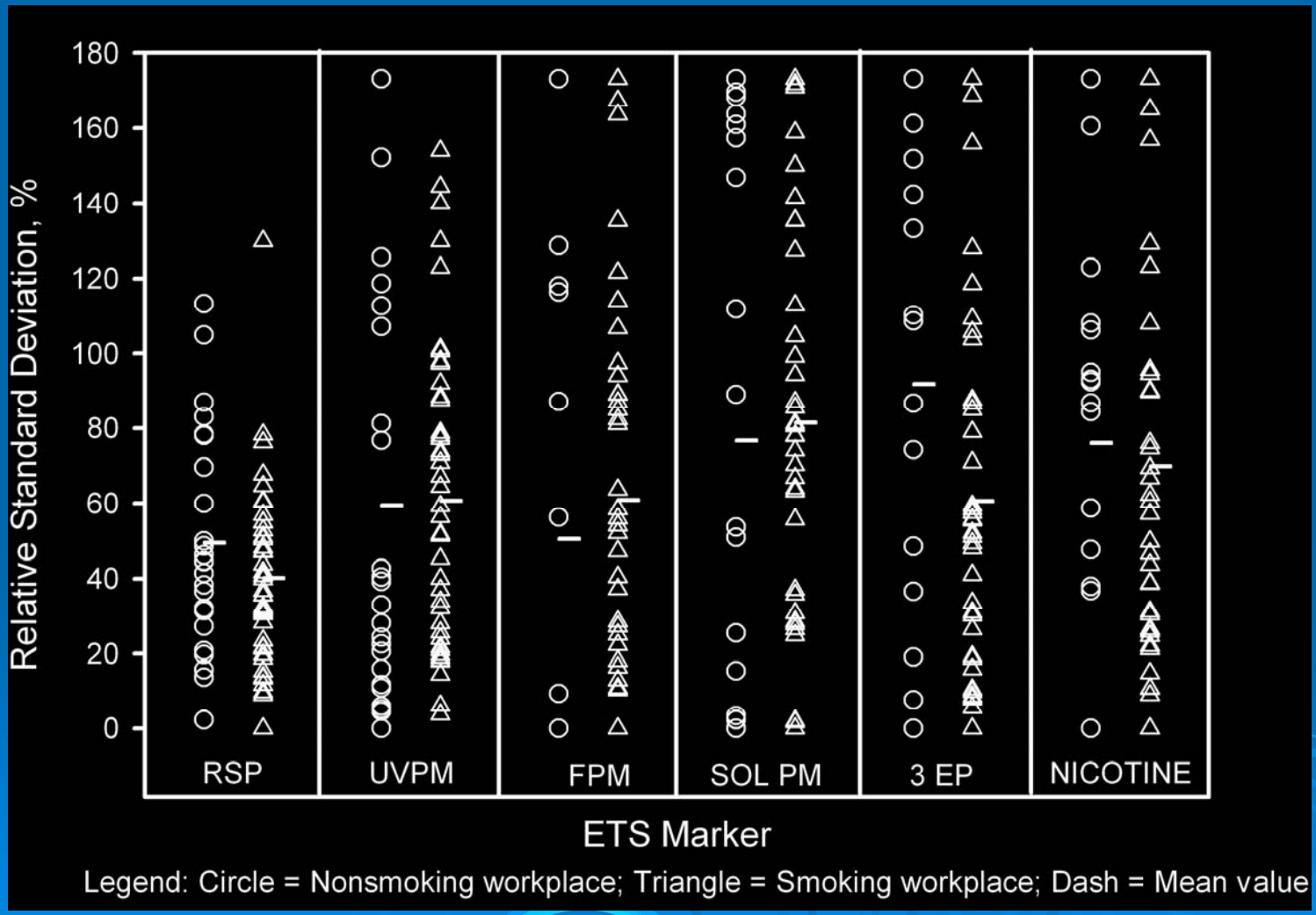


Range of Max/Min Ratios: 1 - 80

Distributions of Away-from-Work Exposure Variations



Workplace Exposure Variation



It’s Not So Simple!

- Jane Cohen

Using Biomarkers for *Quantitative* Assessment of ETS Exposure??

Challenges for the Use of Biomarkers for Exposure Determination

- Finding a tobacco specific marker
  - Present in substantial quantities
  - Is metabolized (or not) to something that can be measured.
- Measuring the component in horribly complex “glop” (ie, biological fluids or tissue).
- Understanding its metabolism sufficiently to make sense of the concentration that is determined.

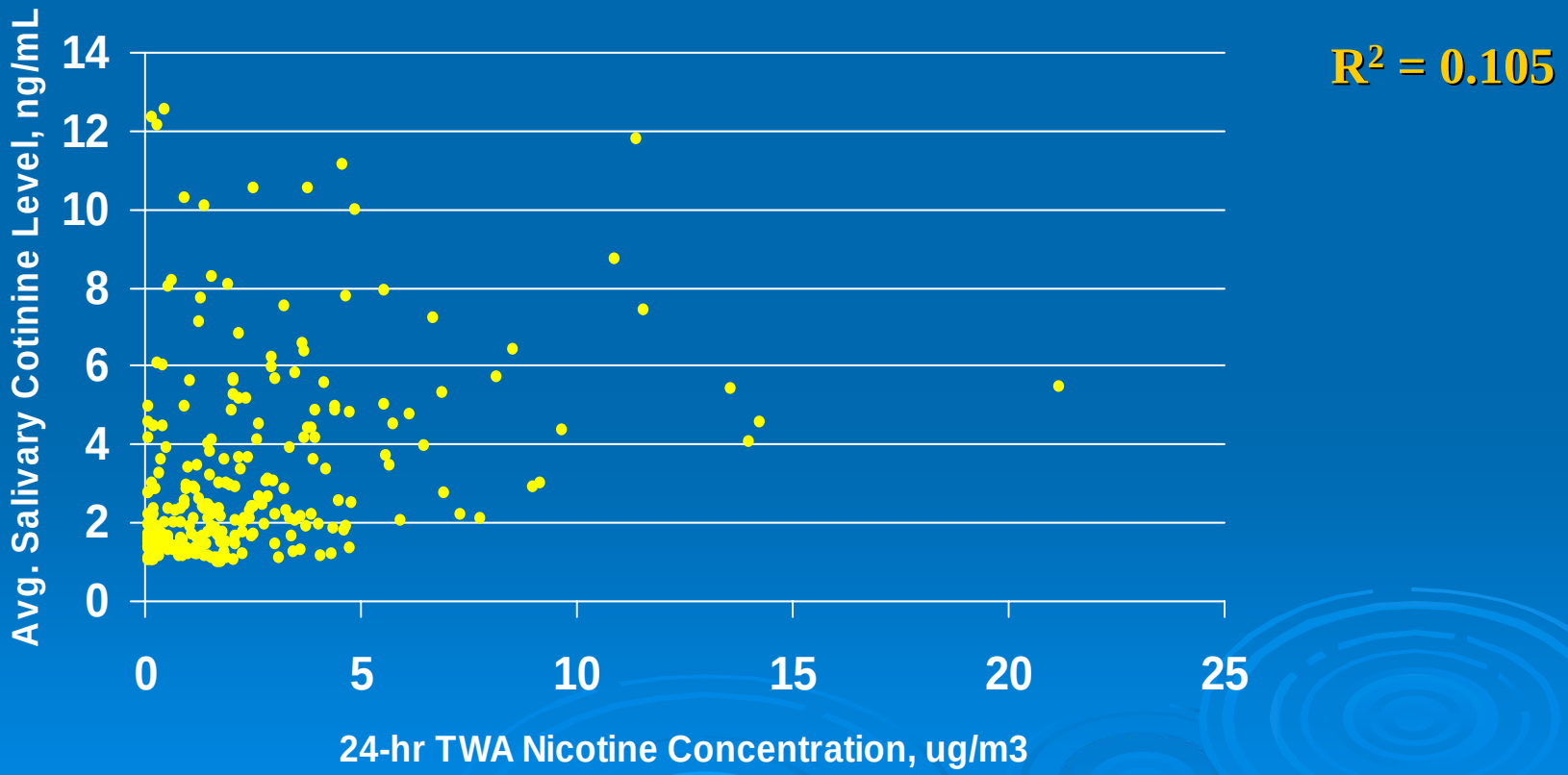
Comparison of Salivary Cotinine Levels and Nicotine Exposure
US 16 Cities Study
Cell Classification by Screening Questionnaire and Diary Observations

Cell No.	Away-from-Work Environment	Work Environment	No. of Participants	Median Nicotine, 24-hr TWA, ug/m3	Median Cotinine, ng/mL
1	S	S	100	2.00	1.94
2	S	NS	138	0.73	0.88
3	NS	S	144	0.16	0.45
4	NS	NS	545	0.03	0.16

Avg. Salivary Cotinine Level as a Function of Nicotine Exposure 16 Cities Study

All Subjects with Both Markers >95% CL above LOD

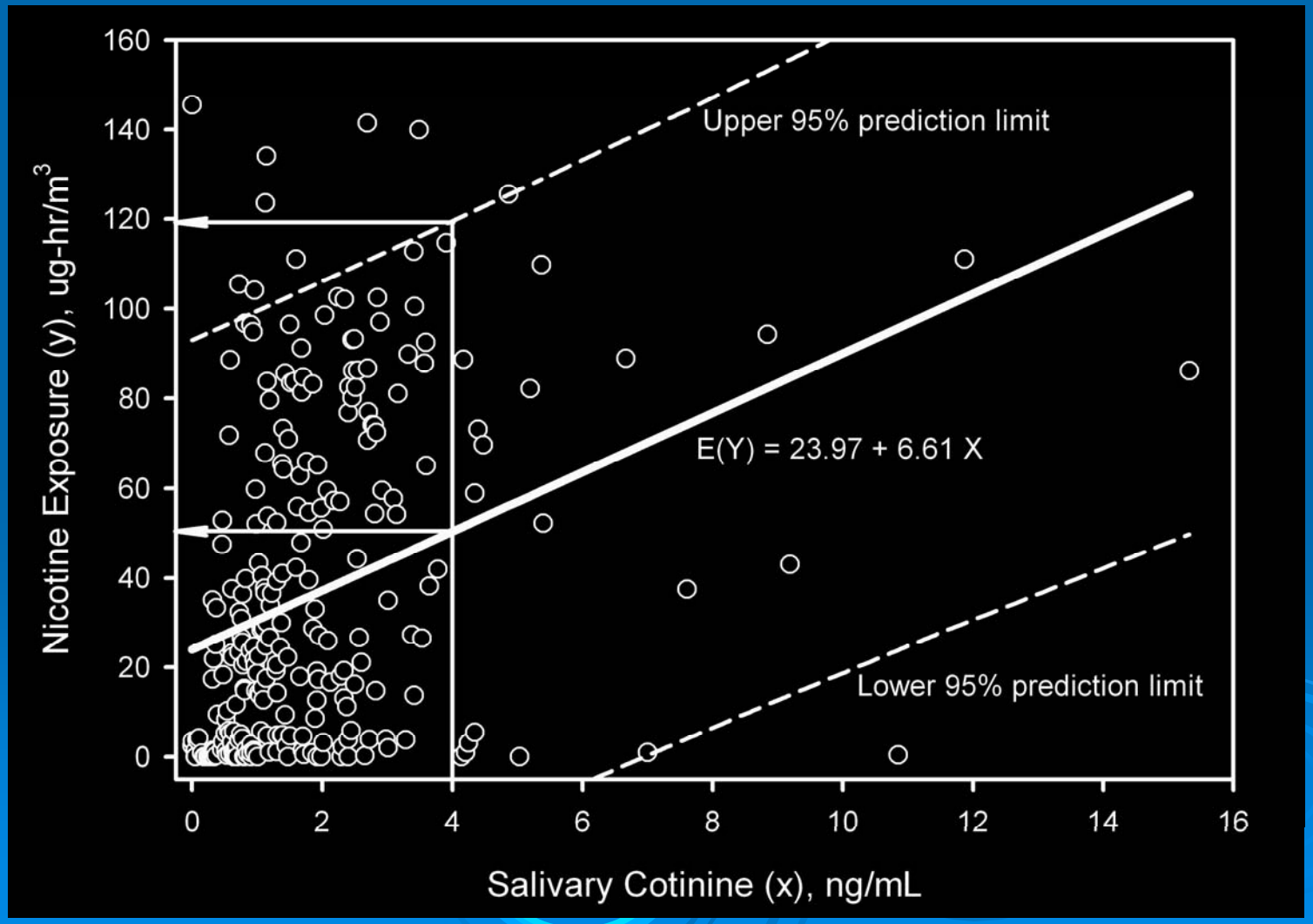
Nicotine: 0.063 ug/m^3; Cotinine: 1.01 ng/mL



$R^2 = 0.105$

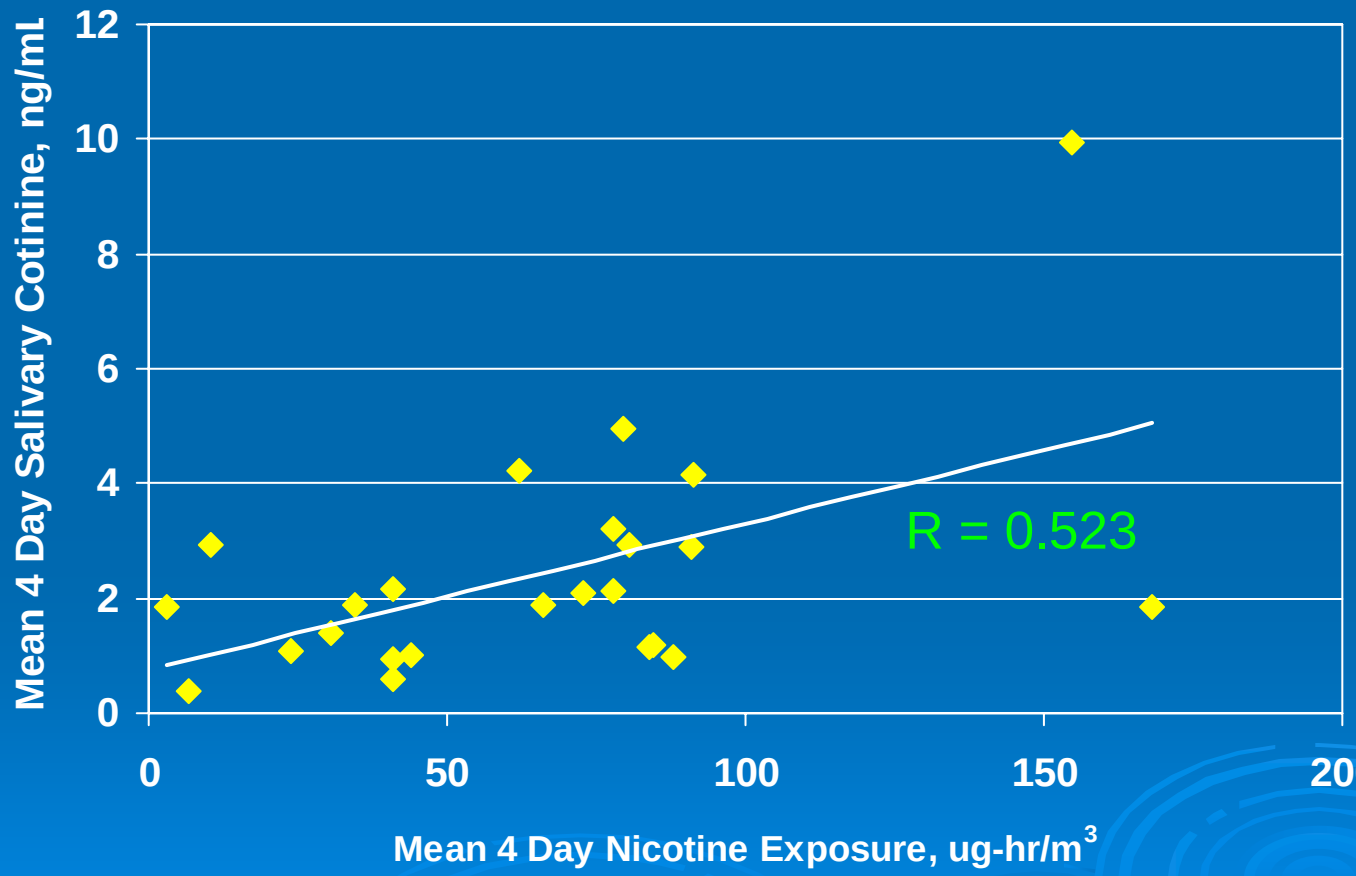
Nicotine Exposure vs Salivary Cotinine

ETS Exposure Variation Study



Any Correlation Among Individual Means?

Mean Four Day Cotinine vs Exposure
Subjects Exposed to ETS at Both Home and Work (Cell 1)



Salivary Cotinine
Comparison of NHANES III vs 16 Cities Study

ETS Exposure Venue	Cell Designation	NHAHES III Geo Mean Levels, est'd from Serum Levels	16 Cities Study Confirmed Subjects below Misclassification Criteria Level
Exposed at Both Home and Work	1	1.16	1.97
Exposed at Home Only	2	0.81	0.89
Exposed at Work Only	3	0.40	0.44
Unexposed at Either Home or Work	4	0.16	0.15

Material Balance

Inhaled/Absorbed Nicotine vs. Systemic Nicotine (as Measured by Salivary Cotinine)

- Estimated systemic dose:
  - N (in ug/day) = Cs*((80 ug/day/ng/mL)*1.25) where Cs: salivary cotinine, in ng/mL
- Potential Inhaled Quantity:
  - Concentration * duration * breathing rate
- Absorption Factor: 71%

Can Airborne Exposure Account for Systemic Dose Estimated from This Model?

	Cal'd Potential Inhaled Quantity of Nicotine from Personal Monitoring ug/day	Estimated Systemic Dose from Salivary Cotinine, ug/day
Median	22.8	141
Mean	36.4	201
20th Percentile	4.1	91
80th Percentile	58.8	293
95th Percentile	114	516

Explanations for Discrepancies Between "Systemic Dose" and Inhaled Quantity

- RIA analysis of cotinine over-reports levels?
  - Comparisons with NHANES III are too good
- Other sources of nicotine (eg. dietary)?
  - Then "unexposed" (NS Home/NS Work) subjects would have higher levels. (Their diets don't seem to be different.)
- Estimation model doesn't work for subjects exposed at low levels?
- *Note that for most highly exposed subjects, difference between systemic and inhaled/absorbed is only a factor of 2.6*

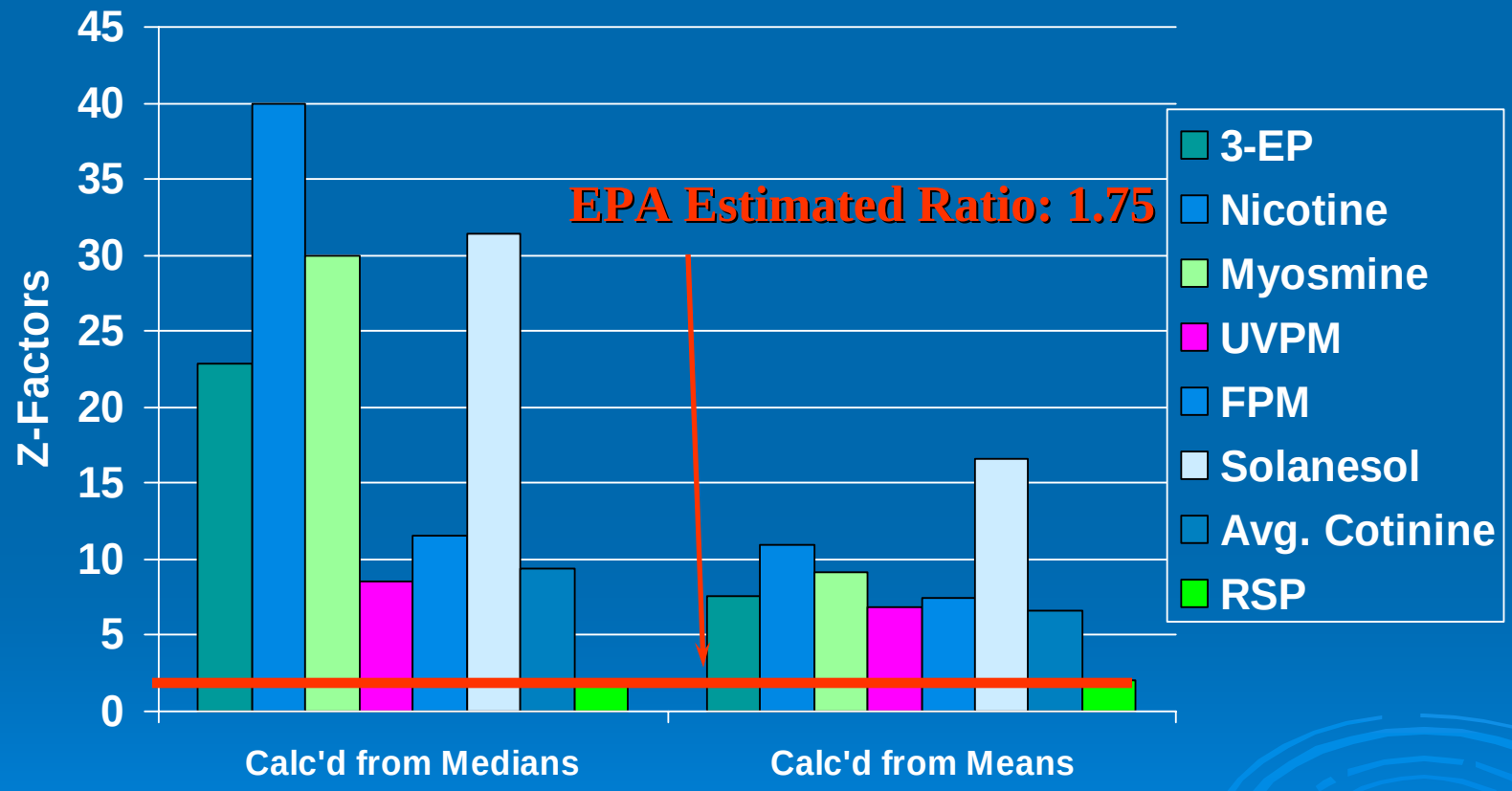
Major Differences in Metabolite Ratios vs Exposure Ratios

- 50 – 100 fold difference in observed levels of cotinine between smokers and those passively exposed.
  - But a 500 – 1000 fold difference in the amount of nicotine inhaled.
- Hecht observes 50 – 100 fold difference in NNK metabolite levels, but we know NNK exposure ratios are a factor of 10X greater.
- Could it just be that people who get a vastly higher dose of a chemical metabolize it differently than those who are exposed to low doses??

How do ORNL Results Fit into THE BIG PICTURE?

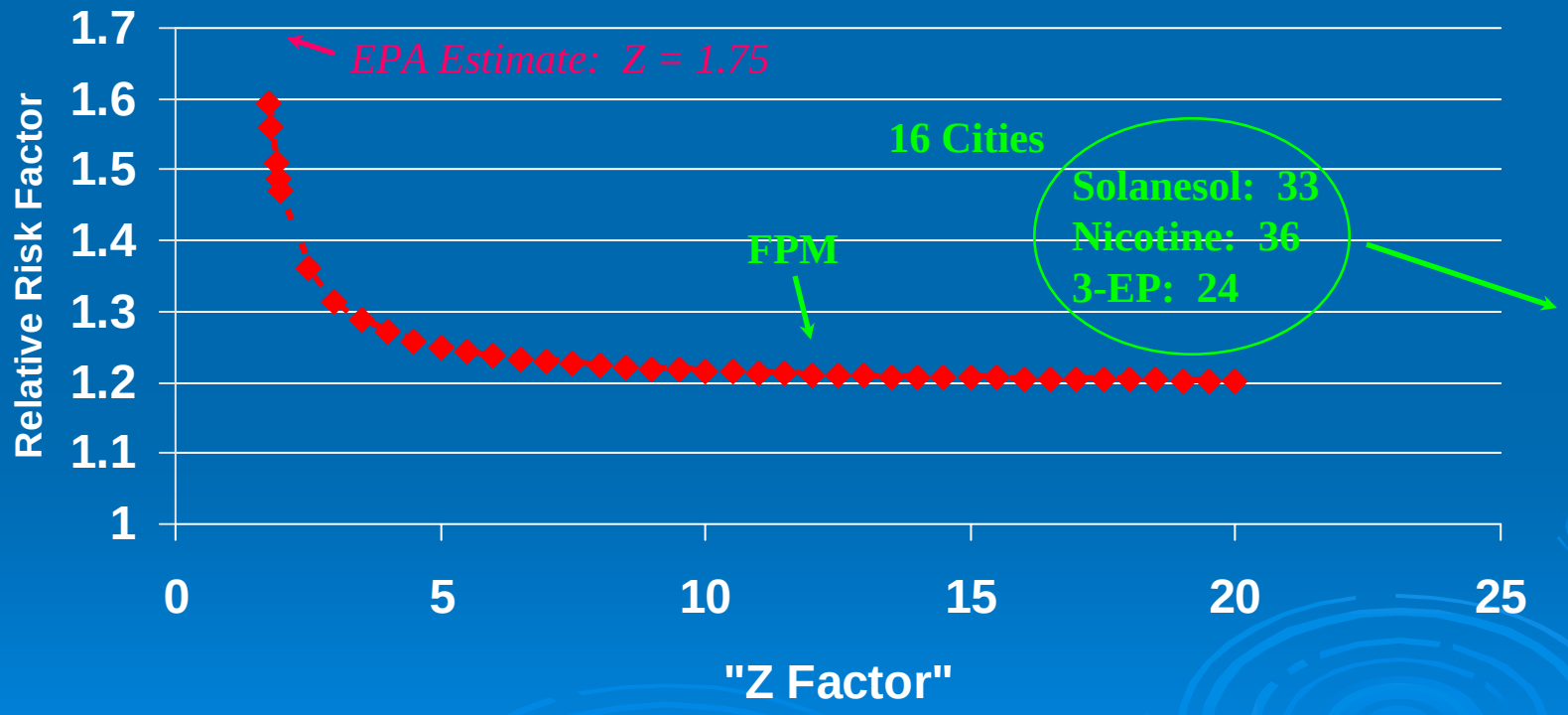
Ratios of 24-hr Exposures of Never Smoking Women:

Married to Smokers vs. Married to Non-Smokers
Comparison of EPA Estimate with 16 Cities Data

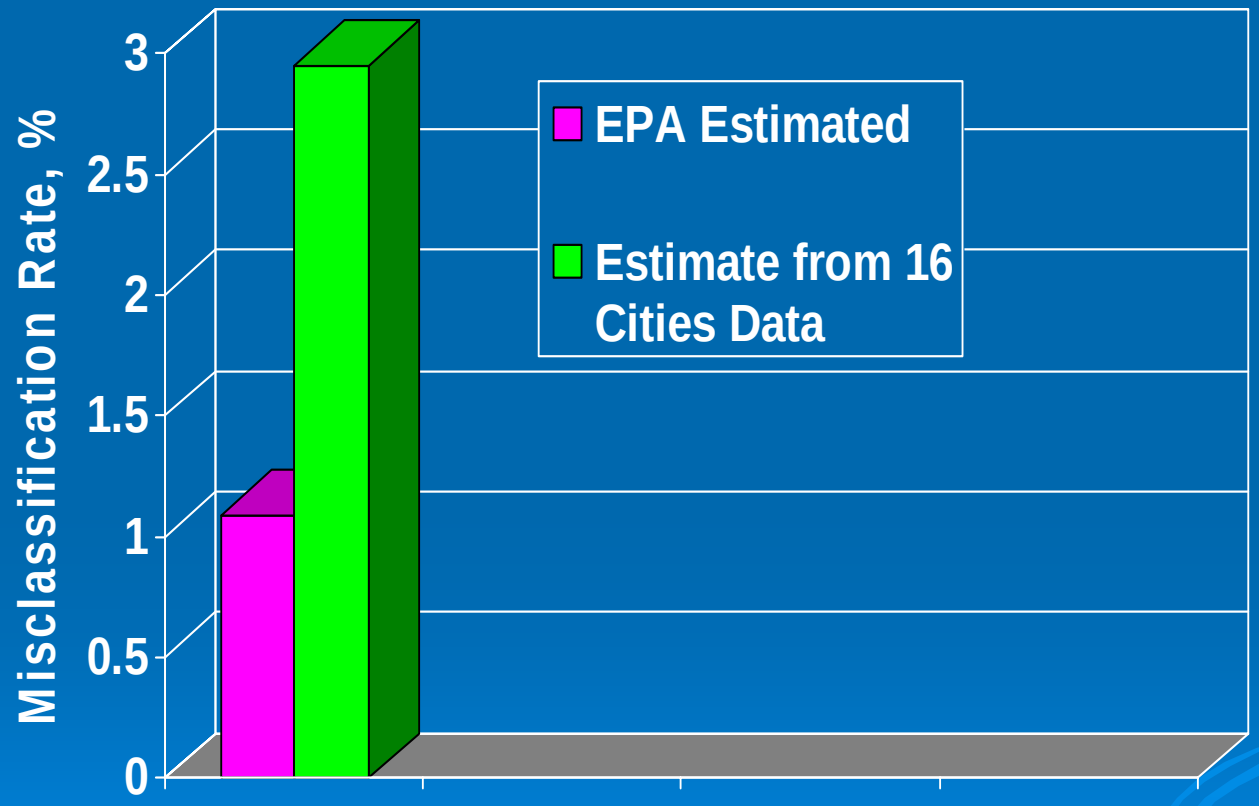


Impact of Differences in Z-Factor: EPA Estimate vs. ORNL 16 Cities Data

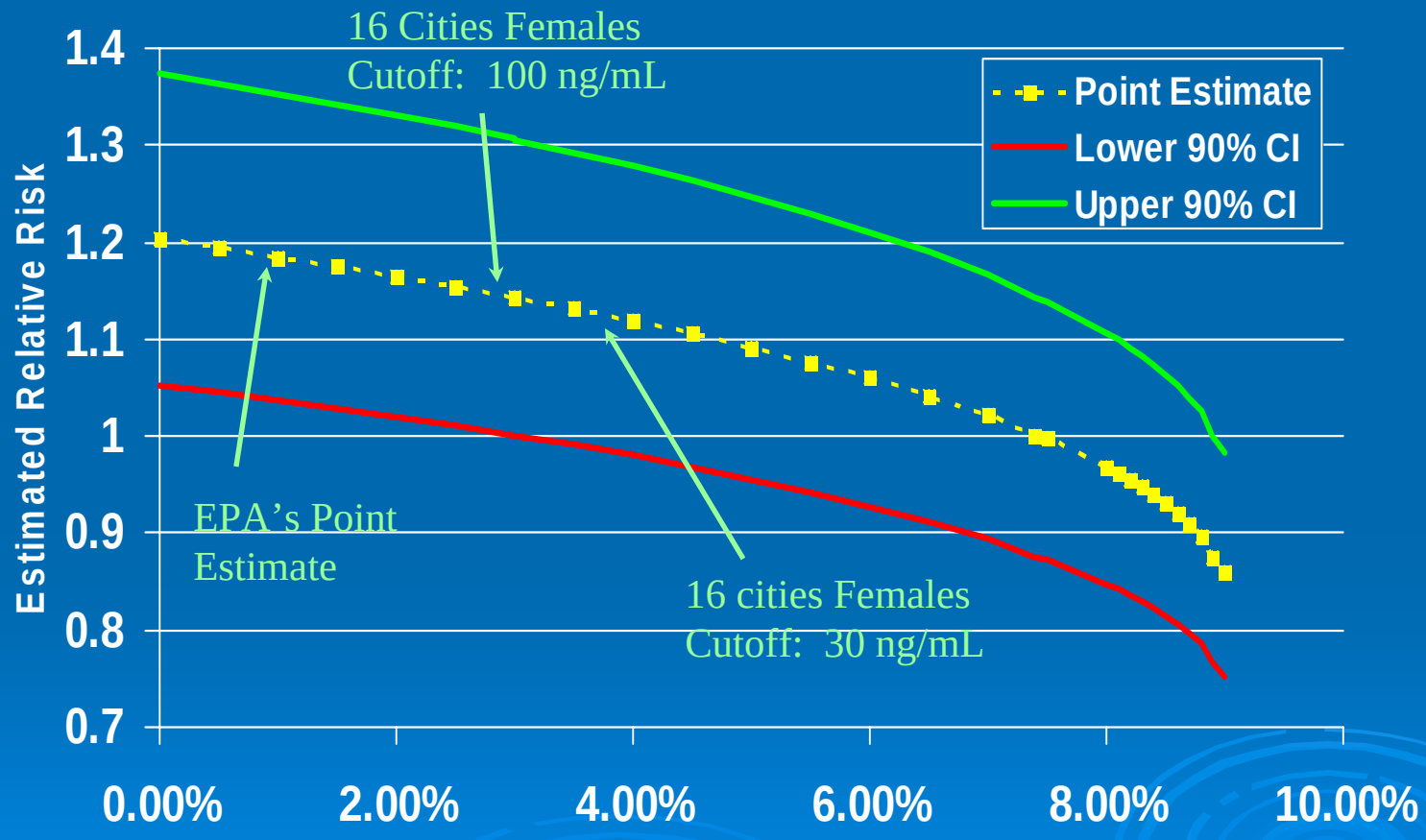
Z = Exposure ratio of women exposed from smoking spouse compared with women not exposed from spouse



Implications for Risk Assessment: Never Smoking Female "Misclassification" Rates



How "Never-Smoker" Misclassification Rates Impact EPA's Relative Risk Estimation



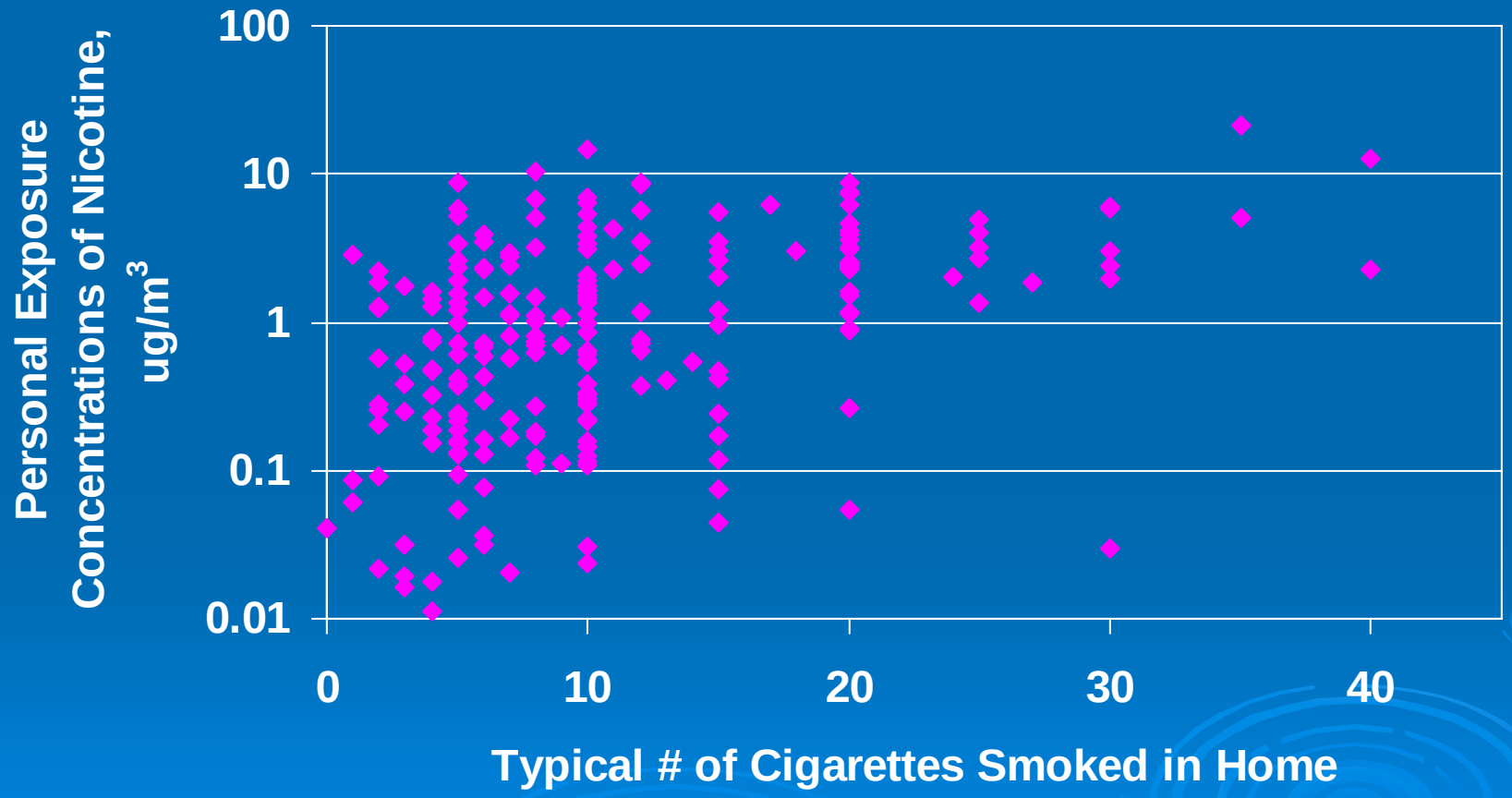
At the ORNL determined mis-classification rate, there is virtually no statistically significance for increased lung cancer risk to never-smokers

Surrogates of Exposure

aka: How good are the measures of exposures used in epidemiological studies?

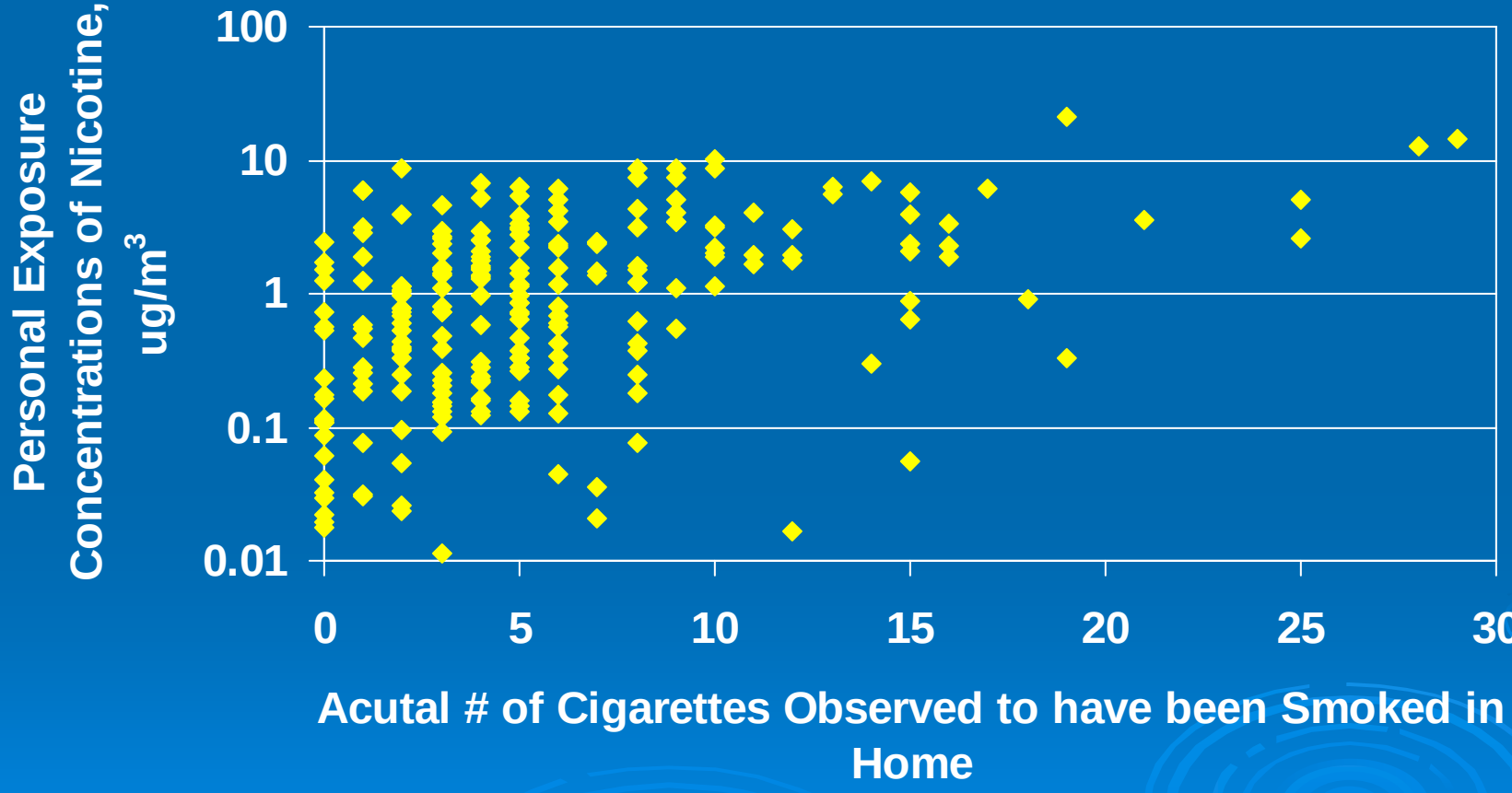
Epidemiological Surrogates of Exposure

Personal Away from Work Nicotine Exposure (16 hr) vs "Typical" Number of Spousal Cigarettes Smoked in the Home



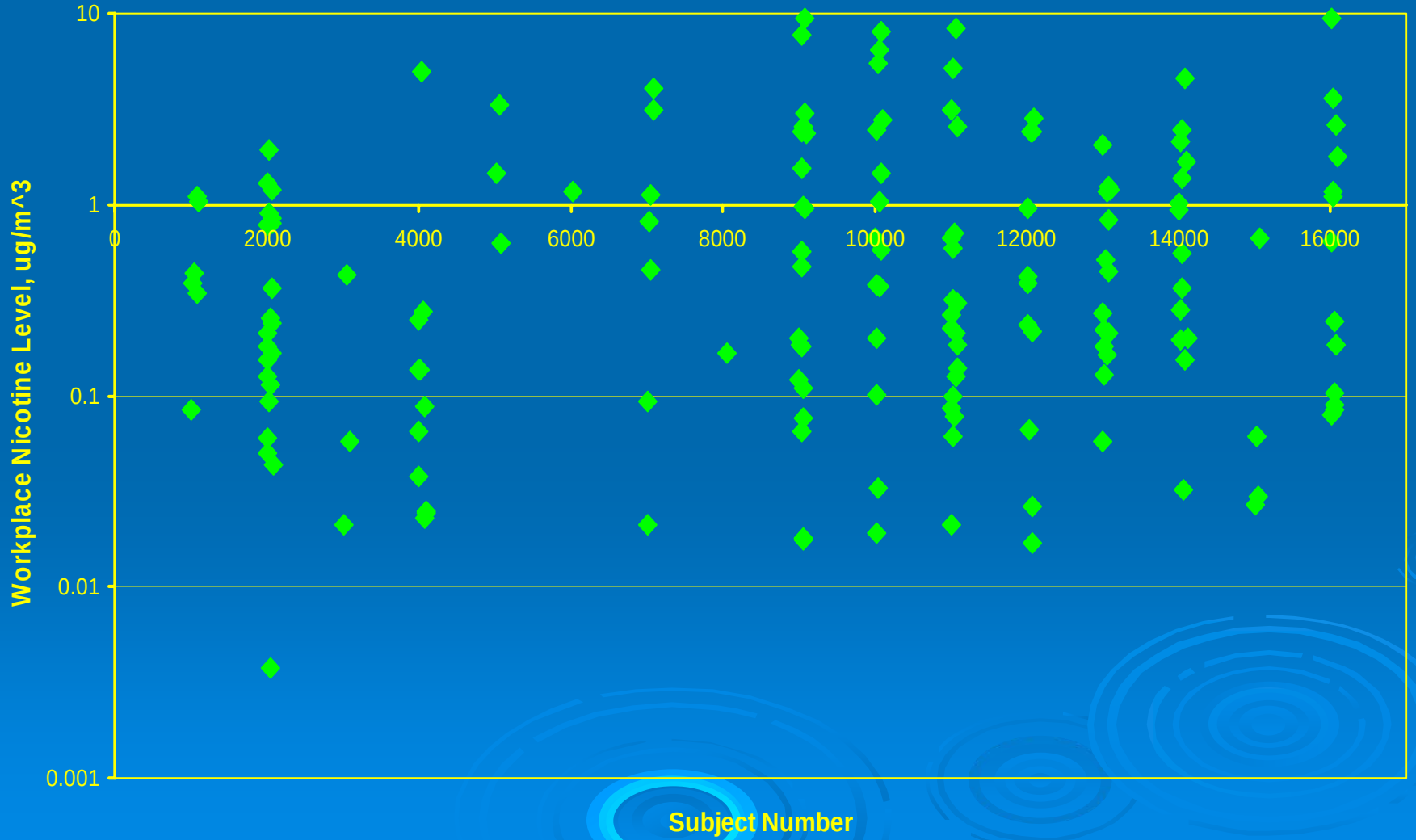
Epidemiological Surrogates of Exposure

Personal Away from Work Nicotine Exposure (16 hr) vs Actual Number of Spousal Cigarettes Observed to have been Smoked in the Home



Are People Good Observers of their Own Exposures?

Workplace Nicotine Exposure Concentrations of Subjects Reporting "A Little" Exposure to ETS



Key Findings from Various Exposure Studies

- For non-smokers in these environments, exposure at home is greater than exposure at work.
- BUT …. “Living with a smoker” can **BE** different things for different people.
- Salivary cotinine not a good quantitative predictor of ETS nicotine exposure.
- Humans, as a class, are not good at estimating their exposure to ETS.
- For non-smoking bartenders (if you can find one) who live with smokers, their exposure to ETS at home is at least as important as their exposure in the workplace.
- For all but the most highly exposed non-smokers living in urban environments, ETS is not likely to be the dominant source of VOC exposure.