

# **Thirdhand Smoke: Exposure Pathways and Biomarkers**

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**OTRU Thirdhand Smoke Workshop**  
May 3, 2012

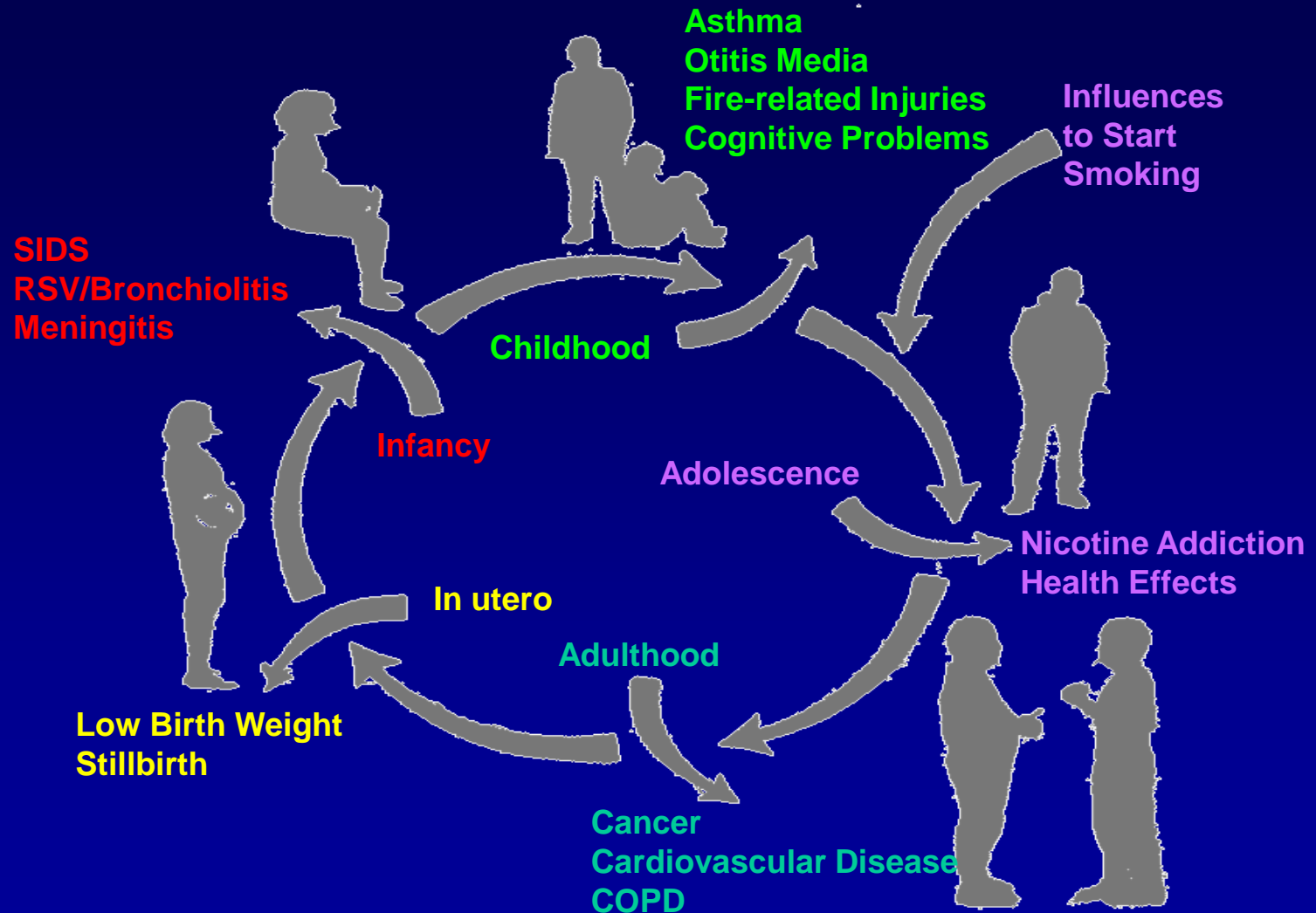
# Tobacco Smoke Ingredients

There is **NO**  
risk-free level of  
exposure to  
tobacco smoke.

## SHS or THS?

The condensate on the glass from a smoking chamber was used in one of the first studies linking smoking and cancer (Wynder, 1953)

# Life Cycle Effects of Tobacco Smoke



# Environments with Potential THS Exposure

- Homes of smokers
- Apartments & homes previously occupied by smokers
- Multi-unit housing where smoking is permitted
- Automobiles of smokers (used cars)
- Hotel rooms

# Evidence of THS Exposure Indoors

- House dust and surfaces contain:  
nicotine

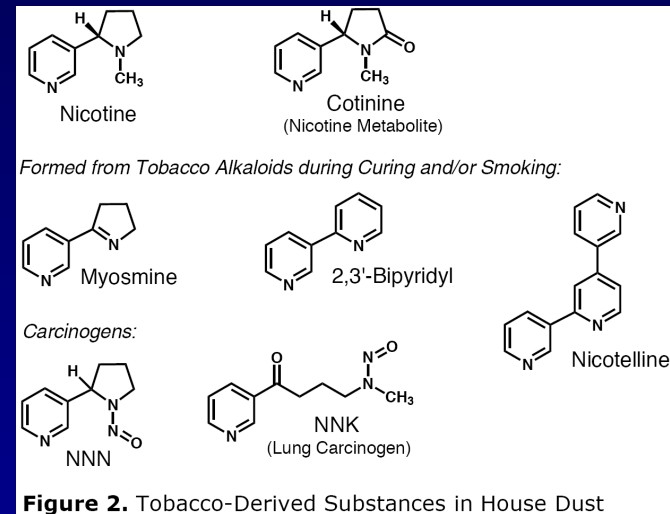
3-ethenylpyridine (3-EP)

polycyclic aromatic hydrocarbons

NNK

nicotelline

- Depending on the compound, rates of these compounds may be 50 times higher in homes where people smoke



# Thirdhand Smoke



# Even at Low Levels of Exposure? Yes

Yolton et al; using NHANES,

- **Demonstrated a significant inverse relationship between cotinine and block design, reading, and math scores**

Wilson, et al; also using NHANES,

- **Relationship between cotinine levels and serum levels of antioxidants, vitamin C, and carotenoids**

# Possible Routes of Exposure—Dermal uptake

- Effective exposure depends on area of skin in contact with contaminated surfaces/body volume
- Sources: surfaces, dust, clothes, bedding--  
Thirdhand smoke dominates
- Children>adults
- Proof of concept
  1. Nicotine toxicity in child harvesters of tobacco
  2. Wynder, painting tobacco condensate on mice

# **Dermal Absorption of TSMAAs**

- Manuela Martins-Green (UC Riverside) and Peyton Jacob III
- Dermal application of NNK in mice
- NNAL and iso-NNAL measured in urine with positive exposure time–urine concentration relationship

# Pathophysiological Implications

- Low level cumulative exposure over long periods of time
- Potential exposure to irritants, oxidants, pro-inflammatory chemicals, carcinogens, vascular toxins

# Possible Routes of Exposure—Ingestion

- Effective Exposure depends on quantity of contaminated dust ingested/body weight
- Sources: dust, toys, food, mouthing behaviors--thirdhand smoke dominates
- Children>adults...might be 20 times greater
- Proof of concept
  1. Children in homes where smoking has occurred in the past have detectable cotinine levels
  2. Level of contamination in dust of bedroom correlates with cotinine levels

# Possible Routes of Exposure—Inhalation

- Effective exposure depends on respiratory exchange rate and body weight
- Source: air--Secondhand smoke usually dominates but THS may dominate when spaces are heavily contaminated and active smoking occurs when child not present
- Children>adults
- Proof of concept: passive air monitoring

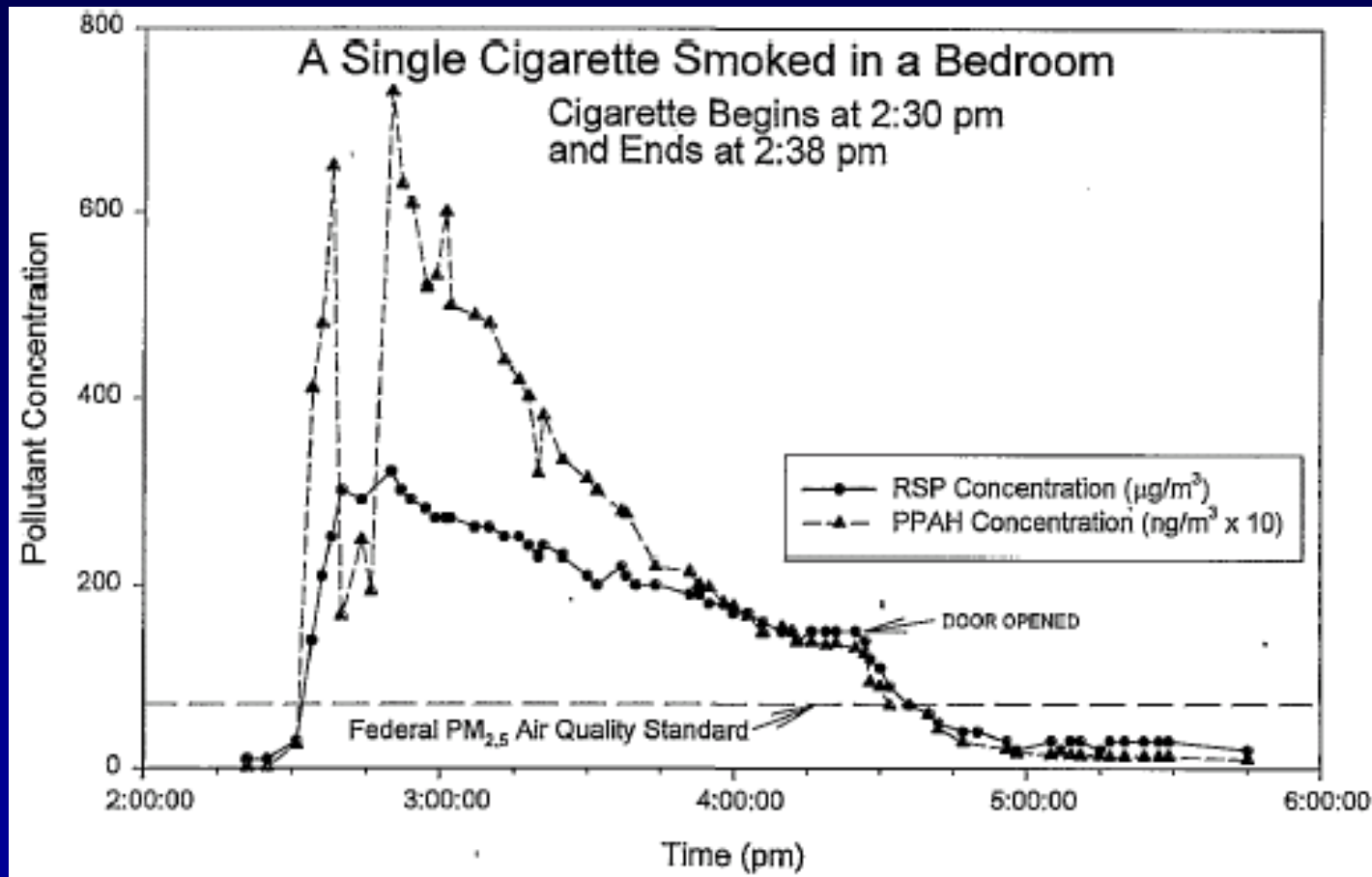
# **Thirdhand Smoke Accumulates**

- **THS accumulates in the homes of people who smoke**
- **Matt et. al. showed that even after a home remain vacant for 2 months and a prepared for the new residents, THS contamination remains on surfaces and in house dust.**
- **Non-smokers living in former smokers homes are exposed to tobacco smoke toxins.**

## **Reason for Concern**

- **Exposure through shared ventilation, along air ducts, leaky walls.**
- **The numbers add up quickly, if just 5 people in a building smoke  $\frac{1}{2}$  pack of cigarettes in their apartment each day— $5 \times 10 \times 365$ ; the load to the building is over 18,000 cigarettes each year.**

## Effect of a Single Cigarette on Indoor Air Quality



...it takes TWO hours for the air quality to return to minimum federal safety standard for fine particles and particulate aromatic hydrocarbons..

# **Can smoking in one unit contaminate another unit?**

- **Kraev et al. (2009) demonstrated, using “Hammond” filters, that air in 89% of non-smoking units was contaminated with nicotine.**
- **When another resident smelled cigarette smoke the levels in that apartment were higher.**
- **But people didn’t need to smell cigarette smoke to be contaminated.**

# Does this Exposure Get into Children?

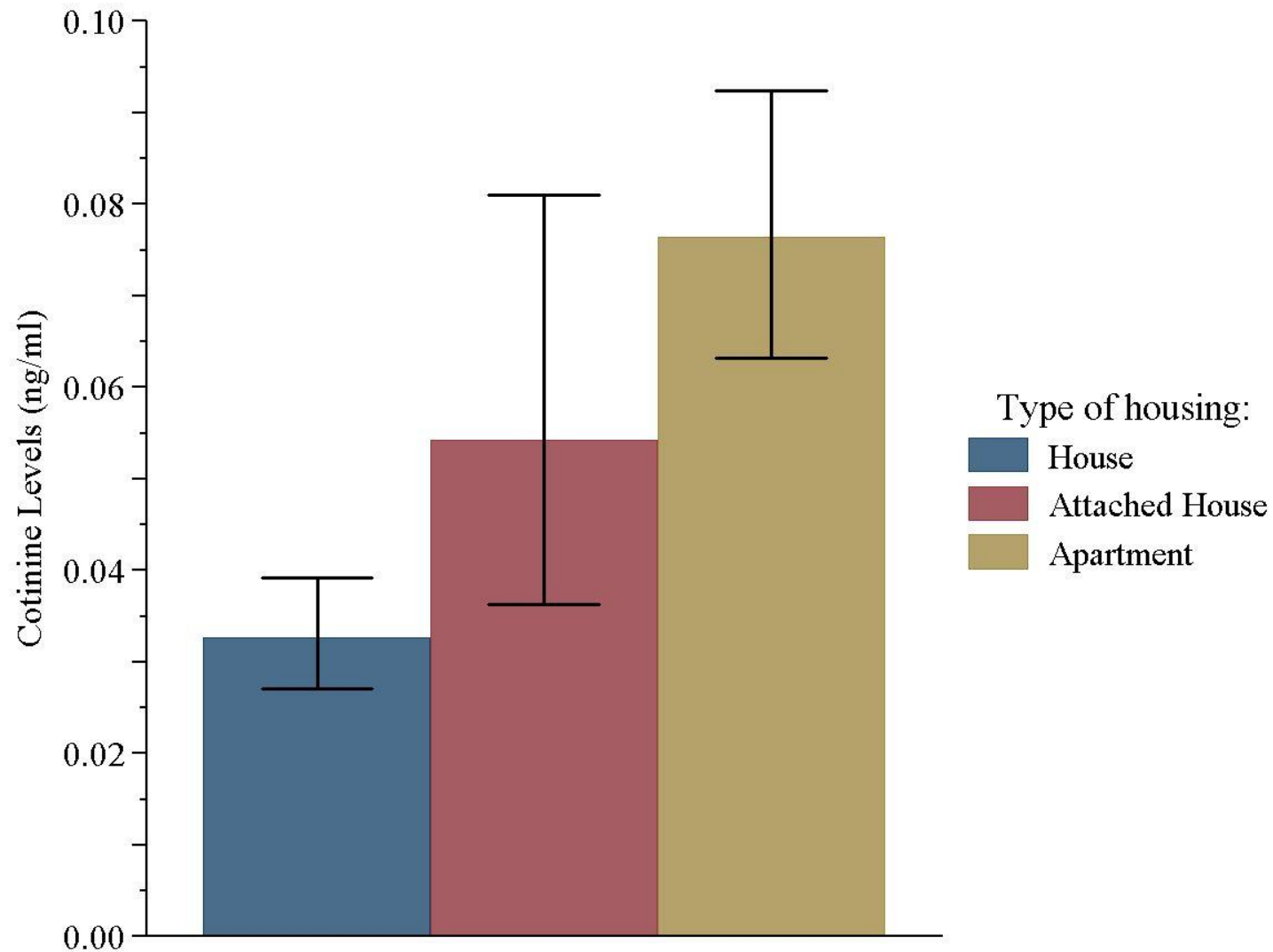
- Whatever the combination of involuntary (SHS+THS) exposure...

Do children who live in multiunit housing have higher cotinine levels than children who live in detached housing

# Cotinine levels in children

- 2001-2006 National Health and Nutrition Examination Survey (NHANES)
- Hypothesized and found that among 4,782 children ages 6 to 18 years, in households that do not allow smoking in their own home, children who live in apartments have a 140% higher cotinine level than children living in detached homes,
- This relationship persists when controlling for poverty and race/ethnicity

## Cotinine levels in children by housing type



## **Future Directions: Biomarker Ratios as a Better Tool to Indentify THS Exposure**

NNK/nicotine – environmental assessment

Urine NNAL/cotinine – human exposure

- Rationale
  - As smoke ages nicotine levels decline and TSNA levels rise
  - Metabolism converts nicotine to cotinine and NNK to NNAL

# The NNAL/Cotinine Ratio in Active and Passive Smokers and in Kids

Urine NNAL/Cotinine Ratio X  $10^{-4}$

<u>Active Smokers</u>	<u>Passive Smokers</u>	<u>Tots<sup>1</sup></u>
1.2	6.6	74

This suggests that measuring cotinine only would underestimate NNK exposure,<sup>2</sup> and is consistent with our hypothesis that the ratio is higher in people exposed to THS as compared to SHS (Hand to mouth behavior in toddlers)

1. Healthy Tots Project - San Diego State University, Mel Hovell and Joy Zakarian
2. Benowitz N, Goniewicz ML, Eisner MD, Lazcano-Ponce E, Zielinska-Danch W, Koszowski B, Sobczak A, Havel C, Jacob P 3rd. Urine cotinine underestimates exposure to the tobacco-derived lung carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone in passive compared with active smokers. Cancer Epidemiol Biomarkers Prev. 2010;2795-800.

## Summary

- Although no safe level of tobacco smoke exposure, quantifying the relative exposure due to SHS and THS is difficult
- Especially across different age ranges in the human life cycle
- However, the state of the science supports smokefree environments for all children

# CEASE Posters

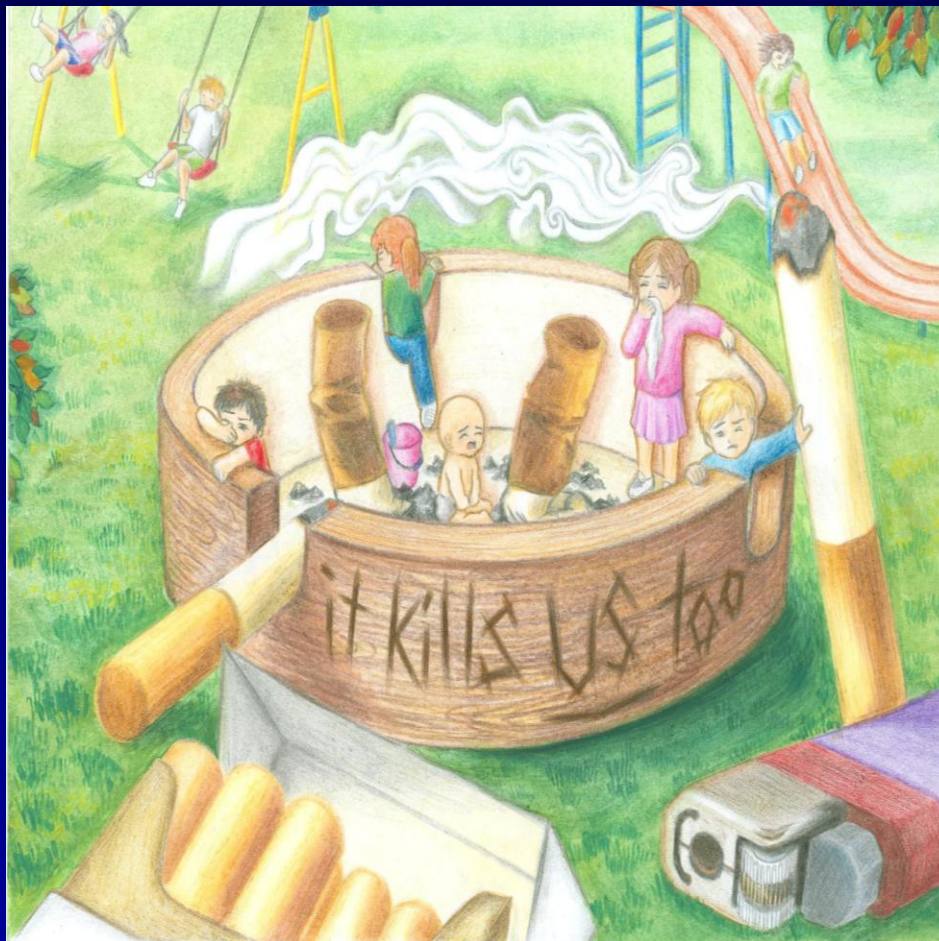
*Sometimes it's easy to see  
what can hurt your kids.*



*But sometimes it's not.  
The toxins from cigarette  
smoke can hurt your children  
long after the cigarette is out.*

*Your child's doctor can  
help you quit smoking  
and have a completely  
smoke-free home and car.*





*Jessica Lin 1<sup>st</sup> Place winner, FAMRI/ AAP/Richmond Center Art Contest  
2009*





# A New Health Message: Tobacco Smoke Contamination, or Third-Hand Smoke...

Sometimes it's easy  
to see what can  
hurt your kids...



But sometimes it's not.



Tobacco smoke stays  
around in your clothes,  
house and car long  
after you put out  
the cigarette.

Quit smoking today.



Keep your home and  
car smoke-free at  
all times.

Talk to your child's  
doctor or nurse for help.

Call the quitline or visit  
[www.ceasetobacco.org](http://www.ceasetobacco.org)  
for more help.

*CEASE*

1-800-QUIT-NOW

1-800-784-8669

[www.ceasetobacco.org](http://www.ceasetobacco.org)



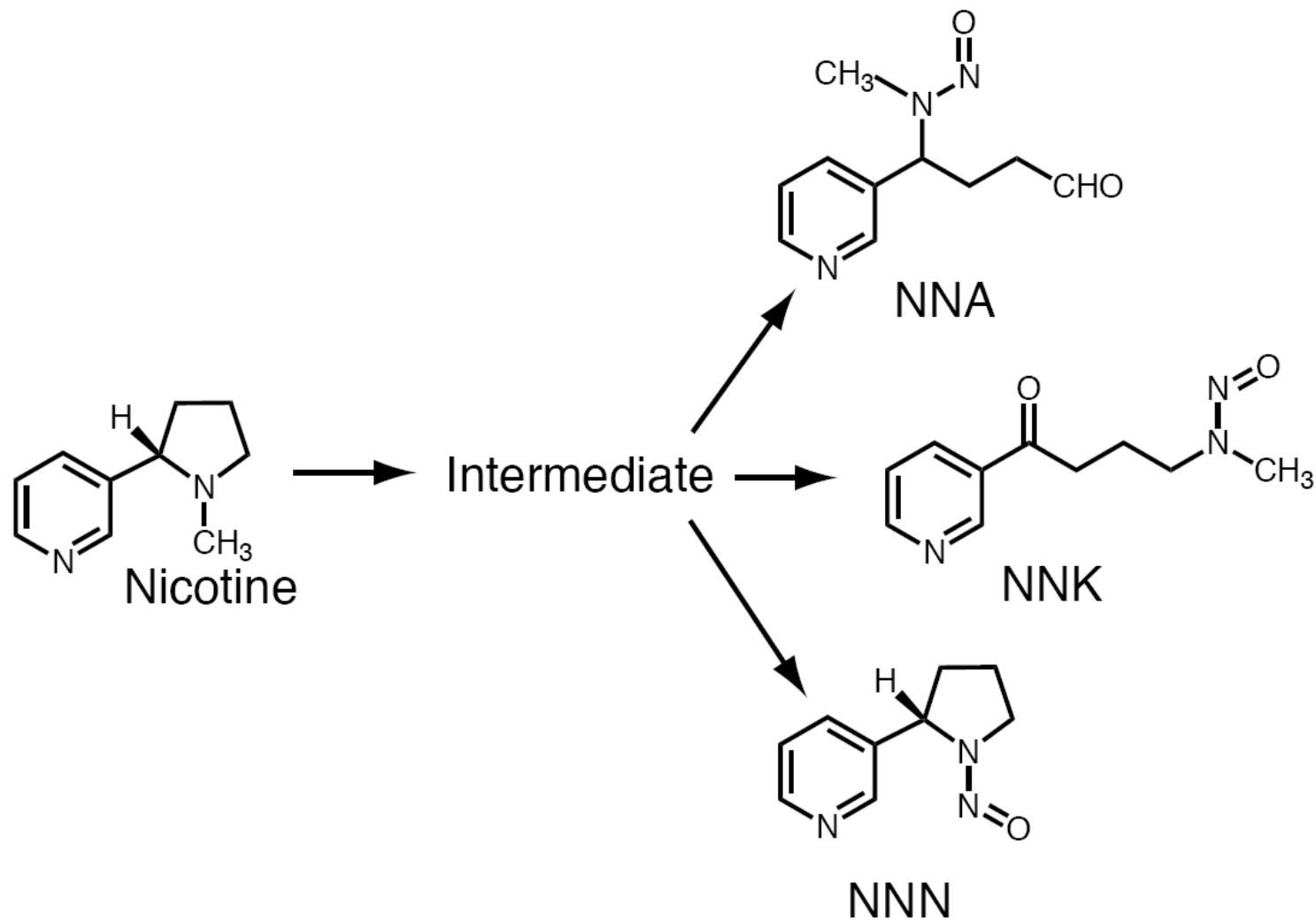
## **Results: Tobit regression analysis**

- Controlling for SES, race/ethnicity
- White children living in apartments had a 208% increase in their cotinine level over those living in detached homes ( $p=.003$ )
- Black children living in apartments had a 45% increase in cotinine over those living in detached homes ( $p=.024$ )

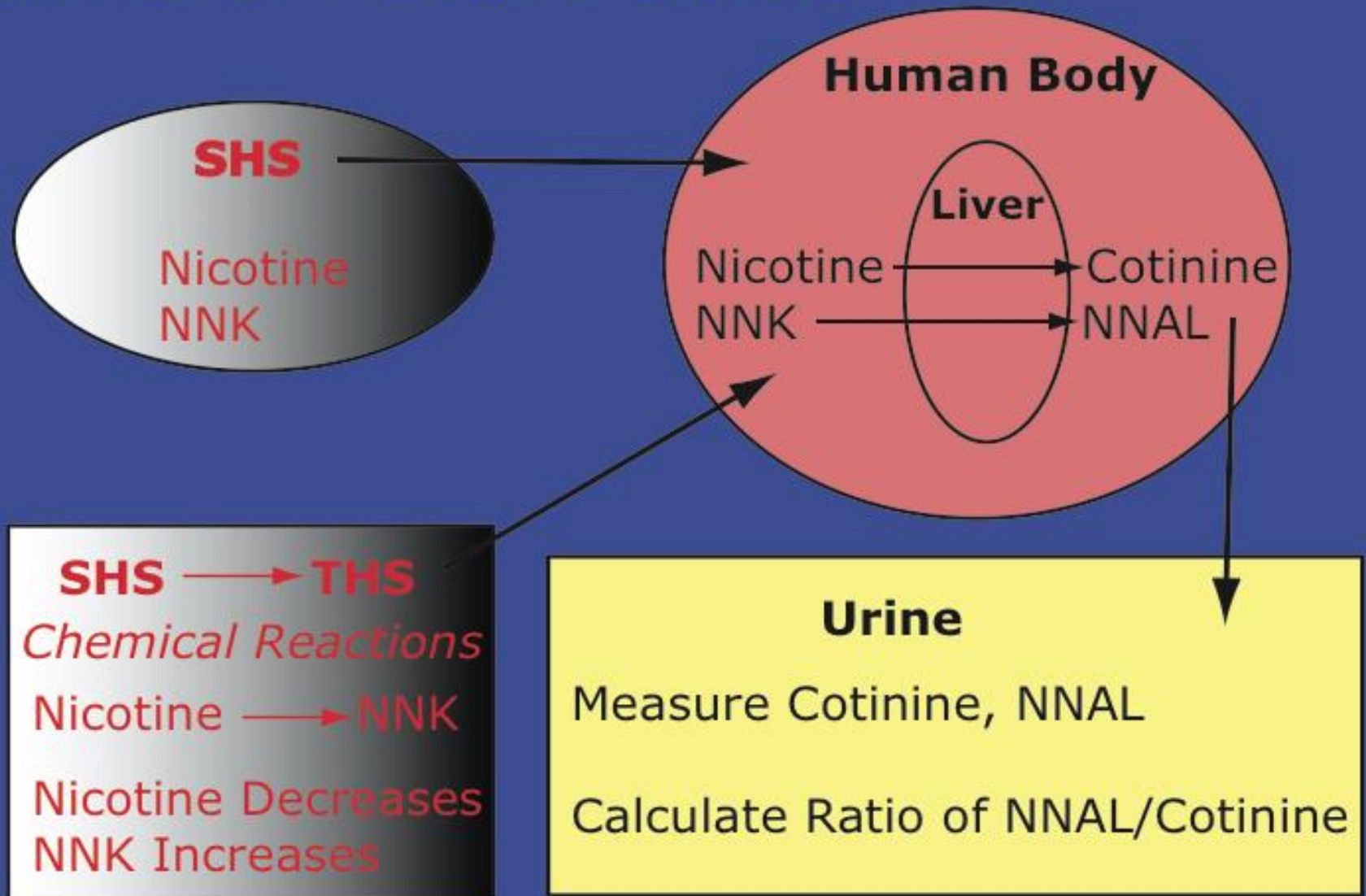
# Potential Clinical Implications

- Children most vulnerable
- Allergies
- Asthma
- Acute Cardiovascular Events
- Cancer

# Formation of Tobacco-Specific Nitrosamines by Reaction of Nicotine with Nitrous Acid

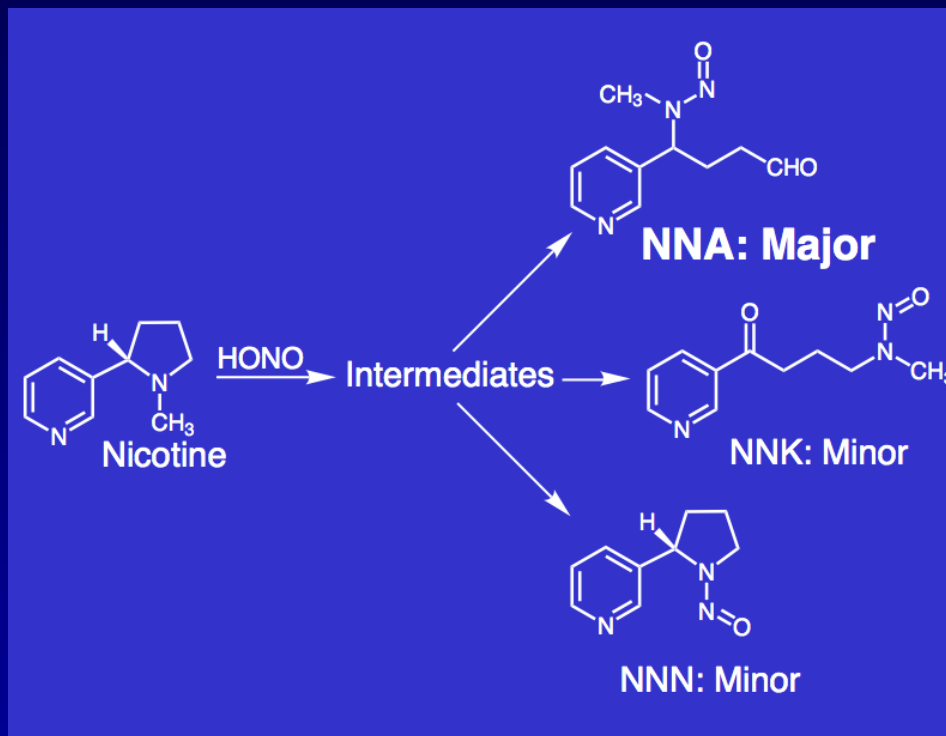


Why we expect a greater NNAL/Cotinine ratio if exposed to THS than if exposed to SHS



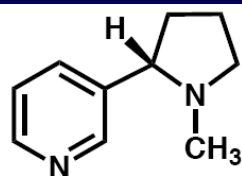
# Biomarkers for Thirdhand Smoke

Interest in THS accelerated with the discovery of TSNA formation from the reaction of nitrous acid with nicotine under typical environmental conditions

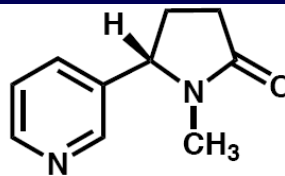


Since NNA is the major TSNA formed in this reaction, and has not been found in tobacco smoke, it is a logical choice for a marker

# Tobacco-Derived Substances in House Dust

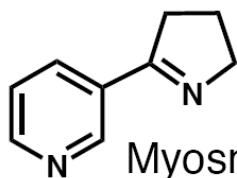


Nicotine

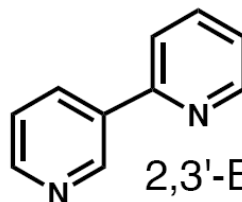


Cotinine  
(Nicotine Metabolite)

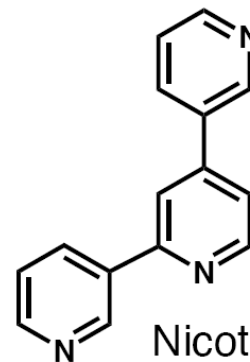
*Formed from Tobacco Alkaloids during Curing and/or Smoking:*



Myosmine

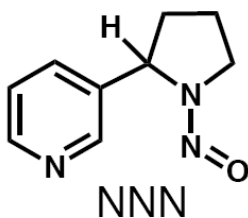


2,3'-Bipyridyl

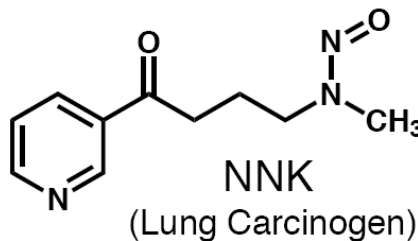


Nicotelline

*Carcinogens:*



NNN



NNK  
(Lung Carcinogen)

**Figure 2.** Tobacco-Derived Substances in House Dust

Sample	Nicotine	Cotinine	Myosmine	2,3'-Bipyridyl	Nicotelline	NNK	NNN
<b>Smokers' Homes</b>							
Smoker's Home #1	184787	4371	11080	1207	298	156.1	66.1
Smoker's Home #2	20242	1921	1708	127	43.9	36.9	5.7
<b>Mean</b>	<b>102515</b>	<b>3146</b>	<b>6394</b>	<b>667</b>	<b>171</b>	<b>96.5</b>	<b>35.9</b>
<b>Non-Smokers' Homes</b>							
Non-Smoker's Home #1	3738	102	279	105	10.1	2.1	1.4
Non-Smoker's Home #2	5000	77	282	151	1.9	2.2	1.2
Non-Smoker's Home #3	441	252	13	53	1.9	0.6	1.3
Non-Smoker's Home #4, Sample #1	991	58	60	13	1.2	7.8	2.5
Non-Smoker's Home #4, Sample #2	518	19	17	5	0.5	1.5	0.3
Non-Smoker's Home #4, Sample #3	1089	51	49	18	0.9	6.9	1.8
<b>Mean</b>	<b>1963</b>	<b>93</b>	<b>117</b>	<b>58</b>	<b>2.8</b>	<b>3.5</b>	<b>1.4</b>
<b>NIST SRM #2585, House Dust</b>	<b>19281</b>	<b>1096</b>	<b>933</b>	<b>163</b>	<b>73.8</b>	<b>33.7</b>	<b>12.8</b>
<b>Clay Soil, Collected in Winter, 6" below surface, oven-dried</b>					<b>ND</b>	<b>ND</b>	<b>ND</b>