Biomarkers of Tobacco Smoke Exposure in the U.S. Population: Result and Resources from the National Health and Nutrition Examination Survey (NHANES)

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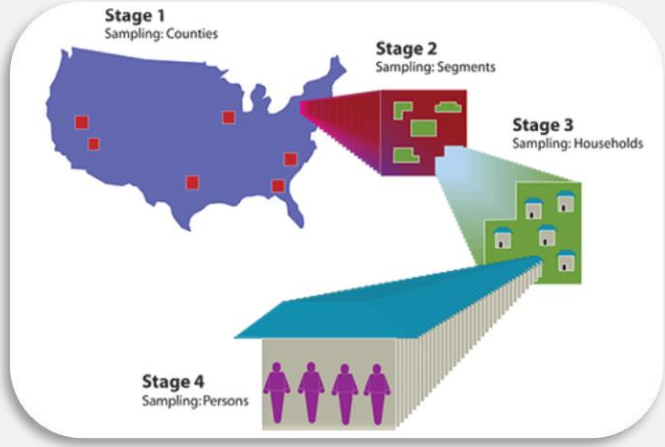
CORESTA 2018

CDC's National Biomonitoring Program

A federal program that establishes U.S. population-based reference ranges and exposure trends for environmental chemicals.

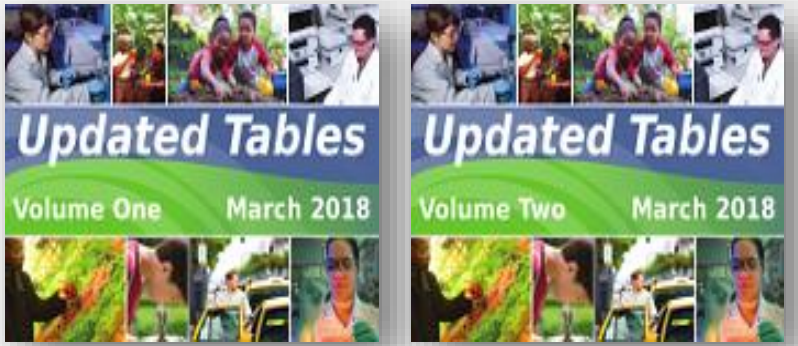
NHANES
Participant Recruitment and Sample Collection



Probability sample of civilian, non-institutionalized Americans that provides population-based results.

CDC
Sample Analysis

National Report on Human Exposure to Environmental Chemicals* and *Updated Tables



A comprehensive, ongoing assessment of American's exposure to environmental chemicals.

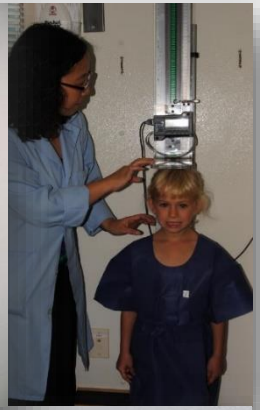
NHANES: National Health and Nutrition Examination Survey

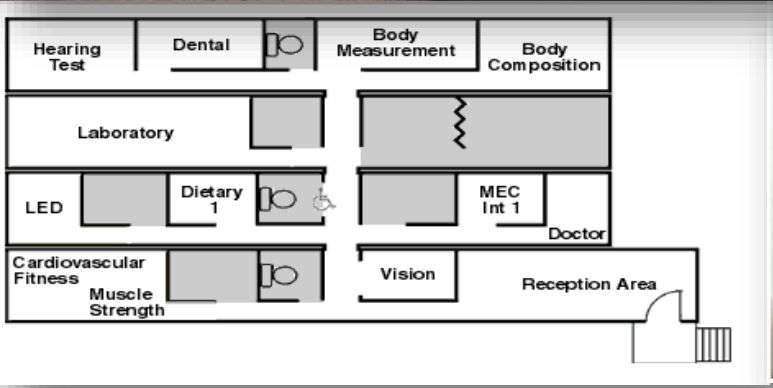
What is NHANES?

- **National Health and Nutrition Examination Survey**
  - Ongoing survey—continuous since 1999
  - Nationally representative sample of civilian, noninstitutionalized US population in the contiguous states
  - About 10,000 participants in 30 counties every 2 years
- **Methods**
  - Face-to-Face and Computer-Assisted Interviews:
    - Demographics/Socioeconomic
    - Dietary/Nutritional
    - Medical History and Health Behavior
    - Physical Examination
  - Biological Specimen Collection: Blood & Urine

More at: https://www.cdc.gov/nchs/nhanes/about_nhanes.htm

Mobile Examination Centers (MEC)





www.cdc.gov/nchs/nhanes.html

Biomonitoring in NHANES

- Not all chemicals are measured in everyone, except:
  - Blood Pb, Cd, Hg, Se, Mn: All persons 1 year and older
  - Serum cotinine: All persons 3 years and older
- Most urinary chemical measurements are made in a 1/3 subsample (n~2500) of the participants
  - Ages 6 years and older*
  - Subsamples are determined so they are representative of the U.S. population
- Biomonitoring results are presented in the ***National Report on Human Exposure to Environmental Chemicals*** and the ***Updated Tables***
- Biomonitoring datasets can be downloaded using SAS

*Starting in 2015, urine is collected from participants ages 3 years and older

CDC's National Report on Human Exposure to Environmental Chemicals (1999–2018)*

Serum Perfluorooctane sulfonic acid (PFOS) (2011 - 2014)‡

Geometric mean and selected percentiles of serum concentrations (in µg/L) for the U.S. population from the National Health and Nutrition Examination Survey.

	Survey years‡	Geometric mean (95% conf. interval)	Selected percentiles (95% confidence interval) 50th	75th	90th	95th	Sample size
Total	11-12	**6.31** (5.84-6.82)	**6.53** (5.99-7.13)	**10.5** (9.78-11.1)	**15.7** (14.7-17.5)	**21.7** (19.3-23.9)	1904
	13-14‡	**4.99** (4.50-5.52)	**5.20** (4.80-5.70)	**8.70** (7.90-9.40)	**13.9** (11.9-15.5)	**18.5** (15.4-22.0)	2165
Age group							
12-19 years	11-12	**4.16** (3.70-4.68)	**4.11** (3.48-4.65)	**5.90** (5.14-7.25)	**9.05** (6.49-10.8)	**10.8** (8.52-14.2)	344
	13-14‡	**3.54** (3.17-3.96)	**3.60** (3.10-4.20)	**5.20** (4.60-6.20)	**7.80** (7.00-8.90)	**9.30** (7.90-11.7)	401
20 years and older	11-12	**6.71** (6.24-7.20)	**7.07** (6.65-7.52)	**11.0** (10.4-11.9)	**17.0** (15.3-18.5)	**22.7** (20.4-24.8)	1560
	13-14‡	**5.22** (4.70-5.81)	**5.60** (5.10-6.00)	**9.10** (8.20-10.2)	**14.5** (12.9-16.1)	**19.5** (15.8-23.0)	1764
Gender							
Males	11-12	**7.91** (7.19-8.70)	**8.31** (7.35-9.15)	**12.5** (11.4-13.5)	**19.3** (15.7-21.4)	**24.1** (22.2-28.5)	966
	13-14‡	**6.36** (5.62-7.20)	**6.40** (5.70-7.30)	**10.2** (8.70-11.5)	**15.5** (13.2-19.8)	**22.1** (16.7-26.9)	1031
Females	11-12	**5.10** (4.70-5.53)	**5.27** (4.67-5.64)	**8.57** (7.87-9.30)	**12.5** (11.0-14.9)	**17.5** (14.9-20.5)	938
	13-14‡	**3.96** (3.60-4.35)	**4.00** (3.60-4.60)	**7.20** (6.40-7.70)	**11.8** (9.70-13.6)	**15.1** (13.9-17.3)	1134
Race/ethnicity							
Mexican Americans	11-12	**4.79** (4.07-5.64)	**5.18** (3.92-6.33)	**7.91** (6.18-9.48)	**10.5** (8.50-12.6)	**12.1** (10.0-14.4)	211
	13-14‡	**3.47** (2.90-4.16)	**3.70** (3.00-4.40)	**5.20** (4.60-6.40)	**8.80** (6.40-10.3)	**10.8** (9.20-11.8)	332
Non-Hispanic blacks	11-12	**6.35** (5.41-7.46)	**6.57** (5.71-7.65)	**11.3** (9.74-13.9)	**21.8** (13.9-31.3)	**30.7** (21.6-45.1)	485
	13-14‡	**5.32** (4.12-6.88)	**5.30** (4.30-6.80)	**10.2** (7.60-13.7)	**17.4** (12.4-24.5)	**24.5** (16.3-39.7)	455
Non-Hispanic whites	11-12	**6.71** (6.15-7.32)	**6.83** (6.07-7.73)	**10.7** (9.89-12.2)	**15.7** (14.8-18.1)	**21.3** (18.7-23.5)	666
	13-14‡	**5.31** (4.72-5.98)	**5.70** (5.10-6.40)	**8.90** (8.20-9.90)	**14.1** (12.2-15.6)	**18.0** (15.5-20.4)	861
All Hispanics	11-12	**4.63** (3.86-5.55)	**5.18** (4.41-6.19)	**8.10** (6.64-9.78)	**11.0** (9.96-12.6)	**13.4** (11.5-16.1)	406
	13-14‡	**3.51** (3.09-3.98)	**3.70** (3.20-4.20)	**5.50** (4.90-6.40)	**8.80** (8.00-9.70)	**10.8** (9.70-12.1)	537
Asians	11-12	**7.10** (5.80-8.68)	**7.53** (5.96-9.25)	**12.6** (10.8-17.0)	**24.6** (19.1-33.3)	**35.1** (26.4-42.3)	291
	13-14‡	**6.18** (5.08-7.52)	**6.30** (5.00-7.90)	**13.2** (9.40-15.4)	**23.8** (15.2-33.9)	**33.6** (20.1-69.0)	234

Limit of detection (LOD, see Data Analysis section) for Survey year 11-12 is 0.2.
‡.See Calculation of PFOS and PFOA as the Sum of Isomers for additional information about Survey years 2013-2014.

- Nicotine, Cotinine
- NNAL
- Anabasine, Anatabine
- PAHs
- Perchlorate, nitrate & thiocyanate
- VOCs and VOC metabolites
- Heterocyclic amines
- Aromatic amines
- Metals
- Dioxins, furans, & PCBs
- Organochlorine pesticides
- PBDEs
- PFAS
- Organophosphate & pyrethroid insecticides
- Other pesticides (e.g., herbicides, insect repellents)
- Parabens
- Phthalates & alternative plasticizers
- PCP chemicals (e.g., phenols, triclocarban)

*www.cdc.gov/exposurereport/

Updated Tables, March 2018

- **Updated Tables reported in two volumes**
  - Volume 1 – U.S. general population
  - Volume 2 – Pooled samples, adult cigarette smokers and nonsmokers:
    - ***Special sample of adult smokers and nonsmokers***
    - POPs and pesticides in individual and pooled samples
- **New chemical data**
  - ***VOCs in blood (10 new)***
  - ***Heterocyclic amines in urine***
  - BPF, BPS in urine
  - Flame retardants in urine (OP FR metabolites)
  - Cobalt, chromium in blood (40+yrs)
  - DiBP, DBP metabolites in urine

Goals of the *National Report* and *Updated Tables*

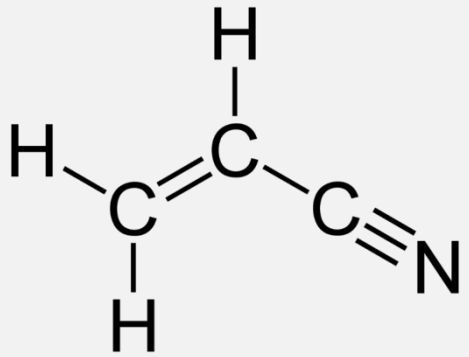
- **Assess exposure to various chemicals**
  - Which chemicals? Who is exposed? How much?
- **Establish US "reference ranges" for these chemicals**
  - By age, sex, and racial/ethnic group
  - By smoker vs. nonsmoker status (adults)
- **Over time, track changes in these "reference ranges"**
- **Help set priorities on studies of exposures and health outcomes**

Data tables are available for more than 300 chemicals, with results from 1999 to 2016

Exploring NHANES data for selective smoke exposure biomarkers

Acrylonitrile

- Possible human carcinogen
- Acute toxicity to multiple physiologic systems
- Clean Air Act Hazardous Air Pollutant

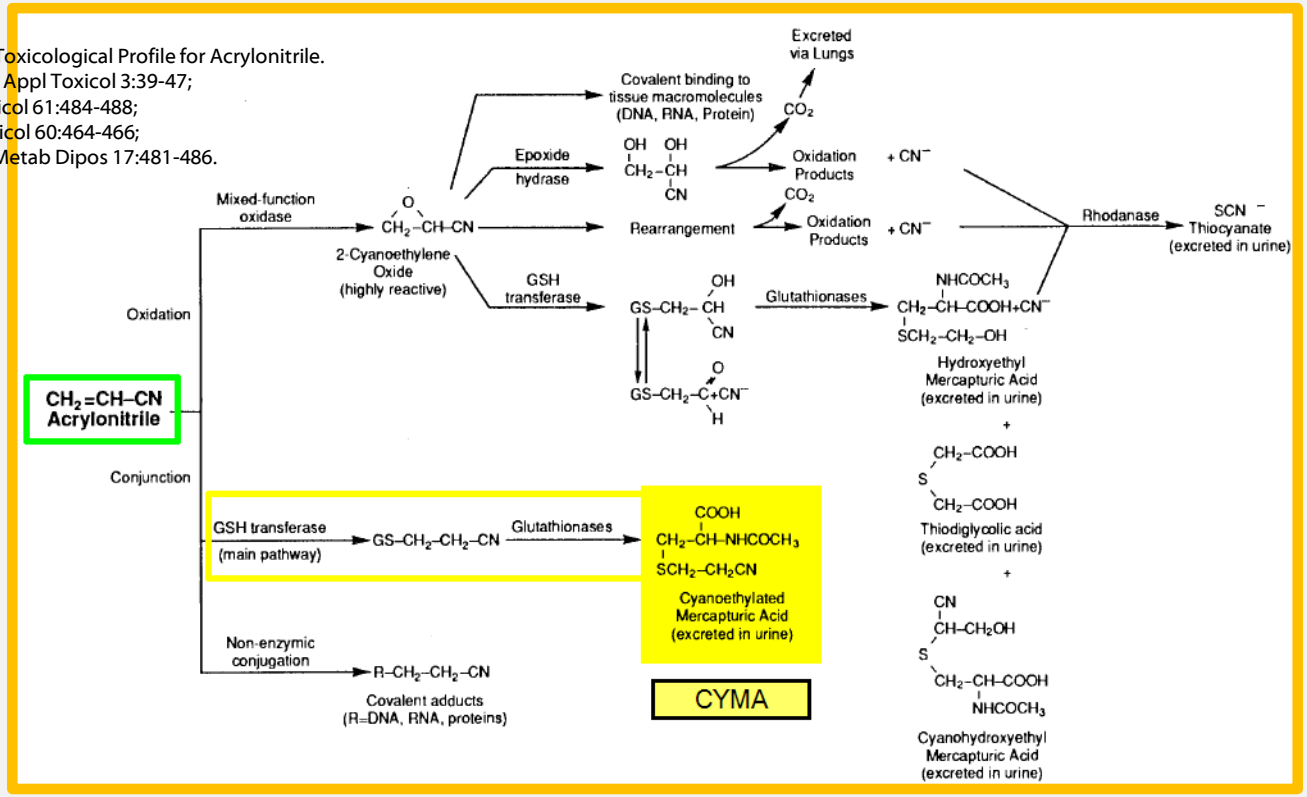


Burning Biomass Forms Acrylonitrile

- Large-scale
  - Smoke plumes from forest fires
- Small-scale
  - Tobacco smoke
  - Marijuana smoke

Acrylonitrile Biomarker: Urinary CYMA

As adapted in ATSDR (1990). Toxicological Profile for Acrylonitrile.
From Ahmed AE, et al. 1983. J Appl Toxicol 3:39-47;
Linhart I, et al. 1988. Arch Toxicol 61:484-488;
Muller G, et al. 1987. Arch Toxicol 60:464-466;
Roberts AE, et al. 1989. Drug Metab Dipos 17:481-486.



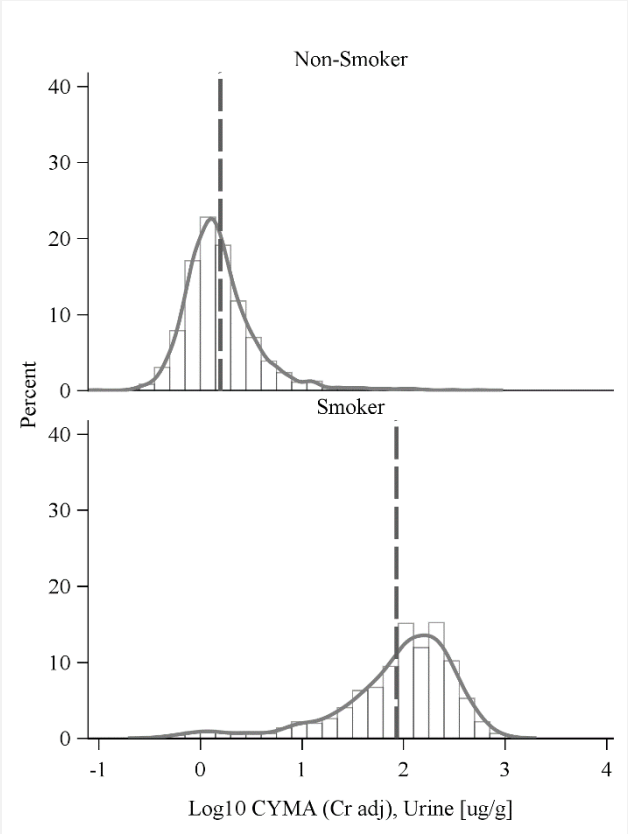
Available CYMA data from NHANES

- National Health & Nutrition Examination Survey
  - United States civilians
  - >4,600 participants ≥6 y
    - 2005 – 2006 One-half sub-sample
    - 2011 – 2012 One-third sub-sample
  - Biomarkers
  - Questionnaires

Objectives

- Characterize population exposure to acrylonitrile based on urinary CYMA
- Evaluate relative source contribution from tobacco smoke and diet
- Evaluate CYMA as a biomarker of tobacco smoke exposure

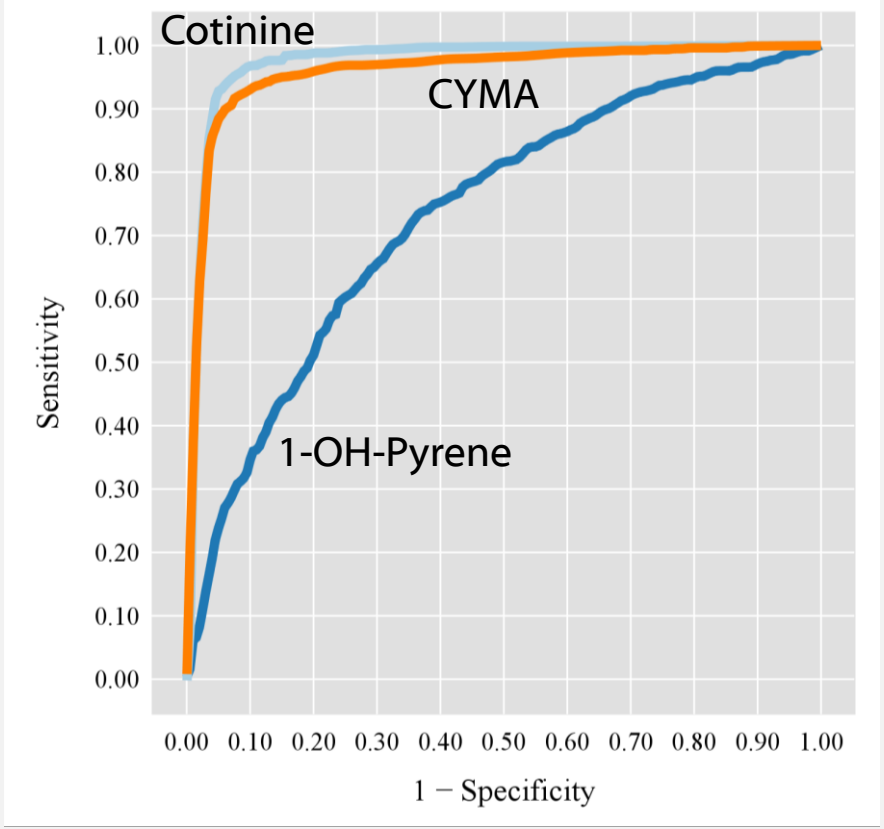
Log10 CYMA, Urine



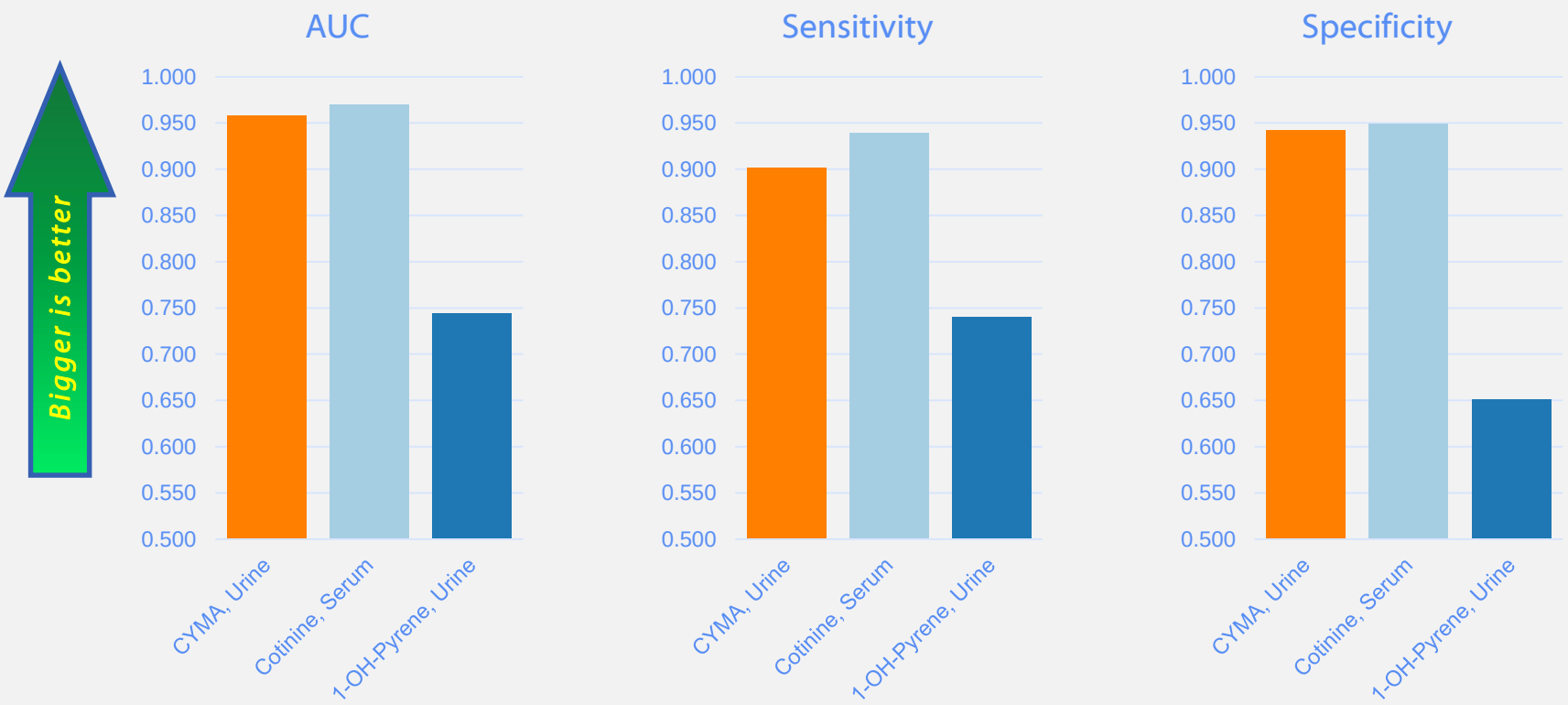
ROC CURVE ANALYSIS

CYMA’s performance as indicator of tobacco smoke exposure

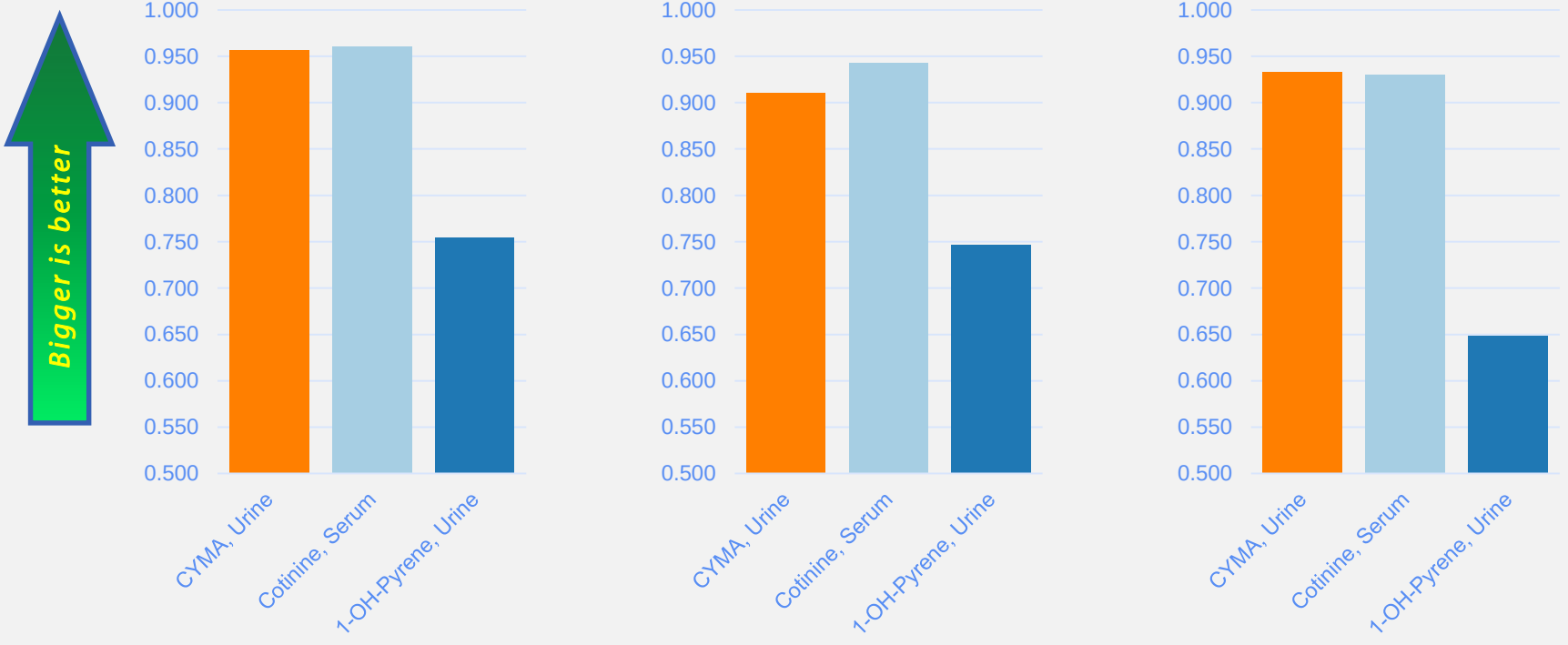
Non-User vs. Exclusive Smoker



Non-User vs. Smoker: Cut-points



SHS-Exposed vs Non-Exposed: Cut-point



MULTIPLE REGRESSION

Predict CYMA, Urine

Primary interest: Tobacco smoke, Diet

Stratification

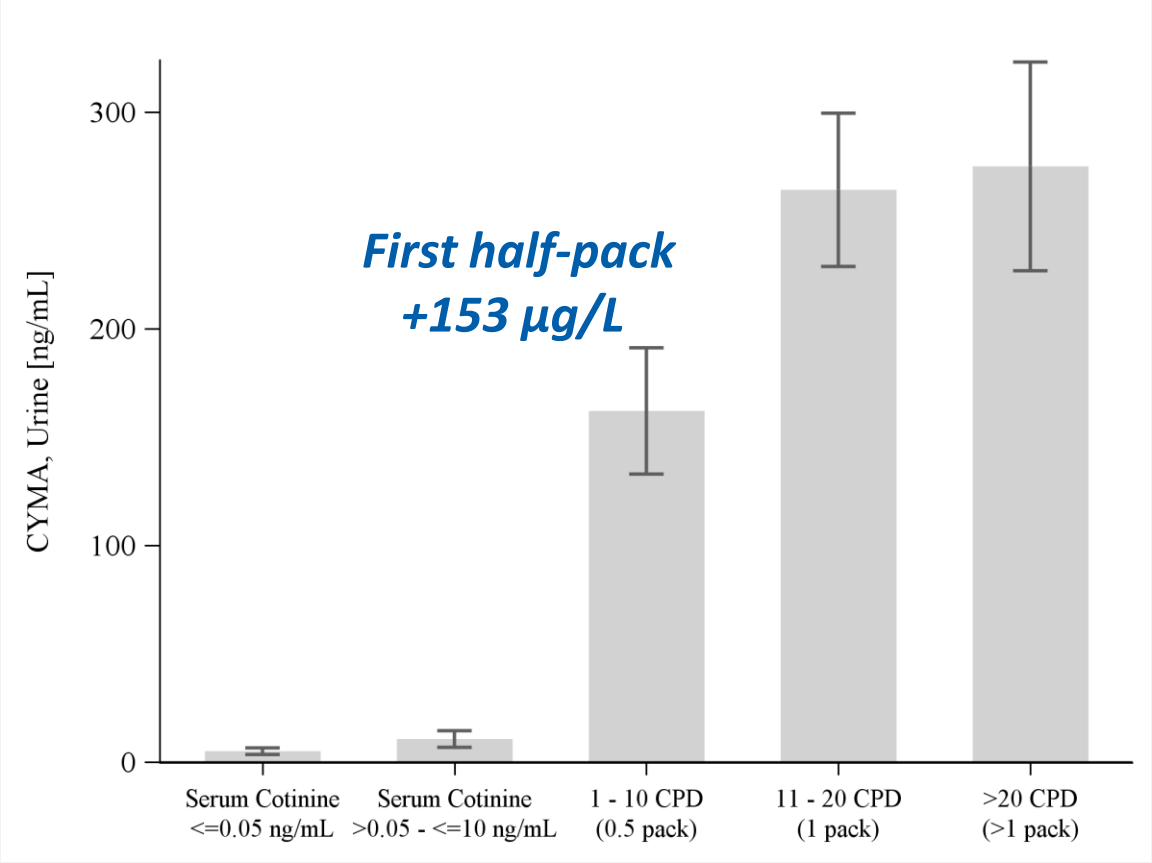
- Exclusive combusted tobacco users (“smokers”)
- Non-users

Urinary CYMA Predictor Variables

- CPD and Serum Cotinine
- Sex
- Age
- Race/ethnicity
- BMI
- Creatinine, Urine
- Fasting time
- Impoverishment
- NHANES Cycle
- Roasted Nuts and Seeds
- Chocolate
- Coffee, Brewed
- Meats, Smoked
- Alcohol
- Plus 9 USDA Major Food Groups

  Milk Products; Meat, Poultry; Eggs; Legumes, Nuts, Seeds; Grain Products; Fruits; Vegetables; Fats, Oils, Salad Dressings; Sugars, Sweets, Beverages

Smoke Exposure Increases Urinary CYMA



Dietary Exposure

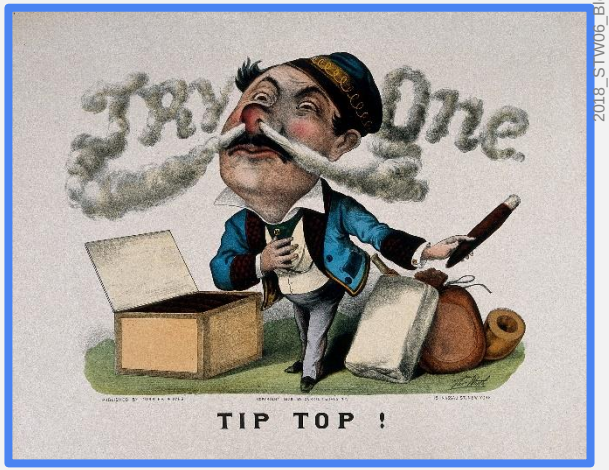
Food Group	Non-Users	Smokers
Meats, Smoked	+	+
Alcohol	+	NS
Fruits	–	–
Nuts & Seeds, Roasted	NS	NS
Chocolate	NS	NS
Coffee, Brewed	NS	NS

Smoking predicts higher CYMA than Diet

- Cigarettes: First half-pack smoked associated with major increase in urinary CYMA (153 µg/L)
- Smoked Meat Consumption
  - Statistically significant but median meat consumed = 0); even at 95th %tile meat consumed, only modest CYMA increase (2.9 µg/L)
- Alcohol Consumption (non-user model only)
  - Median wine consumption (1 glass) predicts 10 µg/L increase in CYMA

Conclusions

- Characterization of US population exposure to acrylonitrile
- Tobacco Smoke is a major source
- Ingested smoked meats and alcohol are minor sources of acrylonitrile exposure



CYMA Smoke Biomarker

- Biomass Combustion
  - General applicability
- Tobacco Smoke Exposure
  - Excellent indicator
- Measurement in Urine
- Frequently Detected (>90%)

Limitations

- Cross-sectional study design
- Smoking, Tobacco Smoke exposure self assessment
- Diet
  - Food classification
  - Sufficient mass

Collaborators

- CDC National Center for Environmental Health
  - Division of Laboratory Sciences
  - Tobacco & Volatiles Branch
    - Rey de Castro, Statistician
    - Victor DeJesus, VOC Laboratory Chief
    - Deepak Bhandari
    - David Chambers

Follow Up

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