

Public Comments of Albert Donnay, MS, MHS

Consulting Toxicologist and Research Associate

Johns Hopkins Center for Sleep Disorders

adonnay@jhu.edu

August 24, 2016

National Academy of Sciences

Division on Earth & Life Sciences

Board on Environmental Studies & Toxicology

*Committee on “Assessing Toxicologic Risks to Human Subjects
Used in Controlled Exposure Studies of Environmental Pollutants”*

History of EPA reliance on Controlled Human Inhalation Exposure Studies (CHIEs) for Setting National Ambient Air Quality Standards

Carbon Monoxide NAAQS is the only NAAQS ...

- * based exclusively on the results of CHIEs
- * that has not changed since adopted in 1971, though its basis has:

1971 : based on vision changes reported in 1 CHIEs (later found irreproducible)

1980 : proposed basing on cardiac changes reported in 8 CHIEs by Aronow et al

1985 : changed basis to cardiac changes reported in 1 CHIEs by EPA staff with n=10

1994 : kept same basis as 1985, citing 3 more cardiac CHIEs (2 EPA \$ and 1 CARB \$)

2011 : kept same basis as 1994, citing 1 more cardiac CHIEs from 1998 (CARB \$)

Table 1 CHIE Studies cited by EPA in 2011 as basis for CO NAAQS

CO CHIE Studies * authors include ≥ 1 EPA staff	Funding Source(s)	Reported number of fully tested subjects all with ischemic heart disease and stable angina (plus number of dropouts if known)
Adams* 1988	EPA intramural and extramural with UNC	30 men (plus 12 dropouts)
Anderson* 1973	EPA intramural	10 men, 5 of them smokers (no dropouts mentioned)
Allred 1989a,b, 1991	EPA extramural commissioned from Health Effects Institute	63 men (plus 7 dropouts, 6 cut, and 31 not reported)
Kleinman 1989	CARB extramural and Southern Occupational Health Center intramural	24 men (plus 2 dropouts)
Kleinman 1998	CARB extramural and Southern Occupational Health Center intramural	17 men, 15 of them ex-smokers (no dropouts mentioned)
Sheps* 1987	EPA intramural and extramural with UNC	25 men and 5 women (no dropouts mentioned)

Table 2 CO Exposures Used in Studies cited by EPA Administrator in 2011

CO CHIE Studies * authors include ≥ 1 EPA staff	CO Exposure Level, Duration and vCOHb Target, if any Note 1: All exposures exceeded EPA 1-hour NAAQS of 35ppm Note 2: None of the studies that varied individual exposure times to reach COHb targets reported the mean, range or SD time
Adams* 1988	Inhaled 100ppm (n=17) or 200ppm (n=13), both for ≥ 1 hour on one day, varying extra time to reach 6% venous COHb
Anderson* 1973	Inhaled 50 and 100ppm for 4 hours each on two days
Allred 1989a,b, 1991	Inhaled 150ppm for 1 hour on 1 st day; 2 nd and 3 rd days varied from 42 to 357 ppm and from 50-70 minutes, varying time to reach targets of 2.2% and 4.4% venous COHb
Kleinman 1989	Inhaled 100ppm for 1 hour on one day to reach mean 3.0% venous COHb without varying individual times
Kleinman 1998	Inhaled 100ppm for ≥ 2 hours each on two days, varying extra time to reach target of 4% venous COHb
Sheps* 1987	Inhaled 100ppm for ≥ 1 hour on one day, varying extra time to reach target of 4% venous COHb

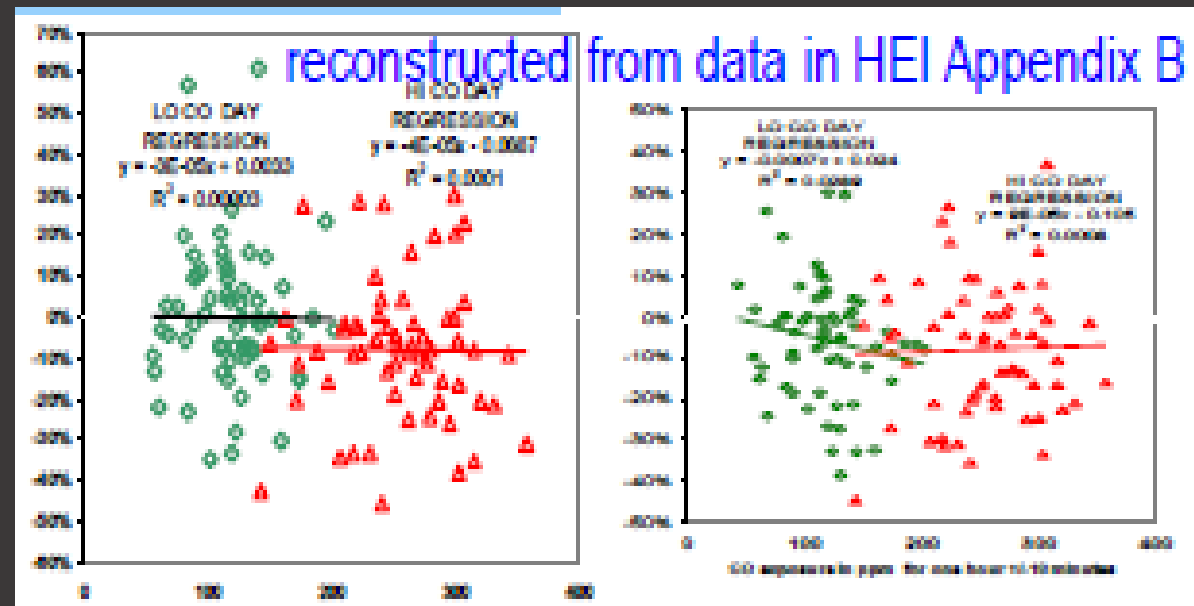
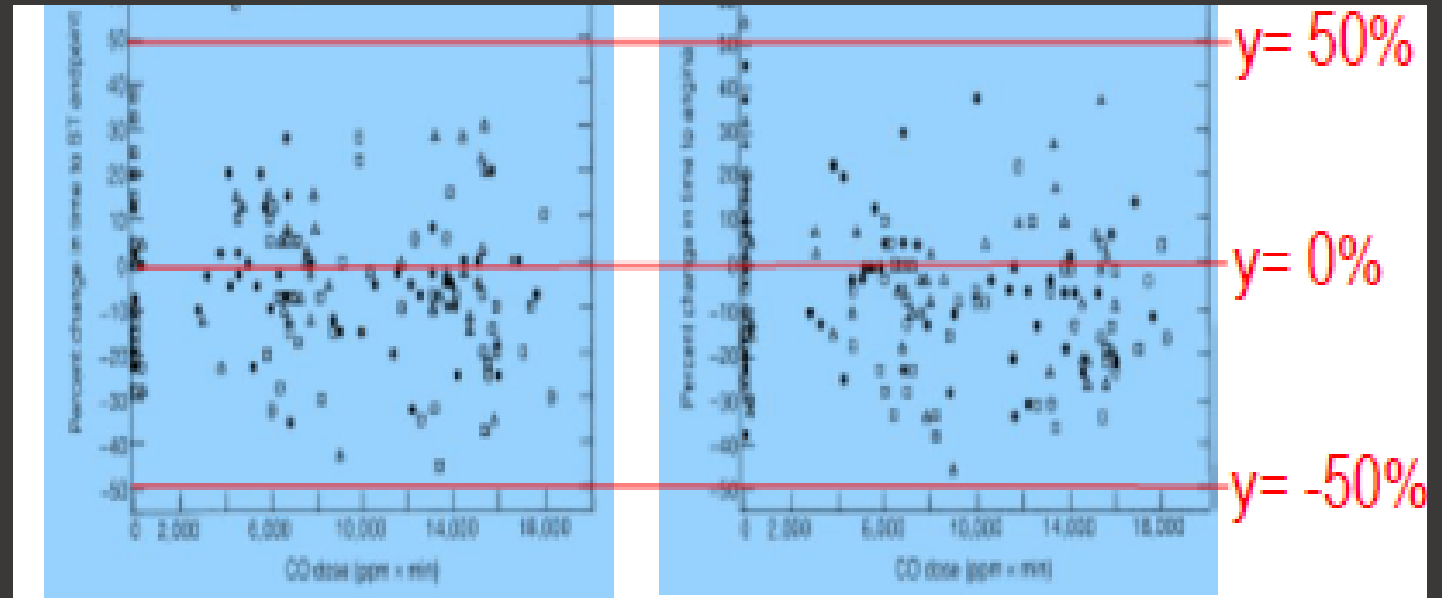
Allred et al

CO Dose-Response Data

x-axis = CO doses in ppm*minutes
y-axis = primary adverse outcomes

In Figure C1 at left,
y = % change in time to abnormal ST-EKG
during exercise post vs pre-exposure
In Figure C2 at right,
y = % change in time to onset of angina
during same exercise

Source: Figures C1 and C2 above are from
Allred 1989, HEI Research Report #25
Replotted below by Donnay showing
low CO range in green and hi CO in red
with flat or falling regression lines

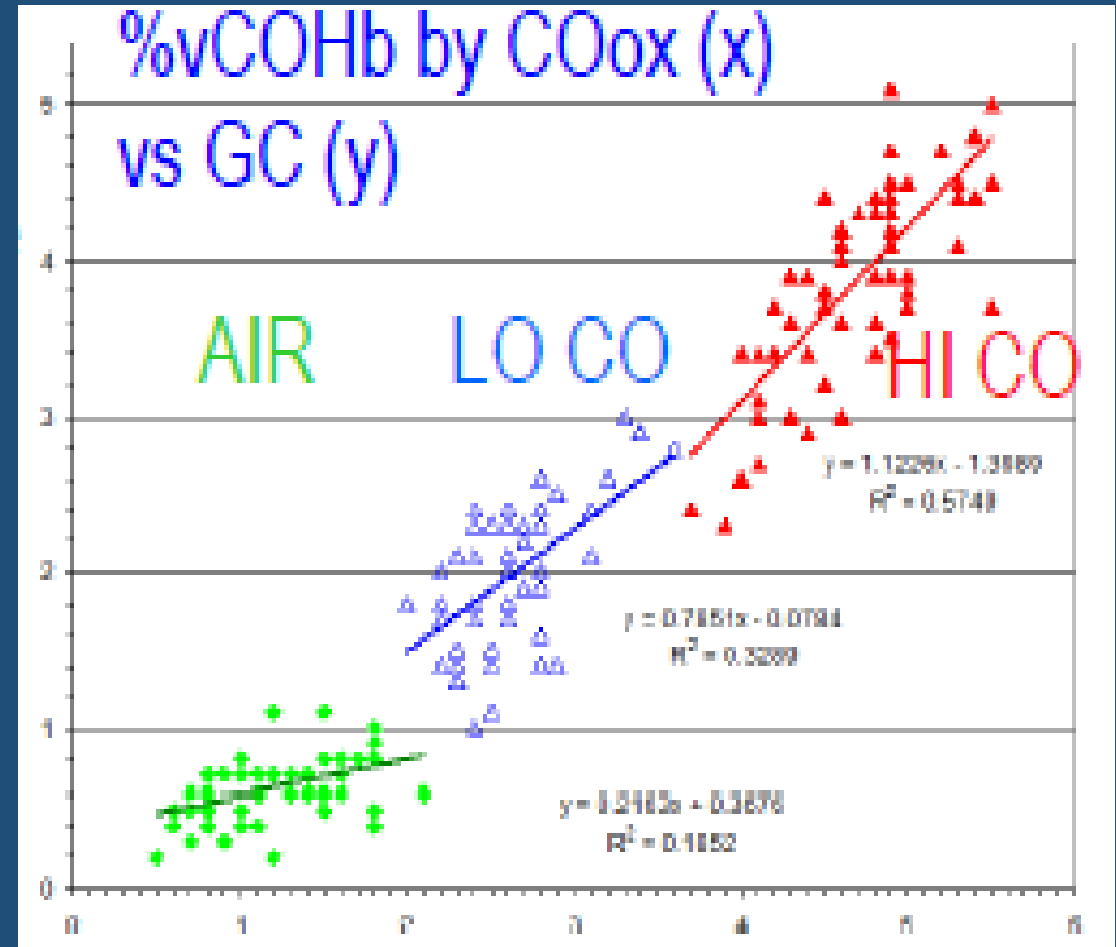


Inconsistent correlation
between venous COHb
as measured by
IL 282 CO-oximeter (x)
compared to Gold Standard
Gas Chromatograph (y)

5 of 6 CHIE studies used IL 282s

*4 of 6 relied on Allred's QC lab to
calibrate their IL282s by this GC method*

Data from Allred 1989
HEI version Appendix B;
Figure by Donnay



Conclusions

EPA use of CHIE studies
in setting National Ambient Air Quality Standards

1. Is inherently unrepresentative and under-powered vs epi studies
2. Violates the Common Rule and other ethical standards
3. Inappropriately focuses on brief indoor exposures above NAAQS
in place of chronic low exposures outdoors below NAAQS

*NAS/DELS/BEST Committee should recommend that
EPA stop conducting, funding and citing CHIE studies
for use in NAAQS rulemakings and focus instead on epi studies*