

FOUNDATION FOR A
SMOKE-FREE WORLD



TOBACCO HARM REDUCTION WEIGHING THE EVIDENCE

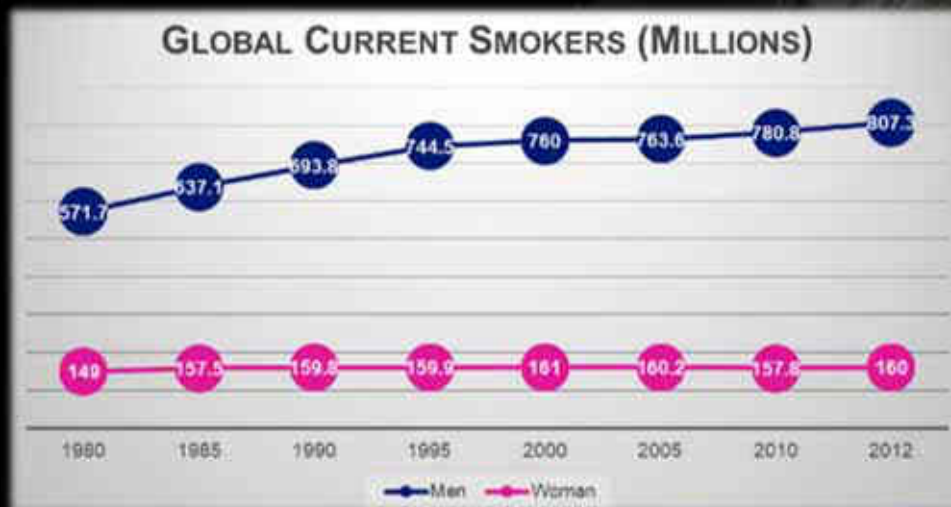
Brian Erkkila, PhD
VP, Health, Science & Technology
TSRC | September 16, 2019

OUTLINE OF TALK

- THE NEED FOR TOBACCO HARM REDUCTION
- EVIDENCE
 - WHAT WE TALK ABOUT WHEN WE TALK ABOUT EVIDENCE
 - WHAT EVIDENCE DO WE ALREADY HAVE
- QUESTIONS

GLOBAL TRENDS IN SMOKING PREVALENCE

THE WHO
ESTIMATES THAT
THERE ARE NOW
1.1 BILLION
SMOKERS
WORLDWIDE



Ng, M., 2014

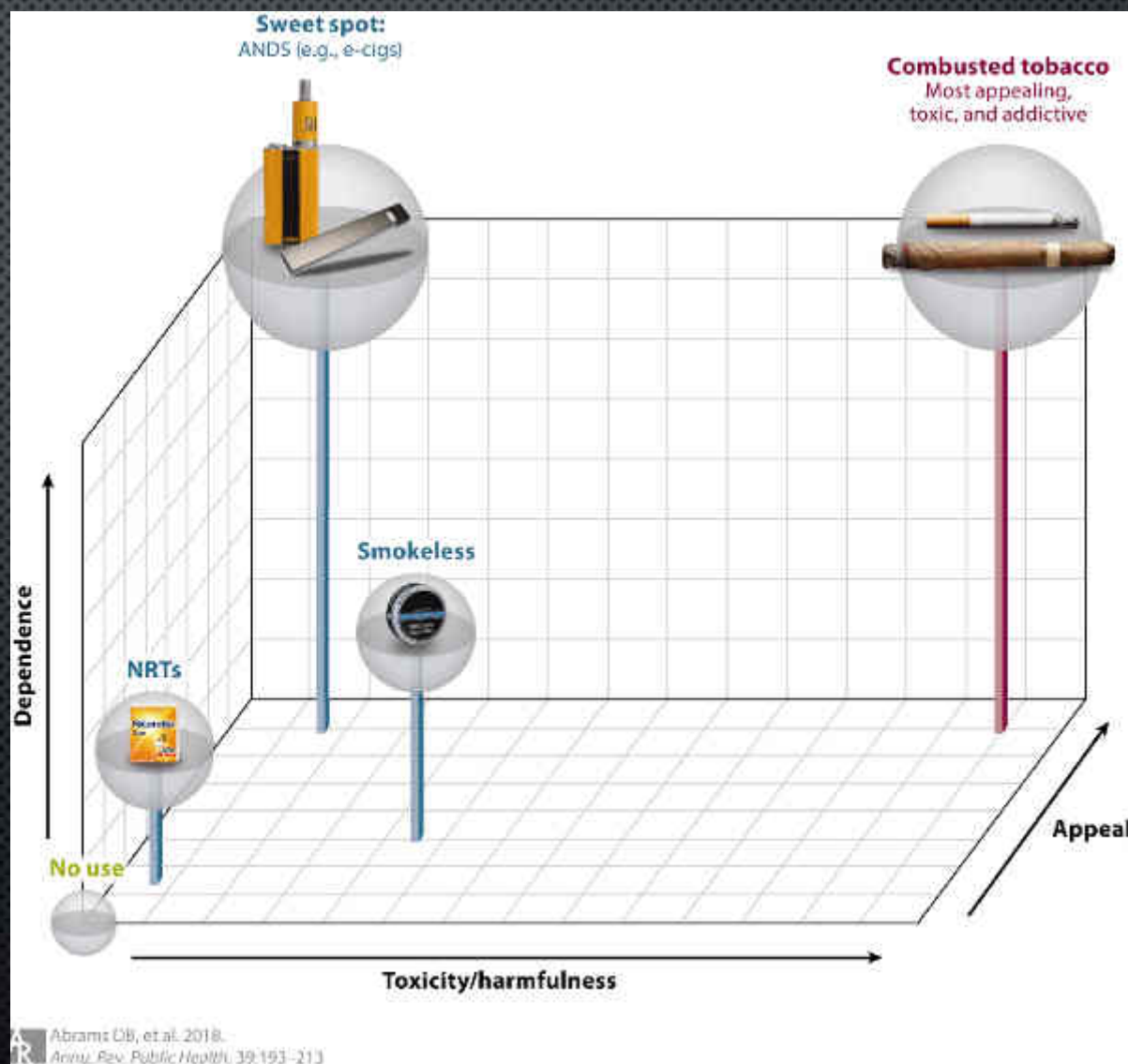
SMOKING

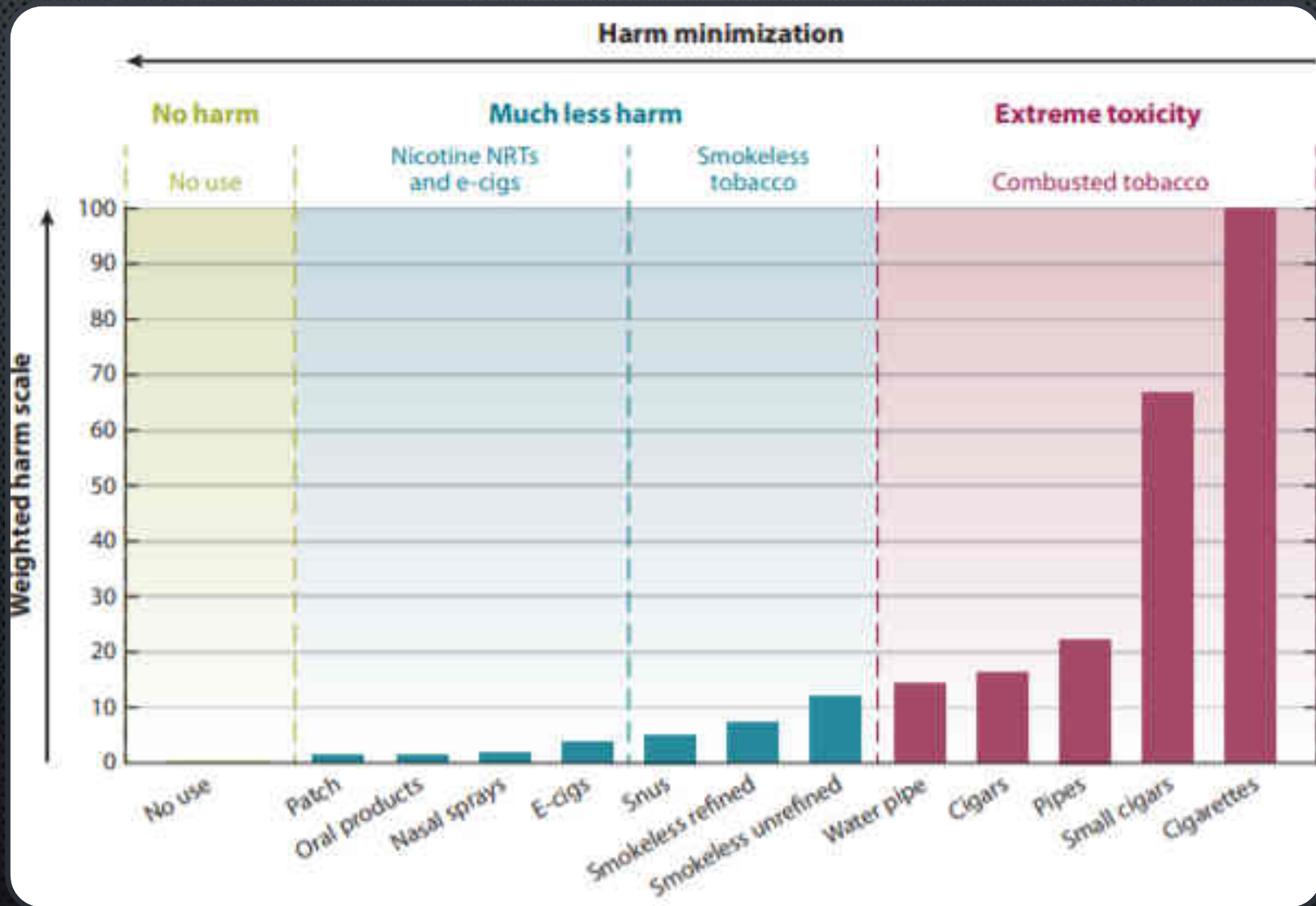


**IS THE LEADING CAUSE OF PREVENTABLE DEATH
AND RESULTS IN MORE DEATHS EACH YEAR
THAN ALL OF THESE COMBINED:**

- HIV
- ILLEGAL DRUG USE
- ALCOHOL USE
- MOTOR VEHICLE INJURIES
- MICROBIAL AGENTS
- TOXIC AGENTS

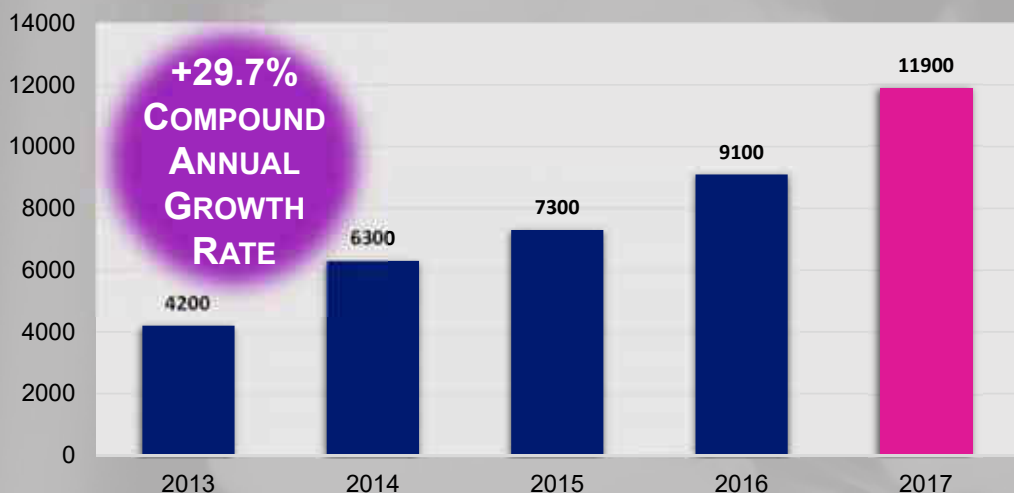
DEFINING CHARACTERISTICS OF THE PRODUCT LANDSCAPE





ABRAMS, D. 2018

ELECTRONIC NICOTINE-DELIVERY SYSTEM SALES

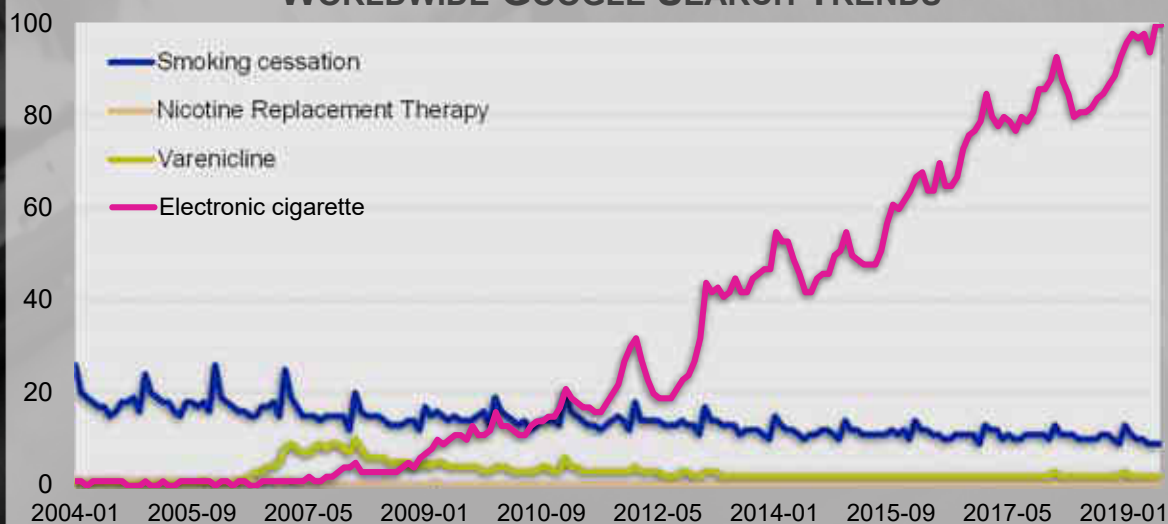


- **ENDS MARKET IS VALUED AT OVER \$10 BILLION, WITH INCREASING DEMAND.**

Smoking Cessation Products and Services, EY- 2018

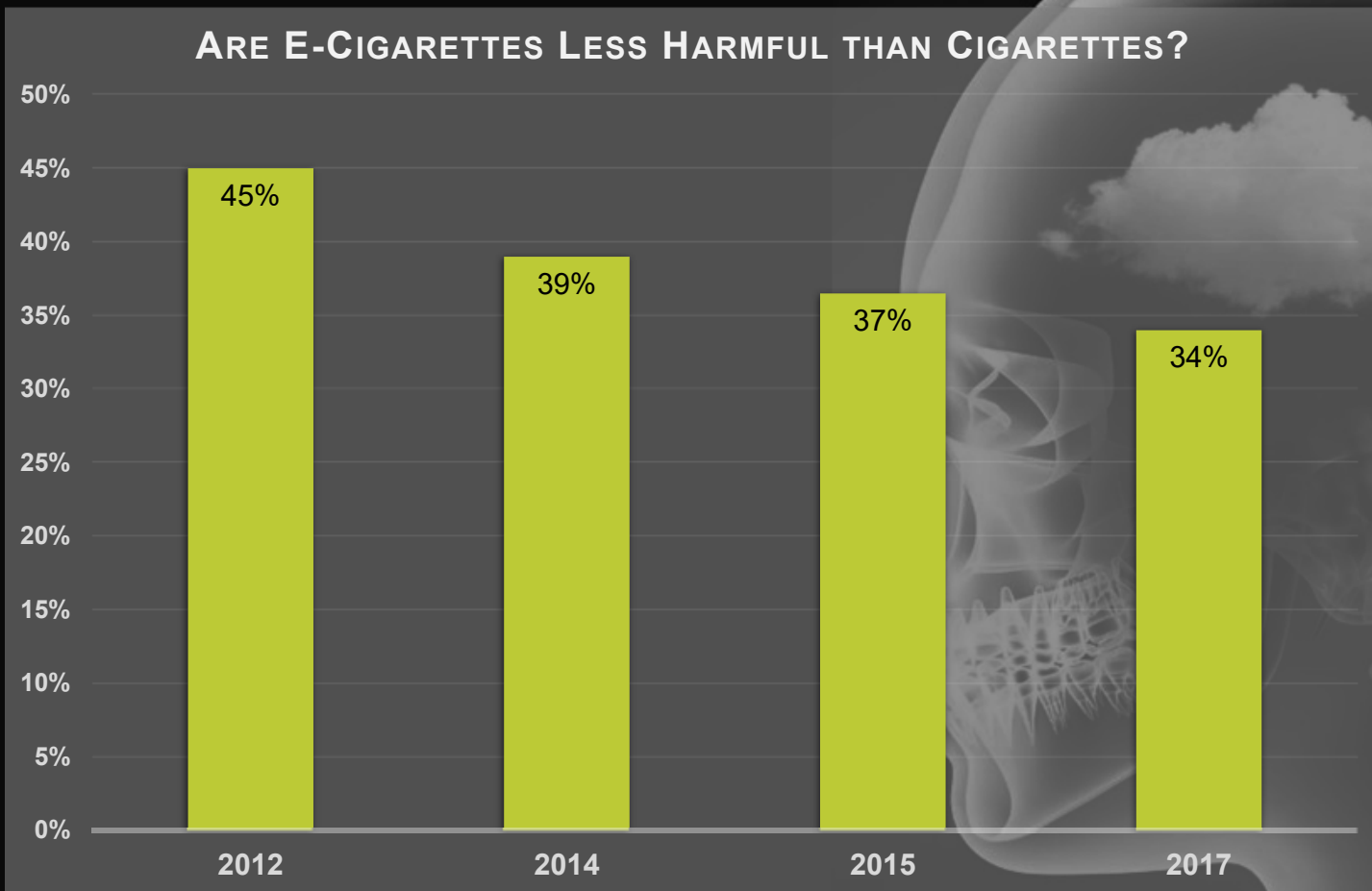
- **E-CIGARETTES HAVE SEEN SIGNIFICANT GROWTH IN INTEREST OVER TIME, OUTSTRIPPING SMOKING CESSATION, VARENICLINE, AND NICOTINE REPLACEMENT THERAPY.**

WORLDWIDE GOOGLE SEARCH TRENDS



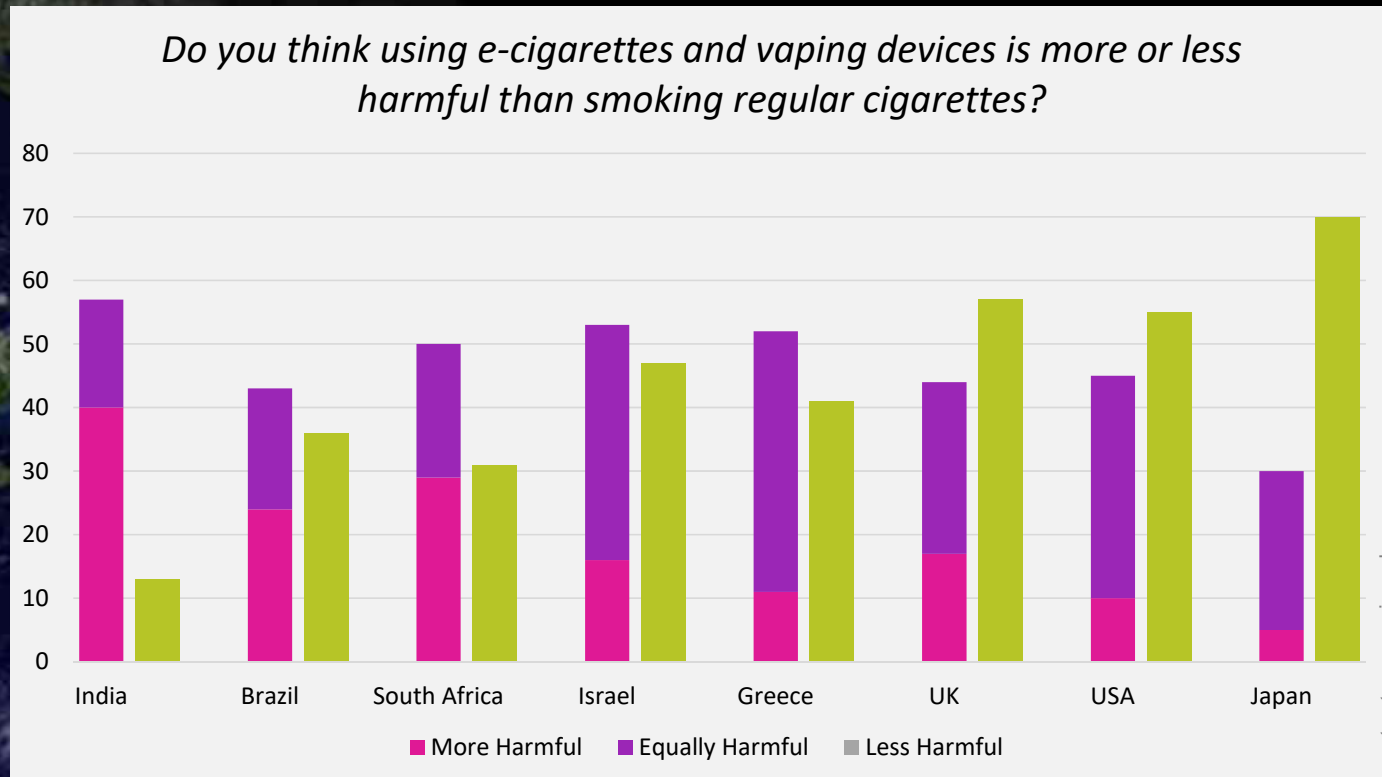
Google Trends, 7/28

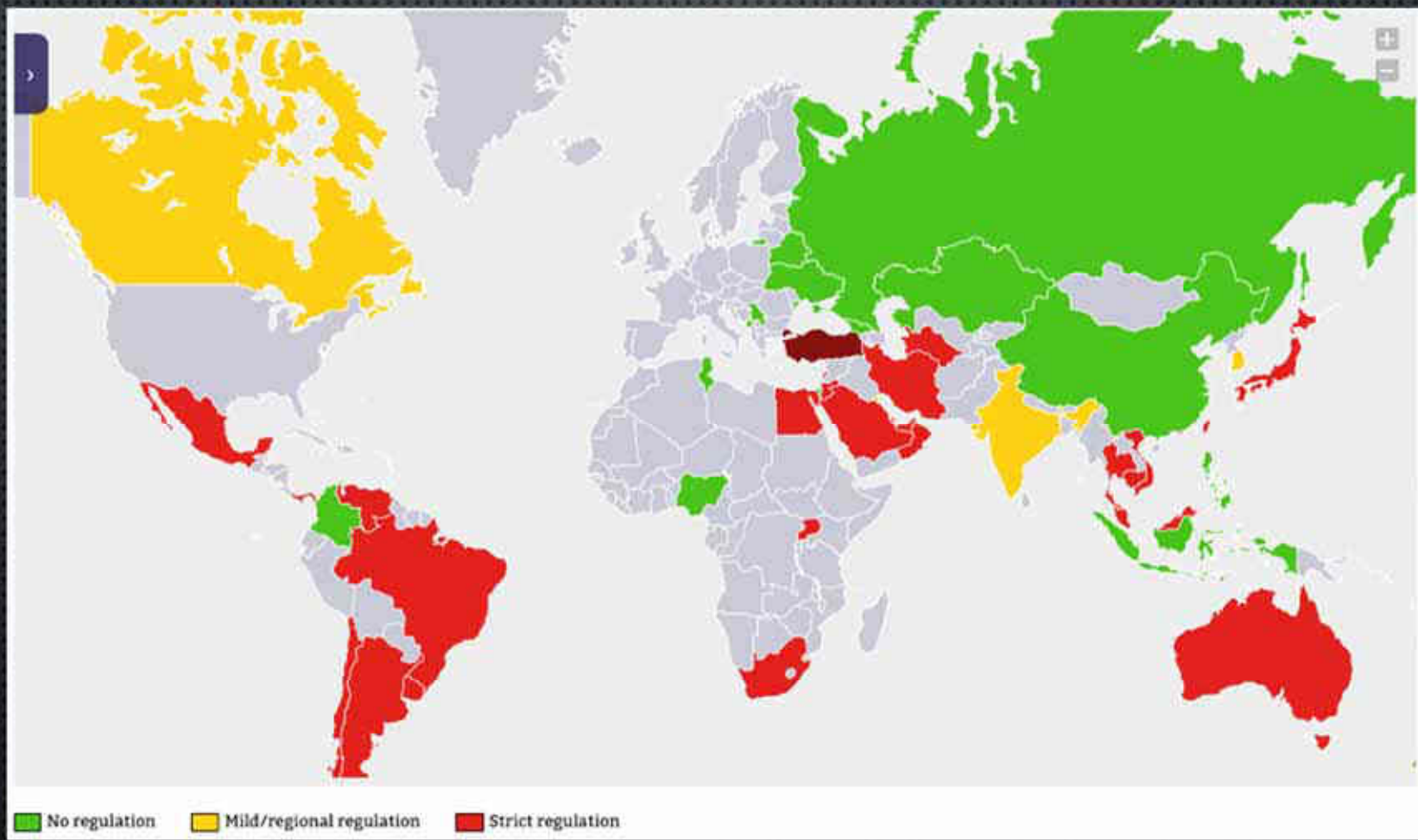
CLOUDED JUDGEMENTS:



MAJEED BA, 2017; HUANG J, 2019; PERSOSKIE A, 2017

GLOBAL OPINIONS OF E-CIGARETTES & VAPING DEVICES





EVIDENCE

WHAT WE TALK ABOUT WHEN WE TALK ABOUT EVIDENCE



SMOKING EVIDENCE: A BRIEF HISTORY





1939: Ochsner A. & DeBakey M. publish review of smoking and lung cancer citing 400+ correlating the increased sale of cigarettes with an increased prevalence of lung cancer.



1958: Hammond EC. & Horn D. publish a pivotal article in JAMA showing an extremely high association between cigarette smoking and death rates for men with lung cancer and cancers of other sites.

1964: First US Surgeon General's report on smoking is released, recognizing the proven link between smoking and lung cancer.



*Lung cancer and cancers of other sites accounted for 27% of excess deaths among regular smokers

1939

1966



1950: Wynder E. & Graham E. publish study of bronchogenic carcinoma in JAMA concluding that tobacco smoking is a possible etiologic factor in the increased incidence of these carcinomas.



1950: Levin M. publishes epidemiologic study linking smoking to lung cancer in JAMA. He reports that heavy smokers as 10x more likely as nonsmokers to contract lung cancer.



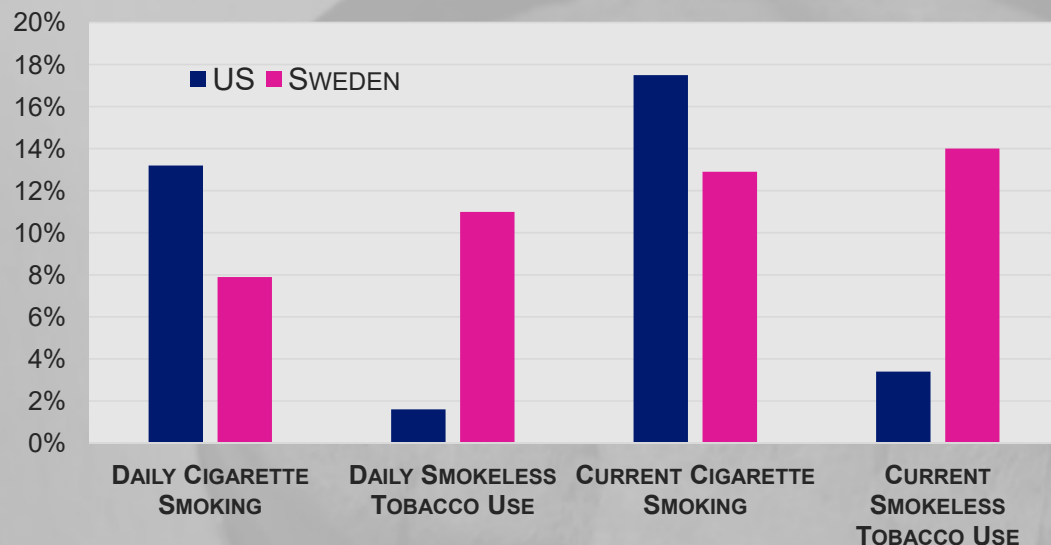
1950: Doll R. & Hill AB. publish preliminary report in BMJ linking smoking and lung cancer about patients in 20 UK hospitals:

"It must be concluded that there is a real association between carcinoma of the lung and smoking."



SNUS

PREVALENCE OF TOBACCO USE - US v. SWEDEN

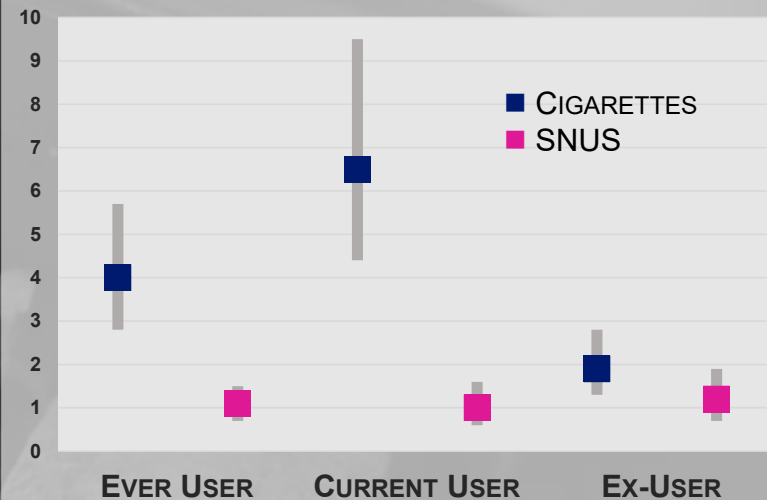


IN 2017, THE ESTIMATED DALY RATE (PER 100,000) FROM ESOPHAGEAL CANCER ATTRIBUTABLE TO SMOKING:

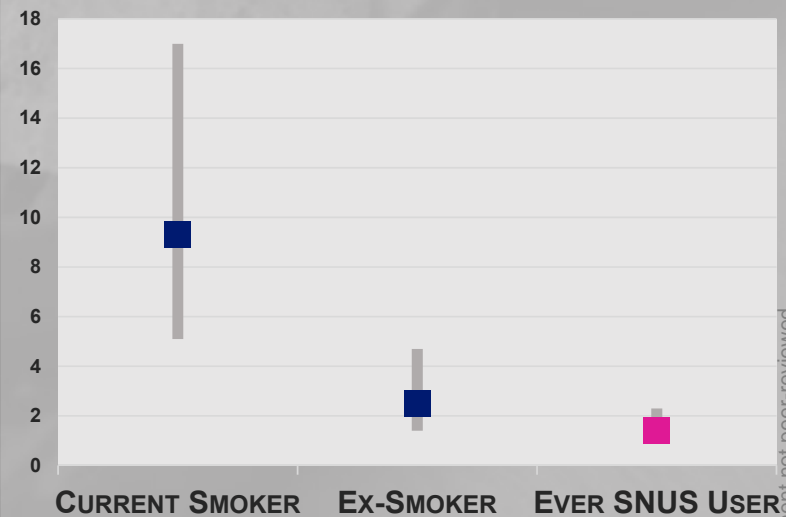
49.3
US

36.4
SE

RELATIVE RISK OF HEAD & NECK CANCER

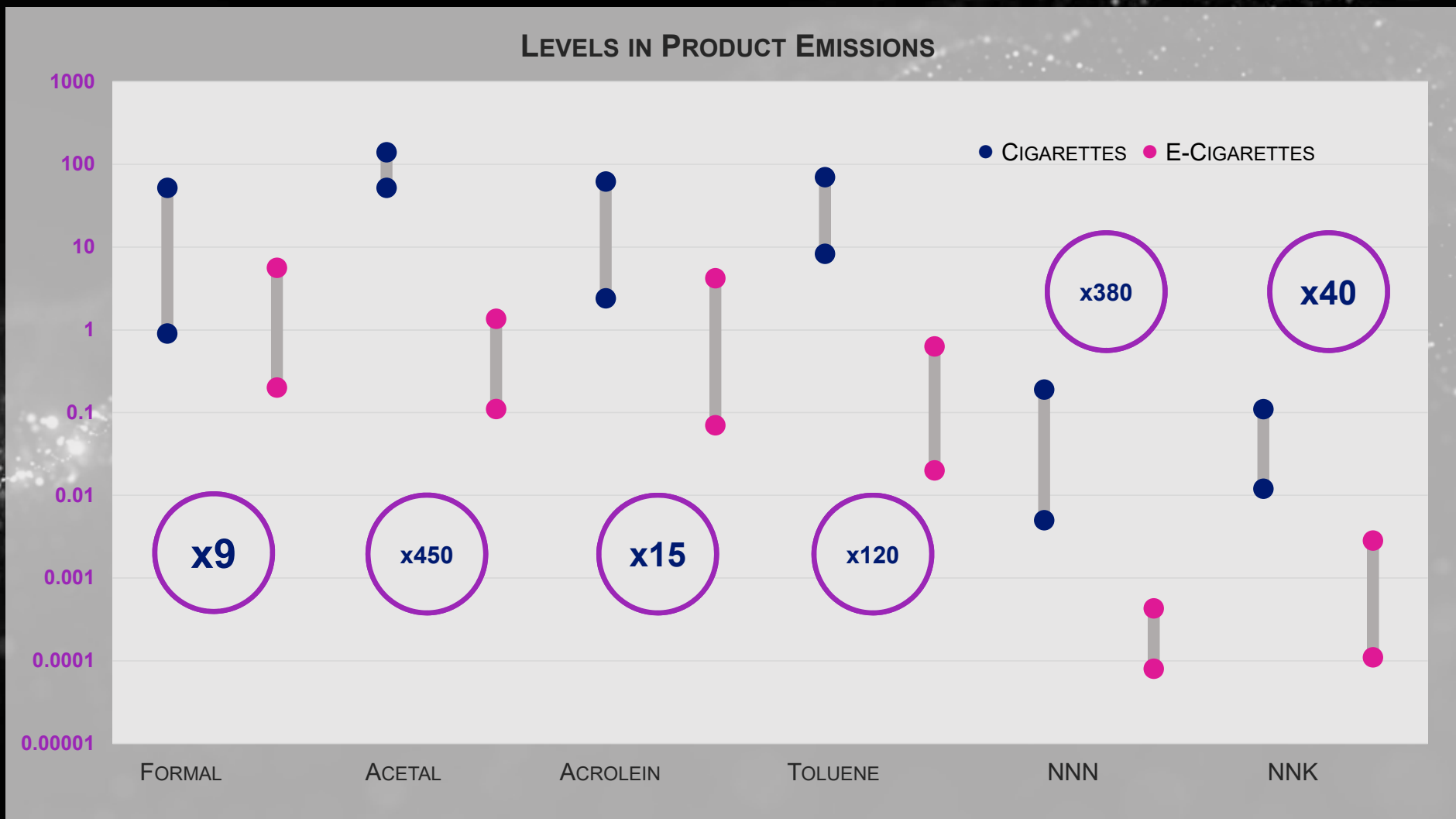


OR FOR DEVELOPING ESOPHAGEAL SCC



COMPOSITION

WHAT ARE IN THESE THINGS?



THE SCIENTIFIC BASIS OF T

Toxicants recommended for mandated lowering

Toxicant	Level in µg/mg nicotine		Criterion for selecting value
	International brands ^a	Canadian brands ^b	
NNK	0.072	0.047	Median value of data set
NNN	0.114	0.027	Median value of data set
Acetaldehyde	860	670	125% of median value of data set
Acrolein	83	97	125% of median value of data set
Benzene	48	50	125% of median value of data set
Benzo[a]pyrene	0.011	0.011	125% of median value of data set
1,3-Butadiene	67	53	125% of median value of data set
Carbon monoxide	18 400	15 400	125% of median value of data set
Formaldehyde	47	97	125% of median value of data set

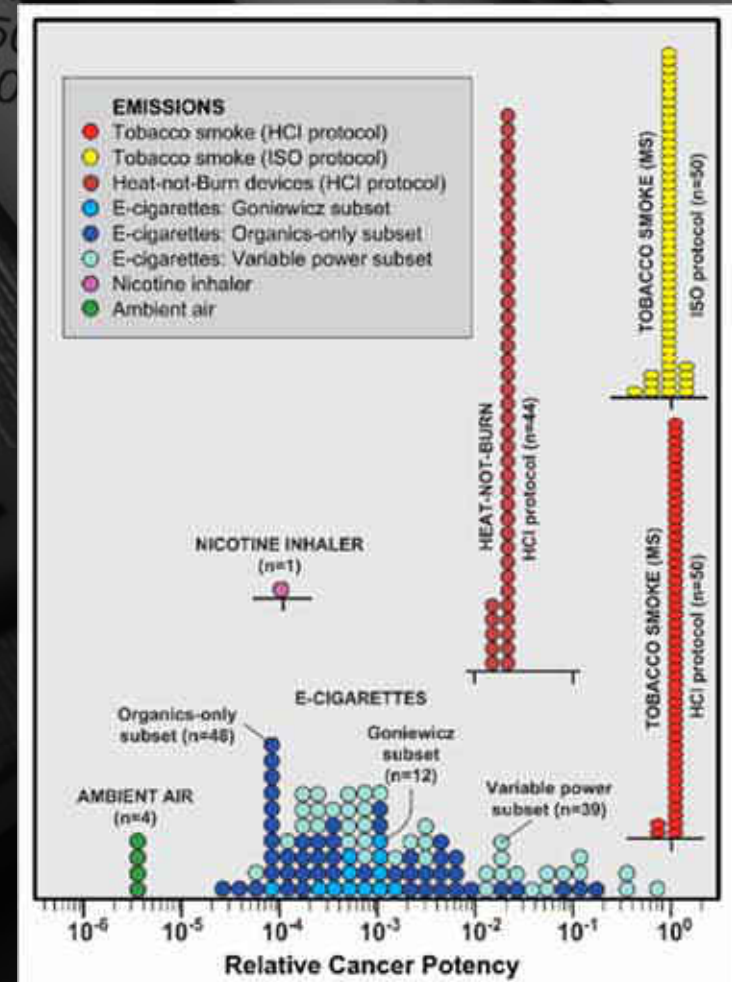


Organization

QUANTITATIVE RISK ASSESSMENT

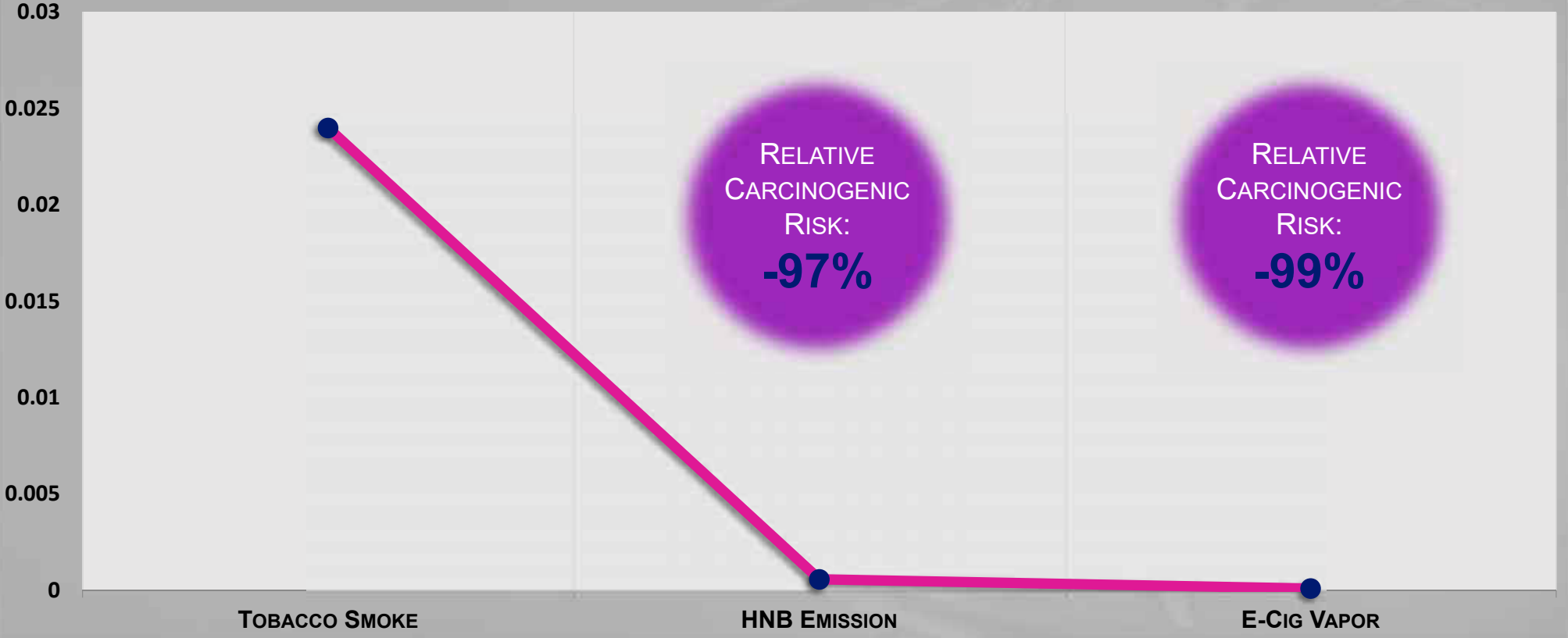
$$\text{RISK} = \text{EXPOSURE} * \text{POTENCY}$$

- COMBINES INFORMATION ABOUT EMISSIONS, PRODUCT USE TOPOGRAPHY, CONSTITUENT POTENCY
- ALLOWS FOR COMPARISONS OF RELATIVE RISK BETWEEN PRODUCTS AND CLASSES OF PRODUCTS



(STEPHENS WE, 2019)

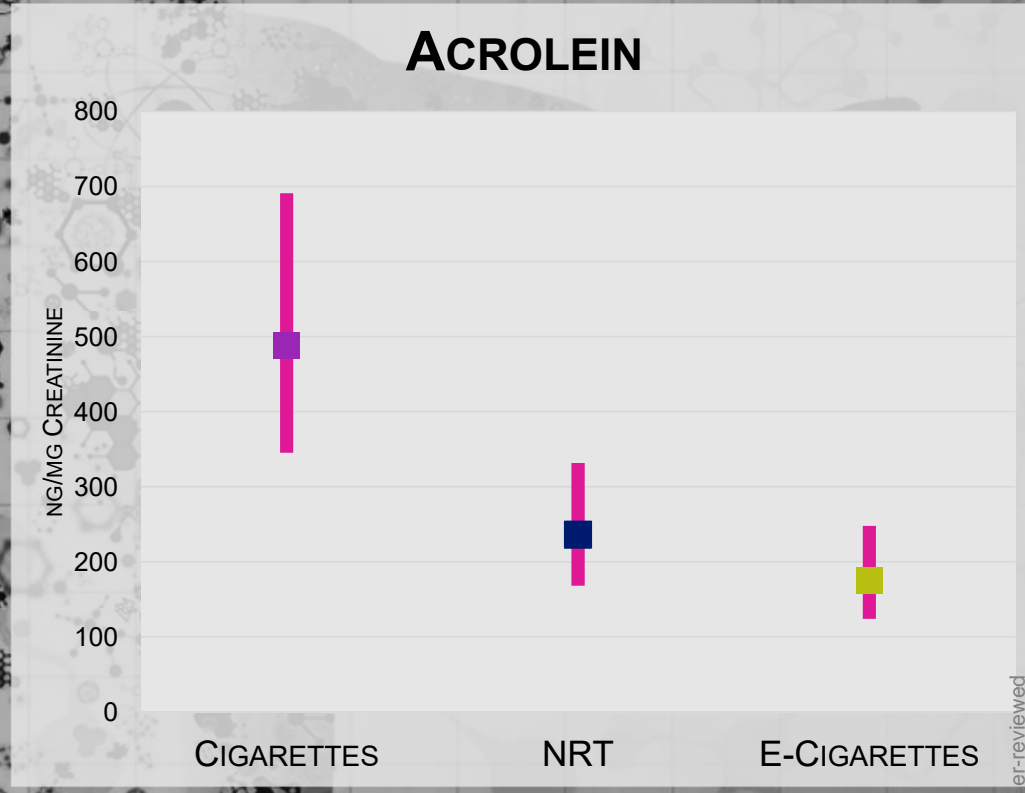
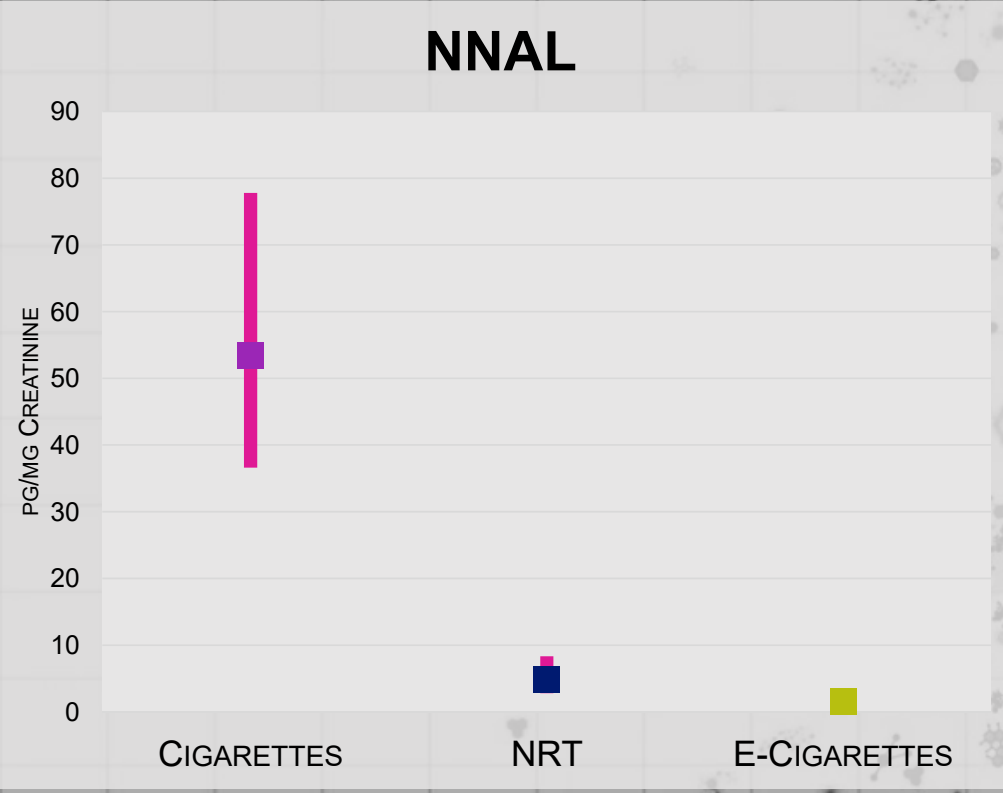
MEAN LIFETIME CANCER RISK

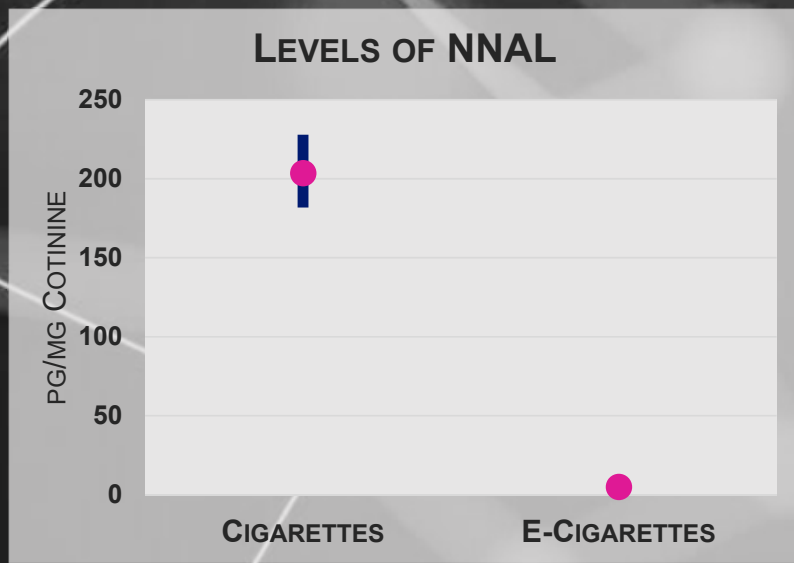
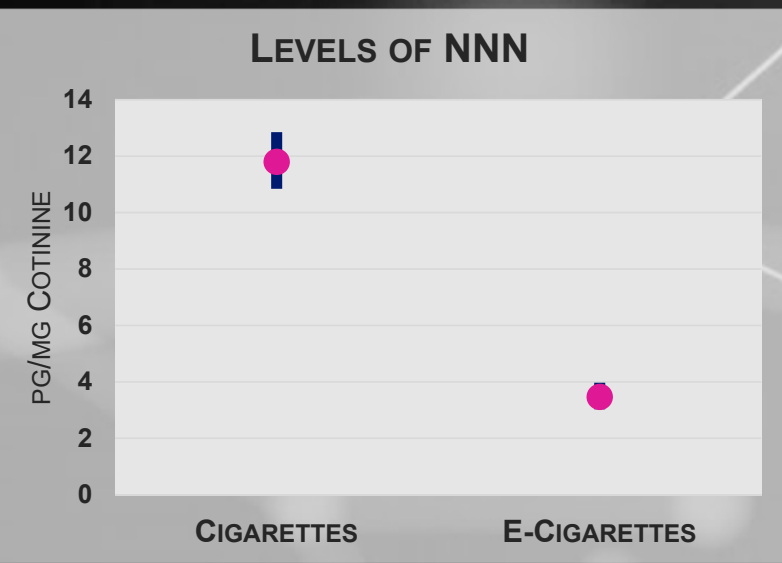
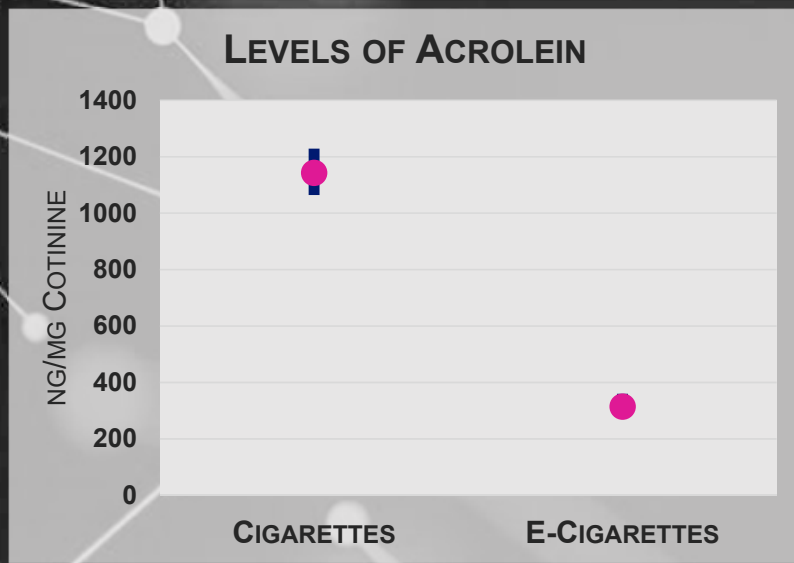
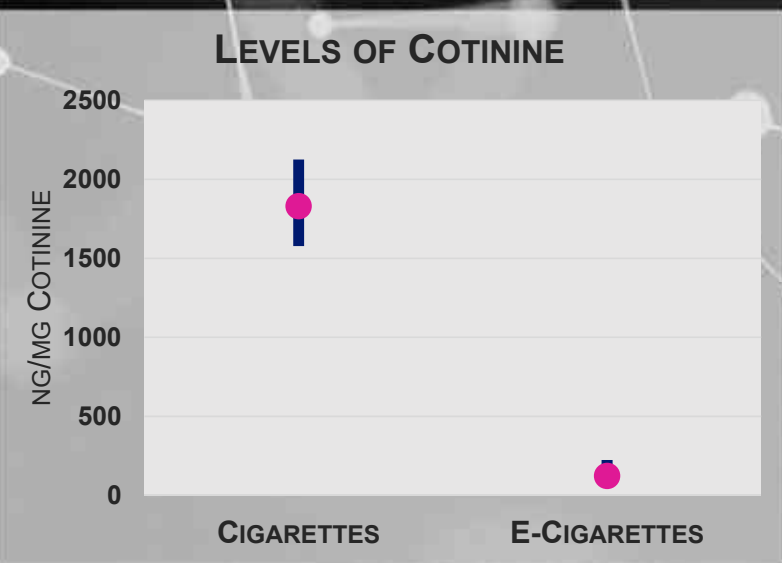


EXPOSURE

WE DON'T KNOW WHAT PEOPLE ARE PUTTING INTO THEIR
BODIES?

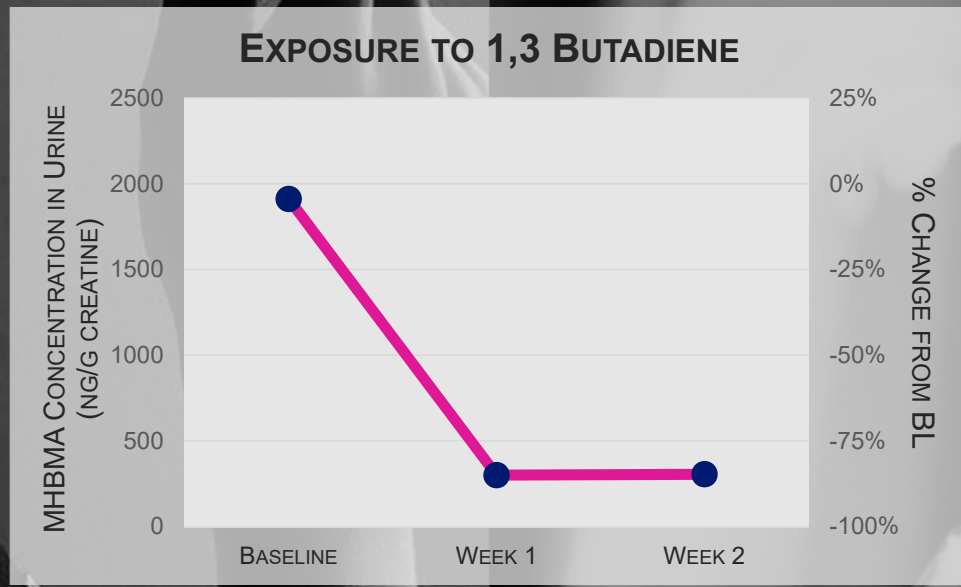
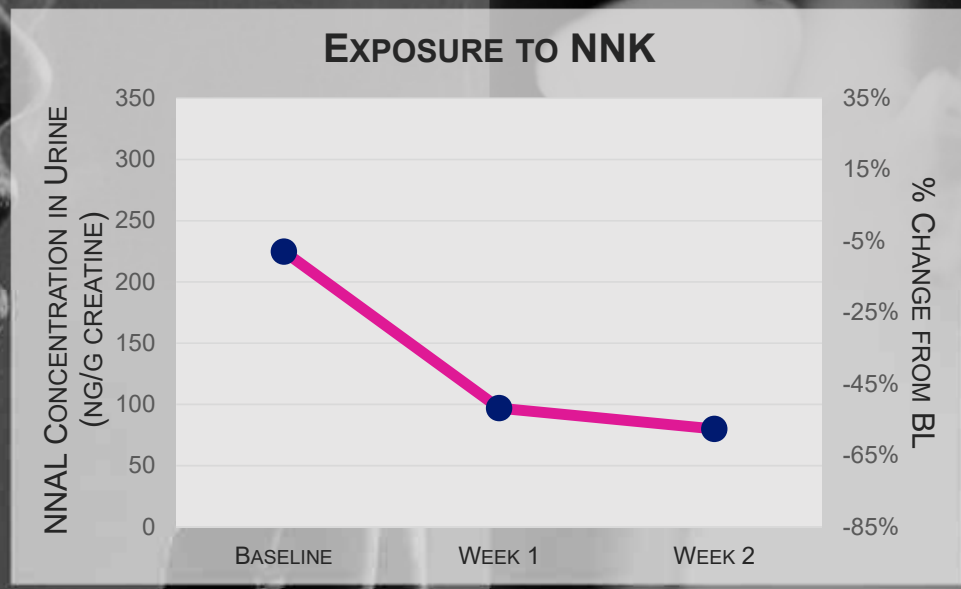
BIOMARKERS OF EXPOSURE



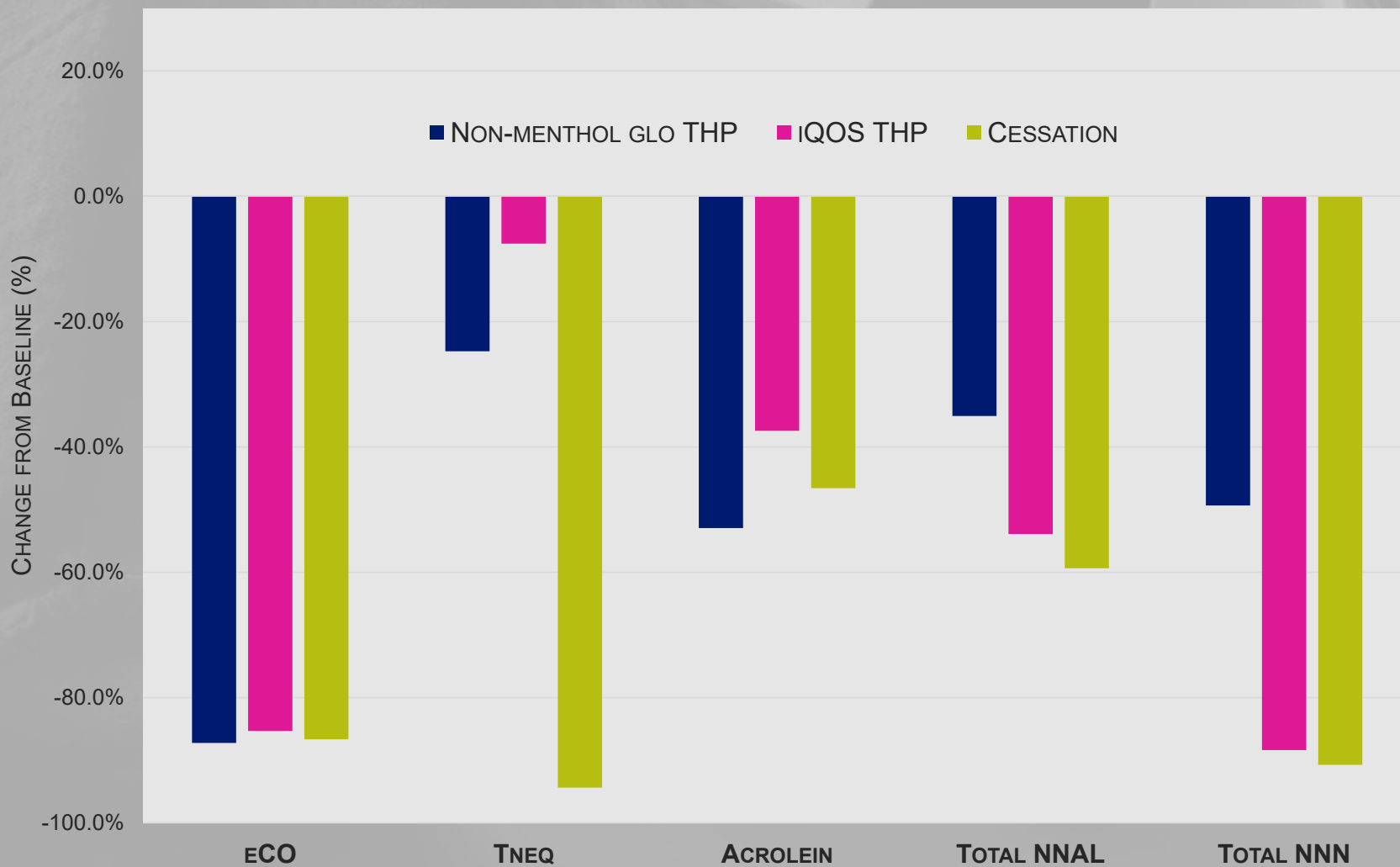


REAL WORLD EVIDENCE: THE PATH STUDY

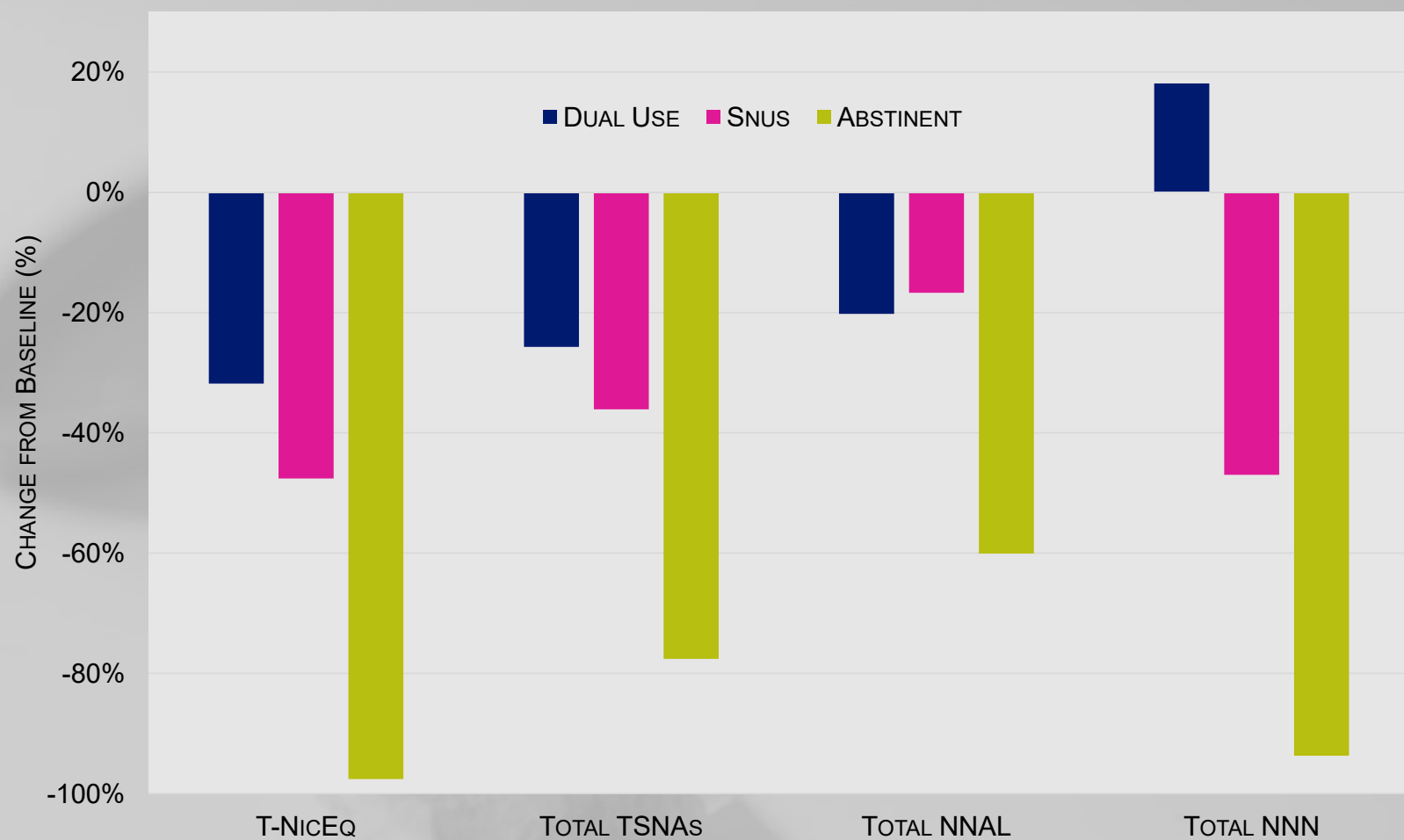
SWITCHING FROM CIGARETTES TO E-CIGARETTES

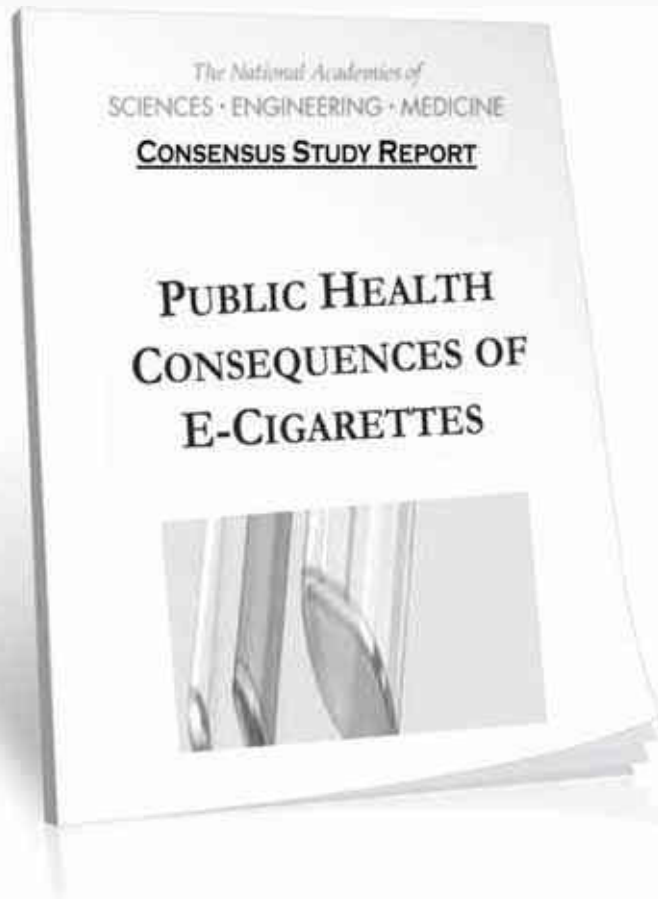


BIOMARKERS OF EXPOSURE CHANGES (HNB)



BIOMARKERS OF EXPOSURE CHANGES (SNUS)





“ THERE IS **CONCLUSIVE EVIDENCE** THAT COMPLETELY SUBSTITUTING E-CIGARETTES FOR COMBUSTIBLE TOBACCO CIGARETTES REDUCES USERS’ EXPOSURE TO NUMEROUS TOXICANTS AND CARCINOGENS PRESENT IN COMBUSTIBLE TOBACCO CIGARETTES.”

BIOMARKERS OF BIOLOGICAL EFFECT

WHAT ARE THE HEALTH EFFECTS?

EXPOSURE & BIOMARKER ASSESSMENT

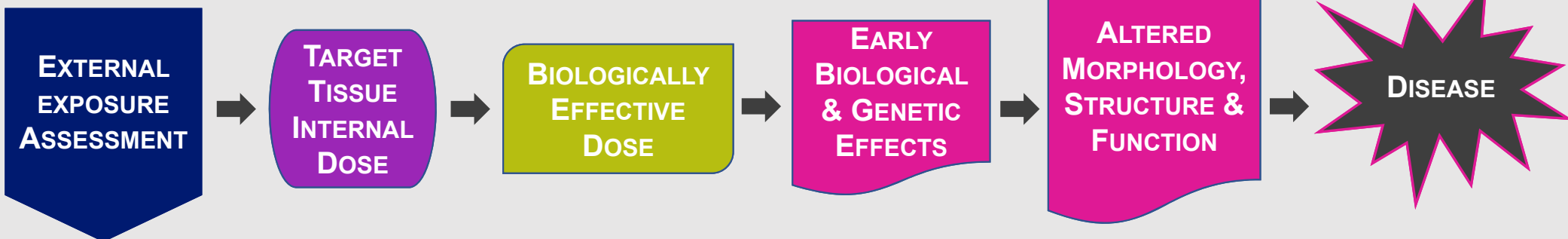
EXTERNAL
EXPOSURE

BIOMARKERS
OF EXPOSURE

BIOLOGICALLY
EFFECTIVE
DOSE

BIOMARKERS OF POTENTIAL
HARM

OUTCOME



**BIOMARKERS
OF POTENTIAL HARM**

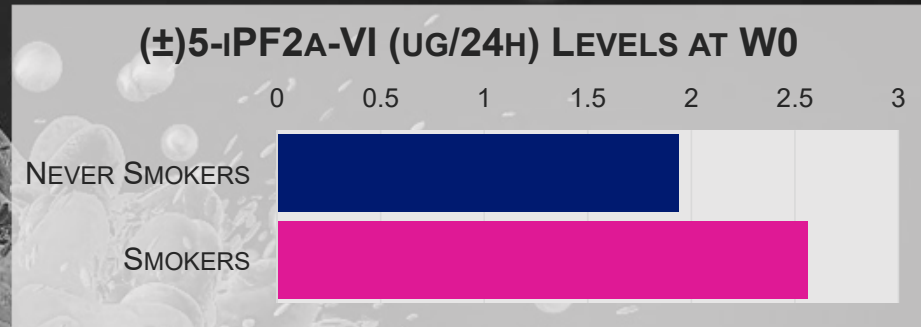
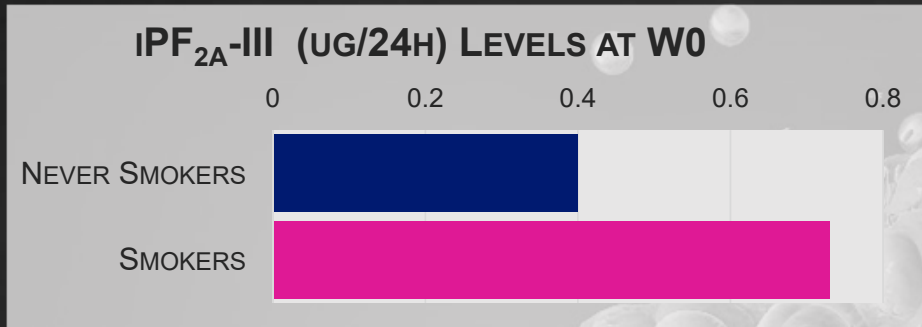
A measurement of an effect due to exposure; these include early biological effect, alternations in morphology, structure, or function and clinical symptoms consistent with harm; also includes “preclinical changes”

BIOMARKERS OF BIOLOGICAL EFFECT

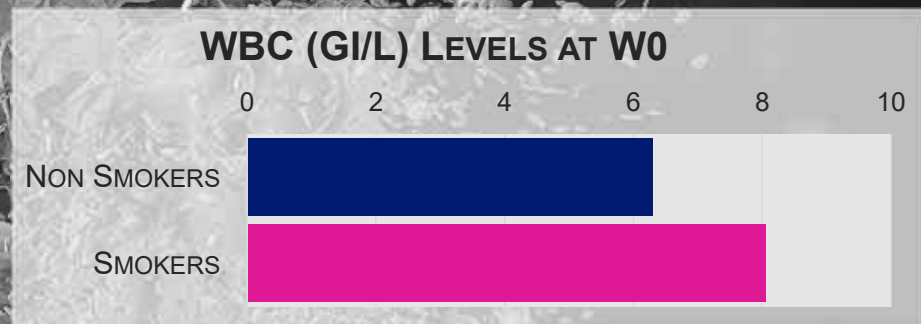
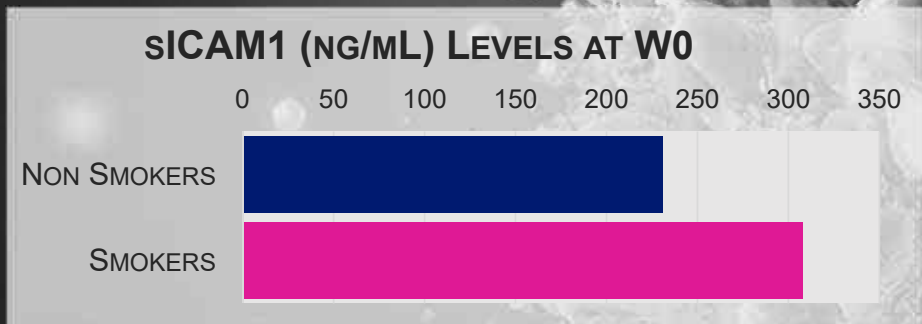
CRITERIA FOR CAUSATION

- **ARE ASSOCIATED WITH A DISEASE OF INTEREST**
- **DISPLAY A DOSE-RESPONSE RELATIONSHIP WITH EXPOSURE**
- **CAN BE DIFFERENTIATED BETWEEN SMOKERS AND NON-SMOKERS**
- **EXHIBIT REVERSIBILITY AND KINETICS WITH SMOKING CESSATION OR SWITCHING**

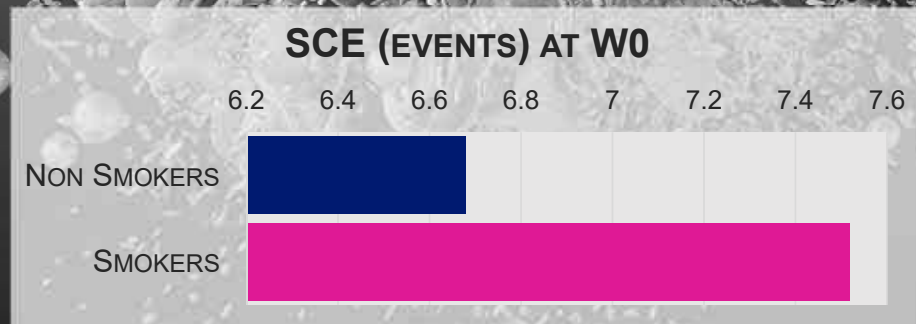
MARKERS OF OXIDATIVE DAMAGE



MARKERS OF INFLAMMATION



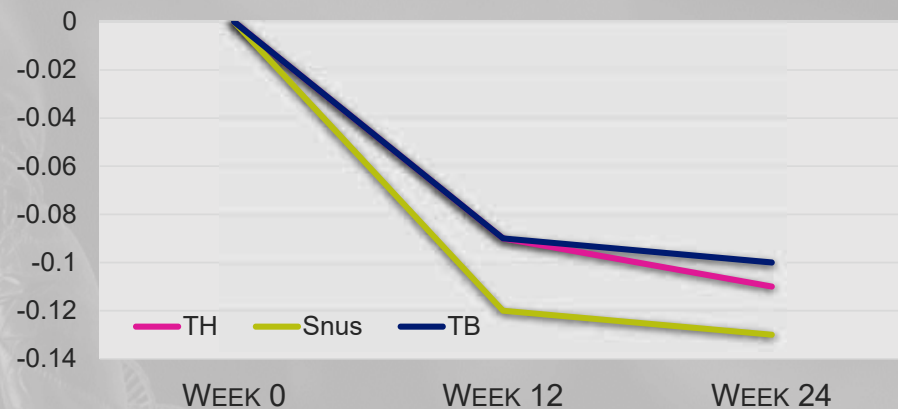
MARKERS OF DNA DAMAGE



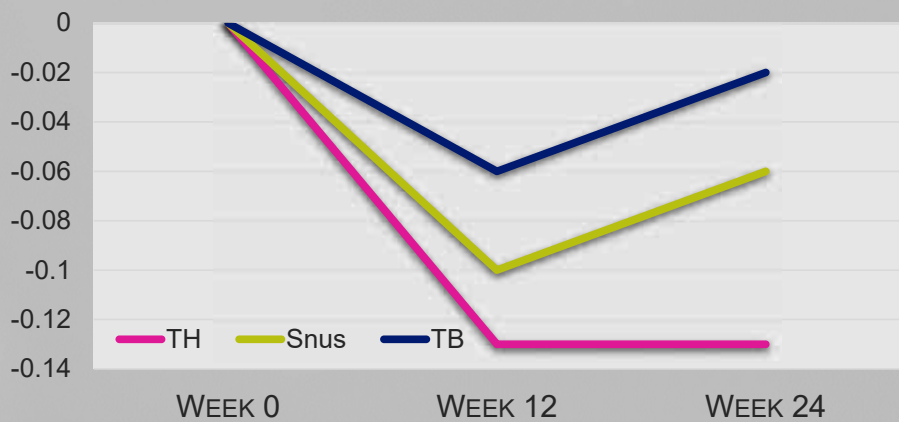
CHANGES IN SMOKERS WHO SWITCHED TO:

- TOBACCO-HEATING CIGARETTES (TH)
- SNUS
- ALTERNATIVE BURN CIGARETTES (TB)

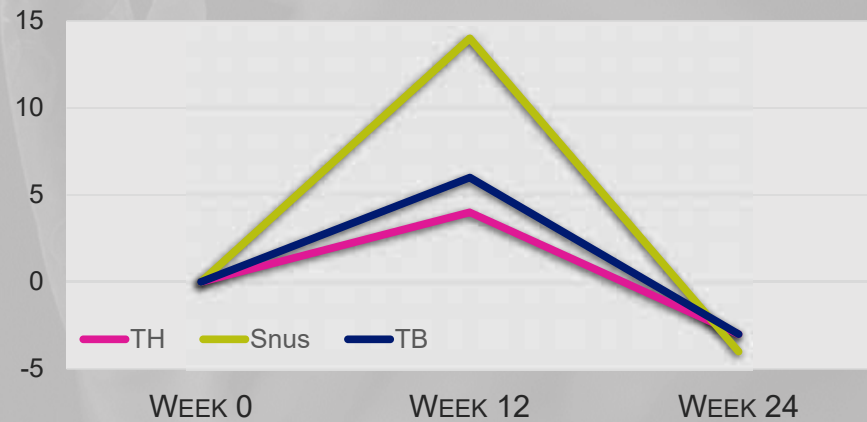
PERCENT CHANGE IN SICAM1 (NG/ML) OVER TIME



PERCENT CHANGE IN WBC (GI/L) OVER TIME



PERCENT CHANGE IN SCE (EVENTS) OVER TIME



LONG-TERM EFFECTS

- RISKS OF CVD, RESPIRATORY DISEASE, AND CANCER ARE KNOWN TO BE REDUCED UPON CESSATION
- MONITORING IMPROVEMENTS REQUIRES STAKEHOLDER (INDUSTRY, ACADEMIC, GOVT) HARMONIZATION CONCERNING
 - STUDY DESIGN
 - APPROPRIATE BIOMARKERS
 - TIME COURSE

SWITCHING

DO THESE THINGS ACTUALLY HELP PEOPLE QUIT
SMOKING?

CONSIDERATIONS FOR RCT DESIGN

CRITERIA

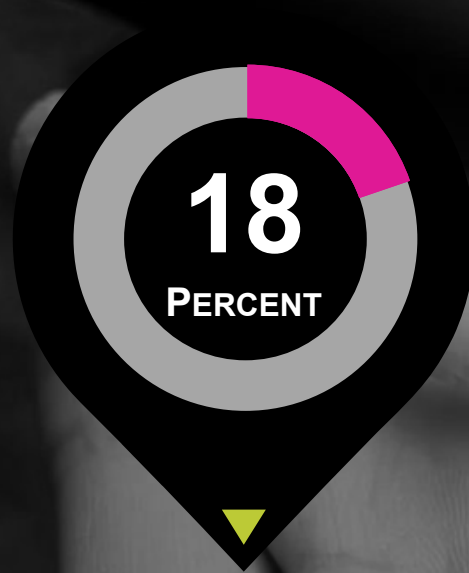
1. EXAMINE THE OUTCOME OF INTEREST
 - a) E.G. CIGARETTE SMOKING CESSATION OR REDUCTION

2. ASSESS *PRODUCT* USE FOR CESSATION OR REDUCTION AS THE EXPOSURE OF INTEREST

3. USE AN APPROPRIATE DESIGN WITH CONTROL / COMPARATOR GROUPS AND MEASURES TO ADDRESS THE POTENTIAL EFFECT OF *PRODUCT* USE ON CESSATION OR REDUCTION WITH MINIMAL CONFOUNDING

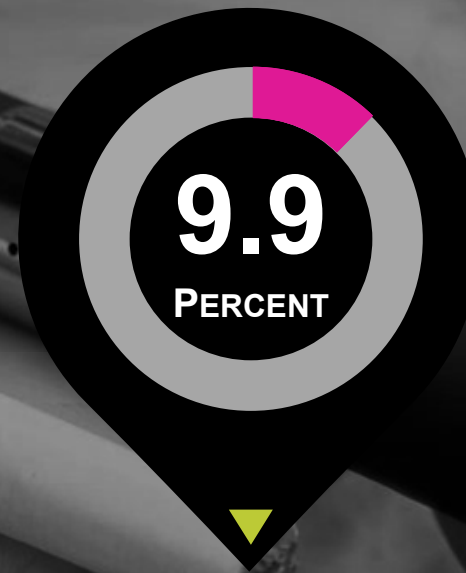
4. PRECISELY MEASURE THE EXPOSURE OF INTEREST
 - a) ESTABLISH TEMPORALITY (EXPOSURE PRECEDES OUTCOME)
 - b) MEASURE DOSE / DURATION OF *PRODUCT* USE
 - c) ASSESS THE *PRODUCT* TYPE

RCT ABSTINENCE RATES



**OF E-CIGARETTE USERS
AT 1-YEAR LATER**

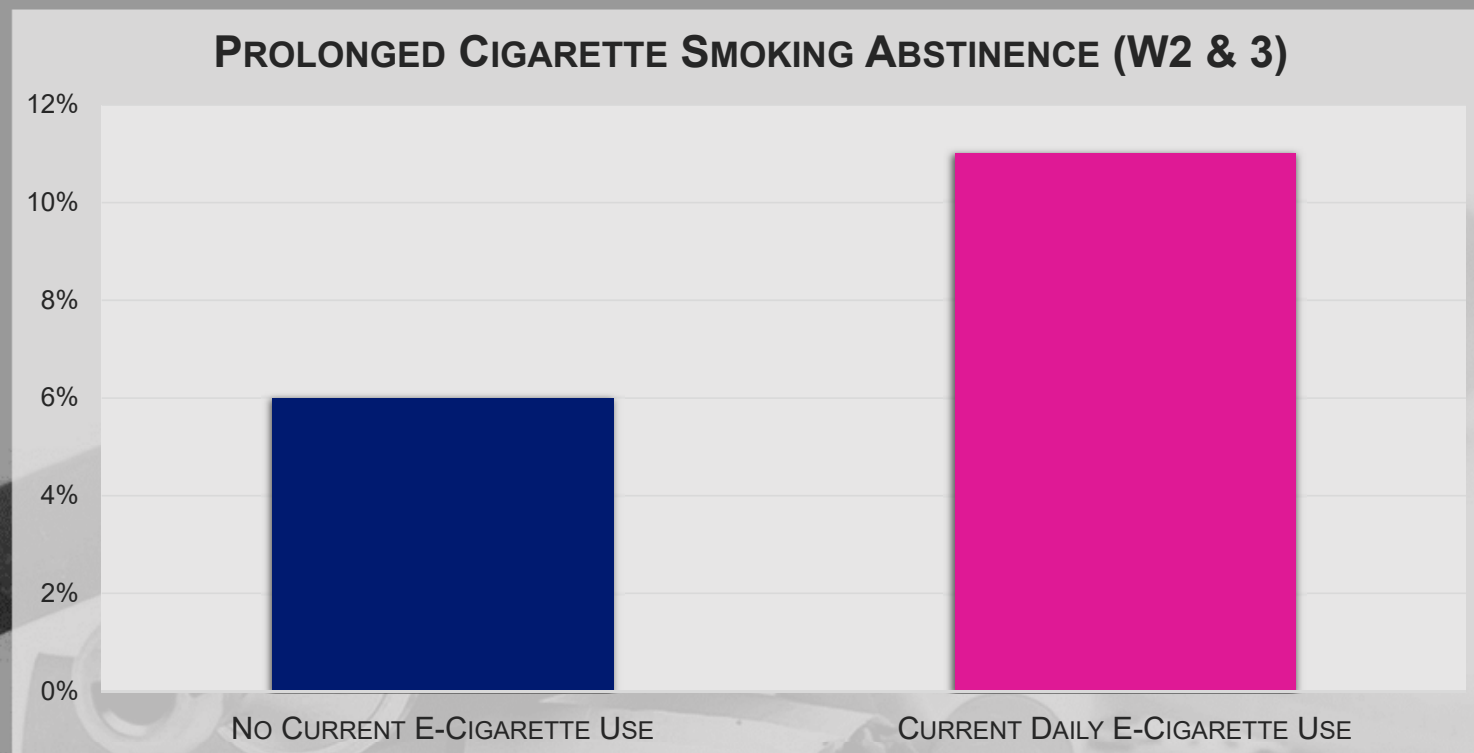
**80% REMAINED E-
CIGARETTE USERS**



**OF NICOTINE-REPLACEMENT
THERAPY AT 1-YEAR LATER**

**9% REMAINED NRT
USERS**

REAL WORLD EVIDENCE

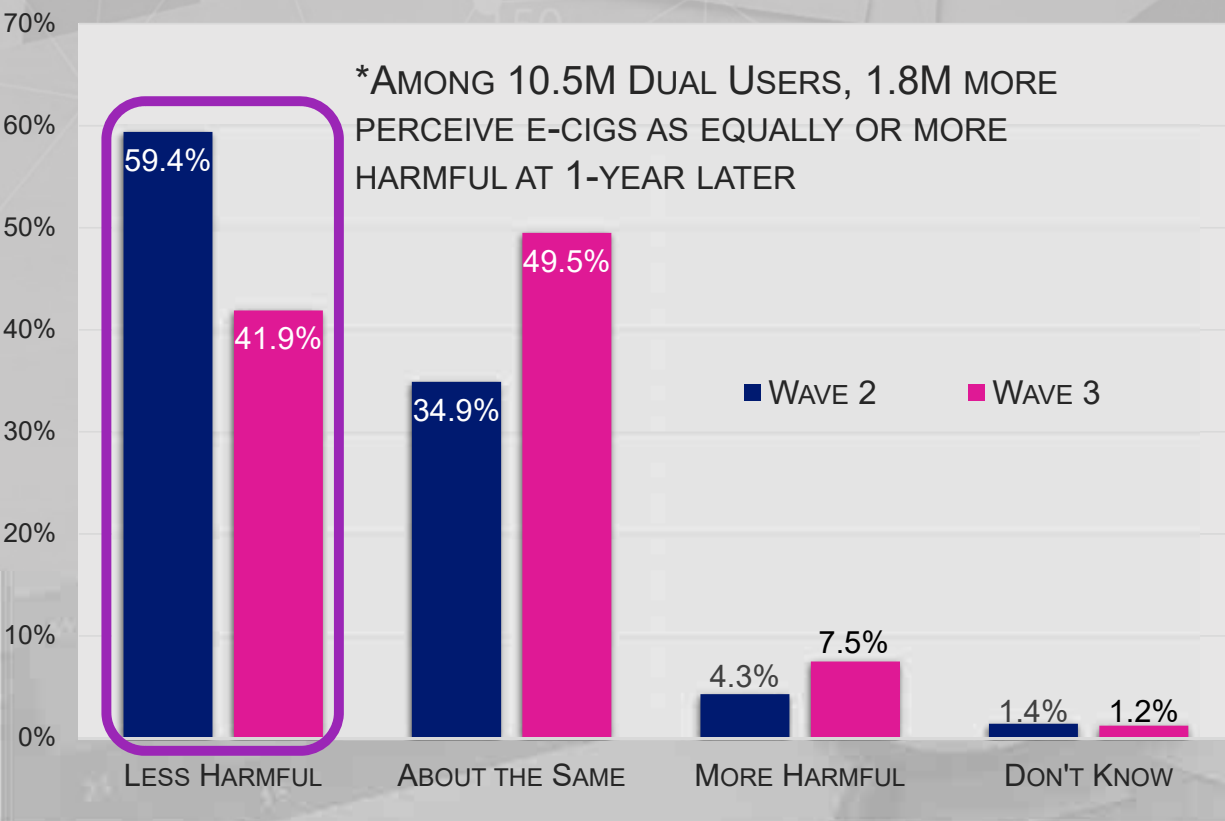


PROLONGED ABSTINENCE = W1 E-CIGARETTE USE STATUS + AGE + SEX + RACE/ETHNICITY + EDUCATION + INCOME + CIGS/DAY + NICOTINE DEPENDENCE

AOR = 1.77 [1.08, 2.89]

PERCEPTIONS OVER TIME

DUAL USER PERCEPTIONS AT PATH W2 AND W3 (CROSS-SECTIONAL)



10.5M
DUAL
USERS

4.3M
DID NOT PERCEIVE E-
CIGS AS LESS HARMFUL

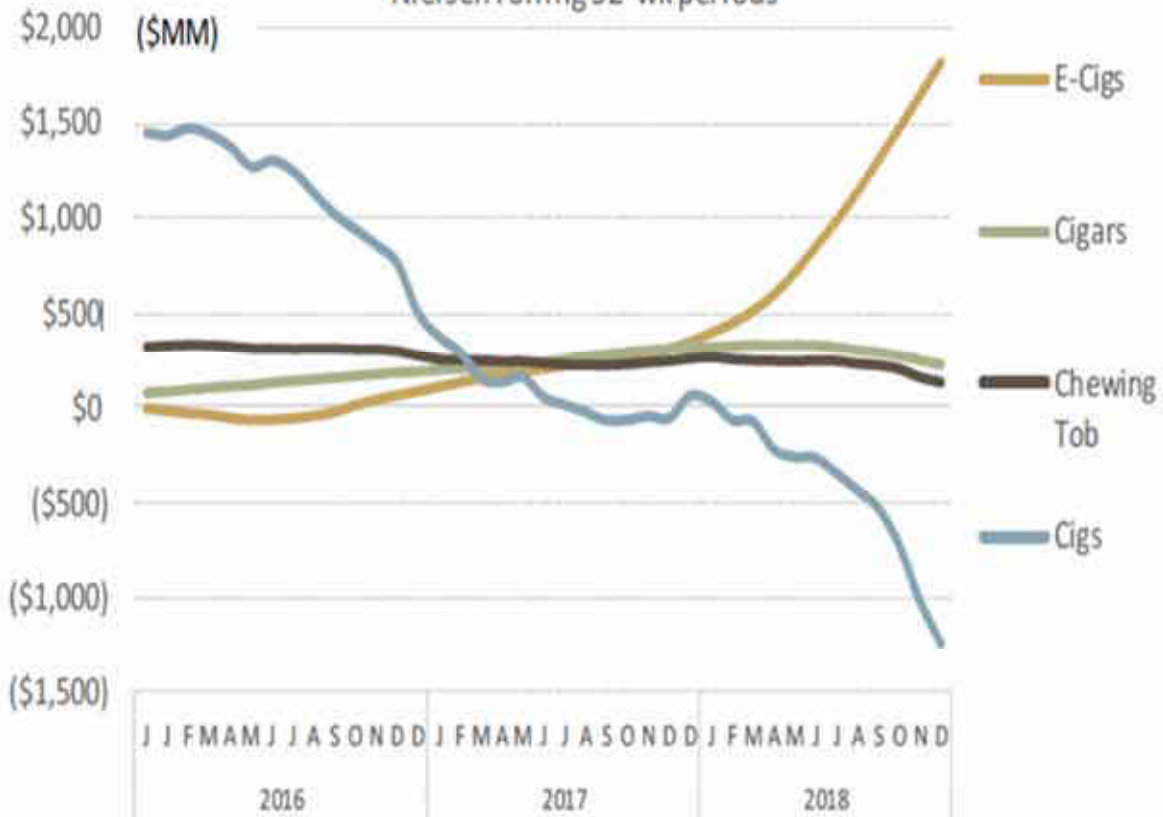
ONLY **115K (2.7%)**
BECAME EXCLUSIVE E-CIG

320K (7.5%)

485K (11.3%)
IF THEY HAD THE SAME RATE AS
THOSE WHO PERCEIVED E-CIGS AS
LESS HARMFUL AT BOTH TIMEPOINTS

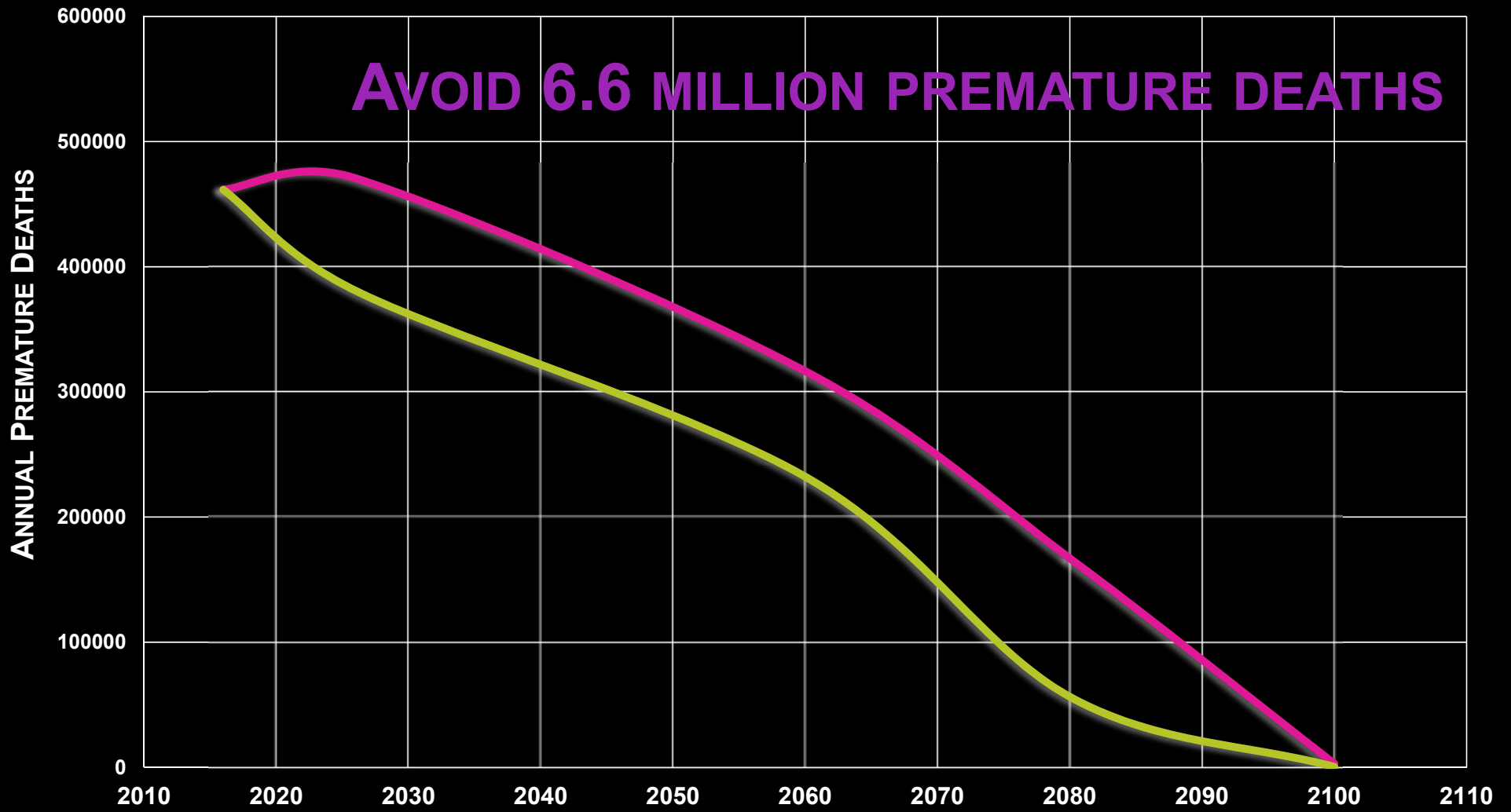
Y/Y \$ Change in Total Tobacco Retail \$ Sales

Nielsen rolling 52-wk periods

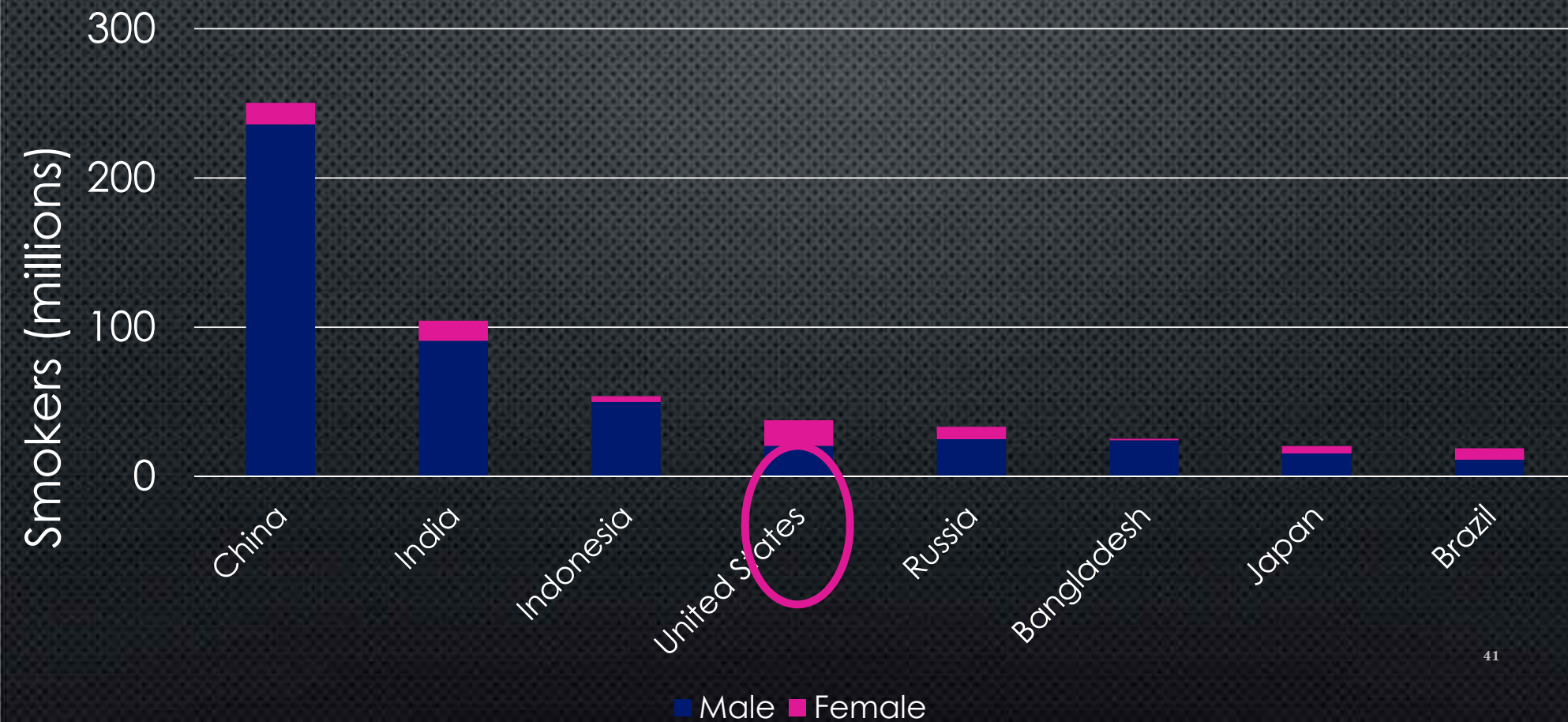


RECOGNIZING THE POTENTIAL

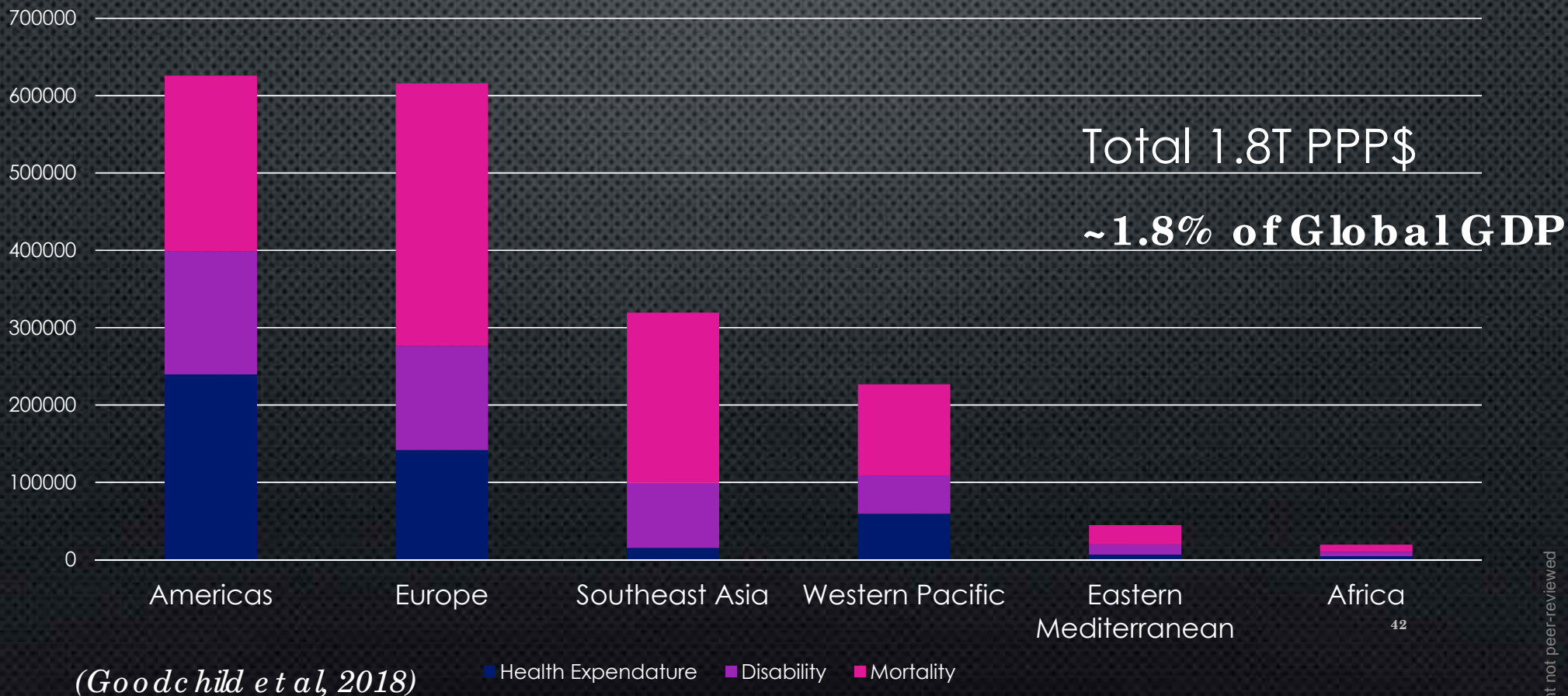




GLOBAL SMOKING



SMOKING ATTRIBUTABLE MORBIDITY AND MORTALITY IMPACT ON GLOBAL ECONOMY



QUESTIONS

FOUNDATION FOR A
SMOKE-FREE WORLD