Schroeder Institute
FOR TOBACCO RESEARCH AND POLICY STUDIES

truth initiative
INSPIRING TOBACCO-FREE LIVES

# Alternative Nicotine Delivery Systems (ANDS):

## FRIEND, FRENEMY, OR ENEMY?

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# Disclosures: David Abrams

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# Big Picture: Reduce Death and Disease Burden from Deadly Combusted Smoke

***"Death is Overwhelmingly Caused By Cigarettes and Other Combustibles…***

***Promotion of E-cigarettes and Other Innovative Products Is…Likely To Be Beneficial…***

***Where The Appeal, Accessibility and Use of Cigarettes Are Rapidly Reduced."***

***50th Anniversary Surgeon General's Report, 2014, Executive Summary, Pages 14-17***

# Brief state of the science: what we know

**OPERATIONALIZE POPULATION IMPACT: BENEFITS AND HARMS**

- **The Public Health Standard** – frameworks matter – blind people and elephants: maximize and minimize.
- **Harms:** relative - to deadly smoke & absolute - to nothing
- **State of The Science: Uptake** by non-tobacco users, especially youth and young adults and former smokers
- **State of The Science: Cessation** by current tobacco users, primarily smokers of deadly cigarettes.

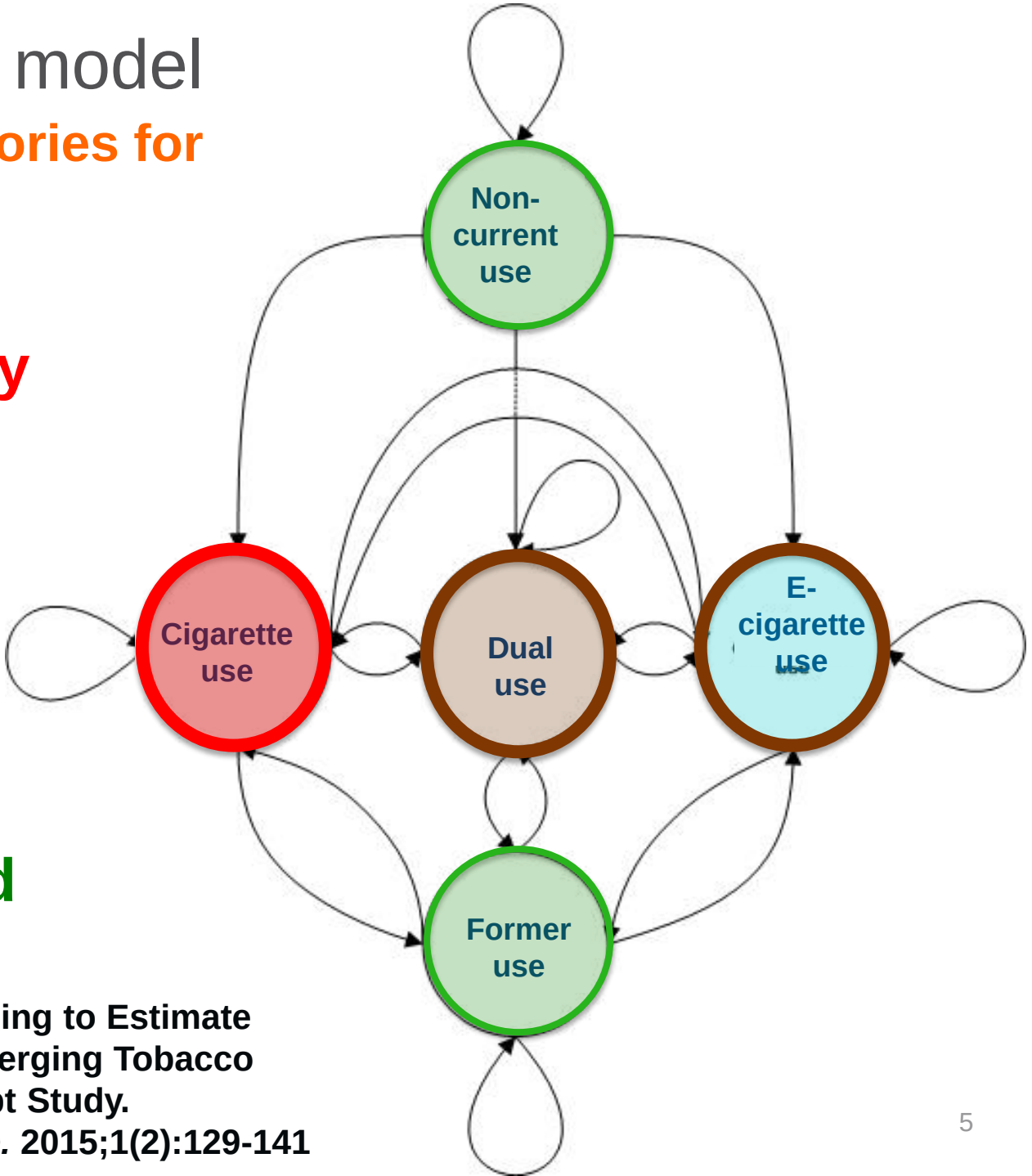
# Frame: markov model

**All states & Trajectories for population impact:**

**Enemy**

**Frenemy?**

**Friend**




**Cobb C. et al. Markov Modeling to Estimate the Population Impact of Emerging Tobacco Products: A Proof-of-Concept Study. *Tobacco Regulatory Science.* 2015;1(2):129-141**

# 1. informing impact: harms

RELATIVE & ABSOLUTE - PRODUCT QUALITY VARIES

**Relative:** vape to combusted smoke and passive exposure to smoke.

**Absolute:** not harmless: No / variable nicotine; humectants (aerosol vapor); additives, flavors… some more harmful than others

**Absolute**: compared to no use: (fetus, accidental poisoning, passive exposure, indoor air, youth and young adult never users).

**Regulation**: needed to ensure quality and make as low in harm as possible

**Common Sense Regulation**: Goldilocks Rule, not too much and not too little

**Core Principle:**

**Policy and Regulation proportional to the harm of the product class**…

# Relative harms of different product classes.

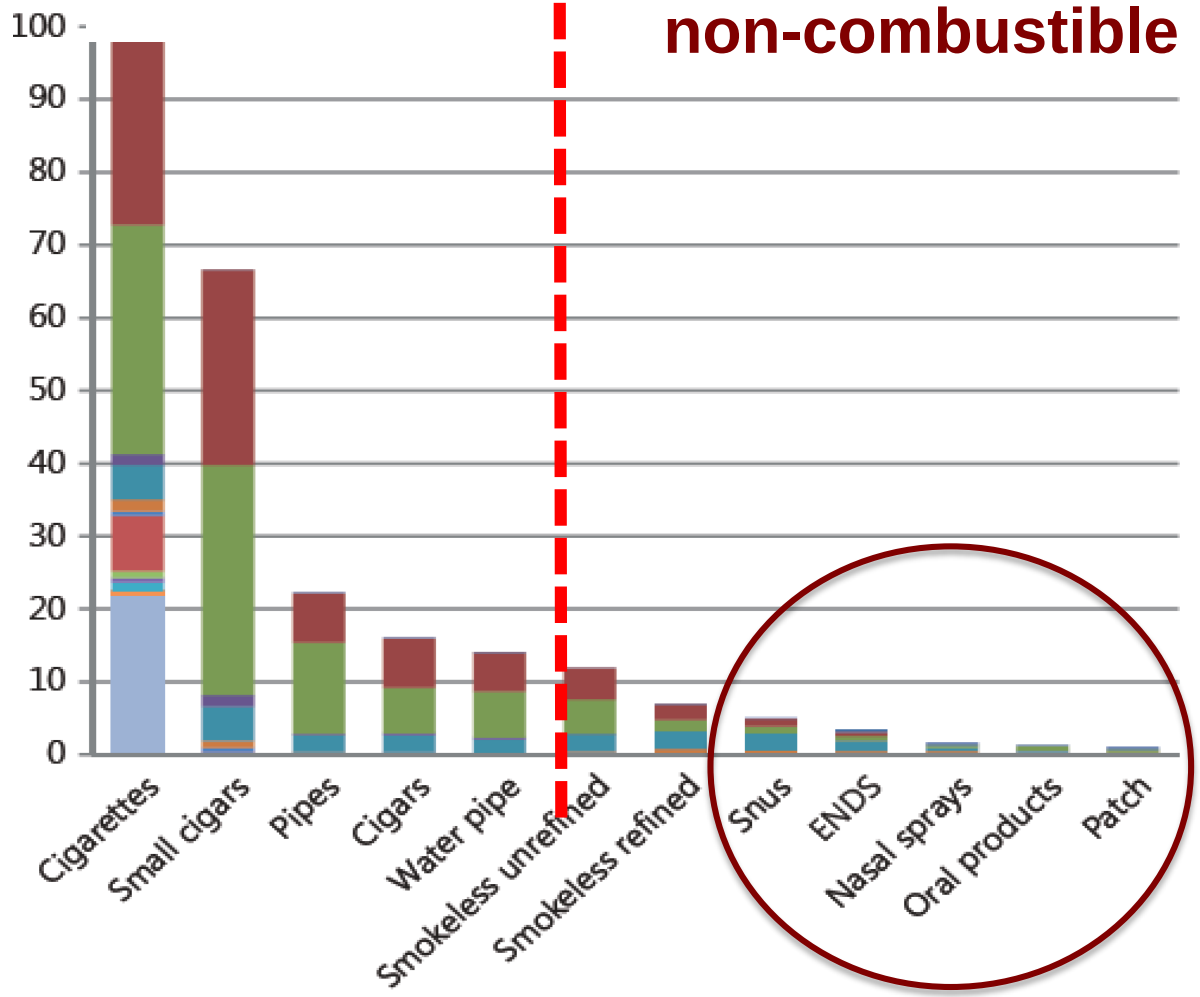
**EXTREME Toxicity**

**Cigs - Combustibles**

**MUCH Less Harm**

**non-combustible**

**No Harm No use at all**

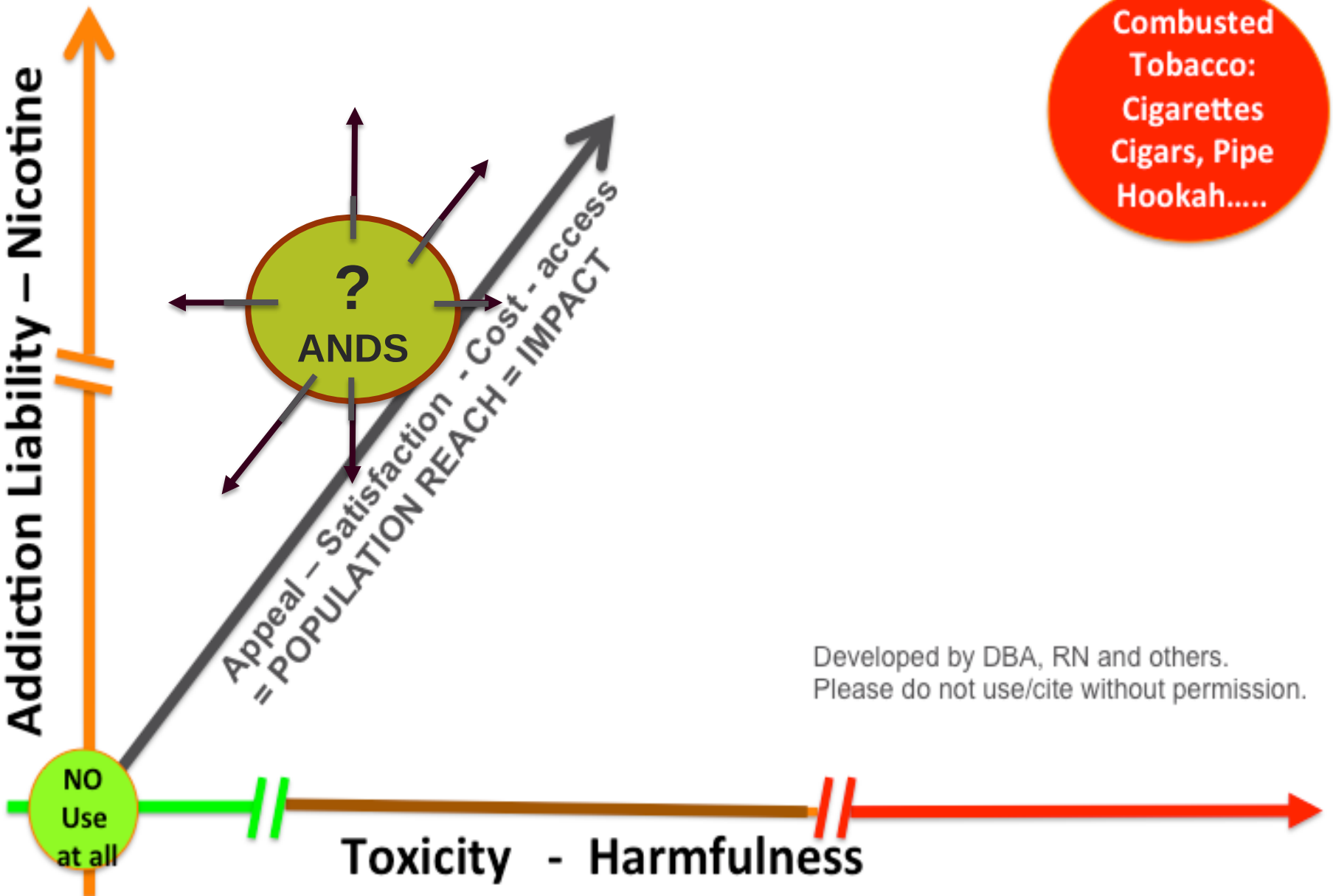



Nutt DJ et al Estimating the Harms of Nicotine-Containing Products Using the MCDA Approach – European Addiction Research March 2014

**Public Health England (PHE)**

McNeill A, Brose LS, et al E-cigarettes: an evidence update. London, England: Public Health England;2015.

# Appeal, Addiction, Harm: A 3-D Framework



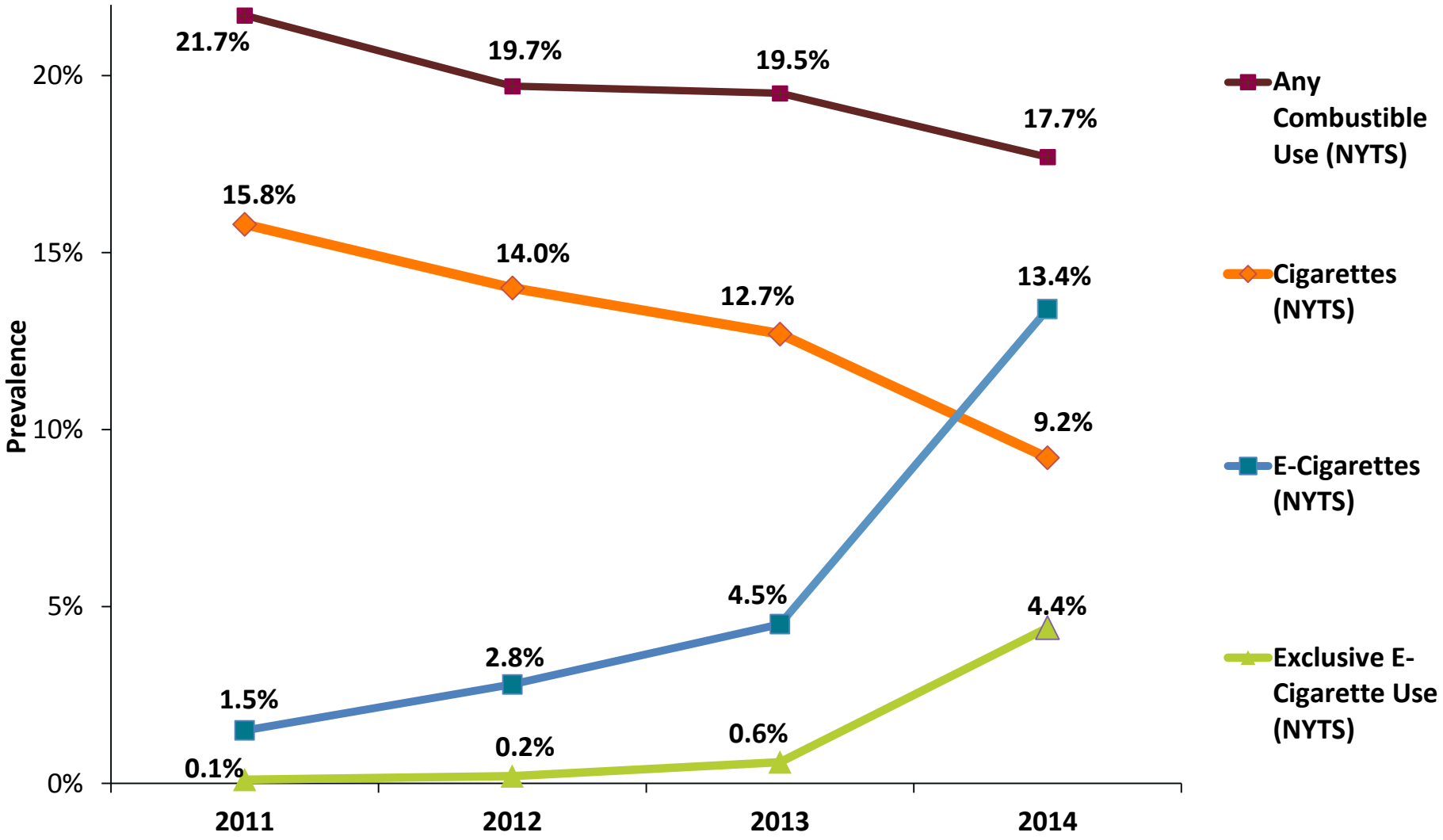

Developed by DBA, RN and others.
Please do not use/cite without permission.

# 2. informing impact : patterns of uptake

**Enemy, Frenemy, Friend?**

- **Uptake of  E-cigarette** use by non-users of tobacco products, especially minors: vigilance and no use enforced
- **Progression:** either into or a deflection out of deadly lifetime combustible / cigarette use
- **Appeal and Addiction:** when decoupled from deadly smoke from combustion?

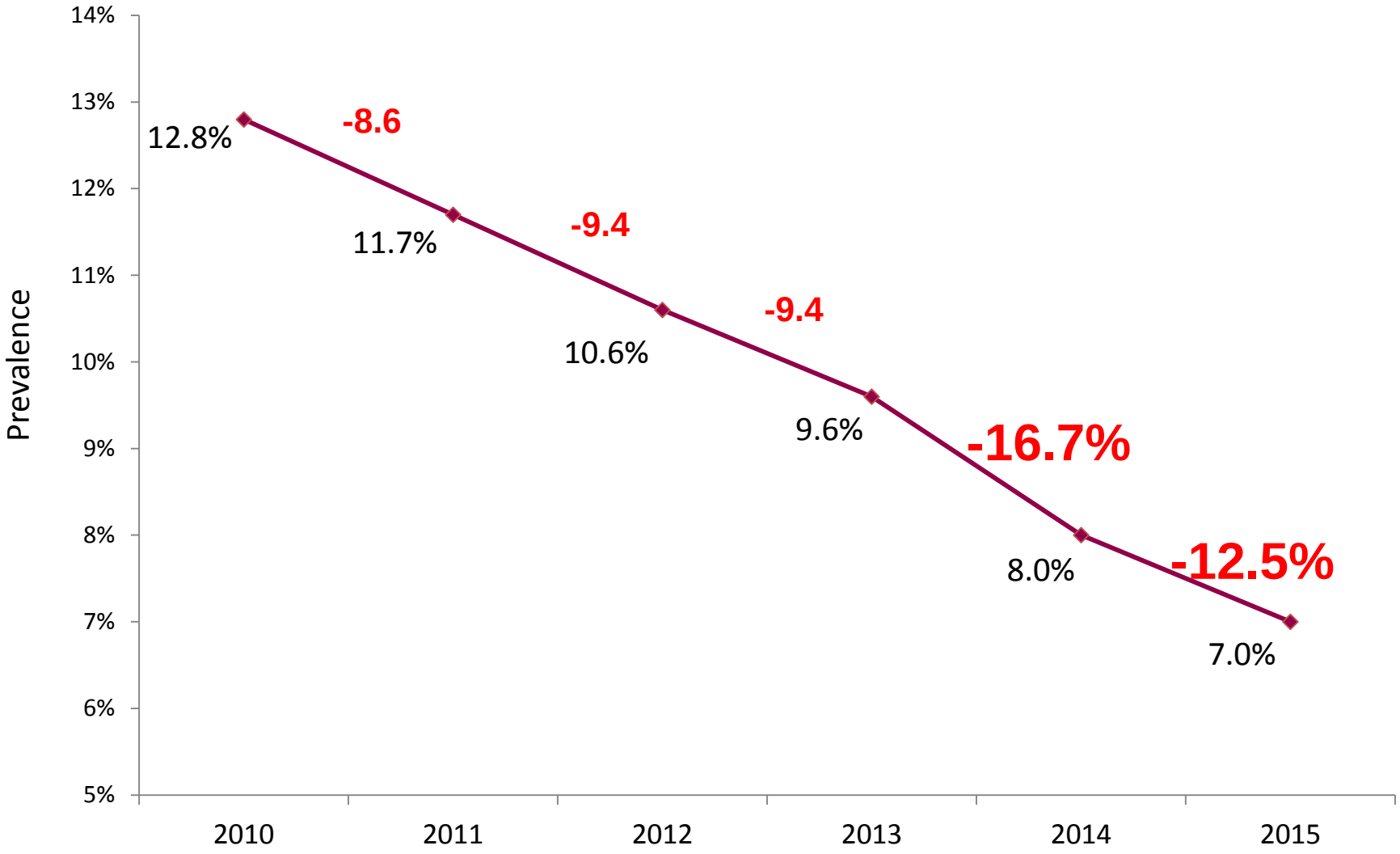
# Past 30-Day Use among High School Students






Source: National Youth Tobacco Survey, 2011 - 2014.

# Past 30-Day Cigarette Use 8, 10, & 12 Graders




**Source: Monitoring the Future, 2015 - Table 1**

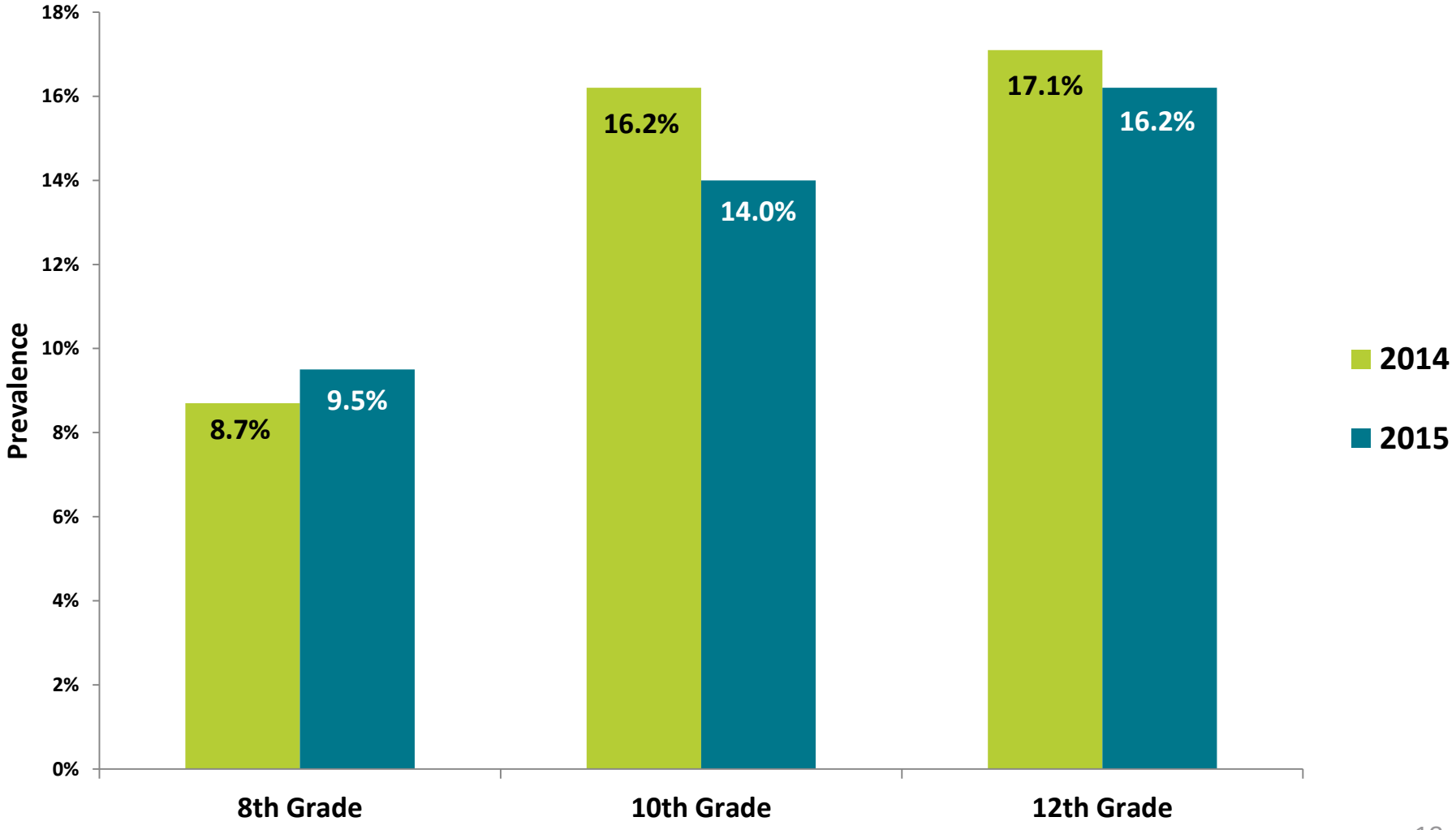
# progression: frequency of use

FREQUENCY OF PAST 30-DAY USE OF E-CIGARETTES AND CIGARETTES (NYTS, 2014)

| Days used/ month | % high school users | | % high school population | |
|---|---|---|---|---|
| | Of ENDS | Of Cigarettes | Using ENDS | Using Cigarettes |
| 1-2 days | **45.4** | **37.0** | 6.1 | 3.4 |
| 3-5 days | 16.2 | 12.3 | 2.2 | 1.1 |
| 6-9 days | 12.0 | 9.7 | 1.6 | 0.9 |
| 10-19 days | 10.9 | 9.4 | 1.4 | 0.9 |
| 20-29 days | 5.8 | 9.0 | 0.8 | 0.8 |
| All 30 days | **9.7** | **22.6** | 1.3 | 2.1 |
| **TOTAL** | **100.0** | **100.0** | **13.4** | **9.2** |

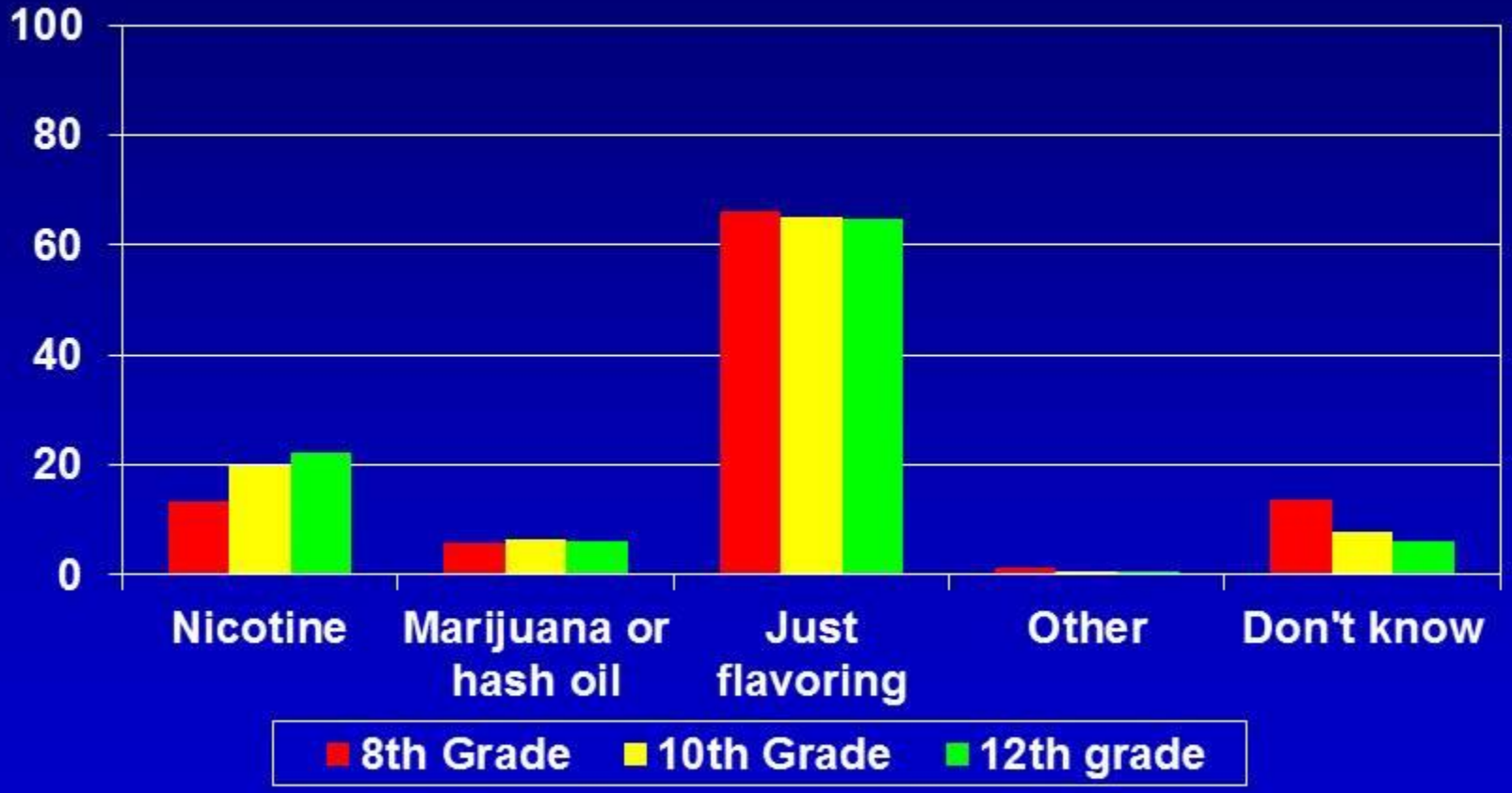
# past 30-Day e-Cig use leveled off / dropped slightly

BY GRADE AND YEAR




Source: Monitoring the Future, 2015 (Table 3)

# Substance Vaporized the Last Time e-Cigarette Used




SOURCE: University of Michigan, 2015 Monitoring the Future Study

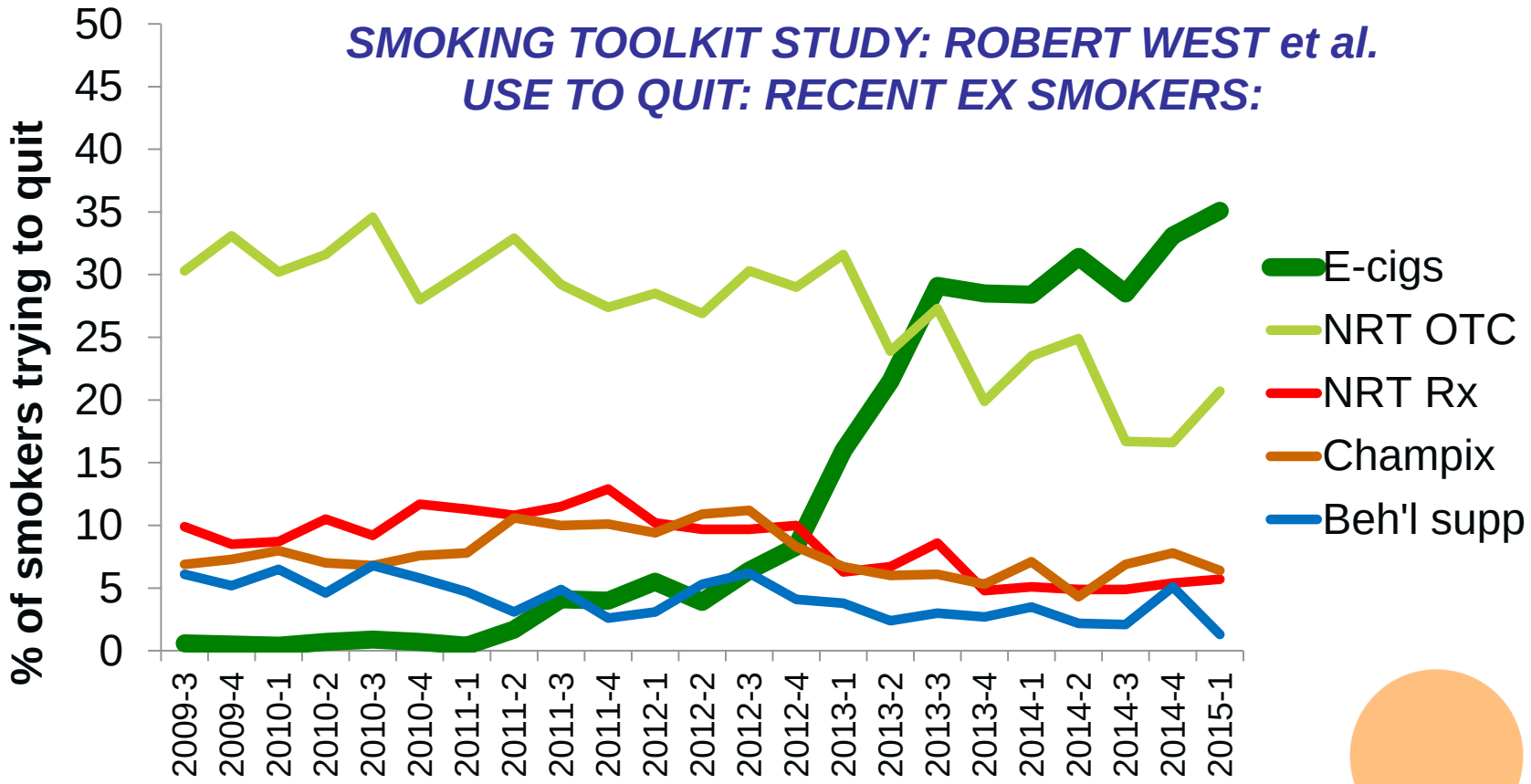
# 3.Informing impact: use in current and former smokers

**Enemy, Frenemy, Friend?**

- **Impact:** on use of cigarettes:
  - at scale:  reach x efficacy, cost, appeal
  - do e-cigs speed or slow population cessation?
- **Dual use:** concern if get stuck on path to exclusive use (a sticky versus a transitional state)?
- **Relapse:** prevention or promotion in former smokers?

# Appeal as a Cessation Aid : IMPACT at Scale: (Reach x Efficacy / Cost Efficiency)

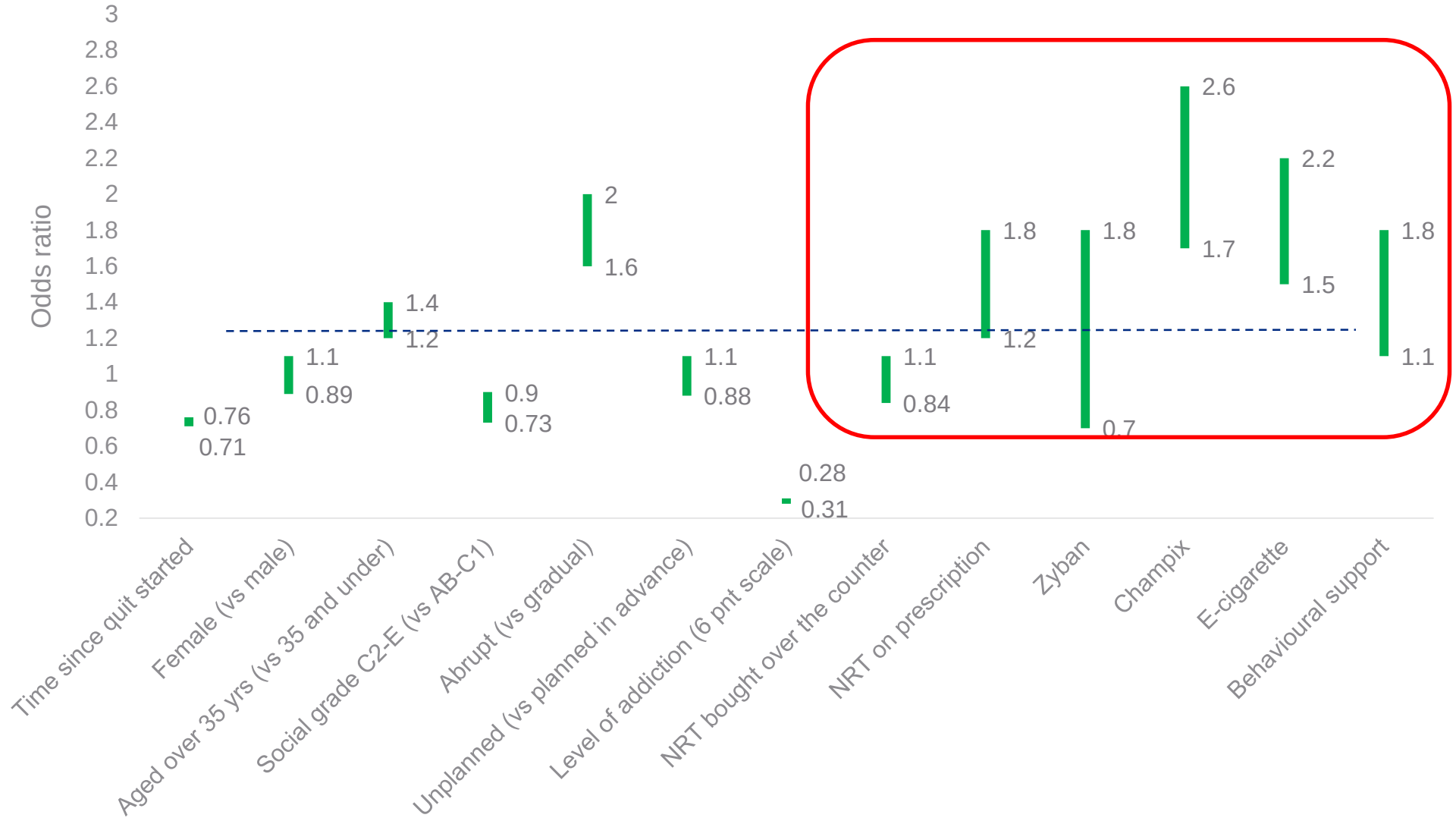
SEE ALSO: COBB NK, ABRAMS DB. (2014) . THE FDA, E-CIGARETTES, AND THE DEMISE OF COMBUSTED TOBACCO. N ENGL J MED 371;16:1469-71




N=10078 adults who smoke and tried to stop or who stopped in the past year

Source: “Trends in e-cigarette use in England Mar 2015”

# Factors Associated with Odds of Success in Most Recent Quit Attempt




Base: 14,813 smokers who tried to quit in past 12 months

# randomized trials: cochrane and PHS clinical guide – comparable to nrt's. (some other ? invalid ? reports)

Findings from meta-analysis of smoking cessation studies with six-month outcomes in "Treating Tobacco Use and Dependence"

| Intervention | Number of arms | Estimated abstinence rate (95% C.I.) |
|---|---|---|
| **Among smokers not willing to quit (but willing to change their smoking patterns or reduce their smoking)** | | |
| Placebo | 5 | 3.6 |
| Nicotine replacement (gum, inhaler, or patch) | 5 | 8.4 (5.9–12.0) |
| Nicotine E-cigarette (Caponnetto 2013) | 2 | 11.0 |
| **Among smokers interested in quitting** | | |
| Placebo | 80 | 13.8 |
| Nicotine Patch (6–14 weeks) | 32 | 23.4 (21.3–25.8) |
| Long-Term Nicotine Patch (> 14 weeks) | 10 | 23.7 (21.0–26.6) |
| Nicotine Inhaler | 6 | 24.8 (19.1–31.6) |
| Nicotine E-cigarette (Bullen 2013) | 1 | 21.1 |
| Patches (Bullen 2013) | 1 | 15.6 |

# observational studies: with better measurement of exposure and use specific to quit intentions..

| Study | Follow-up period | Cigarette smoking abstinence (%) | Other outcomes | |
|---|---|---|---|---|
| **Biener Hargrave (2014)** | **2 years** | | | |
| Intensive e-cigarette users at baseline | | 20.4 | | |
| Intermittent e-cigarette users at baseline | | 8.5 | | |
| E-cigarette non-users/triers at baseline | | 12.4 | | |
| **Brose (2015)** | **1 year** | | ***>50% reduction in CPD from baseline to follow-up*** | ***Quit attempts*** |
| Daily e-cigarette use at baseline | | 8.1 | 13.9 | 64.9% |
| Non-daily e-cigarette use at baseline | | 9.5 | 5.5 | 52.5% |
| Non-use of e-cigarettes at baseline | | 12.9 | 5.7 | 43.7% |
| **Brown (2014)** | **Cross-sectional** | | | |
| E-cigarettes used in last serious quit attempt | | 20.0 | | |
| NRT used in last serious quit attempt | | 10.1 | | |
| No aid in last serious quit attempt | | 15.4 | | |

# device type may matter

**Adapted Table 3.** E-cigarette use, product type, and quit smoking at follow-up

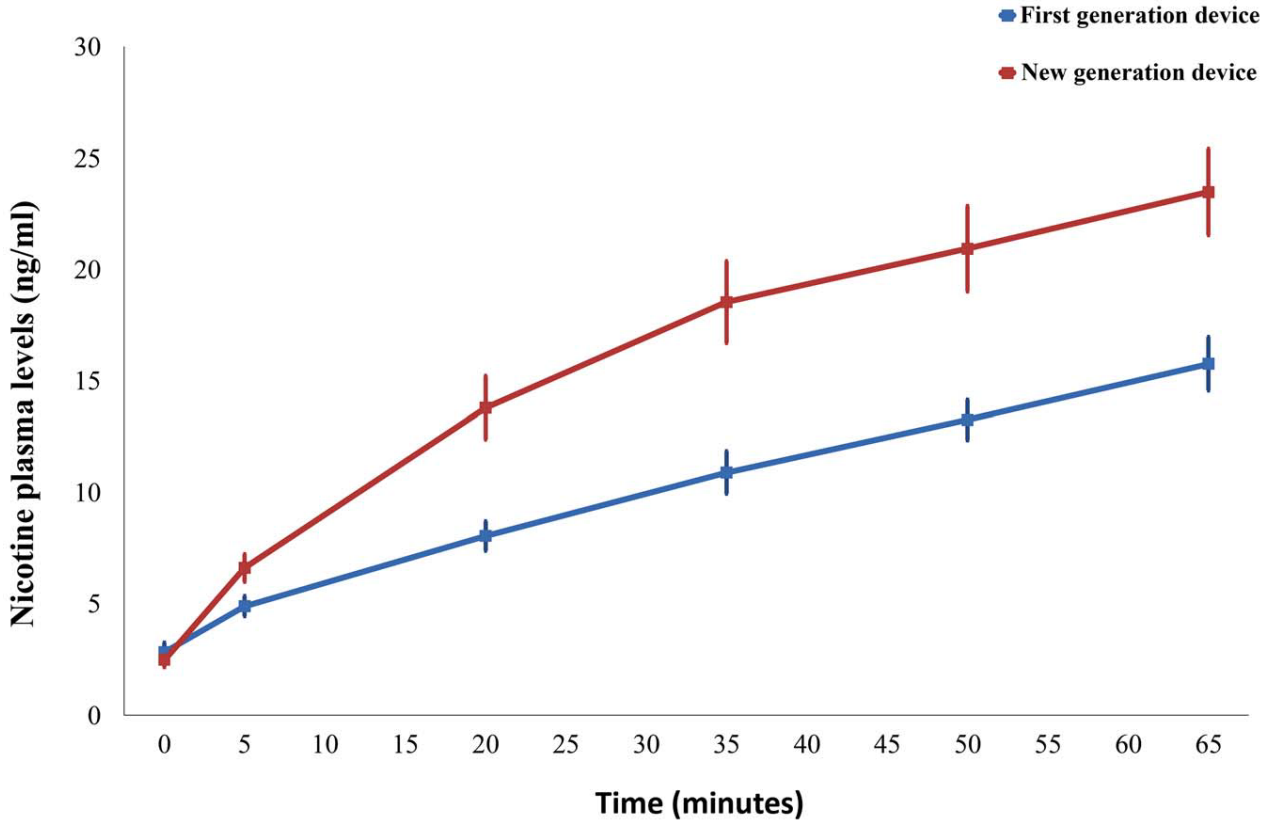
| | % quit smoking | AOR (95% CI) |
|---|---|---|
| E-cigarette type and frequency at follow up | | |
| Non-daily cigalike | 5.2% | **0.35 (0.20, 0.60)** |
| Non-daily tank | 8.6% | 0.70 (0.29, 1.68) |
| Daily cigalike | 10.6% | 0.74 (0.39, 1.42) |
| No e-cigarette use | 13.5% | 1.0 |
| Daily tank | 27.5% | **2.69 (1.48, 4.89)** |

Source: Hitchman, Sara C., et al. (2015) Associations between e-cigarette type, frequency of use, and quitting smoking: findings from a longitudinal online panel survey in Great Britain." *Nicotine & Tobacco Research*. [epub ahead of print]

# device type: improved satisfaction?

- Bigger battery = better nicotine delivery

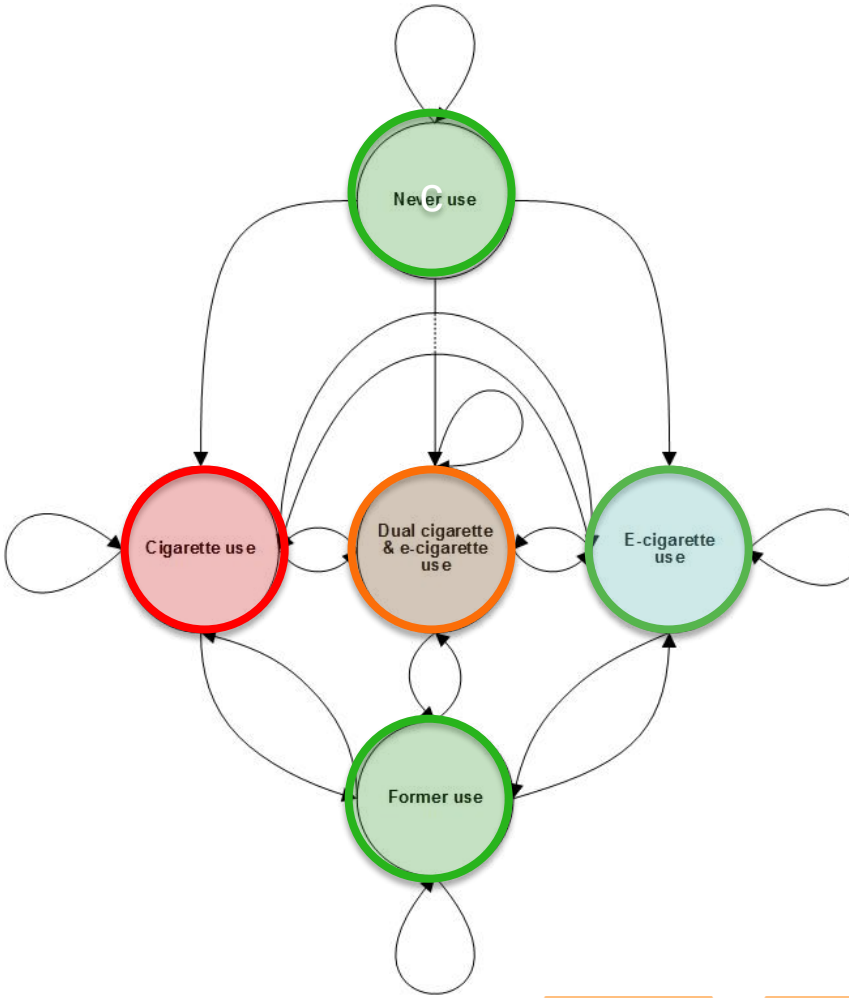
- exclusive users: use open (tank/Mod) systems; flavors help them to extinguish tobacco/menthol cue reminders of cigs.




Farsalinos et al (2014). Nicotine absorption from electronic cigarette use: comparison between first and new-generation devices. Sci. Rep; 4: 4133.

# Summary: friend of cessation / switching?

- More rigorous studies and randomized trials needed.
- Uninformative studies must be excluded entirely
- Promising when intended for cessation and used regularly. Likely at least as good as and more impact/reach than NRT
- Dual use not desirable, except if like NRT, used for a limited time on a trajectory to cessation or exclusive use (reduce to quit)?



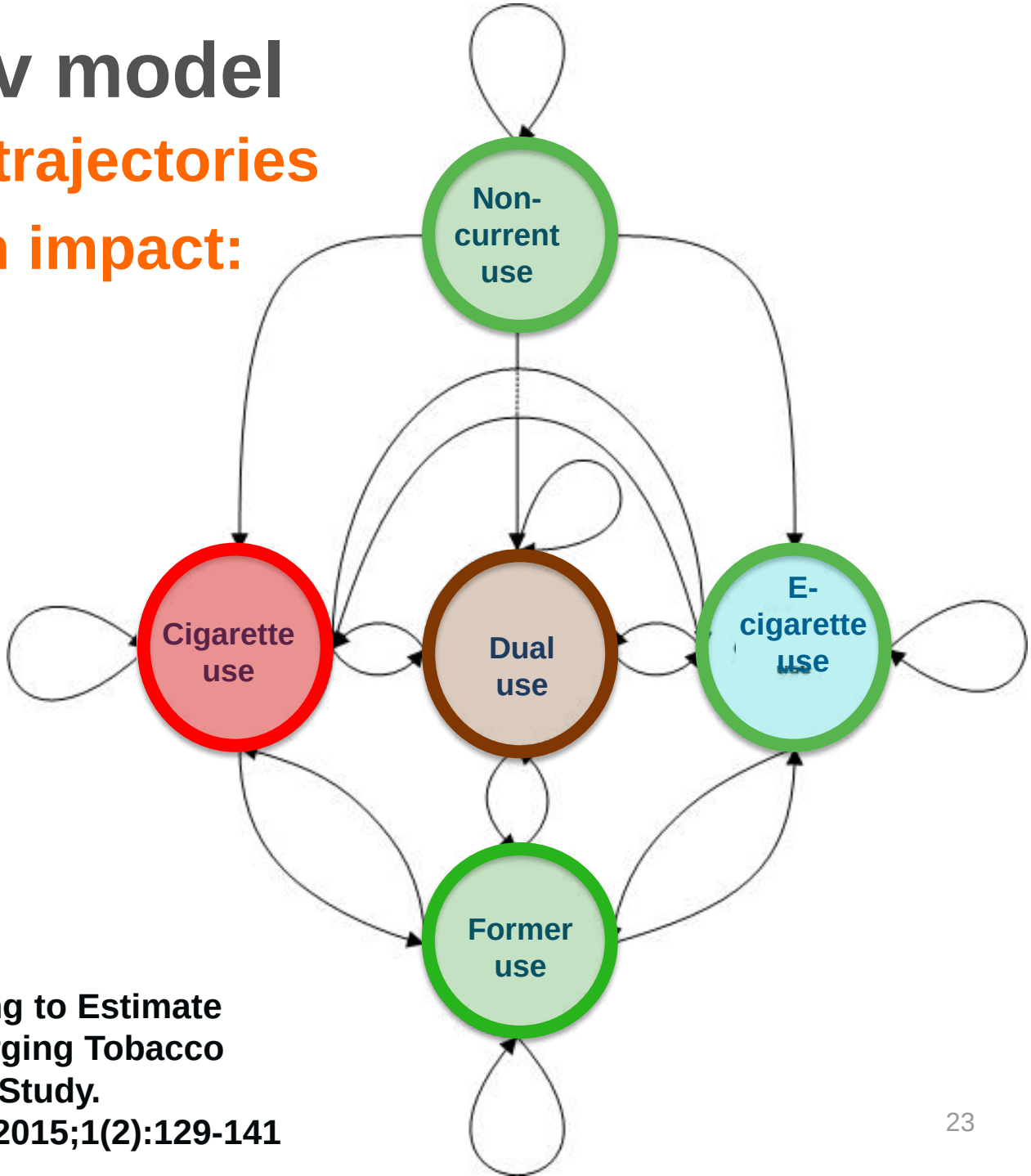
# formal markov model

## need all states & trajectories for net population impact:

**Enemy?**

**Frenemy**

**Friend**





**Cobb C. et al. Markov Modeling to Estimate the Population Impact of Emerging Tobacco Products: A Proof-of-Concept Study. *Tobacco Regulatory Science.* 2015;1(2):129-141**

# summary: can nicotine in less harmful delivery modes be a friend or frenemy to speed the obsolescence of combustible tobacco?

1. **Youth**: Despite dramatic declines in cigarette use, total combustible tobacco use (cigars and hookah) is of great concern – most toxic, appealing, addictive and overwhelming cause of progression and death

2. **Increases in youth trial use has leveled off**: Current data cannot confirm whether a pathway in or out of combustible use. Trajectory to regular use >20 days is miniscule. No sign of progression to cigarettes

3. **Larger than usual drops** in youth and adult cigarette prevalence: e-cigs?

4. **Use for cessation/switching promising**: RCTs and real world trials needed with the newer, better products and with treatment support

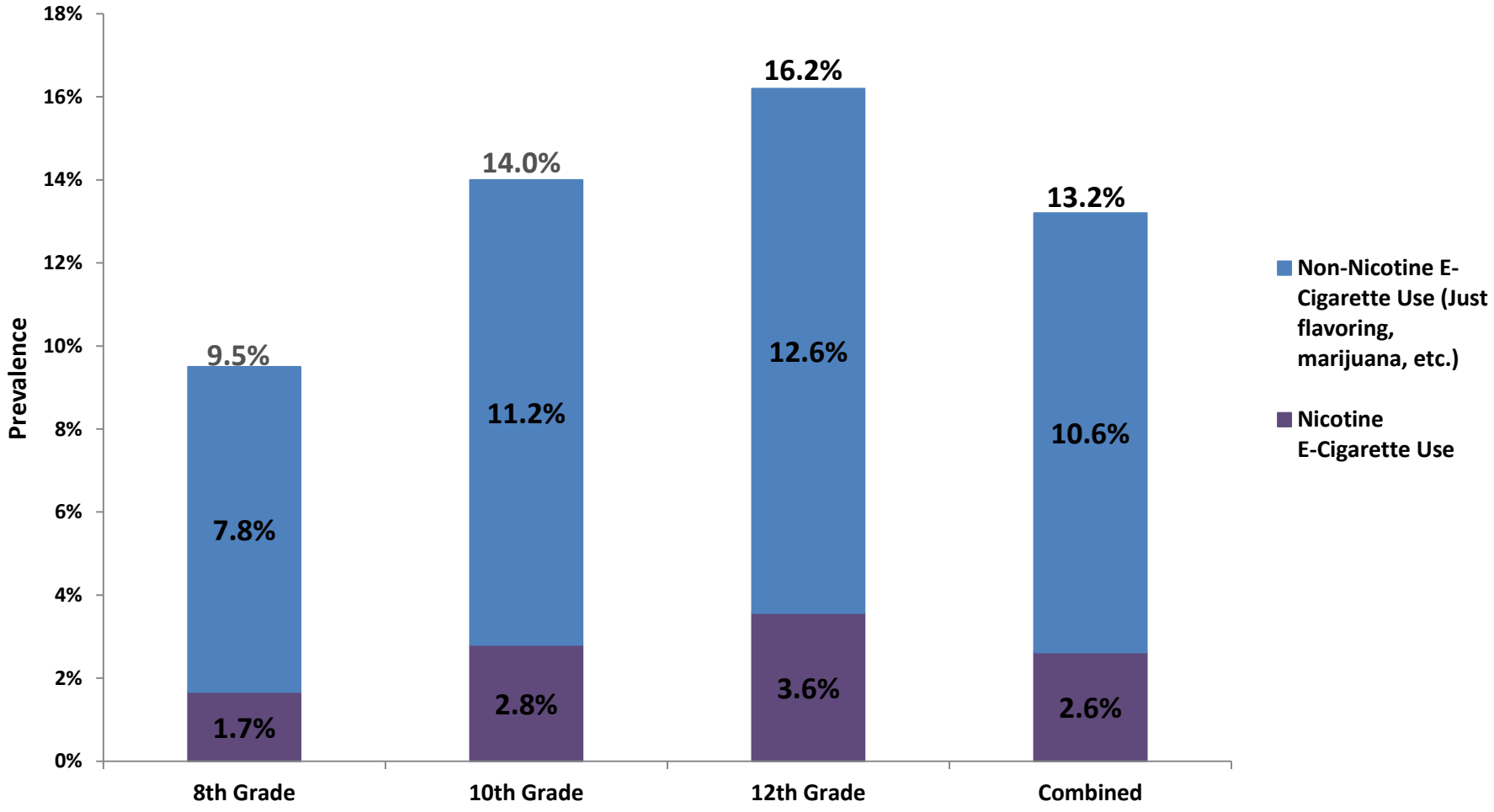
5. **Blind People and Elephants**: ALL moving parts, not one aspect. Big picture – relative harm - combustibles cause the deaths. Longitudinal Data + Modeling to capture dynamic interplay and net population impact.

6. **Goldilocks: just right regulation**: data (science) not dogma (ideology)

# Thank You

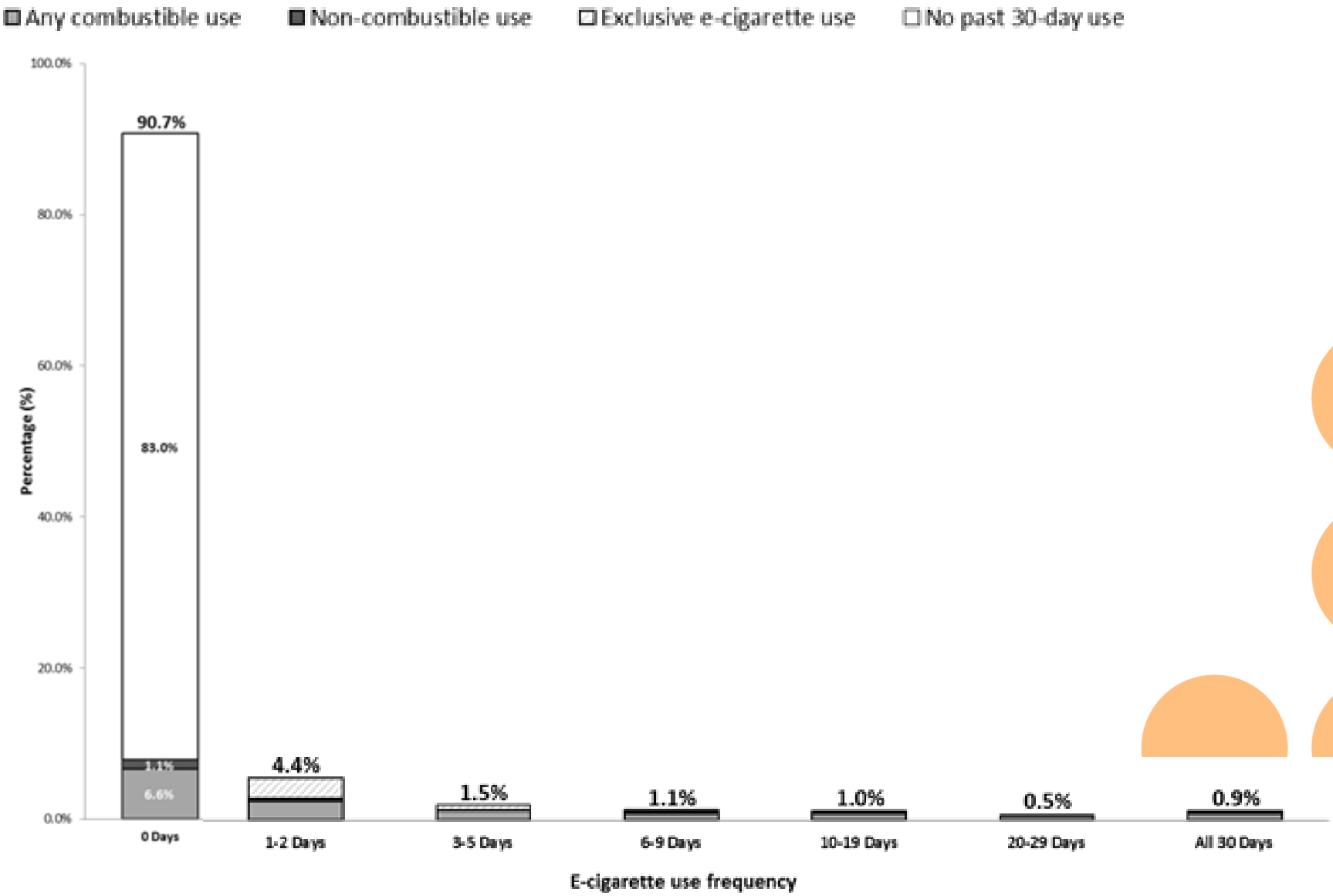
Dabrams@truthinitiative.org

# Past 30-Day E-Cigarette Use Among 8th, 10th, and 12th Graders – MTF, 2015

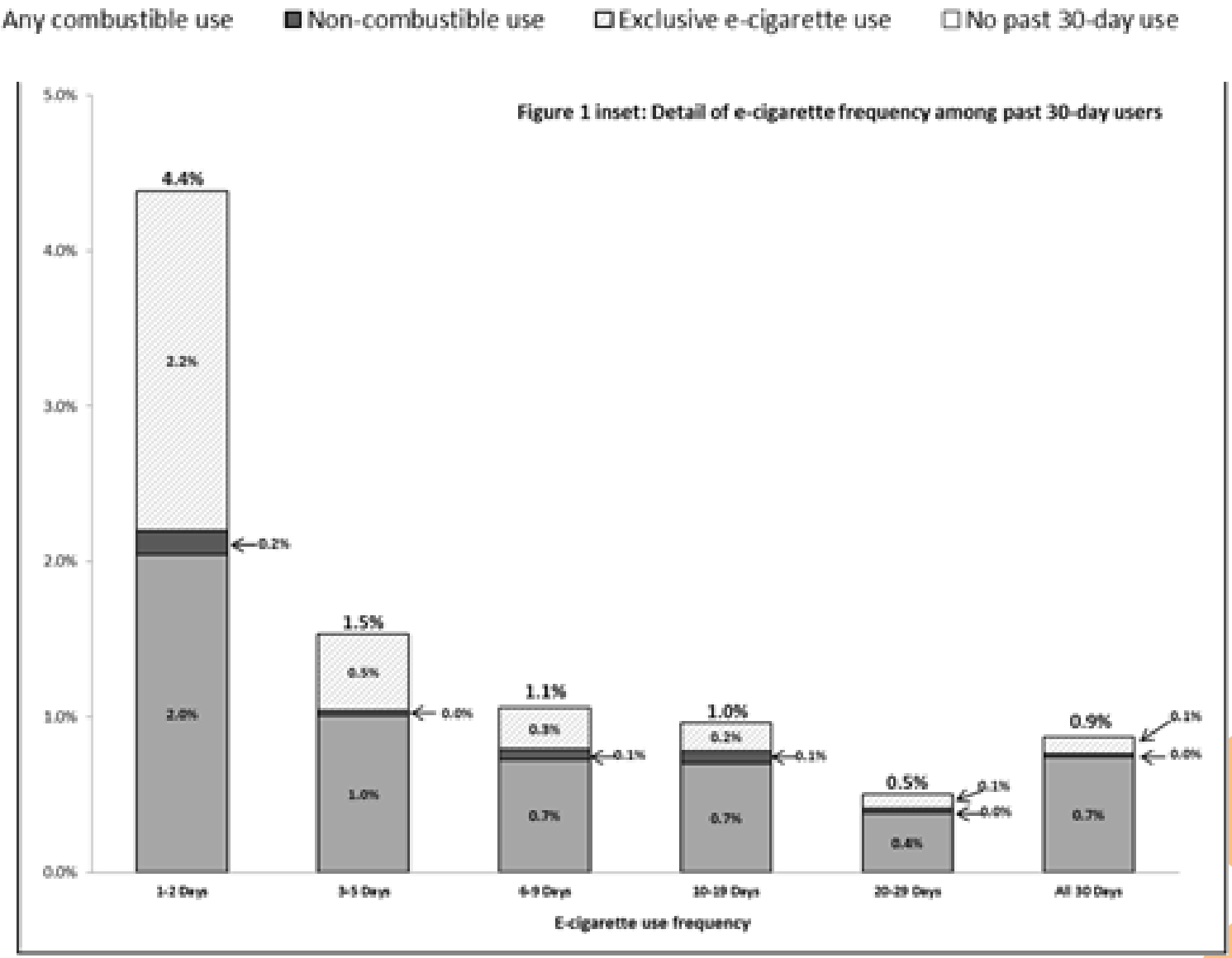



Source: Monitoring the Future, 2015

# E-cigarette Use Frequency

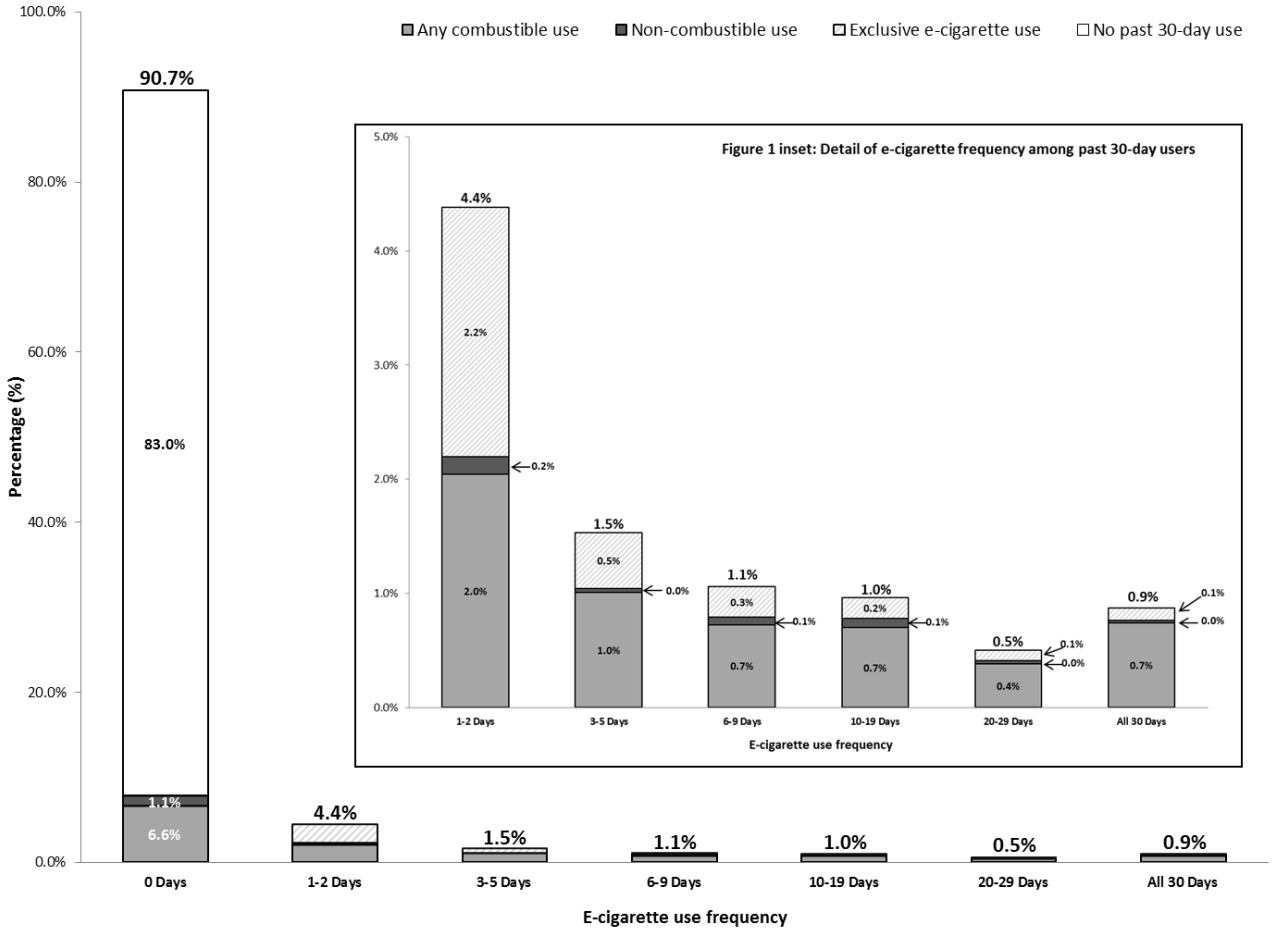


# Past 30-day users



# Youth Patterns of Use

DISTRIBUTION OF TOBACCO AND E-CIGARETTE USE AMONG U.S. MIDDLE AND HIGH SCHOOL STUDENTS (WEIGHTED); NATIONAL YOUTH TOBACCO SURVEY, 2014[A]

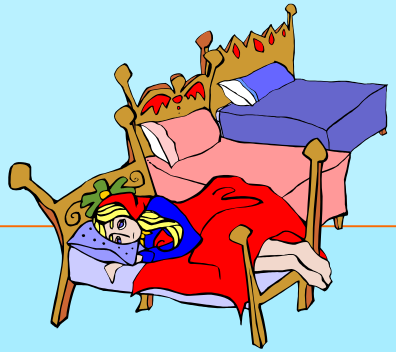


# Regulatory Implications

The swirl of data on trial e-cigarette uptake, dual use and use for cessation **does not** change many policy recommendations –

- Prudent Product standards to ensure safety and quality BUT without over burden – favors big tobacco
- Integrated Fast Track nicotine regulation: maximize benefits for cigarette cessation (CDER) and harm minimization (CTP)
- Accurate Education on harms and benefits of e-cigarettes
- Prevent sales, marketing, flavors or targeting to appeal to youth of any and all tobacco and nicotine products

# Appeal, Addiction, Harm: The Triple Continua Framework



Flavored
Combustible Tobacco;
Menthol, little cigars…….

Unflavored
Combustible
Tobacco ….>

Unflavored,
less addictive
combustible
Tobacco ….>

Flavored
E-cigs


Inexpensive, small packs in convenience stores (Zonnic)


Flavored NRT's


Addiction Liability - Nicotine + ?

Toxicity - harmfulness

Appeal - satisfaction

# Regulatory Tools: Complement Traditional T.C.

**FDA-Center for Tobacco Products (CTP) can: Regulate and Educate:**

- **Product Standards: Individual Safety & Efficacy**
- **New Product and Substantial equivalence applications**
- **Modified Risk Reduced Harm Product (MRTP) designations**
- **Public Education: Correct Misperceptions**
- **Pre- and post-market surveillance: PATH patterns, trajectories**
- **CTP separate from CDER (Therapeutics for Cessation Tx)**
- **Need for Comprehensive Nicotine Policy**

**KEY ISSUE: Rethinking Nicotine in light of new delivery modes**