

Methods: Mind the Gap Webinar Series

The Role of Computational Models on Assessing the Population Health Consequences of Menthol Cigarettes and the Benefits of a Menthol Ban

Presented by:

David Mendez, Ph.D.

University of Michigan School of Public Health



National Institutes of Health
Office of Disease Prevention

The Role of Computational Models on Assessing the Population Health Consequences of Menthol Cigarettes and the Benefits of a Menthol Ban

David Mendez, Ph.D.
Department of Health Management and Policy
School of Public Health
University of Michigan

Acknowledgments

- **I want to acknowledge my colleague Dr. Thuy TT Le, from the University of Michigan Health Management and Policy, who is my co-author in two of the publications mentioned in this talk.**
- Several of the studies mentioned in this talk were performed under the umbrella of the Center for the Assessment of Tobacco Regulations (CAsToR) TCORS, funded by grant 2U54CA229974 from the National Institutes of Health, the National Cancer Institute, and the Food and Drug Administration.

Acknowledgments (cont'd)

- I want to acknowledge my colleague Dr. Thuy TT Le, from the University of Michigan Health Management and Policy, who is my co-author in two of the publications mentioned in this talk.
- **Several of the studies mentioned in this presentation were performed under the umbrella of the Center for the Assessment of Tobacco Regulations (CAsToR) TCORS, funded by grant 2U54CA229974 from the National Institutes of Health, the National Cancer Institute, and the Food and Drug Administration.**

Peppermint



Menthol

Menthol is an organic substance extracted from the mint family of plants. It has cooling and anesthetic properties.



Commercial Uses of Menthol

- Oral hygiene products
- Confectionery
- Pharmaceuticals
- Cosmetics
- Flavoring agent
- Tobacco
- Food preservative

Menthol-Containing Products





Menthol in Cigarettes

- Menthol in 90% of tobacco products
- Characterizing flavors – 0.12% or greater; most 0.3% or higher
- Non-menthol cigarettes up to 0.07 mg/cig; menthol cigarettes 1.5 mg/cig or more
- 5-20% menthol absorbed from cigarettes, depending on ventilation



Menthol in Cigarettes (cont'd)

- Cigarettes with a menthol characterizing flavor are called **“menthol cigarettes.”**
- When added to cigarettes, as a characterizing flavor, menthol masks the harshness of the smoke, **facilitating smoking initiation.** It also makes cigarettes more addictive, **delaying smoking cessation.**

Menthol in Cigarettes (cont'd)

- The 2009 Family Smoking Prevention and Tobacco Control Act charges the Food and Drug Administration's (FDA) Tobacco Products Scientific Advisory Committee (TPSAC) with developing a report and recommendations that address **“the issue of the impact of the use of menthol in cigarettes on the public health including such use among children, African Americans, Hispanics, and other racial and ethnic minorities.”**



Menthol in Cigarettes (cont'd)

- In 2011, the TPSAC submitted a report to the FDA with the following conclusions:
 - **Menthol cigarettes have an adverse impact on public health in the United States.**
 - There are no public health benefits of menthol compared to non-menthol cigarettes.



Menthol in Cigarettes (cont'd)

- In 2011, the TPSAC submitted a report to the FDA with the following conclusions:
 - Menthol cigarettes have an adverse impact on public health in the United States.
 - **There are no public health benefits of menthol compared to non-menthol cigarettes.**



Menthol in Cigarettes (cont'd)

- Consequently, the TPSAC Menthol Report made the following overall recommendation to the FDA:
 - **Removal of menthol cigarettes from the marketplace would benefit public health in the United States.**
- In 2013 and again in 2018, the FDA sought public comment, research results, and other information on the impact of menthol cigarettes on smoking initiation, prevalence, and other factors to inform regulatory actions that the FDA might take on mentholated cigarettes.

Menthol in Cigarettes (cont'd)

- **In April 2021, the FDA announced plans to ban menthol cigarettes, in response to a lawsuit filed by the African American Tobacco Control Leadership (AATCLC), Action on Smoking and Health (ASH), the American Medical Association (AMA), and the National Medical Association (NMA) on Saving Black Lives.**
- In April 2022, the FDA proposed rules prohibiting menthol cigarettes and flavored cigars to prevent youth initiation and significantly reduce tobacco-related disease and death.



Menthol in Cigarettes (cont'd)

- In April 2021, the FDA announced plans to ban menthol cigarettes, in response to a lawsuit filed by the African American Tobacco Control Leadership (AATCLC), Action on Smoking and Health (ASH), the American Medical Association (AMA), and the National Medical Association (NMA) on Saving Black Lives.
- **In April 2022, the FDA proposed rules prohibiting menthol cigarettes and flavored cigars to prevent youth initiation and significantly reduce tobacco-related disease and death.**



Modeling Studies

- **The population health consequences of smoking menthol cigarettes and the benefits of a ban on menthol cigarettes have been estimated using simulation models.**

Modeling Studies (cont'd)

Publication	Benefits of Menthol Ban	Menthol Harm	Population	Period	Premature Deaths Caused / Averted
Mendez, TPSAC Report 2011		X	General US	2010-2050	328,000
Le & Mendez, Tob Ctrl 2021		X	General US	1980-2018	378,000
Mendez & Le, Tob Ctrl 2021		X	African American	1980-2018	157,000
Levy et al., AJPH 2011	X		General US	2011-2050	633,000
Levy et al., Tob Ctrl 2021	X		General US	2021-2060	650,000
Issabakhsh et al., Tob Ctrl 2022	X		African American	2021-2060	256,000

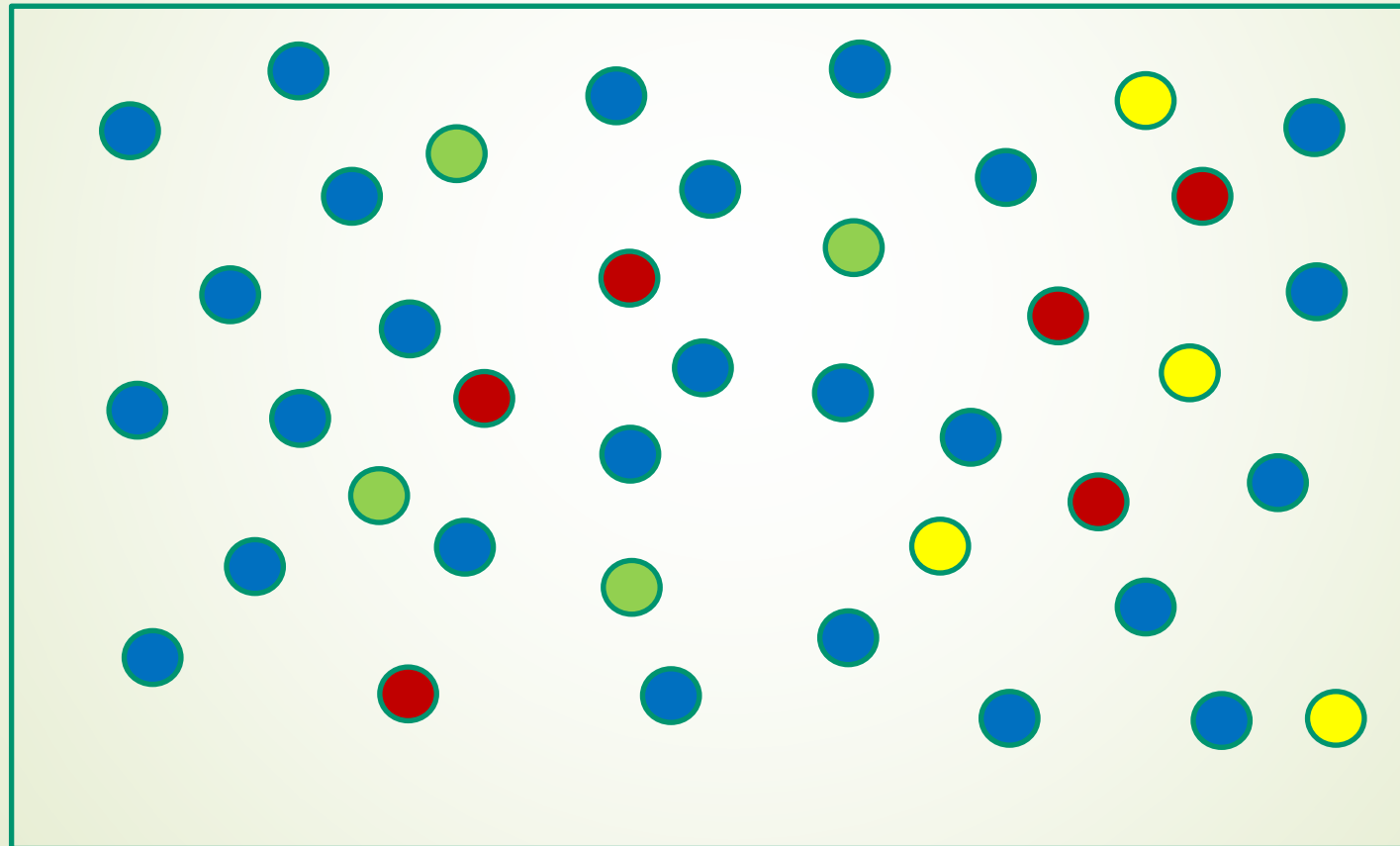


Modeling Studies (cont'd)

- The population health consequences of smoking menthol cigarettes and the benefits of a ban on menthol cigarettes have been estimated using simulation models.
- **The models employed have been aggregate/compartmental, dynamic, and linear.**

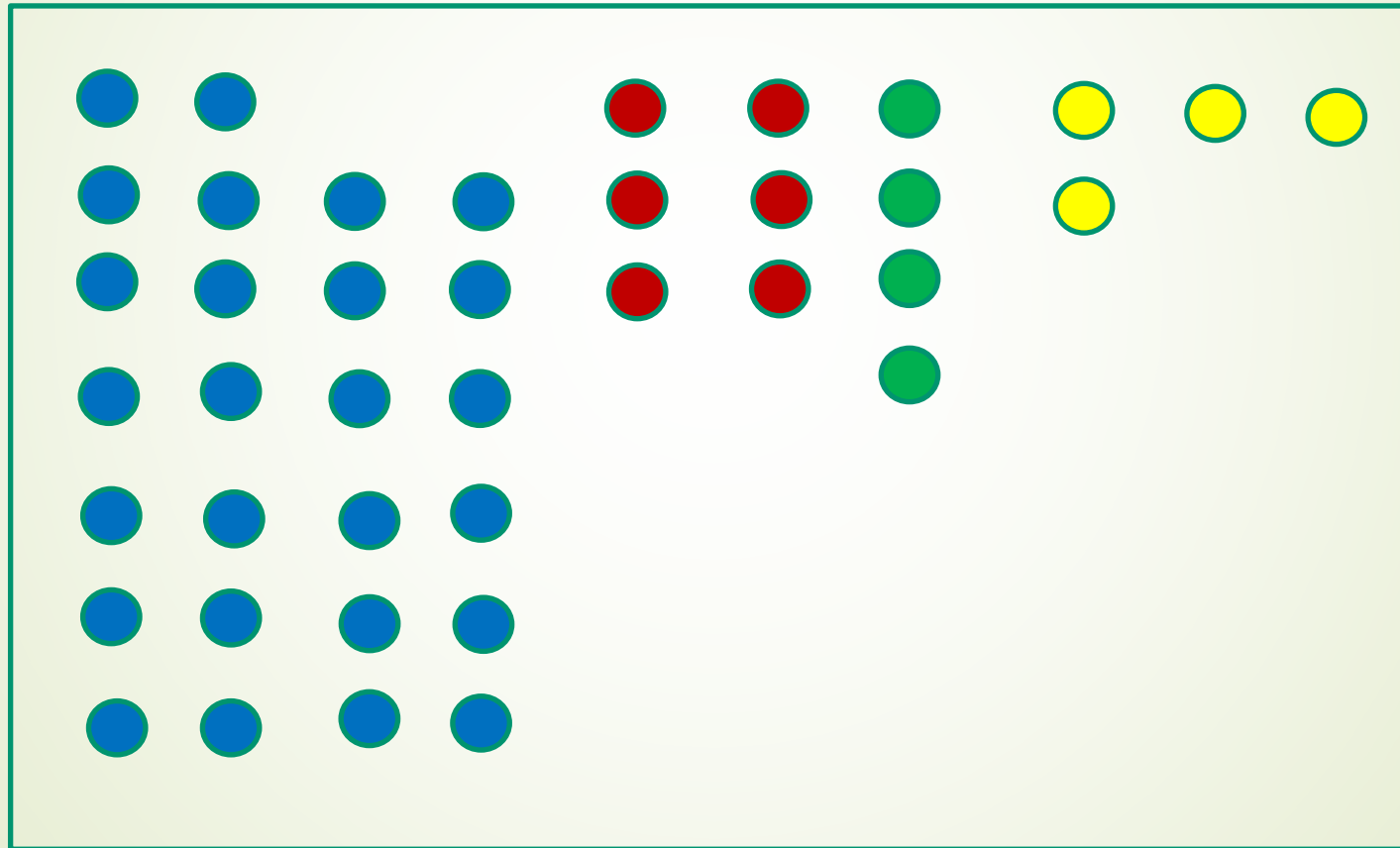
Compartmental Models

● Never Smoker ● Non-menthol Smoker ● Menthol Smoker ● Former Smoker

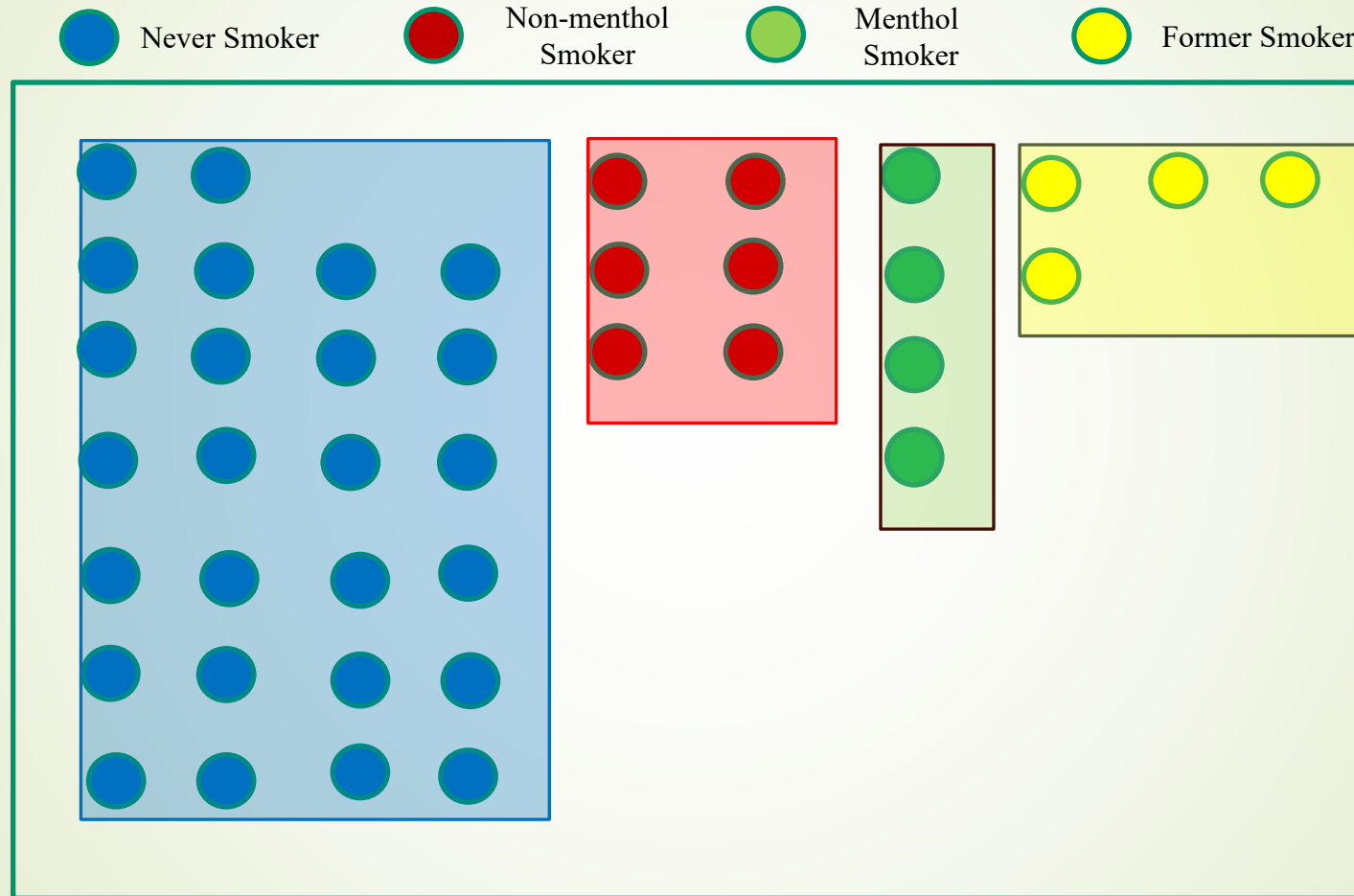


Compartmental Models (cont'd)

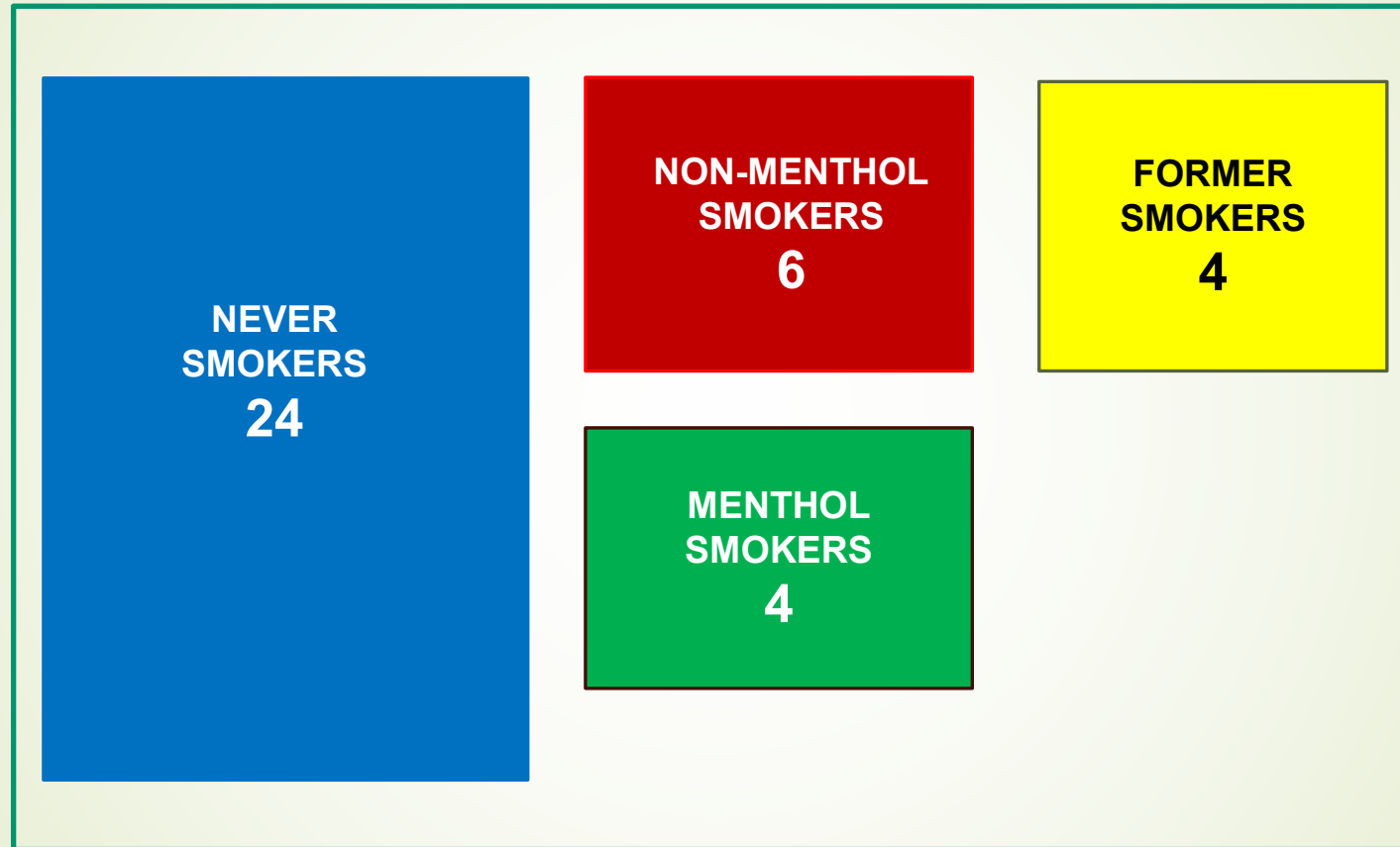
● Never Smoker ● Non-menthol Smoker ● Menthol Smoker ● Former Smoker



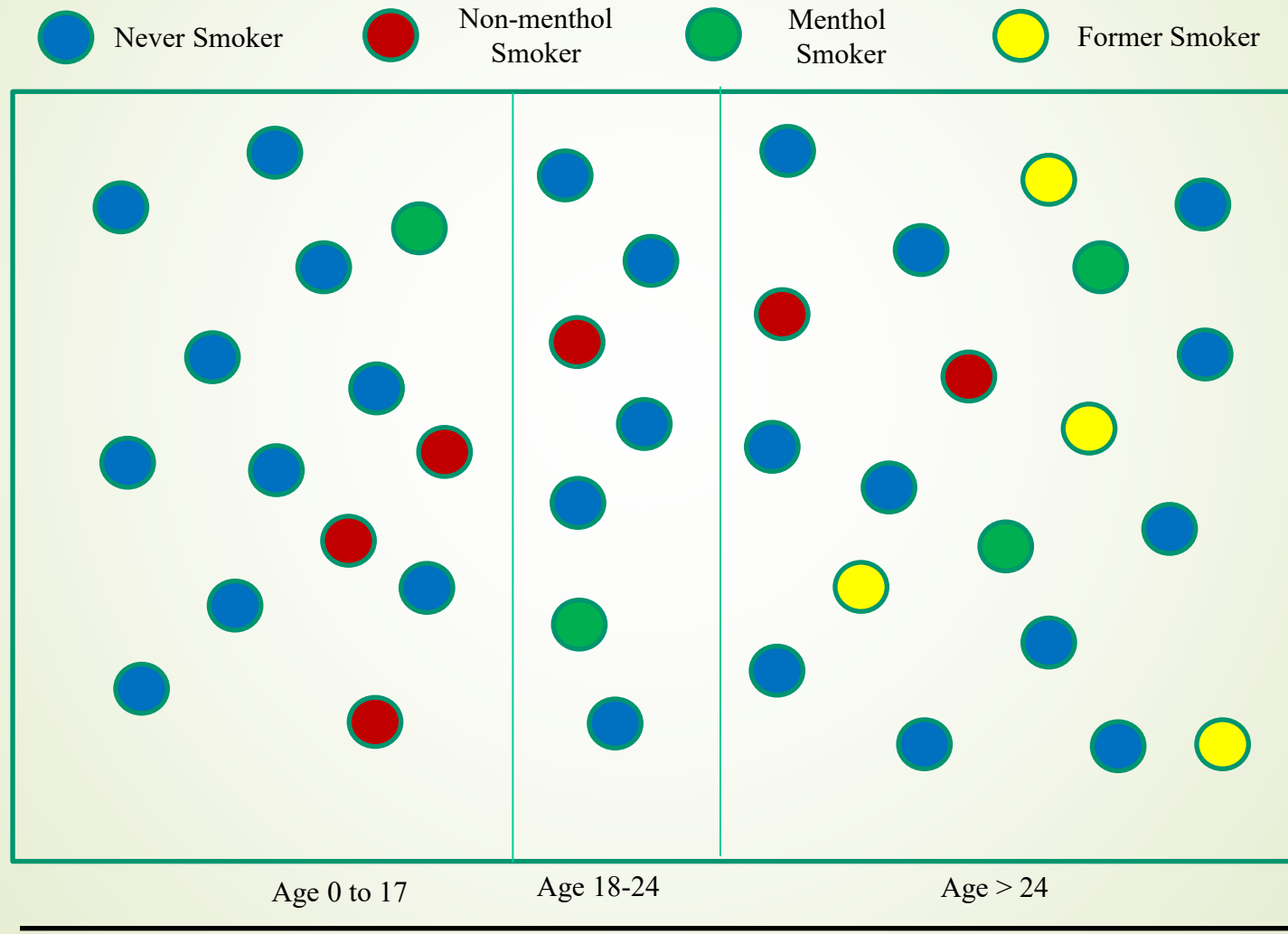
Compartmental Models (cont'd)



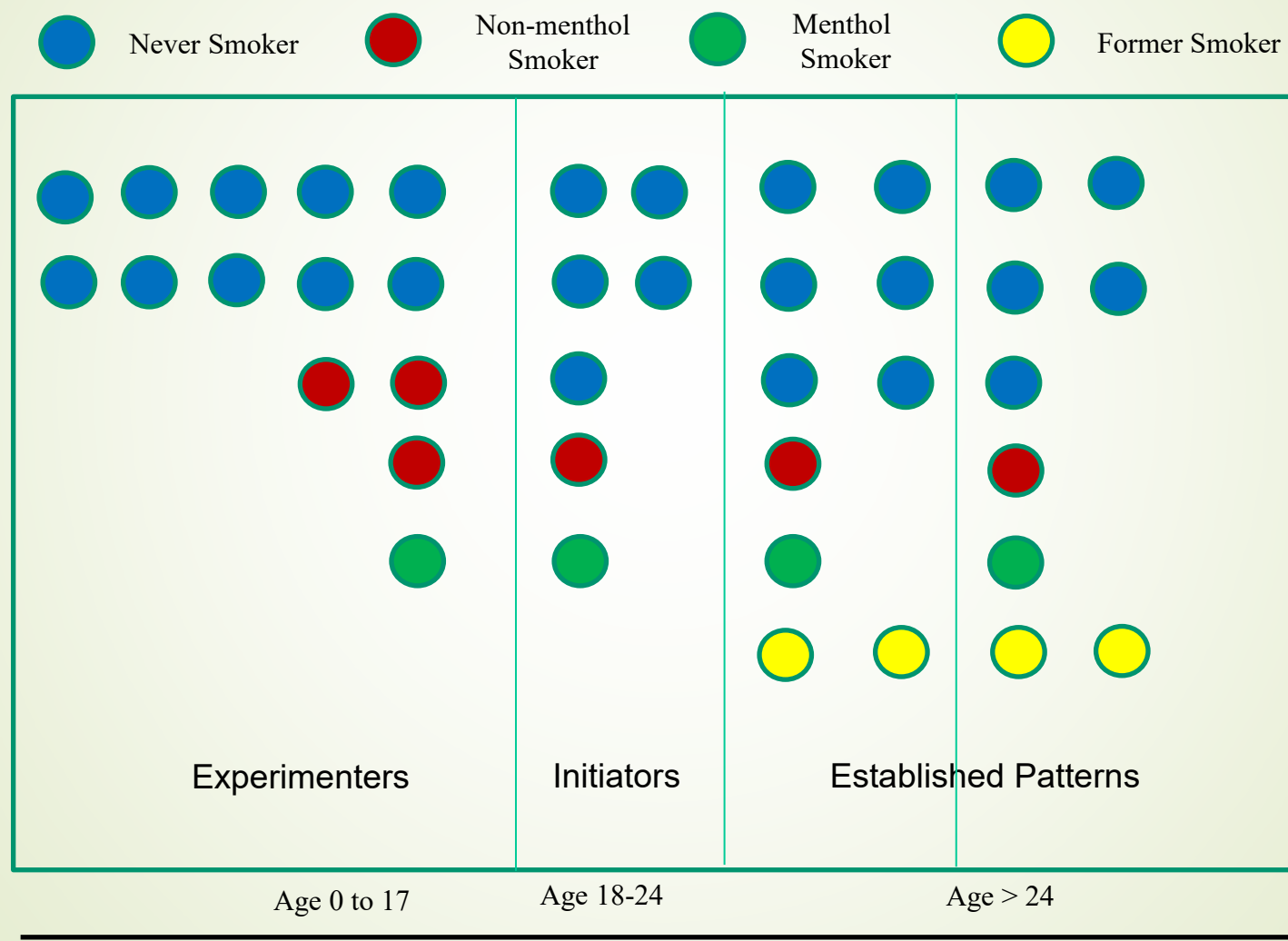
Compartmental Models (cont'd)



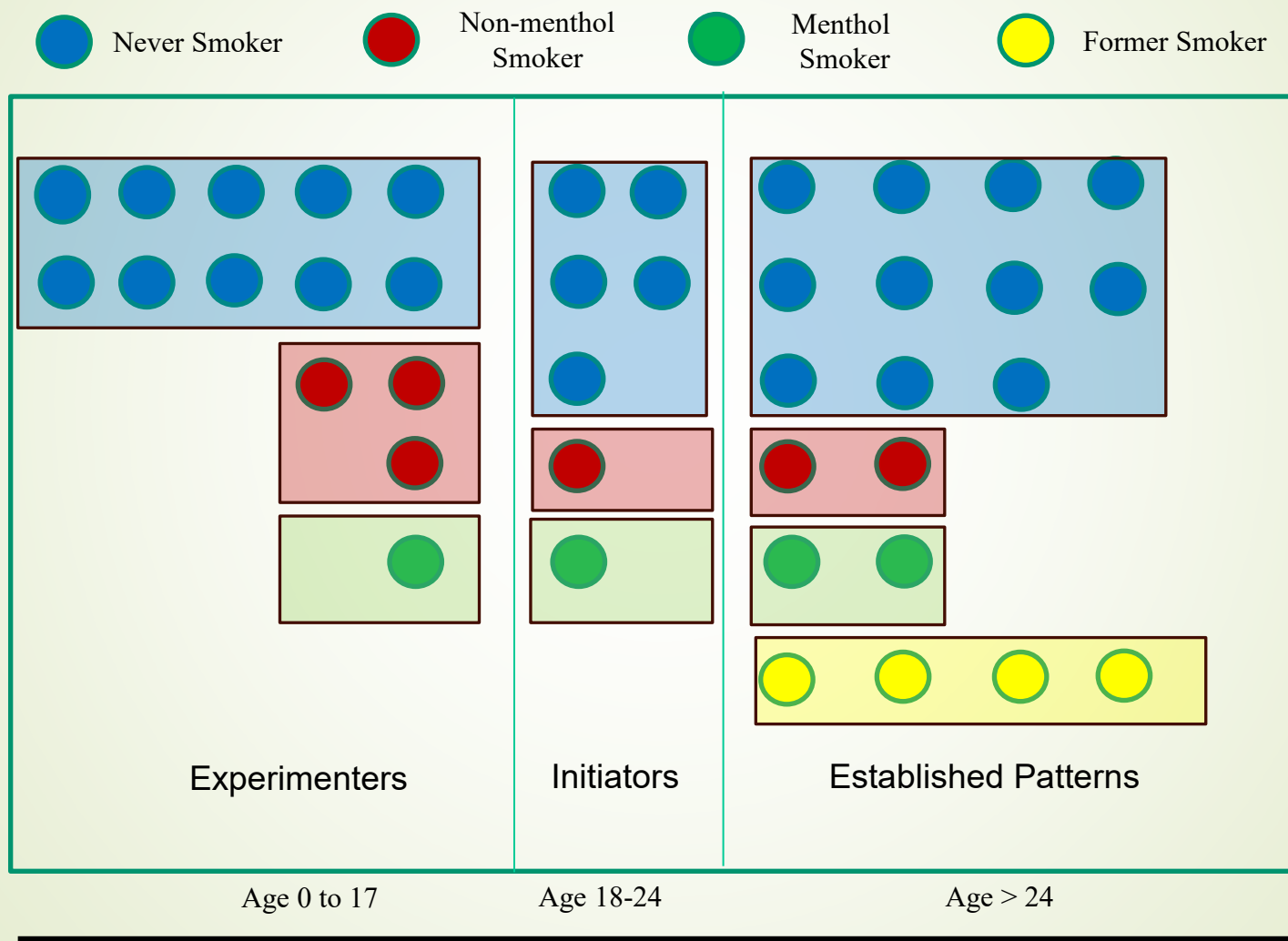
Compartmental Models (cont'd)



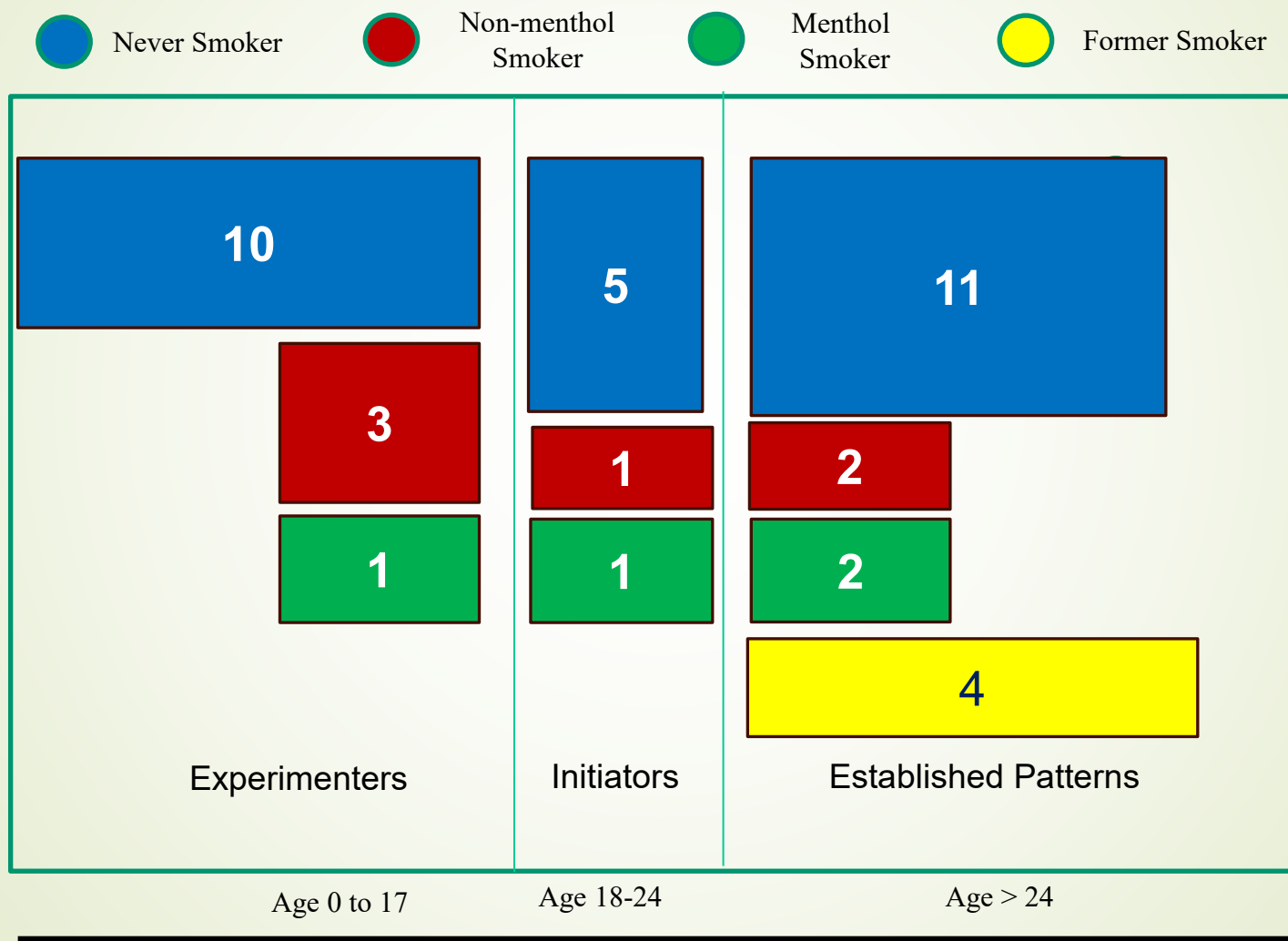
Compartmental Models (cont'd)



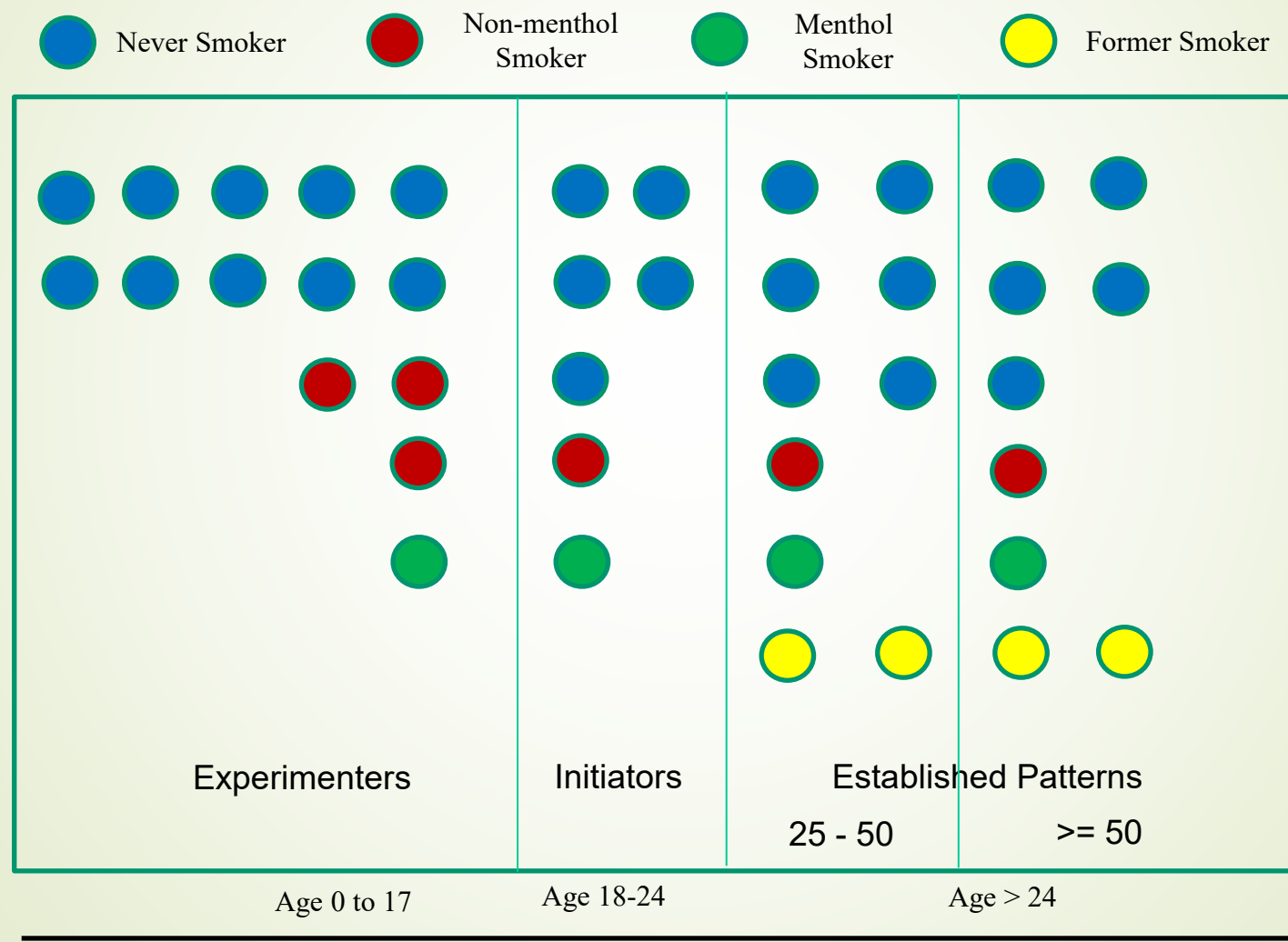
Compartmental Models (cont'd)



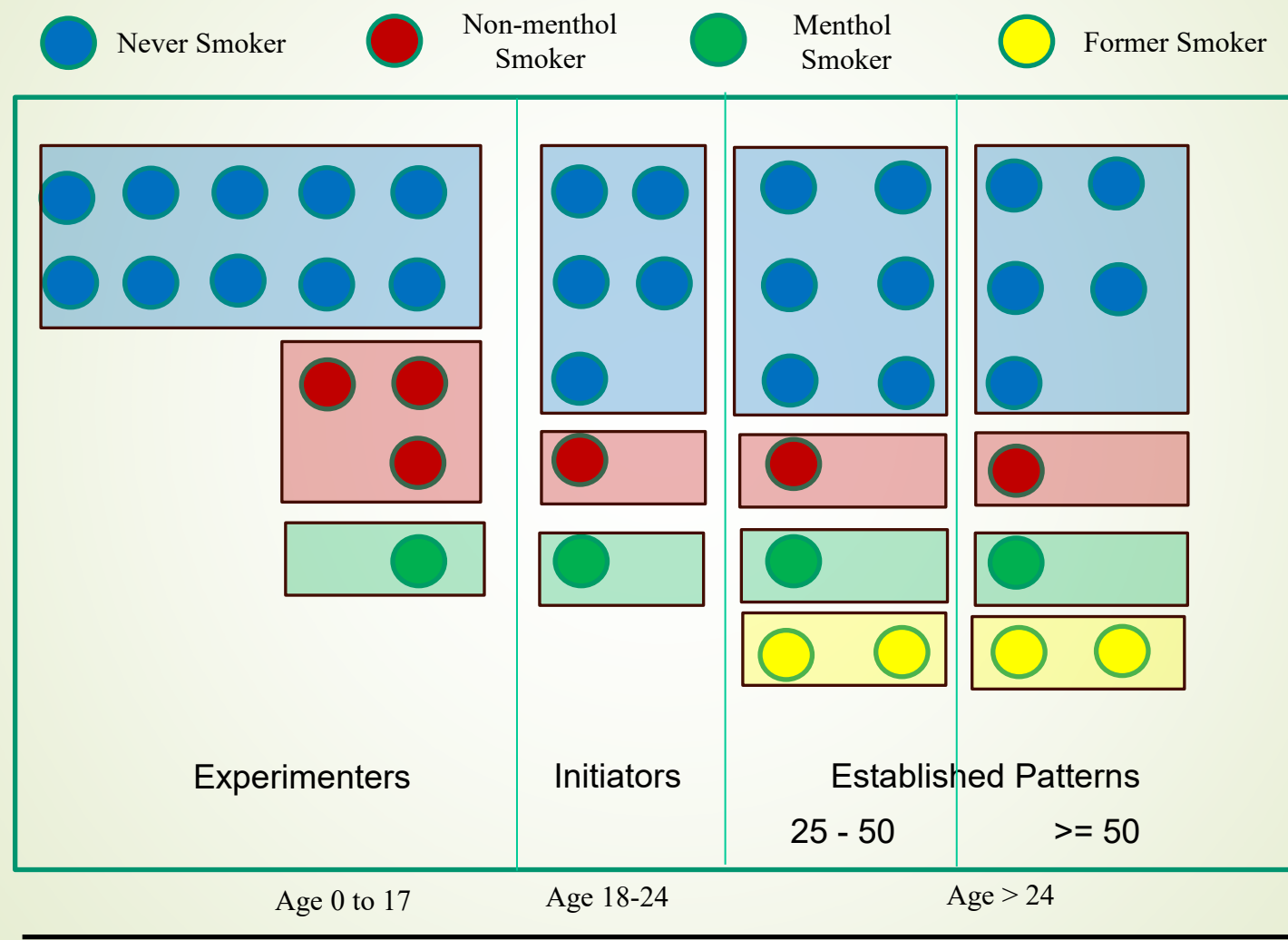
Compartmental Models (cont'd)



Compartmental Models (cont'd)

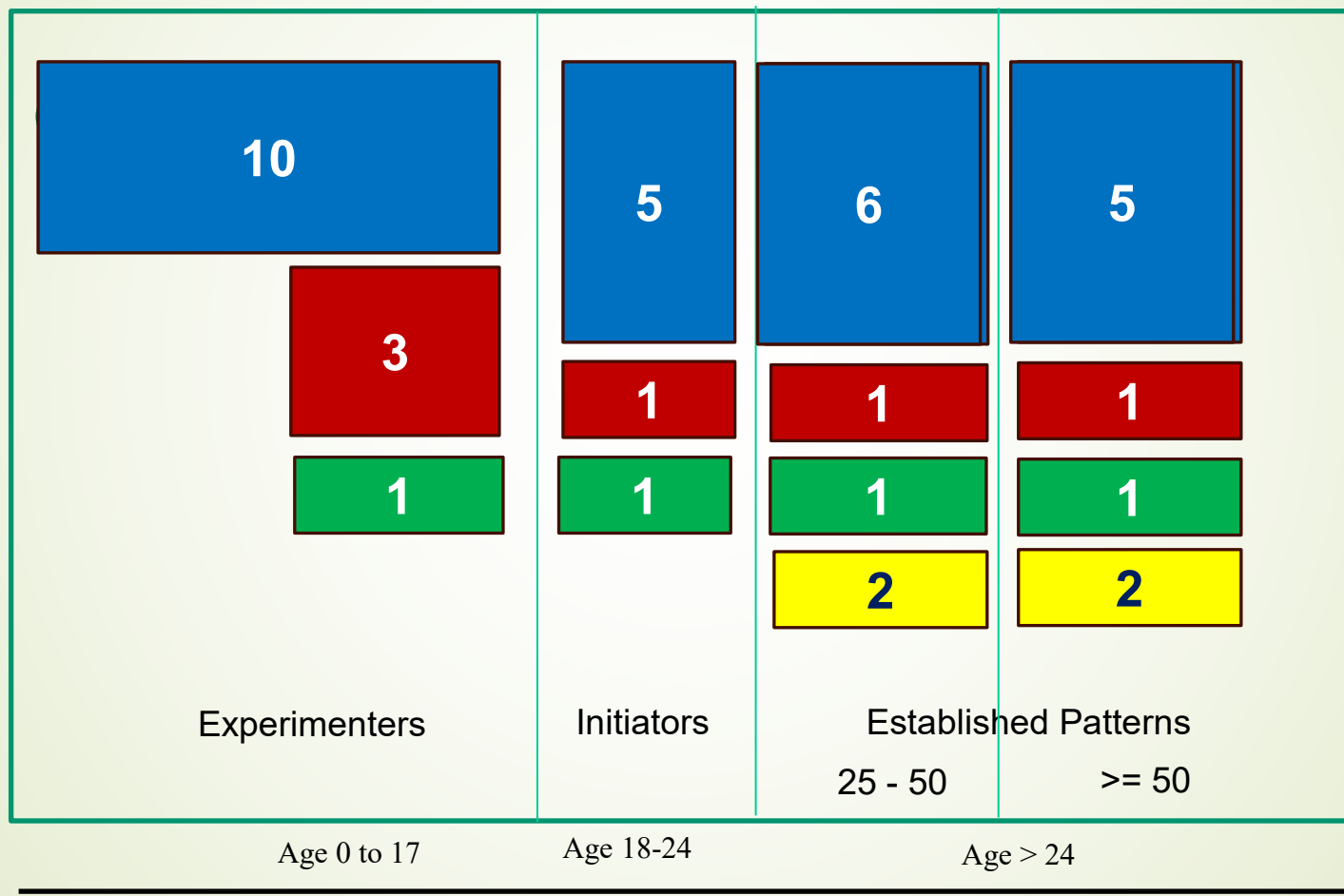


Compartmental Models (cont'd)

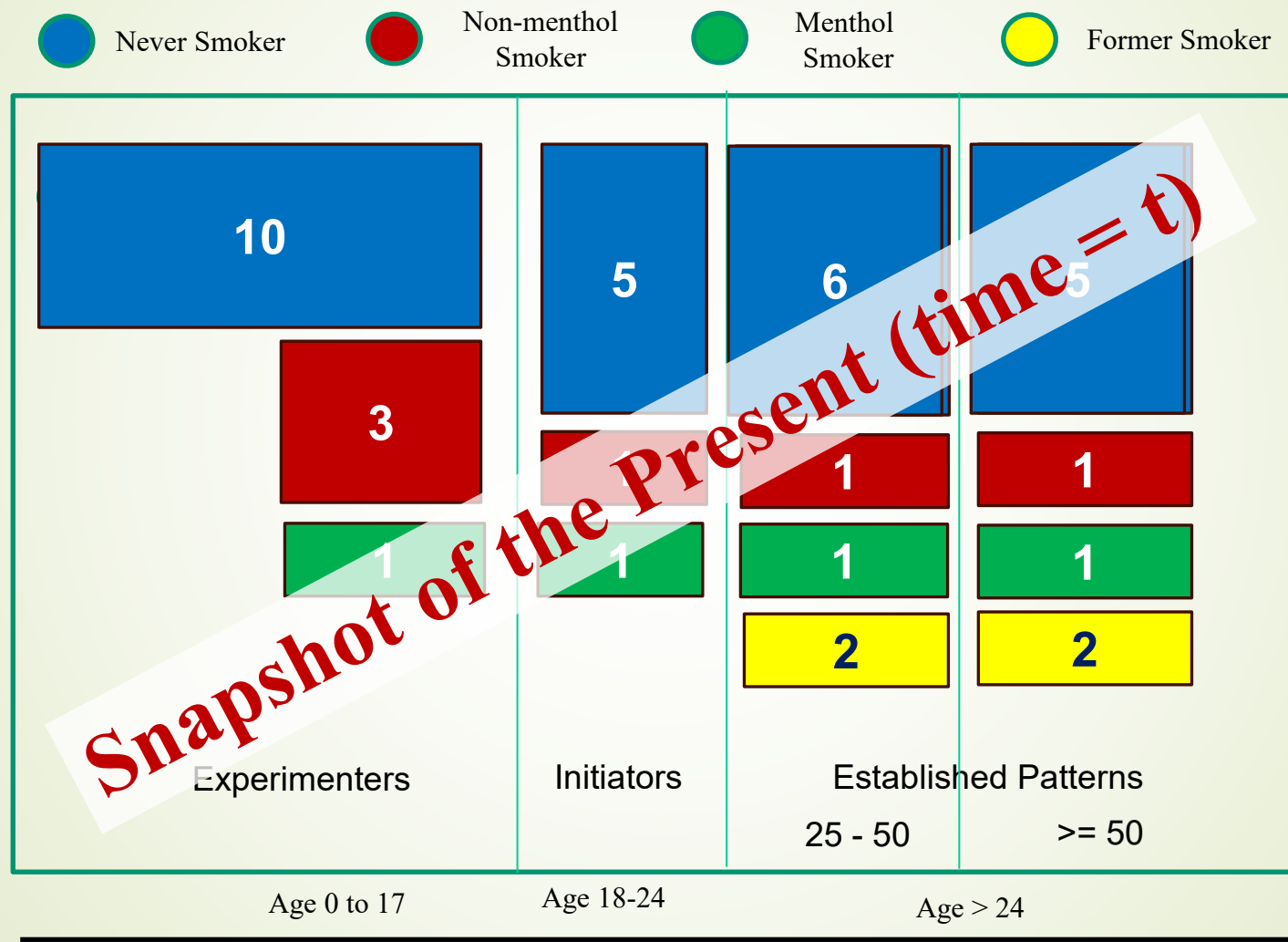


Compartmental Models (cont'd)

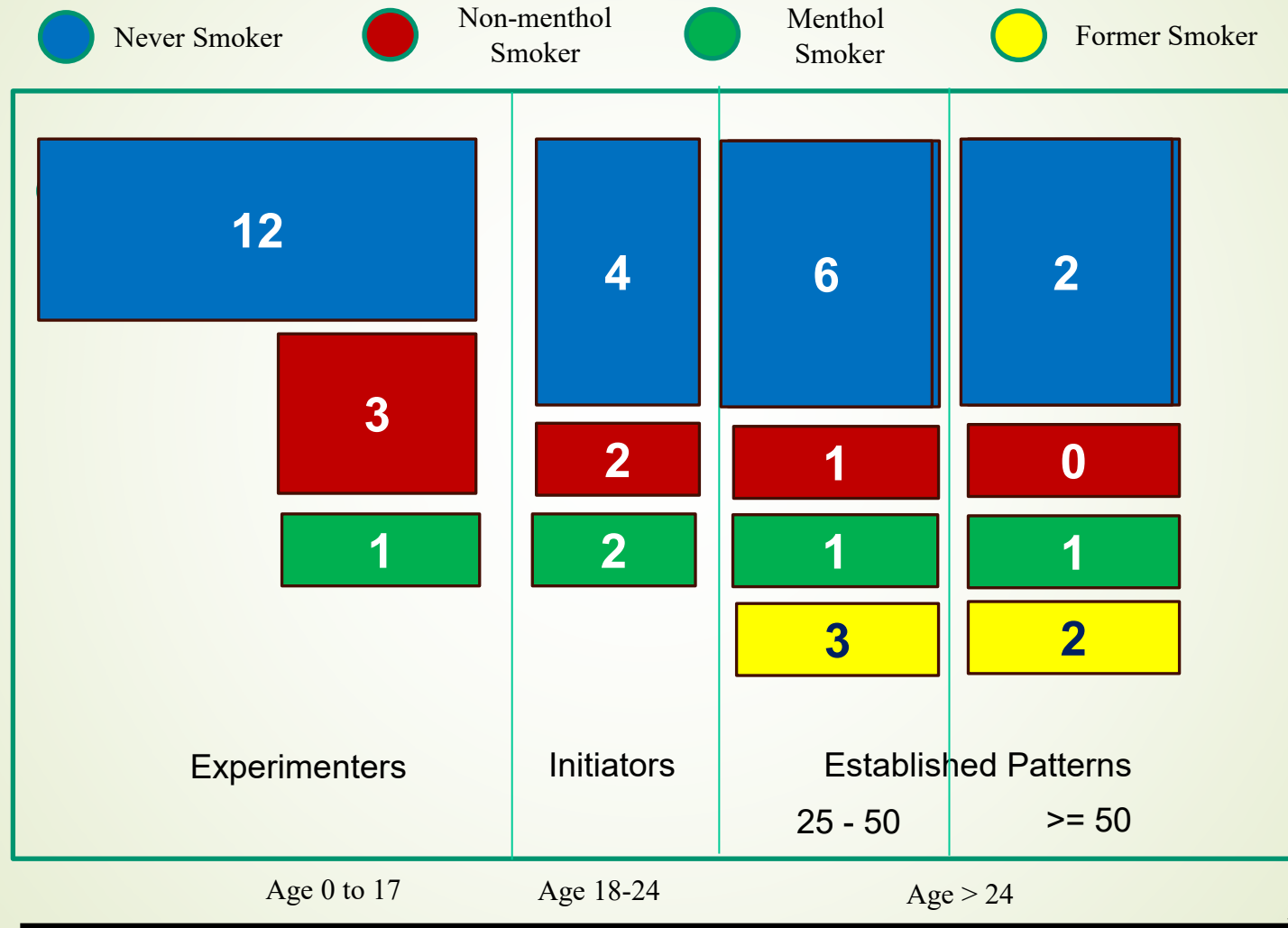
● Never Smoker
 ● Non-menthol Smoker
 ● Menthol Smoker
 ● Former Smoker



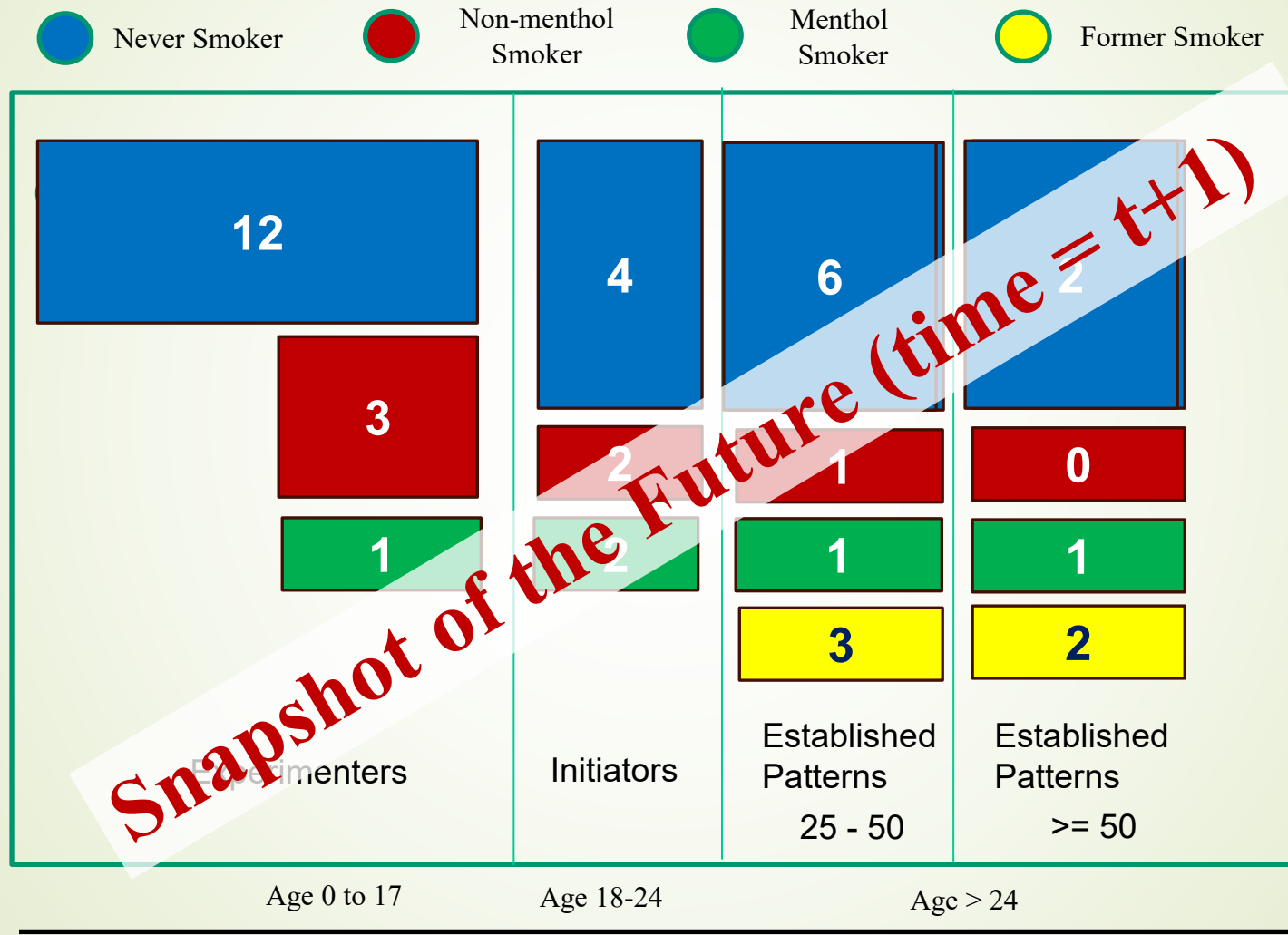
Compartmental Models (cont'd)



Model Dynamics



Model Dynamics (cont'd)



Model Dynamics (cont'd)

Future = Present + Change

$$\textit{Menthol Smokers } (t+1) = \textit{Menthol Smokers}(t) + [\textit{Inflows}(t) - \textit{Outflows}(t)]$$

Model Dynamics (cont'd)

Future = Present + Change

$$\textit{Menthol Smokers (t+1)} = \textit{Menthol Smokers(t)} + [\textit{Inflows(t)} - \textit{Outflows(t)}]$$

Model Dynamics (cont'd)

Future = **Present** + Change

$$\textit{Menthol Smokers } (t+1) = \textit{Menthol Smokers}(t) + [\textit{Inflows}(t) - \textit{Outflows}(t)]$$

Model Dynamics (cont'd)

Future = Present + **Change**

Menthol Smokers (t+1) = Menthol Smokers(t) + [Inflows(t) – Outflows(t)]

Model Dynamics (cont'd)

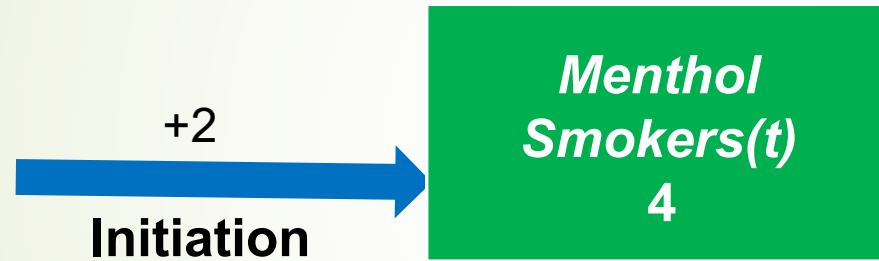
Present

*Menthol
Smokers(t)*

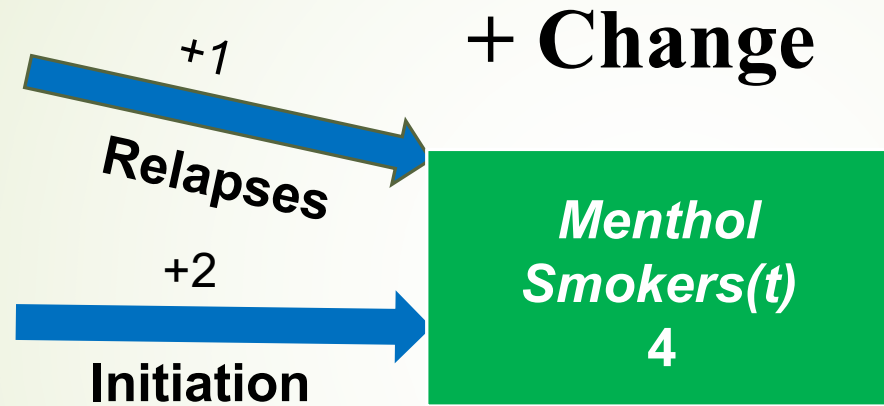
4

Model Dynamics (cont'd)

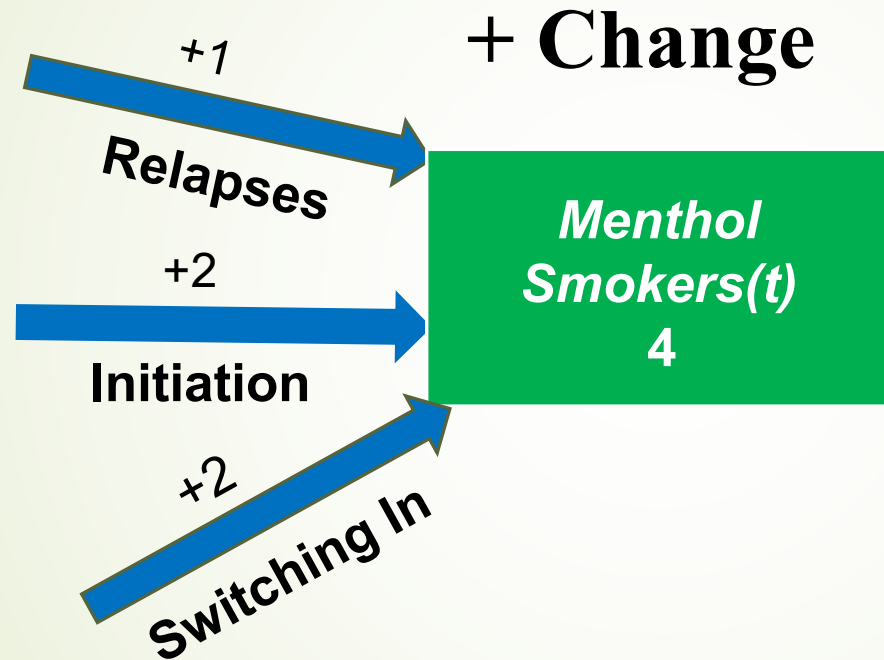
+ Change



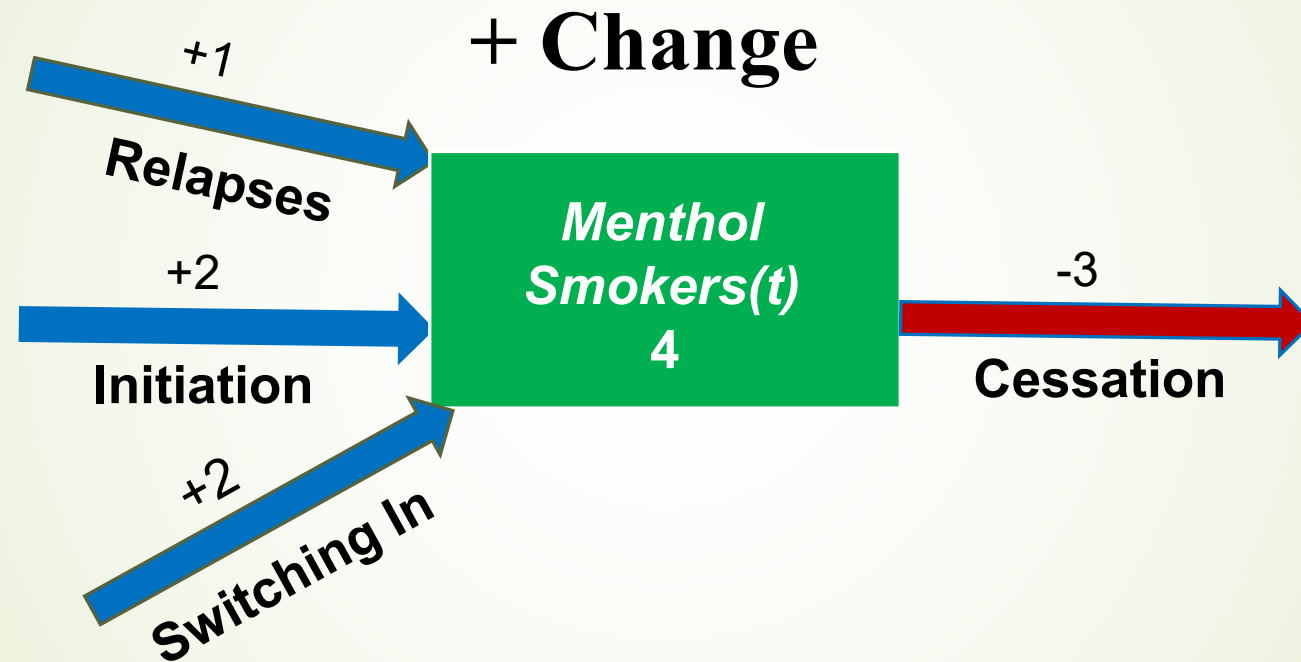
Model Dynamics (cont'd)



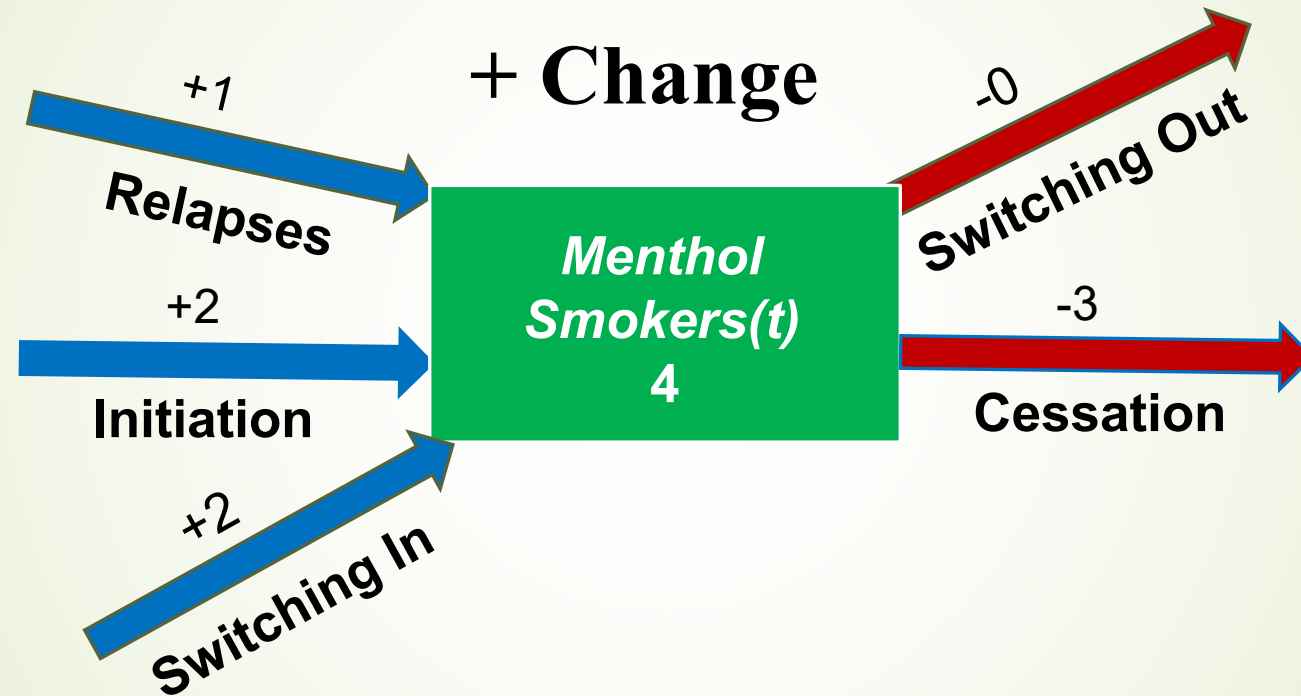
Model Dynamics (cont'd)



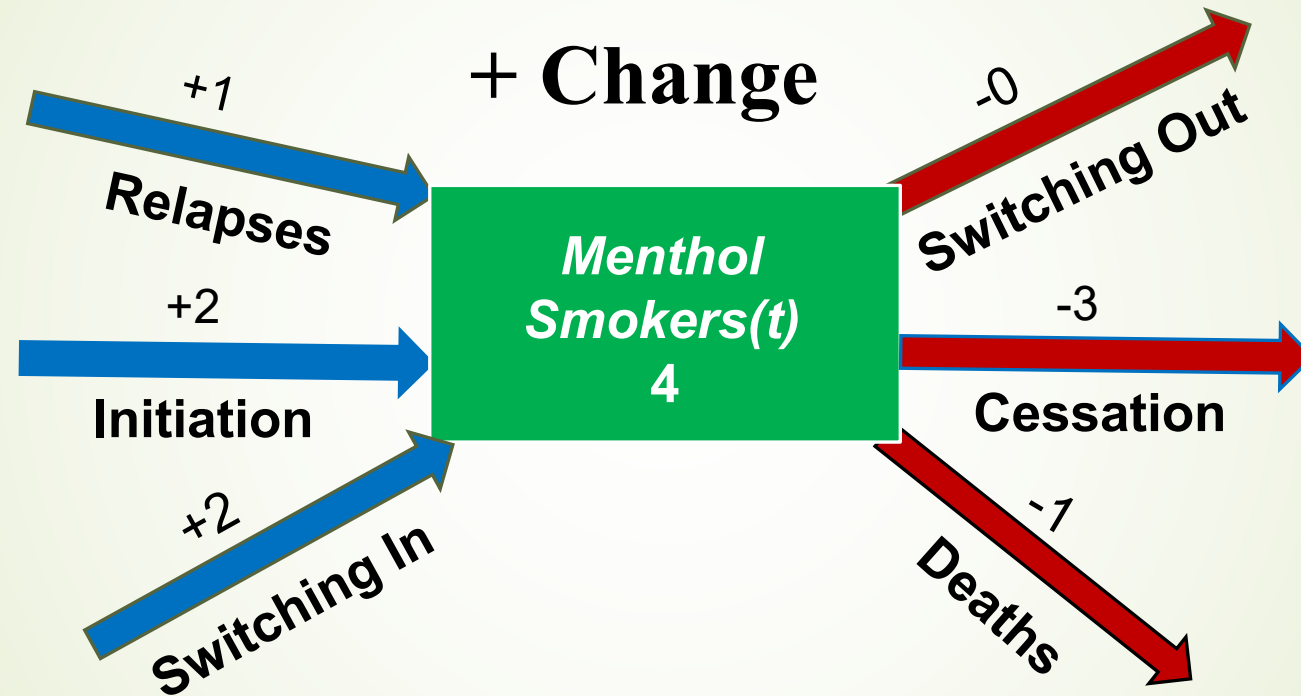
Model Dynamics (cont'd)



Model Dynamics (cont'd)



Model Dynamics (cont'd)



Model Dynamics (cont'd)

= Future

*Menthol
Smokers(t+1)*
5

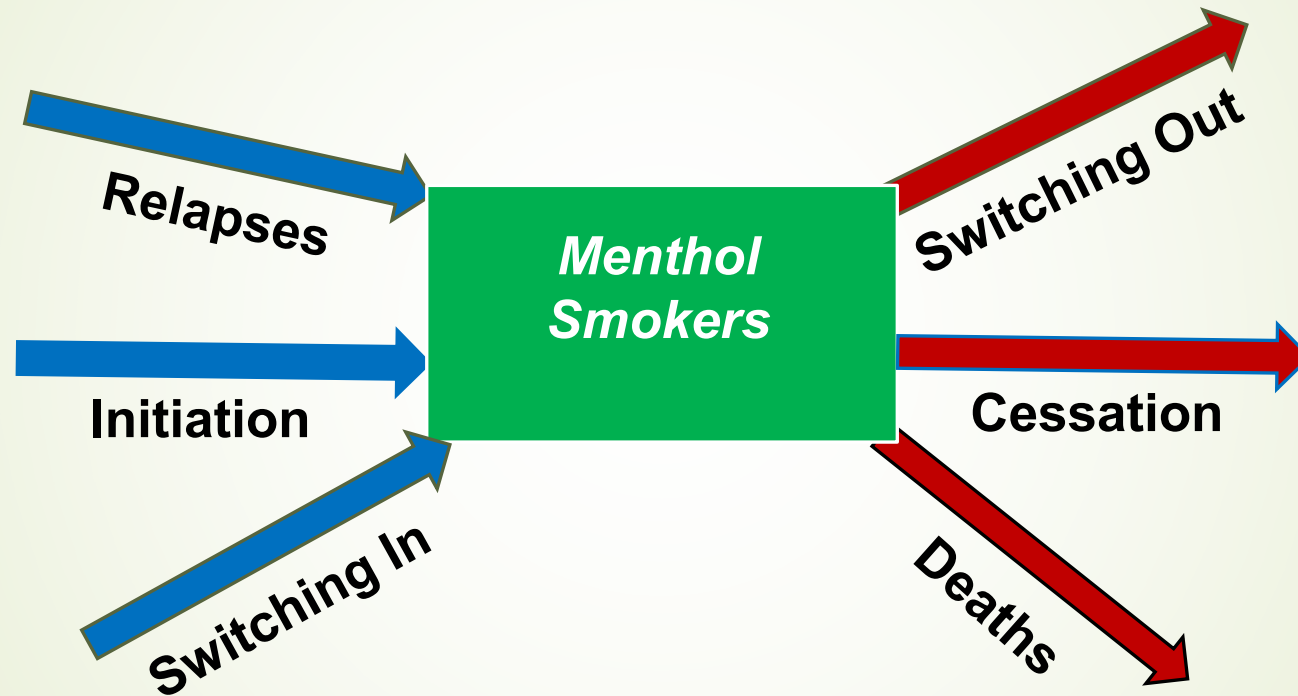
Future = Present + **Change**

$$\begin{array}{ccccccc} \textit{Menthol Smokers (t+1)} & = & \textit{Menthol Smokers(t)} & + & (\textit{Inflows(t)} - \textit{Outflows(t)}) \\ 5 & & 4 & & + (5 - 4) \end{array}$$

Model Dynamics (cont'd)

Inflows

Outflows



Model Dynamics (cont'd)

Stocks and Flows

$$\text{Flow} = \text{Stock} * \textit{Exit Rate} * \Delta t$$

e.g.

$$\text{Initiation}(t) = \text{Never Smokers}(t) * \textit{Initiation Rate}(t) * \Delta t$$

$$\text{Cessation}(t) = \text{Current Smokers}(t) * \textit{Cessation Rate}(t) * \Delta t$$

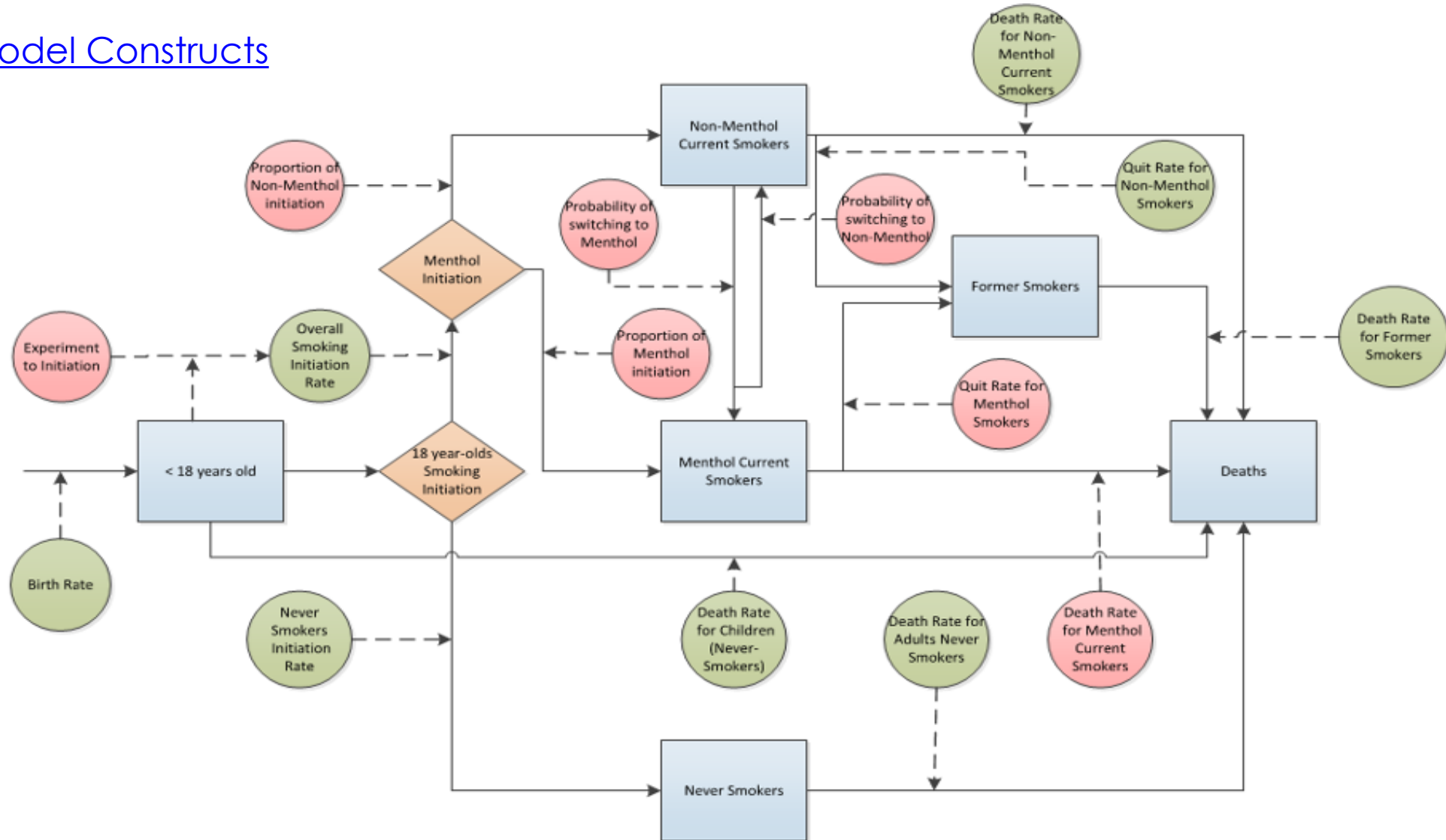
Initiation Rate(t) & *Cessation Rate(t)* are model parameters

Modeling of Menthol Cigarette Effects on Mortality

- An established simulation model of smoking prevalence and health effects (the Mendez-Warner model) was modified to track menthol smokers.
- The modified model was set to compare the health effects of cigarette smoking on the US population over the **next** and **past** 40 years under two scenarios:
 - Status-quo – simulating smoking trajectories from 1980 through 2018 and 2010 through 2050 under existing and current conditions.
 - No menthol scenario – same scenarios as in the status quo, assuming that menthol cigarettes were not available in the market during the simulation periods.
- The analysis was repeated for the African American population.

TPSAC Report Menthol Model

Model Constructs



Model Parameters

Model parameters were updated employing the following sources:

- Birth cohorts from the National Vital Statistics Reports
- Overall death rates: US Life Table [NVSR 1980-2018]
- Menthol and non-menthol smoking prevalence data from the 1980-2018 National Health Interview Survey (NHIS)
- Menthol cessation multiplier: [Mills et al. 2020]
- Probability of switching between Nonmenthol and Menthol cigarettes: [TPSAC Menthol Report, 2011]
- Menthol Mortality Multiplier: [Munro et al. 2016]
- Relative risk of mortality of current, and former smokers: [Mendez et al. 2014, Michael Thun from the American Cancer Society]

Model Parameters (cont'd)

Model parameters were updated employing the following sources (cont'd):

- Ratio of yields from experimenter to established smoker (menthol/non-menthol): [Nonnemaker et al. 2013 and 2019].
- Smoking-related death rates: estimated from overall death rates and relative risk of mortality.
- Overall cessation rates: Mendez et al. 1998 for 1980 and rescaled based on Mendez et al. 2016 for 2018.
- Cessation rates of menthol and nonmenthol smokers: based on overall cessation rates and menthol cessation multiplier.

Model Settings

To project the harm of menthol cigarettes over 1980-2018, we:

- Populated the model with the 1980 data and parameters. Then, a simulation scenario from 1980-2018 was conducted, updating all parameters frequently to match historical conditions (**status quo scenario**).
- Constructed an alternative (**counterfactual**) scenario over the same period in which the effect of menthol cigarettes was removed over 1980-2018.
- Compared both scenarios to quantify the public health harm attributable to menthol over the 1980-2018 period.

Model Settings (cont'd)

Initiation rates:

- Under the status quo scenario (γ): average smoking rates among 18-24-year-olds in the 1980-2018 NHIS.
- Under Counterfactual Scenario (γ')

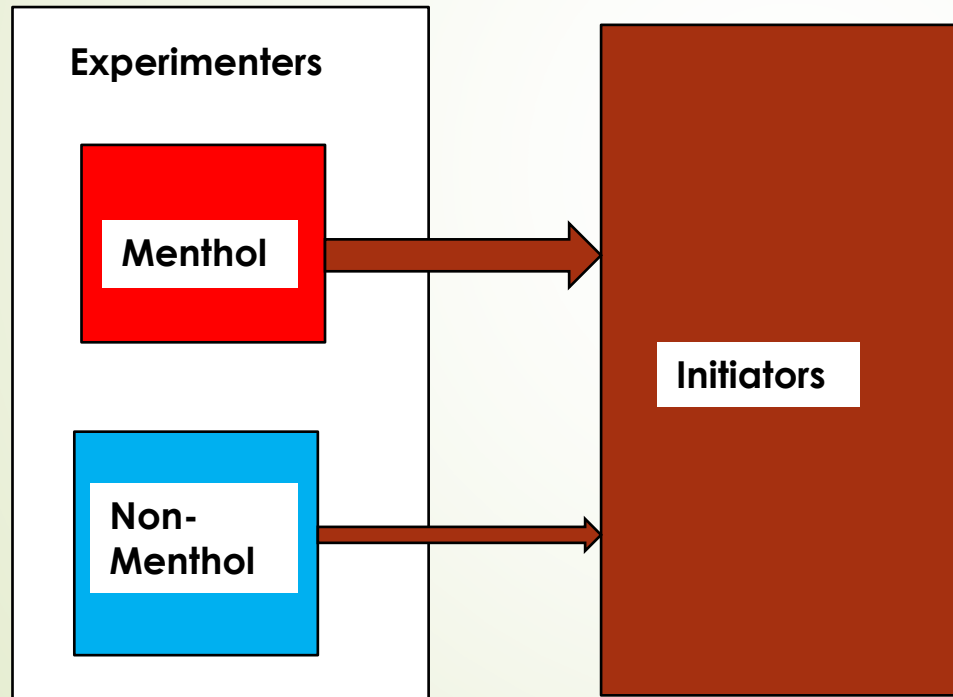
$$\gamma' = \frac{\gamma}{K_4 \times K_5 + (1 - K_4)}$$

γ = Initiation rate under status-quo

γ' = Initiation rate under counterfactual

K_4 = Proportion of Menthol experimenters

K_5 = Ratio of Yields from experimenter to smoker (Menthol/Non-Menthol)



Model Settings (cont'd)

Values of menthol-related parameters for the **General US** and **African American** population

General Population

Parameters	Baseline
Ratio of Yields from Experimenter to Smoker	1.8
Menthol Cessation Multiplier	0.76

African American Population

Parameters	Baseline
Ratio of Yields from Experimenter to Smoker	1.8
Menthol Cessation Multiplier	0.47

Model Fitting and Validation

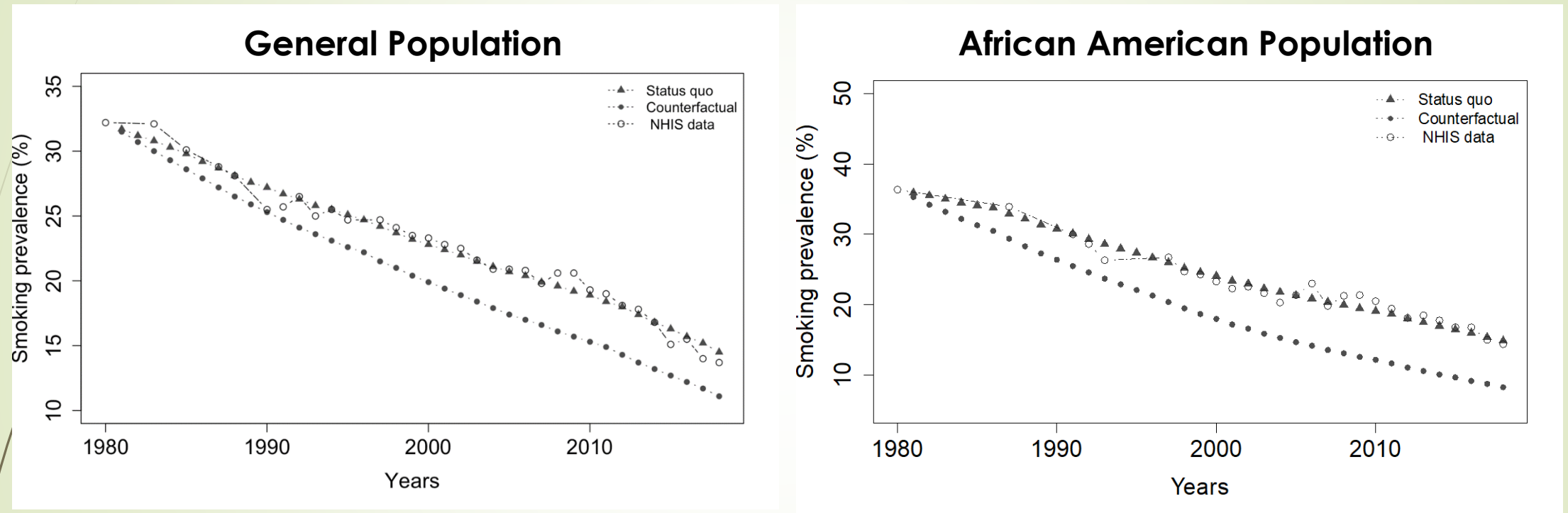


Figure 1: Simulated smoking prevalence under status quo ante and counterfactual scenarios and reported NHIS smoking prevalence over **1980–2018** in the general Population (left, pseudo- $R^2=0.98$) and African American (right, pseudo- $R^2=0.95$).

Performance Measures

Our Public Health performance measures are:

- Number of menthol-smoking-related premature deaths
- Number of Life Years Lost (LYL)
- Number of new smokers due to menthol

Model Results

	Cumulative Excess Smoking Initiators	Cumulative Excess Deaths	Cumulative Excess Life Years Lost	Average Percentage of Population
General population	10,137,808 (100%)	377,528 (100%)	2,951,533 (100%)	(100%)
African American population	1,508,913 (15%)	156,471 (41%)	1,476,198 (50%)	(12%)
Hypothetical low menthol African American population	1,286,848 (13%)	61,132 (16%)	606,840 (21%)	(12%)

Table 1: Excess smoking initiation, smoking-related deaths, and life-years lost due to menthol cigarettes over 1980-2018 for the adult general, African American, and hypothetical low menthol African American population.

The Cost of Delaying a Menthol Ban

- **Question 1:** Between 2011 and 2021, how many premature deaths and life-years lost attributable to menthol cigarette smoking could have been prevented if menthol cigarettes had been banned in 2011?
- **Question 2:** How many premature deaths and life-years would ultimately occur because of a 10-year delay (from 2011) in implementing a menthol cigarette ban?

Methods

- We employed an established population dynamics simulation model of smoking prevalence and health effects that we have used elsewhere to quantify the excess mortality caused by menthol cigarettes from 1980-2018
- To answer each question, we compared two scenarios. One in which a menthol cigarette ban was enacted in 2011 and another in which the ban was enacted in 2021. This allowed us to calculate the effect of delaying the ban for ten years

Question 1: How many preventable menthol-smoking-related premature deaths and life-years lost occurred between 2011 and 2021 among the 2011 cross-section of the population?

- **Scenario 1** – No births from 2011 on. Menthol cigarettes continued in the market after 2011. Observed initiation and cessation rates reflect the effect of menthol cigarettes.
- **Scenario 2** – Menthol cigarettes were removed from the market in 2011, removing their effects on smoking initiation and cessation rates. We assumed that all the people who smoked menthol cigarettes switched to non-menthol brands after the ban.
- **Scenario 3** – This is the same as Scenario 2, but after the ban, all the menthol cigarette users have quit.

Results

Harm Caused from 2011 to 2021 by Failing to Implement a Ban on Menthol Cigarettes in 2011

Menthol Smokers' Behavior After a 2011 Menthol Ban	Premature Deaths	Life-Years Lost
Menthol Smokers Switch to Non-Menthol	14,491	35,186
Menthol Smokers Quit	184,519	585,925

Question 2: What is the lifetime menthol cigarette-related harm to the 2011 population because of a delay of 10 years in implementing a menthol cigarette ban?

- **Scenario 1** – No births from 2011 on. Menthol cigarettes continued in the market until 2021 when a menthol ban would be implemented. Observed initiation and cessation rates were adjusted according to the availability of menthol cigarettes in the market.
- **Scenario 2** – Menthol cigarettes were removed from the market in 2011, removing their effects on smoking initiation and cessation rates. We assumed that all the people who smoked menthol cigarettes switched to non-menthol brands after the ban.

Question 2: What is the lifetime menthol cigarette-related harm to the 2011 population because of a delay of 10 years in implementing a menthol cigarette ban? (cont'd)

- **Scenario 3** – This is the same as Scenario 2, but now all the menthol cigarette users have quit after the ban.
- All three scenarios ran from 2011 to 2104, when all adults alive in 2011 have died.
- The long-term menthol harm reflects that of individuals who started smoking because of menthol between 2011 and 2021.

Results

Lifetime Harm Caused to the 2011 US Population by Delaying a Menthol Cigarette Ban from 2011 to 2021

Menthol Smokers' Behavior After a 2011 Menthol Ban	Premature Deaths	Life-Years Lost
Menthol Smokers Switch to Non-Menthol	577,945 (100%)	9,587,392 (100%)
Menthol Smokers Quit	806,128 (100%)	19,022,277 (100%)

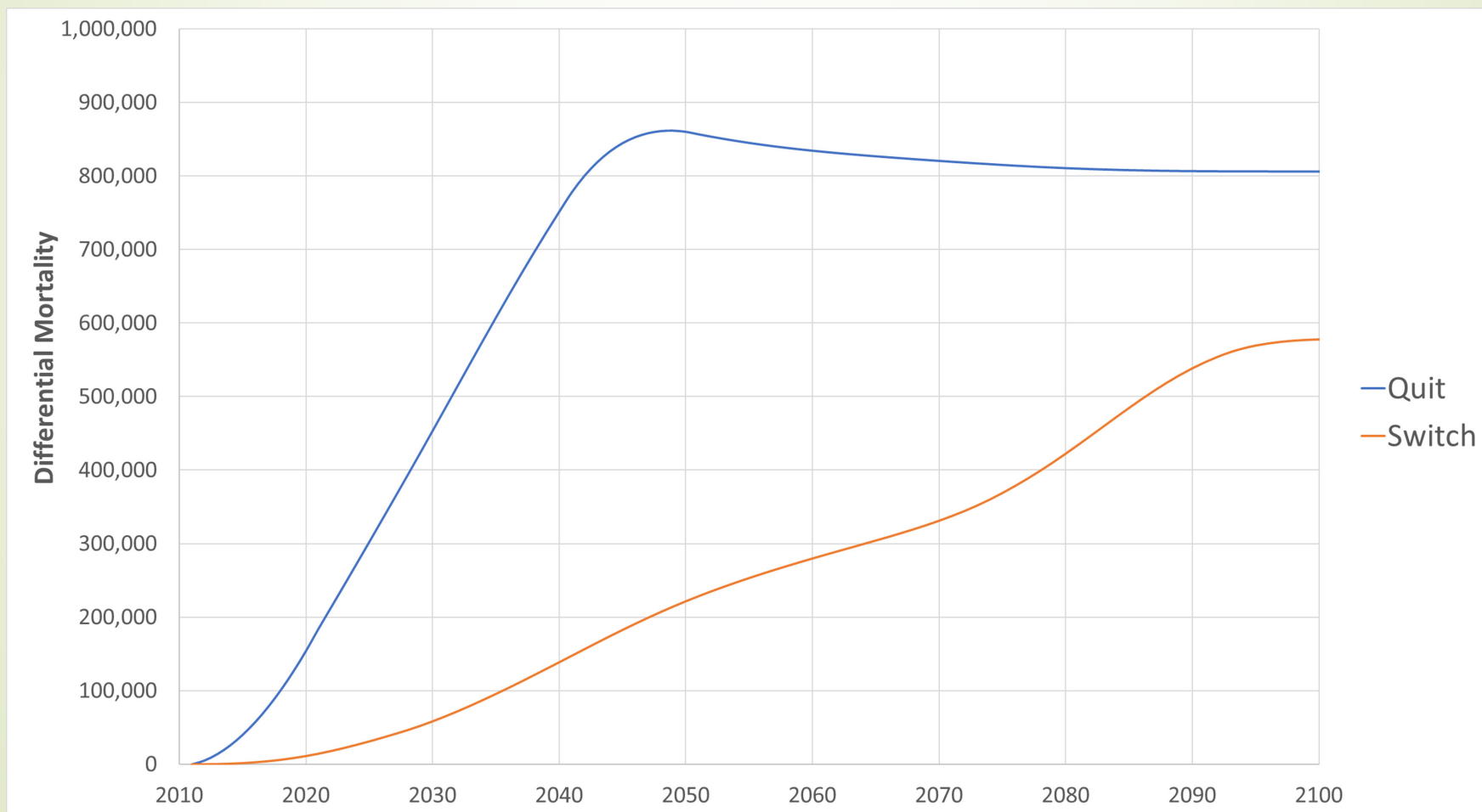
Results (cont'd)

Harm Caused from 2011 to 2021 by Failing to Implement a Ban on Menthol Cigarettes in 2011

Menthol Smokers' Behavior After a 2011 Menthol Ban	Premature Deaths	Life-Years Lost
Menthol Smokers Switch to Non-Menthol	14,491 (2.5%)	35,186 (0.4%)
Menthol Smokers Quit	184,519 (22.9%)	585,925 (3.1%)

Results (cont'd)

Differential Cumulative Premature Deaths Due to a 10-Year Delay in Implementing a Menthol Cigarette Ban



Final Remarks

- **Models on menthol cigarettes have helped to quantify the damage those products have caused, and will likely continue causing, to the US population.**
- All these models have been subject to extensive sensitivity analyses to assess the robustness of their findings.
- The most helpful information produced by these models is not the specific point estimates but the appraisal of the magnitude of the problem and the timing of causes and effects.
- Promoting the corroboration of these findings through different independent modeling studies is key to establishing trust in results supporting regulatory actions.

Final Remarks (cont'd)

- Models on menthol cigarettes have helped quantify the damage those products have caused, and will likely continue causing, to the US population.
- **All these models have been subject to extensive sensitivity analyses to assess the robustness of their findings.**
- The most helpful information produced by these models is not the specific point estimates but the appraisal of the magnitude of the problem and the timing of causes and effects.
- Promoting the corroboration of these findings through different independent modeling studies is key to establishing trust in results supporting regulatory actions.

Final Remarks (cont'd)

- Models on menthol cigarettes have helped quantify the damage those products have caused, and will likely continue causing, to the US population.
- All these models have been subject to extensive sensitivity analyses to assess the robustness of their findings.
- **The most helpful information produced by these models is not the specific point estimates but the appraisal of the magnitude of the problem and the timing of causes and effects.**
- Promoting the corroboration of these findings through different independent modeling studies is key to establishing trust in results supporting regulatory actions.

Final Remarks (cont'd)

- Models on menthol cigarettes have helped quantify the damage those products have caused, and will likely continue causing, to the US population.
- All these models have been subject to extensive sensitivity analyses to assess the robustness of their findings.
- The most helpful information produced by these models is not the specific point estimates but the appraisal of the magnitude of the problem and the timing of causes and effects.
- **Promoting the corroboration of these findings through different independent modeling studies is key to establishing trust in results supporting regulatory actions.**



Thank You

Methods: Mind the Gap Webinar Series

- Updates on Research Methods Resources (researchmethodsresources.nih.gov)
 - Time-varying intervention effects in Stepped Wedge Designs
 - Group Regression Discontinuity Design section with background, key references, and a sample size calculator.