

AN EXAMINATION OF THE DIFFERENTIAL POPULATION HEALTH IMPACT BETWEEN AN IMMEDIATE VS GRADUAL NICOTINE REDUCTION IN CIGARETTES: A SIMULATION ANALYSIS

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I. Introduction

- In 2022, the US Food and Drug Administration (FDA) issued a public announcement renewing its intention to reduce nicotine in combustibles to non-addictive levels.
- A 2018 *NEJM* study estimated that an instantaneous reduction in nicotine to non-addictive levels in 2020 would prevent 8.5 million smoking-related premature deaths, totaling 134.4 million life-years-saved by 2100. Since then, the background smoking initiation rate has continued to fall, and the cessation rate has increased.
- Due to these changes, the potential impact of implementing the nicotine reduction policy must be re-evaluated. Additionally, the FDA must consider different implementation timelines for potential regulatory actions.
- While a 2018 *JAMA* paper reported that immediate nicotine reduction in cigarettes produced a larger decline of biomarkers of smoke exposure compared to a gradual reduction, the implications of these findings at the population level have not yet been studied

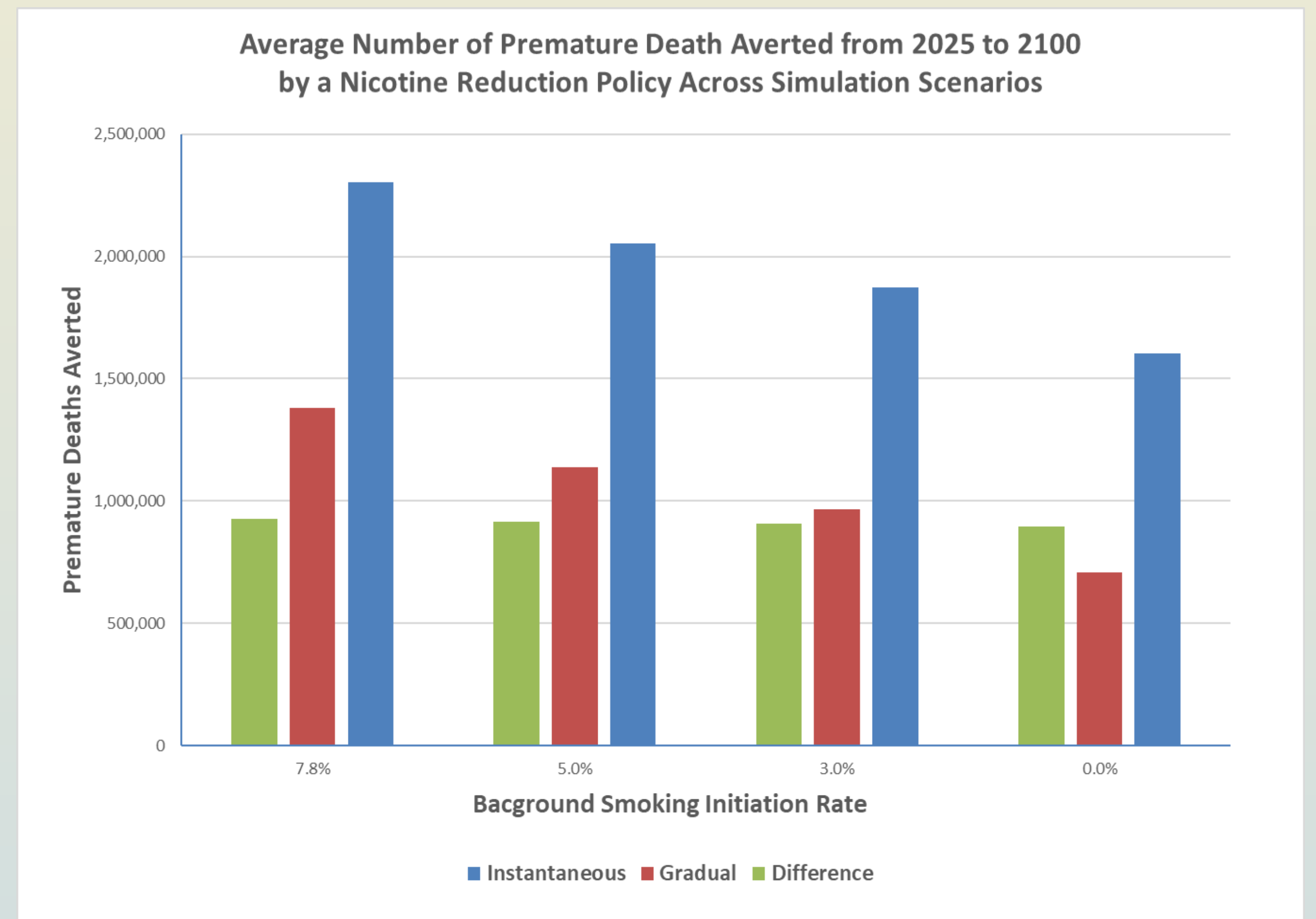
II. Study Objectives

- To develop estimates of the public health effect of a policy to reduce the nicotine levels in combustible to non-addictive levels using more current initiation and cessation rates.
- To evaluate the difference in effectiveness between an instantaneous and a gradual nicotine reduction policy.
- To evaluate the public health cost of delaying the reduction of nicotine in combustibles to non-addictive levels.

III. Methods

- We used a population-dynamics simulation model of smoking prevalence and health effects (the Mendez-Warner model) to calculate and contrast the cumulative mortality over 2025 – 2100 between an immediate and a gradual (over ten years) nicotine reduction regime.
- We parameterized the model with NHIS data and published results of RCTs of nicotine reduction and recommendations from an expert panel.
- We then performed a sensitivity analysis by simulating 40 different scenarios varying the effects of nicotine reduction in the smoking cessation rate (100%, 133%, 167%, 200% increase) and the persistence of those effects indefinitely and increasing to 80% cessation after 15 years, under five different background initiation rates (13%, 7.8%, 5%, 3%, and 0%).
- Each of the simulated scenarios consisted of two runs, depicting an immediate and gradual reduction of nicotine in cigarettes. We then reported the difference in cumulative mortality between the immediate and gradual runs for each scenario.
- We performed sensitivity analyses, assuming the background cessation rate will continue to increase at the same rate it has for the past ten years; we also investigated the potential effect of a black market that would reduce the effect of the nicotine reduction policy on smoking cessation by 10% and 20%

IV. Results



- An instantaneous nicotine reduction policy enacted in 2025 will prevent, on average, between 1.6 and 2.3 million premature deaths and 30-45M Life-years lost (LYL) by 2100 if current smoking initiation and cessation rates persist.
- A gradual implementation of the policy (2025-2035) will prevent, on average, between 0.7 and 1.3 million premature deaths by 2100.
- On average, an instantaneous policy implementation will save around 900K more lives than a gradual policy implementation by 2100. This figure represents a 39% - 56% reduction of the benefits attained by an instantaneous policy.
- On average, the difference in LYS between the two policy implementations would be between 12 and 21 million by 2100.

V. Conclusions

- Gradually implementing a nicotine reduction policy is tantamount to delaying its effects since there will not be population effects until nicotine levels are near non-addictive levels. This implies that the cost of delaying the nicotine reduction policy for 10 years will be around 900K premature deaths and between 12 and 21 million LYL by 2100.
- A nicotine reduction policy will become less effective as background cessation rates and initiation rates decrease. However, even in the extreme case of smoking initiation rates dropping down to zero, the policy will still save more than 1M lives by 2100.
- Time is of the essence. Only around 40% of smoking-related premature deaths between 2025 and 2100 can be prevented. Of those, our results show that around 50% could be prevented by an instantaneous nicotine reduction policy implemented in 2025.

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