The Public Health Gains Had Cigarette Companies Chosen to Sell Very Low Nicotine Cigarettes

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Background and Purpose

- The US Food and Drug Administration has proposed lowering the nicotine content of cigarettes to a minimally addictive level to increase smoking cessation and reduce initiation. Apelberg et al (NEJM, 2018) has projected potential future impacts.
- This study examines potential impacts of past implementation by the industry and their dependence on time of implementation. Based on a paper by Levy et al. NTR (2021) entitled *The Public Health Gains Had Cigarette Companies Chosen to Sell Very Low Nicotine Cigarettes: https://academic.oup.com/ntr/article/23/3/438/5868042*.
- This study had two direct aims: 1) to determine when cigarette manufacturers had the technical capability to reduce cigarette nicotine content; and 2) to estimate the lost public health benefits from not implementing a standard in 1965, 1975, or 1985.

Past history

- To assess when cigarette manufacturers had the technical capability to lower nicotine in the tobacco used in cigarettes, we conducted a review of public patents on nicotine removal in tobacco and internal cigarette company business records accessed from the Truth Tobacco Industry Documents website housed at University of California San Francisco.
- We found patents and internal company documents dating back to the 1920s and 1930s which describe methods to extract nicotine from tobacco. Clearly, capabilities were available by 1964 after the SGR.

Status Quo Model (absence of industry policy)

- The model is initialized in 1964 with separate prevalence rates classified by never, current, and former cigarette smokers from NHIS. To project smoking rates forward from 1964, we apply age-, sex-, and year-specific initiation, cessation, and mortality probabilities developed by applying an age-period-cohort statistical model to data from the 1965-2018 NHIS.
- Initiation is based on respondents' stated ages of initiation. Cessation is measured as the percent quit from smoking for $\leq$ 2 years to approximate cessation net of relapse, assuming those who quit $\leq$ 2 years are offset by those who relapse > 2 years. The initiation and cessation probabilities were validated by comparing projections from 1965-2018 against NHIS smoking prevalence rates.
- A percentage of never, current, and former smokers die each year based on smoking status- age-, sex- and year-specific mortality probabilities.

Modeling the Impact of Nicotine reduction Policy

- We rely primarily on Apelberg et al. (NEJM 2018) for impacts of an industry standard for VLNCs. Applying an expert elicitation (EE) technique, experts provided a range of probabilistic estimates of the impact on initiation, cessation and product switching in response to a very low nicotine standard on cigarettes, taking into account other product use. Besides using their midpoint estimates as the most plausible parameters, we used the 25th and 75th percentile estimates from their lower and upper estimates to develop initiation and cessation multipliers and examined more recent literature.

Multipliers of smoking initiation and cessation rates by age and sex in the *Status Quo Scenario* and *Reduced Nicotine Scenarios* (midpoint, lower bound, and upper bound)

	Status Quo		Reduced Nicotine Midpoint		Reduced Nicotine Lower Bound		Reduced Nicotine Upper Bound	
	Male	Female	Male	Female	Male	Female	Male	Female
Initiation year 1	100%	100%	50%	50%	65%	70%	25%	25%
Initiation year N	100%	100%	50%	50%	65%	70%	25%	25%
Cessation year 1 (≤ 64)	100%	100%	600%	600%	300%	300%	1000%	1000%
Cessation year 1 (≥ 65)	100%	100%	300%	300%	200%	200%	500%	500%
Cessation year N (≤ 64)	100%	100%	300%	300%	200%	200%	500%	500%
Cessation year N (≥ 65)	100%	100%	200%	200%	150%	150%	250%	250%

Public Health Impacts

- We conducted three sets of analyses with start dates when normal cigarettes (Status Quo) are replaced by very low nicotine cigarettes (VLNCs) in 1965, 1975 and 1985.
- The public health impacts are gauged in terms of the relative difference in current and former smoking prevalence and the absolute difference in smoking-attributable deaths (SADs) and life years lost (LYL) between the status quo and VLNC Scenarios.
- The impact of VLNCs on smoking prevalence and deaths is projected over a 100-year horizon in order to incorporate the effects on mortality of those impacted at early ages when initiation takes place. The cumulative public health impact is determined by summing SADs and LYLs between the *Status Quo* and *Very Low Nicotine Scenarios* over the 100-year horizon.

Population impacts on male smoking prevalence, smoking attributable deaths, and life-years-lost in the *Status Quo Scenario* and *Very Low Nicotine Scenarios* (midpoint, lower bound, and upper bound) if very low nicotine content cigarettes begin in 1965

Male		Prevalence				Cumulative Impact*		
		1964	1990	2015	2064	1965-1990	1965-2015	1965-2064
Status Quo	Current	56.9%	34.8%	20.0%	6.3%	-	-	-
	Former	16.1%	25.3%	25.5%	20.6%	-	-	-
	SADs	250,701	284,725	295,371	172,499	7,191,782	14,370,583	26,505,181
	LYLs	2,956,834	3,406,323	3,892,702	1,337,864	85,813,480	178,617,477	293,682,931
VLNC: Mid-point	Current	56.9%	12.1%	4.0%	1.3%	-65.3%	-80.0%	-79.5%
	Former	16.1%	24.9%	13.8%	4.9%	-1.7%	-45.8%	-76.1%
	Averted SADs	-	109,115	169,830	133,762	2,143,512	5,461,853	13,922,577
	Averted LYLs	-	1,813,044	2,919,507	1,092,477	31,828,245	93,283,758	184,122,616
VLNC: Lower Bound	Current	56.9%	19.4%	8.1%	2.4%	-44.2%	-59.7%	-62.1%
	Former	16.1%	26.0%	18.7%	9.0%	2.5%	-26.7%	-56.1%
	Averted SADs	-	76,664	123,647	100,269	1,323,666	3,730,136	9,989,982
	Averted LYLs	-	1,240,005	2,179,537	856,810	19,426,216	63,799,750	134,256,734
VLNC: Upper Bound	Current	56.9%	4.4%	1.0%	0.4%	-87.4%	-94.8%	-93.6%
	Former	16.1%	21.5%	6.9%	1.5%	-15.3%	-72.8%	-92.6%
	Averted SADs	-	129,515	209,341	161,211	2,889,890	6,885,155	17,382,498
	Averted LYLs	-	2,233,913	3,454,269	1,266,465	43,941,649	117,868,590	224,382,828

Notes: VLNC = very low nicotine cigarette, SADs = smoking attributable deaths, Av SADs = averted SADs, LYL is life-years lost, and LYG is life-years gained.
* Cumulative impact = the cumulative SADs or LYLs in the *Status Quo* minus the cumulative SADs or LYL under the *Very Low Nicotine Scenario.*

Population impacts on female smoking prevalence, smoking attributable deaths, and life-years-lost in the *Status Quo Scenario* and *Very Low Nicotine Scenarios* (midpoint, lower bound, and upper bound) if very low nicotine content cigarettes begin in 1965

Female		Prevalence				Cumulative Impact*		
		1964	1990	2015	2064	1965-1990	1965-2015	1965-2064
Status Quo	Current	35.4%	30.3%	16.4%	5.8%	-	-	-
	Former	5.3%	16.3%	21.3%	13.8%	-	-	-
	SADs	36,062	143,063	140,210	69,488	2,466,932	6,019,333	11,874,669
	LYLs	535,523	1,693,556	1,802,867	506,462	32,660,960	75,509,106	130,100,508
VLNC: Mid-point	Current	35.4%	10.9%	3.0%	1.1%	-64.0%	-81.8%	-80.6%
	Former	5.3%	17.6%	12.4%	3.7%	8.1%	-41.8%	-73.4%
	Averted SADs	-	65,996	86,991	54,470	709,421	2,743,448	6,979,170
	Averted LYLs	-	930,881	1,446,923	433,375	11,093,005	42,058,134	87,770,714
VLNC: Lower Bound	Current	35.4%	18.2%	6.7%	2.3%	-40.0%	-59.0%	-60.3%
	Former	5.3%	17.6%	16.8%	7.0%	8.3%	-20.9%	-48.9%
	Averted SADs	-	42,163	65,896	39,875	417,804	1,877,048	5,032,362
	Averted LYLs	-	595,637	1,095,339	343,862	6,498,068	28,666,477	64,466,439
VLNC: Upper Bound	Current	35.4%	3.9%	0.7%	0.3%	-87.0%	-95.7%	-94.2%
	Former	5.3%	16.2%	6.8%	1.1%	-0.7%	-68.2%	-91.9%
	Averted SADs	-	84,414	99,593	65,101	1,008,200	3,377,404	8,432,576
	Averted LYLs	-	1,203,894	1,629,609	486,213	16,111,287	52,286,157	103,633,965

Notes: VLNC = very low nicotine cigarette, SADs = smoking attributable deaths, Av SADs = averted SADs, LYL is life-years lost, and LYG is life-years gained.
* Cumulative impact = the cumulative SADs or LYLs in the *Status Quo* minus the cumulative SADs or LYL under the *Very Low Nicotine Scenario.*

Population impacts on male smoking prevalence, smoking attributable deaths, and life-years-lost in the *Status Quo Scenario* and *Very Low Nicotine Scenarios* (midpoint, lower bound, and upper bound) if very low nicotine content cigarettes begin in 1985

		Prevalence				Cumulative Impact*		
		1984	2010	2035	2084	1985-2010	1985-2035	1985-2084
Status Quo	Current	38.3%	23.0%	9.8%	6.0%	-	-	-
	Former	23.8%	25.3%	25.0%	19.1%	-	-	-
	SADs	293,713	277,917	266,517	140,838	7,402,872	14,446,092	23,926,684
	LYLs	3,452,870	3,758,528	2,494,757	1,106,055	92,848,239	175,020,600	249,947,585
VLNC: Mid-point	Current	38.3%	6.5%	1.6%	1.3%	-71.8%	-84.2%	-79.2%
	Former	23.8%	24.6%	11.9%	4.4%	-2.7%	-52.6%	-77.1%
	Averted SADs	-	97,462	112,980	114,188	1,969,861	4,657,324	10,788,561
	Averted LYLs	-	1,987,480	1,635,166	917,122	35,504,840	84,454,901	141,932,779
VLNC: Lower Bound	Current	38.3%	11.7%	3.2%	2.3%	-49.1%	-67.1%	-61.7%
	Former	23.8%	25.5%	16.5%	8.1%	0.9%	-33.9%	-57.6%
	Averted SADs	-	67,008	82,036	88,312	1,207,009	3,159,122	7,671,983
	Averted LYLs	-	1,335,622	1,263,731	727,749	21,483,723	57,391,419	102,322,668
VLNC: Upper Bound	Current	38.3%	1.9%	0.4%	0.4%	-91.6%	-95.4%	-93.5%
	Former	23.8%	21.8%	6.8%	1.4%	-13.9%	-72.9%	-92.8%
	Averted SADs	-	117,818	143,389	132,991	2,648,680	5,884,081	13,487,304
	Averted LYLs	-	2,471,537	1,936,857	1,050,105	48,845,449	106,894,149	174,224,056

Notes: VLNC = very low nicotine cigarette, SADs = smoking attributable deaths, Av SADs = averted SADs, LYL is life-years lost, and LYG is life-years gained.
* Cumulative impact = the cumulative SADs or LYLs in the *Status Quo* minus the cumulative SADs or LYL under the *Very Low Nicotine Scenario.*

Population impacts on female smoking prevalence, smoking attributable deaths, and life-years-lost in the *Status Quo Scenario* and *Very Low Nicotine Scenarios* (midpoint, lower bound, and upper bound) if very low nicotine content cigarettes begin in 1985

		Prevalence				Cumulative Impact*		
		1984	2010	2035	2084	1985-2010	1985-2035	1985-2084
Status Quo	Current	30.2%	18.5%	8.3%	5.6%	-	-	-
	Former	13.3%	20.3%	19.8%	12.1%	-	-	-
	SADs	110,276	125,285	128,213	50,040	3,287,700	6,505,976	10,662,178
	LYLs	1,451,209	1,607,498	1,238,318	403,852	40,277,255	78,485,526	110,013,751
VLNC: Mid-point	Current	30.2%	5.0%	1.3%	1.1%	-72.8%	-84.5%	-80.6%
	Former	13.3%	20.4%	10.8%	3.2%	0.7%	-45.3%	-73.9%
	Averted SADs	-	61,430	63,601	41,086	1,183,954	2,776,873	5,466,989
	Averted LYLs	-	1,030,903	892,943	351,161	17,836,252	44,403,732	69,547,665
VLNC: Lower Bound	Current	30.2%	9.6%	2.9%	2.2%	-47.9%	-64.6%	-60.2%
	Former	13.3%	21.0%	14.7%	6.1%	3.8%	-25.7%	-49.6%
	Averted SADs	-	42,202	48,822	30,934	719,291	1,908,987	3,895,300
	Averted LYLs	-	695,776	703,727	281,352	10,779,356	30,463,873	50,445,154
VLNC: Upper Bound	Current	30.2%	1.4%	0.4%	0.3%	-92.3%	-95.7%	-94.2%
	Former	13.3%	18.4%	6.8%	1.0%	-9.2%	-65.8%	-92.0%
	Averted SADs	-	72,645	73,969	47,512	1,587,175	3,393,696	6,649,224
	Averted LYLs	-	1,250,409	1,000,678	389,493	24,351,522	54,605,585	82,971,737

Notes: VLNC = very low nicotine cigarette, SADs = smoking attributable deaths, Av SADs = averted SADs, LYL is life-years lost, and LYG is life-years gained.
* Cumulative impact = the cumulative SADs or LYLs in the *Status Quo* minus the cumulative SADs or LYL under the *Very Low Nicotine Scenario.*

Summary

- Based on our review of public patents on nicotine removal from tobacco and company business records, commercially feasible designs for VLNCs have long existed. Cigarette companies had the opportunity to market VLNCs once the 1964 Surgeon General Report made clear that their cigarettes were deadly.

- Had cigarette companies chosen to sell VLNCs starting in 1965, we estimate that 20.9 (15.0-25.8) million SADs and 271.9 (198.7-328.0) million LYLs would have been averted over 100 years, representing a 54% reduction in SADs and a 64% reduction in LYLs. If VLNCs were implemented in 1975, 18.9 (13.3-23.3) million SADs and 245.4 (178.6-296.3) million LYLs would have been averted. Delaying to 1985 would avert 16.3 (11.6-20.1) million SADs and 211.5 (152.8-257.2) million LYLs.

- Apelberg et al. (2018) estimated that a government-imposed cigarette nicotine reduction standard would now avert 8.5 million SADs and 33.1 million LYLs by 2100.

Limitations

- VLNC effect sizes are based on an FDA expert elicitation, much of which is is based on clinical trials, with potential non-compliance, or self-reported reactions by smokers. Clinical studies have not considered smoking initiation impacts for ethical reasons. We also did not incorporate the potential role of compensation, e.g., inhaling deeper, but evidence indicates that problem may be temporary.
- We did not consider that smokers may substitute other forms of nicotine delivery products tobacco, such as smokeless tobacco, cigars and most notably e-cigarettes. However, the FDA EE attempted to distinguish switching to alternative delivery products. Our results are based primarily on those quitting all nicotine use.
- The status quo results are based on smoking rates from 1964-2018 and do not incorporate the impact of policies nor industry counter-marketing.

Final thoughts

- The results of this study demonstrate lives lost as a result of choices made by the cigarette companies, providing evidence of the impact of past industry marketing practices. Our sensitivity analyses indicate that even pessimistic assumptions about VLNC impacts yield major public health gains.
- We also show the need for rapid action to mitigate continued public health harm. Timing matters. Policy delay yields less policy impact.
- Alternative nicotine-delivery products are likely to play a key role by providing a substitute for cigarettes and reducing illicit market use. We now have better information about those impact. We may soon have evidence Re: an actual policy in New Zealand.

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