

Nicotine: Role of nicotine in harm reduction and misperceptions on the harm of nicotine

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1

That humanity at large will ever be able to dispense with Artificial Paradises seems very unlikely. Most men and women lead lives at the worst so painful, at the best so monotonous, poor and limited that the urge to escape, the longing to transcend themselves if only for a few moments, is and has always been one of the principal appetites of the soul.

Aldous Huxley

2

CULTURAL DRUGS

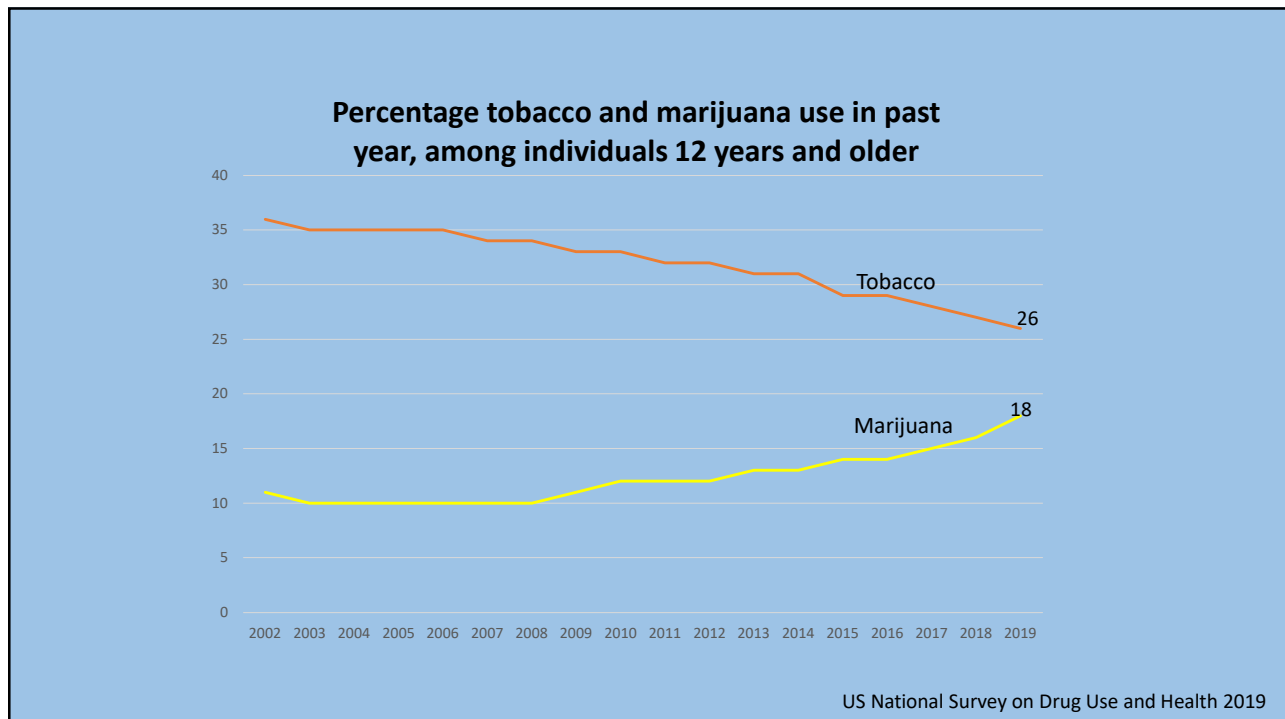
- ALCOHOL, BEER, WINE, HARD LIQUER
- CAFFEINE, SODA, TEA, COFFEE
- NICOTINE, CLEAN NIC. SMOKELESS, COMBUSTIBLES

Semi cultural

- THC, marijuana etc



3



4

Nicotine/Tobacco is an ideal area for harm reduction.

Used largely because of nicotine.

Pure nicotine, and even unburned tobacco, is not a big part of the problem: the health consequences.

5

Harmful effects from nicotine

- Adversely affects the foetus and can complicate delivery
- Can possibly increase risk of diabetes typ 2 in very heavy users
- Can make the consequences of myocardial infarction and stroke worse

Positive effects from nicotine

- A cognitive enhancer
- Can prevent Parkinsons disease, ulcerative colitis and possibly multiple sclerosis
- Appetite supressant and increases energy turnover

6

Examples with products and countries where HR is in operation

7



8

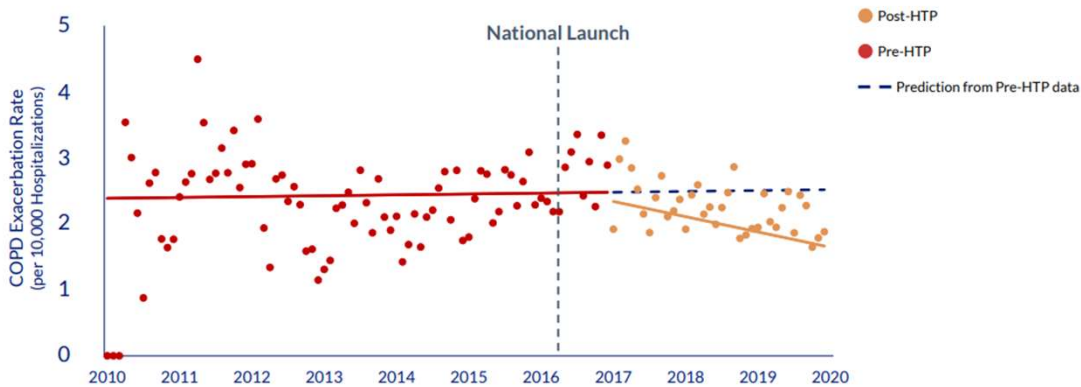
Diapositive 8

KF1 Karl Fagerström; 12/11/2021

Real-World Evidence: Japan Study on COPD



COPD Exacerbation Hospitalization Rate Over Time
MDV Hospital Records

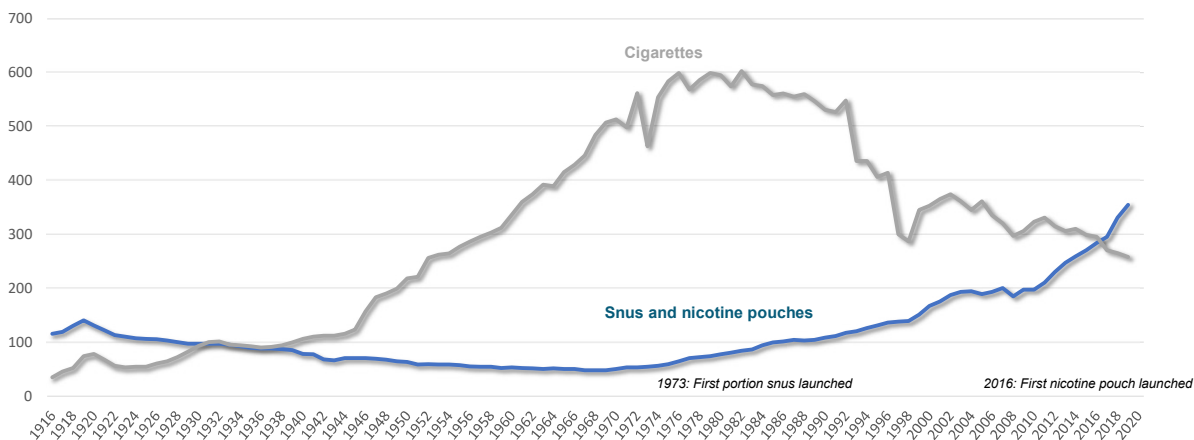


Note: Model adjusting for age and sex. COPD stands for Chronic Obstructive Pulmonary Disease. Observational time-trend analysis looking at temporal associations and not designed to assess cause and effect. Specific factors associated with changing hospitalization rates over time have not been fully analyzed. Subject to inherent limitations of ecological analysis. Source: MDV Diagnosis Procedure Combination Data. <https://en.mdv.co.jp/> (January 13, 2021)

10

9

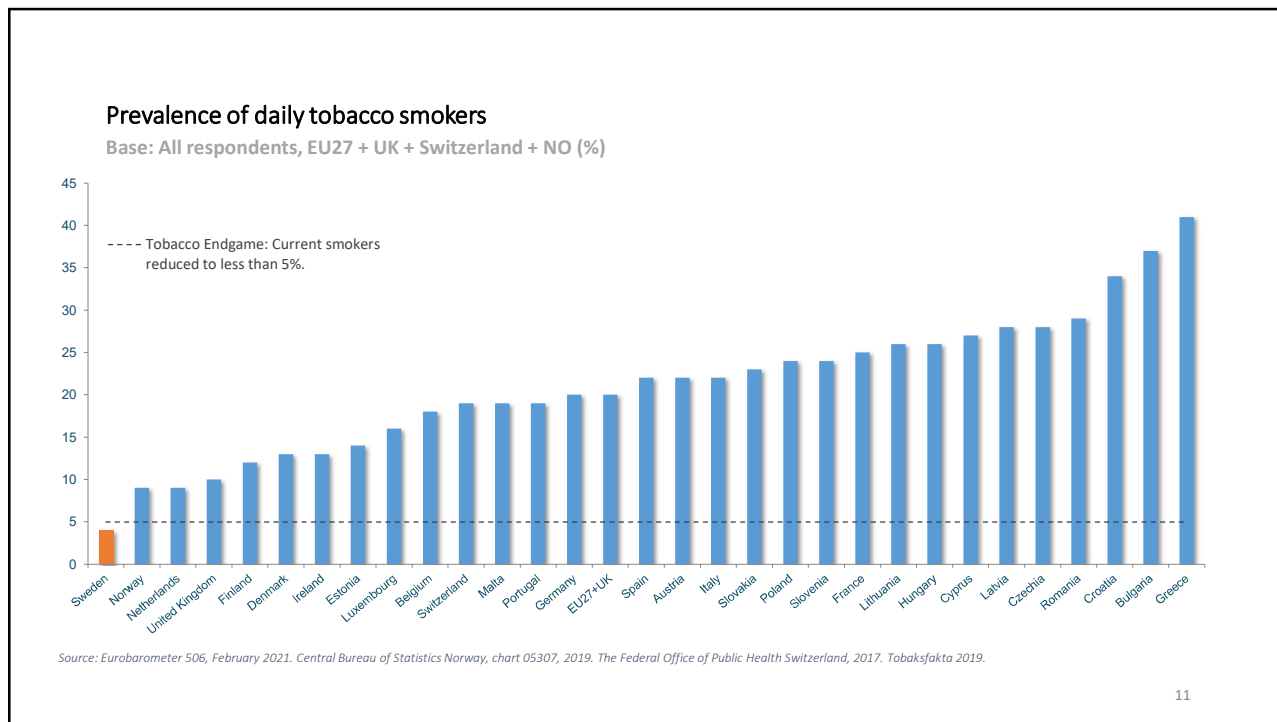
Volumes sold per year, in million packs/cans in Sweden



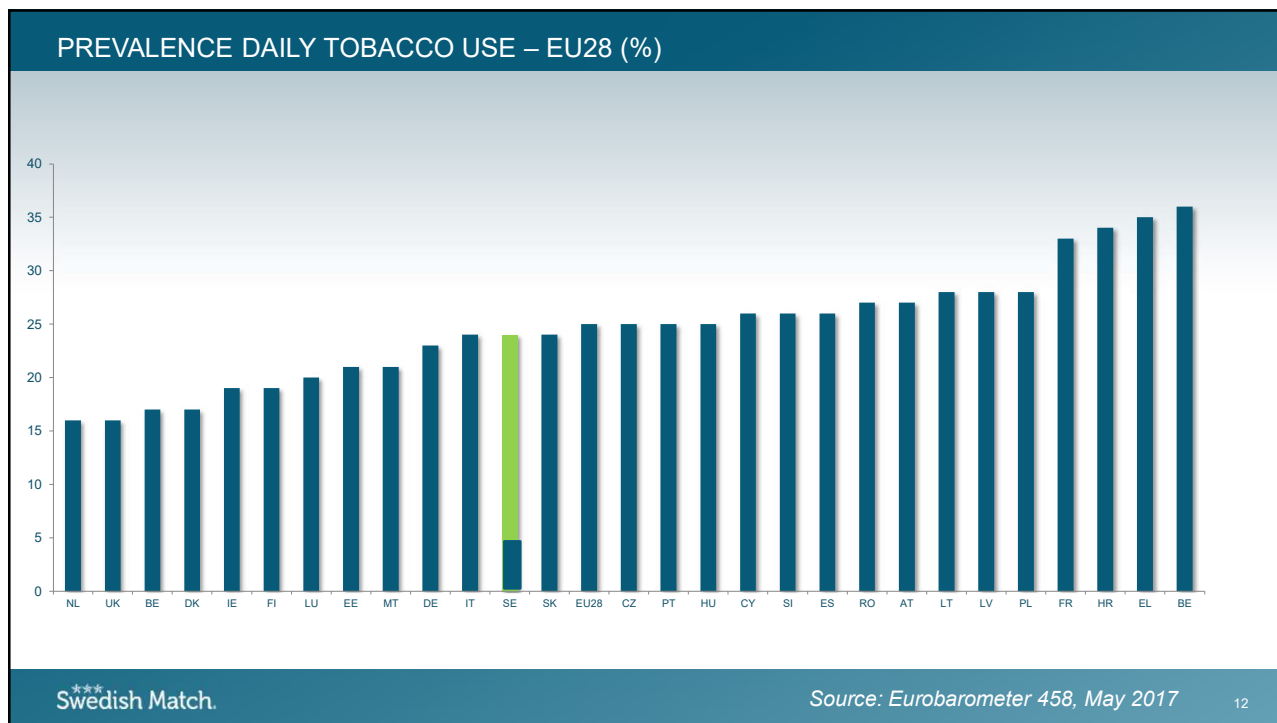
Source: Swedish Match estimates, SMD Logistics.

10

10



11



12

DEATH RATES (PER 100000) ATTRIBUTABLE TO TOBACCO, WHO 2012

	Sweden	European Union Member States other than Sweden		
		Min	Median	Max
MEN (age 60-69)				
Lung cancer	87	91	220	399
Other cancer	36	41	105	217
All cardiovascular	72	107	170	618
All causes	222	378	550	1388

THE GLOBAL BURDEN OF DISEASE STUDY, SWEDEN AND THE REST OF EU 2017

	Sweden	European member states other than Sweden		
		Lowest	Weighted mean	Highest
Total all cases				
Men total population	70	76	125	252
Men age 50-54	38	61	130	412
Women total population	52	19	44	79

Data calculated by Lars Ramström lr@tobaccostudies.com

13

Tobacco-related deaths among men over the age of 30 in the EU+Norway 2004

http://snuskommissionen.se/wp-content/uploads/2017/06/Snuskommissionen_rapport3_eng_PRINT.pdf

Country	Population (number of men over 30, millions)	Tobacco-related deaths per year	If mortality rate were in line with Swedish rate	Different in no. of deaths
Belgium	3,196	15 660	4 511	-11 149
Bulgaria	2,371	12 566	3 406	-9 160
Cyprus	0,221	422	284	-138
Denmark	1,674	6 160	2 254	-3 906
Estonia	0,358	2 277	445	-1 832
Finland	1,589	3 766	2 105	-1 661
France	17,896	59 057	25 364	-33 693
Greece	3,484	13 483	5 223	-8 260
Ireland	1,092	3 286	1 292	-1 994
Italy	19,080	65 444	28 284	-37 160
Croatia	1,349	7 150	1 781	-5 369
Latvia	0,624	4 100	767	-3 333
Lithuania	0,916	5 249	1 105	-4144
Luxembourg	0,138	428	164	-264
Malta	0,116	339	144	-195
Netherlands	5,050	18 180	6 219	-11 961
Poland	10,430	59 034	12 304	-46 730
Portugal	3,107	8 948	4 410	-4 538
Romania	6,140	31 314	7 882	-23 432
Slovakia	1,459	6 843	1 600	-5 243
Slovenia	0,609	2 625	734	-1 891
Spain	13,260	47 736	18 655	-29 081
Great Britain	17,939	61 890	25 438	-36 452
Sweden	2,807	4 267	4 267	0
Czech Republic	3,025	13 492	3 738	-9 754
Germany	26,858	80 843	36 370	-44 473
Hungary	2,878	20 117	3 654	-16 463
Austria	2,597	6 415	3 319	-3 096
Whole EU	150,263	561 091	205 719	-355 372
Norway	1,386	3 396	1 880	-1 516

14

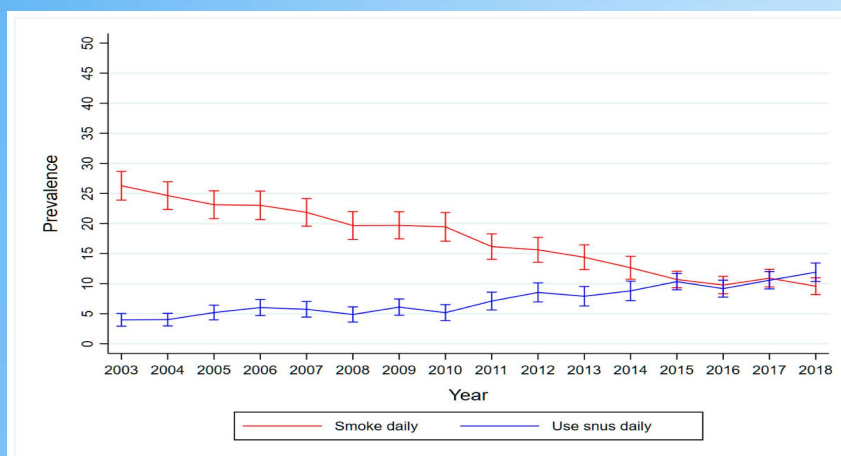
Swedish snus was the first, and so far the only, product to be recognised as a less harmful tobacco product by the US Federal Food and Drug Administration

“the available scientific evidence, including long-term epidemiological studies, shows that relative to cigarette smoking, exclusive use of these specific smokeless tobacco products poses lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis”

<https://www.fda.gov/news-events/press-announcements/fda-grants-first-ever-modified-risk-orders-eight-smokeless-tobacco-products>

15

Smoking and snus use in Norway



Lund et al. Int. J. Environ. Res. Public Health 2019

16

Nicotine intake in perspective.

The nicotine intake among snus users is similar or somewhat higher than from cigarettes [Russell et al., 1981](#)

The nicotine intake from snus is clearly higher than from NRT products. [Lunell and Curvall 2011](#)

17

Nicotine pouches. The most recent harm reduction product.



In 2008, Nicovum registered the first non-tobacco nicotine pouch Zonic as a medicinal NRT

Products normally contain between 2 and 12 mg nicotine/pouch



18

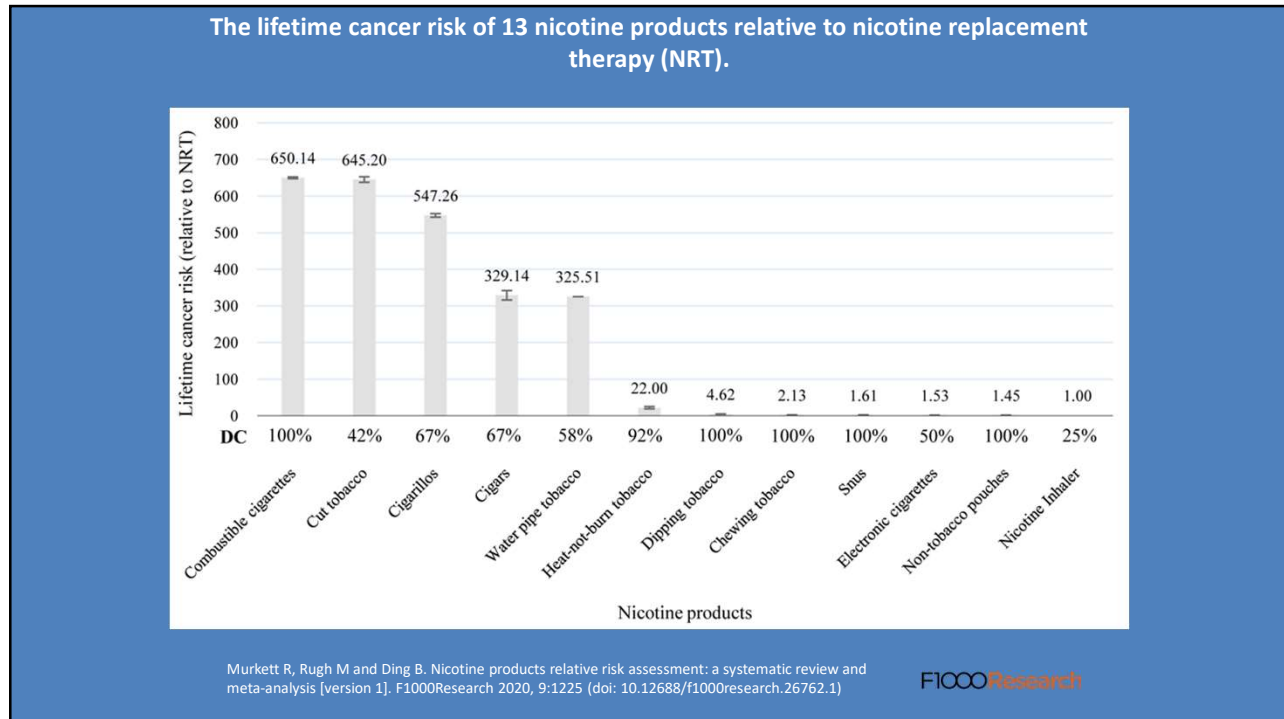
Ingredients in Zonic (NRT)	Ingredients in the market leader Zyn (consumer product)	Ingredients in Nicorette chewing gum
Pharma grade nicotine	• Pharma grade nicotine	Pharma grade nicotine
Microcrystalline cellulose	• Hydroxypropyl cellulose.	Gum base
Trisodium phosphate	• Microcrystalline cellulose	Glycerine
Acesulfame potassium E950	• Malitol	
Ascorbyl palmitate	• Sodium carbonate	Sodium carbonate
Flavorings mint	• Sodium bicarbonate	Sodium bicarbonate
Aspartame E951.	• Acesulfame potassium	Acesulfame potassium
	• Flavourings	Flavourings

The health and adverse effects would be very similar to NRTs

19

Analytes	Unit	Average for nicotine gum 4mg and lozenge 4mg (Nicorette)	Average for 4 different nicotine pouches (Lyft)	
Formaldehyde	µg/g	<1.0	<1.0	<p>Harmful and potentially harmful constituents</p> <p>Red = NRT>Pouch Yellow= Pouch >NRT</p> <p>Azzopardi et al. 2021</p>
Acetaldehyde	µg/g	<1.0	<1.0	
Acrolein	µg/g	<0.05	<0.05	
Crotonaldehyde	µg/g	<0.05	<0.05	
NAB	ng/g	<10	<10	
NAT	ng/g	<10	<10	
NNN	ng/g	<10	<10	
NNK	ng/g	<10	<10	
NDMA	ng/g	<0.2	<0.2	
Benzo(a)pyrene	ng/g	<1.0	<1.0	
1,3 Butadine	ng/g	<20	<20	
Benzene	ng/g	<5.0	<5.0	
Cadmium	ng/g	<20	<10	
Chromium	ng/g	397	113	
Mercury	ng/g	<20	<20	
Nickel	ng/g	151	<50	
Arsenic	ng/g	<50	<50	
Lead	ng/g	37	<20	
Nitrate	µg	<1.0	<1.0	
Aflatoxin B1	ng/g	<1.0	<1.0	
Aflatoxin B2	ng/g	<0.5	<1.0	
Aflatoxin G1	ng/g	<0.5	<1.0	
Aflatoxin G2	ng/g	<0.5	<1.0	
Ochratoxin A	ng/g	<0.5	<0.5	

20



21

NRT: dual use, long term use and dependence.

MHRA in UK.

Indicated as "a safer alternative to smoking and can be used long term"
([medicines.org.uk/emc](https://www.medicines.org.uk/emc))

FDA in USA

"Use of NRT products with cigarettes or with other nicotine-containing products does not raise significant concerns".

"Current marketed NRT products do not appear to have significant potential for abuse or dependence"

(<https://www.federalregister.gov/documents/2013/04/02/2013-07528/modifications-to-labeling-of-nicotine-replacement-therapy-products-for-over-the-counter-human-use>)

Important studies for the above Murray et al. 1996, 2009 and Joseph et al. 2011.

22

Flavourings can be important for adult consumers but...



23

Tobacco free nicotine pouches is likely to have the best potential for harm reduction among

a) smokers who switch completely

and among

b) naive subjects who otherwise would have started with other nicotine and tobacco containing products.

24

Nicotine in perspective.

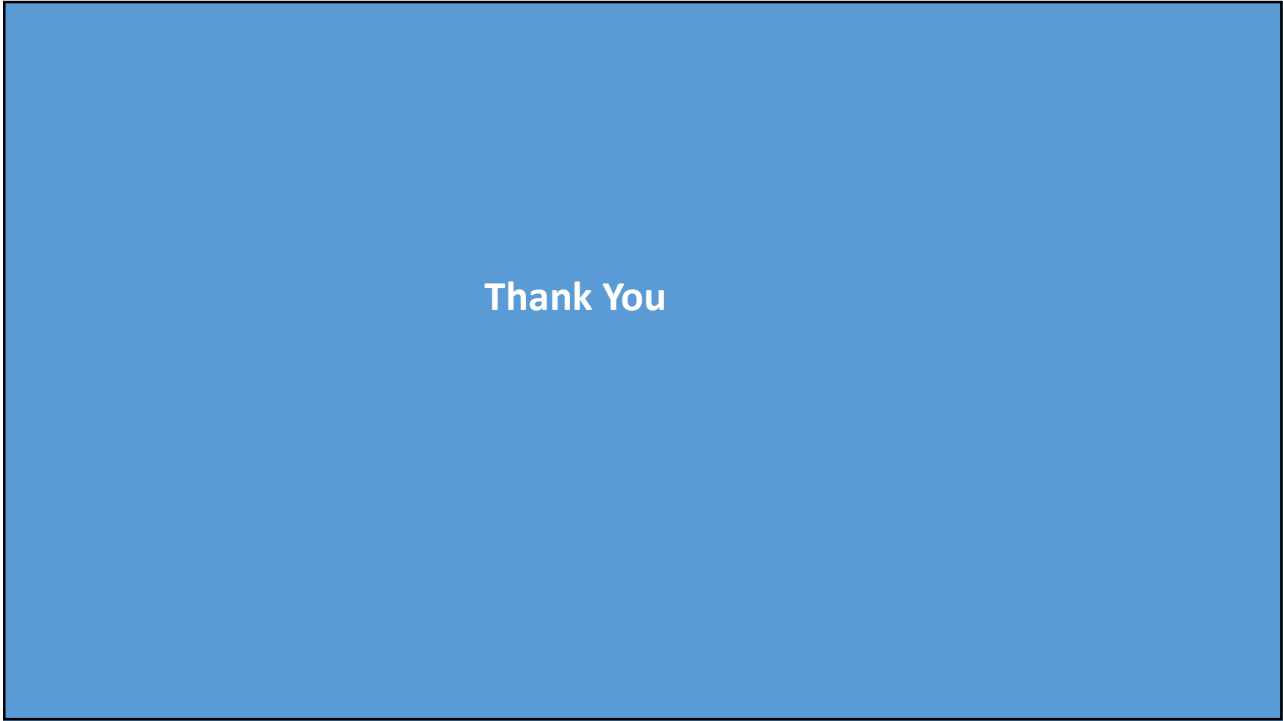
The purest nicotine products may have health effects not far from caffeine and most certainly less harmful effects than alcohol on users and non-users.

25

Key Issues

- Is a drug free world a realistic goal. If not what are the implications.
- Long term use of NR products is allowed by many authorities. What are the implications if tobacco/nicotine products without a medical license have the same safety profile.
- What are the implications of the multitude of flavourings in the new ANDS for how the society perceives the tobacco industry.

26



27