



International Tobacco Control
Policy Evaluation Project

What's Happening With Heated Tobacco Products in Japan? Findings from the ITC Japan Project

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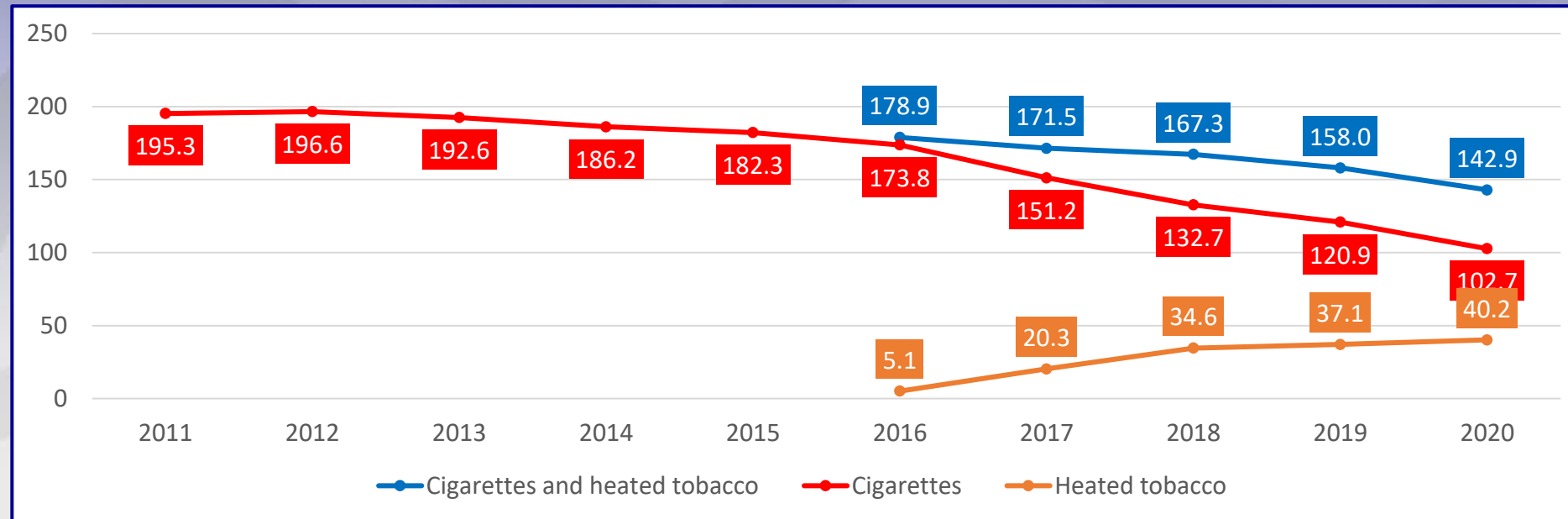


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- Member of the Expert Group for Article 9 (Regulation of the contents of tobacco products) and Article 10 (Regulation of tobacco product disclosures) of the WHO Framework Convention on Tobacco Control
- Member of the Brazil Health Regulatory Agency (ANVISA) Working Group on Tobacco Additives
- Member of the WHO Expert Group on COVID-19 and Tobacco Use
- Paid expert witness or consultant for governments defending their country's policies or regulations in litigation (Australia at WTO challenge; Uruguay at a bilateral investment treaty dispute)
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Introduction: The emergence of HTPs in Japan and the decline of cigarettes



- Japan's tobacco landscape has changed significantly with the introduction of HTPs
- Before HTPs came on the market, cigarette sales were slowly decreasing.
- After HTPs were introduced nationally in September 2015:
 - Cigarette sales have decreased more rapidly.
 - HTP consumption continued to increase.

Article

What Is Accounting for the Rapid Decline in Cigarette Sales in Japan?

K. Michael Cummings^{1,*}, Georges J. Nahhas¹ and David T. Swenor²

International Tobacco Control Policy Evaluation Project (the ITC Project)



Canada



United States



Australia



United Kingdom



Greece



Vietnam



Ireland



Thailand



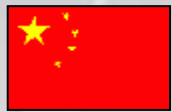
Malaysia



Republic of Korea



Hungary



China



Uruguay



Mexico



New Zealand



Poland



France



Germany



Netherlands



Bangladesh



Romania



Brazil



Mauritius



Bhutan



India



Spain



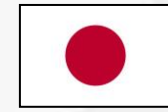
Zambia



Kenya



Abu Dhabi



Japan



Israel

- 31 countries, covering over half of the world's population and over 2/3 of the world's tobacco users
- Only international cohort study of tobacco use
- Key objective: evaluation of tobacco control policies
- Recent objective added: understanding use of other nicotine products across countries with emphasis on evaluating policies on different products

ITC Cohort Surveys

- 180+ survey waves across 31 countries (most are national surveys)
- Common measures, harmonized across countries and over time
- Content has evolved as the policy and product landscape has evolved.
- Global database (400,000 data records, about 150M data points) created and maintained at the University of Waterloo.



The ITC Japan Cohort Surveys

- 4 waves conducted: JP1 in 2018, JP2 in 2018-19, JP3 in 2020, JP4 in 2021
- Recruitment from high quality national web panel (Rakuten Insight)
- Survey design: Longitudinal with replenishment; quotas on those who...
 - Use cigarettes only
 - Use HTPs only
 - Use both products (dual),
 - have recently (≤ 2 yrs) quit smoking
- Survey weights calibrated to results from the JASTIS survey make the data representative of the adult population at each wave.
- Retention between waves: 66%

Table 3: JP3 target and valid sample with retention and replenishment numbers by subsample

Subsample group	JP2 final N	JP3 target N	JP3 recontacted N	JP3 replenished N	JP3 final N
Current exclusive smokers (including recontact cigarette quitters)	1,911	2,000	1,205	643	1,848
Current exclusive HTP-users (including recontact HTP-only quitters)	931	1,000	468	501	969
Current cigarette-HTP dual users (including recontact cigarette-HTP quitters)	895	1,000	660	249	909
Never or non-users	491	500	462	294	756
Total	4,228	4,500	2,795	1,687	4,482

Three ITC Japan Project studies

- 1. Retrospective analysis:** What percentage of IQOS consumers (and HTP consumers more generally) have “completely transitioned” from cigarettes?
- 2. Prospective analysis:** What do we know about transitions between cigarettes and HTPs over time? Are HTPs associated with transitions away from smoking?
- 3. Prospective analysis:** How does consumption change when people transition from smoking to dual use, and when they transition away from dual use to exclusive smoking and exclusive HTP use?

An Examination of Philip Morris International's Estimate of IQOS Consumers Who Have “Completely Transitioned” From Cigarettes: Findings From the 2018/19 and 2020 ITC Japan Surveys

Shannon Gravely¹, Gang Meng¹, Steve Shaowei Xu¹, Christian Boudreau¹,
Mary Thompson¹, Takahiro Tabuchi², Kota Katanoda³, Itsuro Yoshimi⁴,
K. Michael Cummings⁵, Andrew Hyland⁶, and Geoffrey T. Fong^{1,7}

¹ University of Waterloo, Canada; ² Cancer Control Center, Osaka International Cancer Institute, Japan; ³ Japan National Cancer Center, Japan; ⁴ National Cancer Center Japan; ⁵ Medical University of South Carolina, USA; ⁶ Roswell Park Comprehensive Cancer Center, USA; ⁷ Ontario Institute for Cancer Research

Background: PMI's quarterly reports

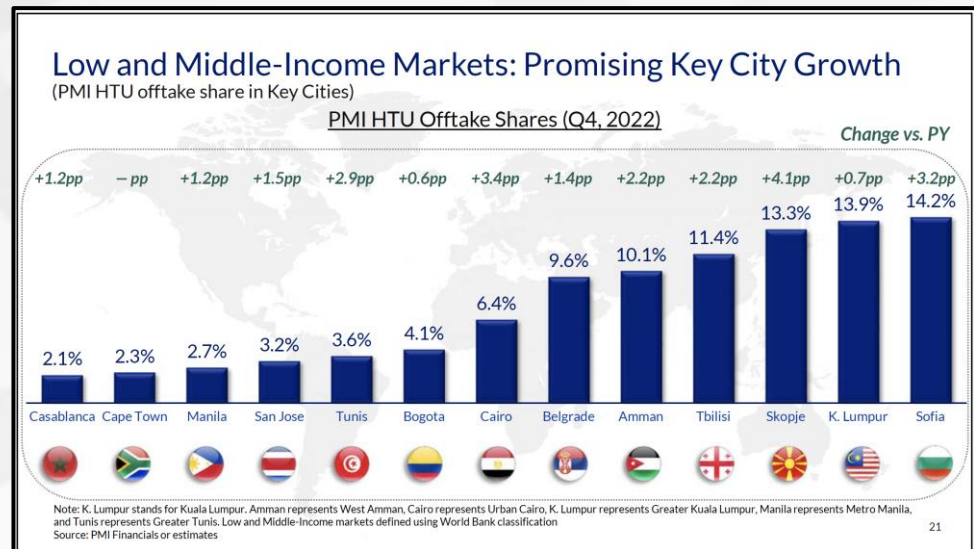
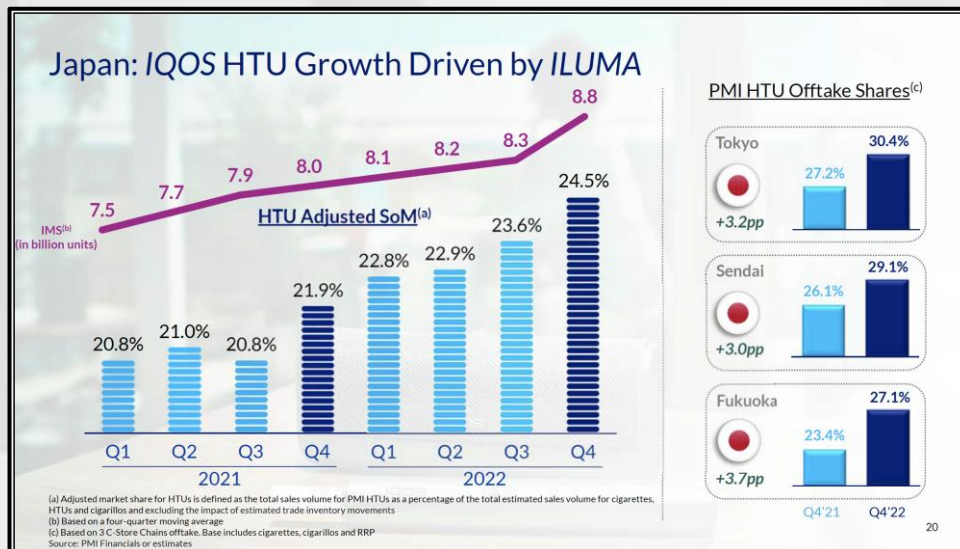
2022 Fourth-Quarter and Full-Year Results

February 9, 2023

2022: Remarkable Year for Our Smoke-Free Transformation

- Very strong delivery despite exceptional challenges
- Second consecutive year of total volume growth
- ~1/3 smoke-free net revenues for total PMI
- Outstanding IQOS performance supported by ILUMA and 2-tier HTU portfolio
- Robust growth in combustible net revenues and share of segment
- Major steps forward in our smoke-free transformation – IQOS in the U.S. and Swedish Match acquisition^(a)

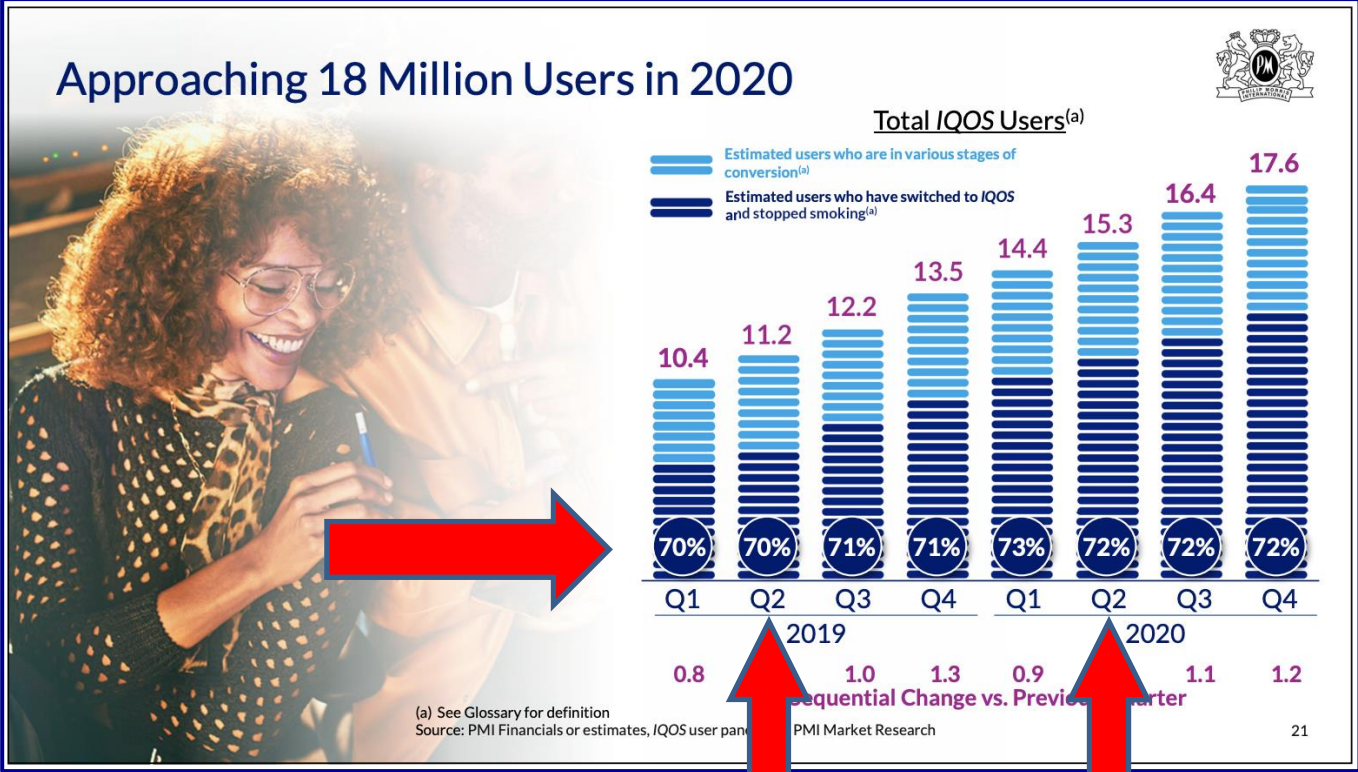
(a) As of April 30, 2024 PMI will have the full rights to commercialize IQOS in the U.S. Source: PMI Financials or estimates



Have IQOS consumers stopped smoking?

PMI Definition

“Completely Transitioned”:
At least 95% of total tobacco consumption is from HTPs



PMI reports that in their IQOS Customer Survey, the percentage of IQOS consumers who had completely transitioned from cigarettes was:

Q1 2019
70%

Q2 2020
72%

ITC Japan Survey & PMI Japan IQOS Customer Survey



	ITC	PMI
Survey type	Online	Online
Survey design	Cohort sample with replenishment	Cross-sectional
Respondent Source	Rakuten Insight (survey firm)	IQOS users registered on the PMI IQOS User Database
Data source	Wave 2 (Dec 2018-Feb 2019) Wave 3 (May-Jun 2020)	Year 3 (2019). Source: Q1 2019 report Year 4 (2020-2021). Source: Q2 2020 report
Eligibility criteria	Use HTPs \geq weekly	Past 30-day IQOS consumers
	Aged 20+ years	Aged 20+ years
	Used \geq 100 HTP sticks/lifetime	Used \geq 100 HTP sticks/lifetime
HTPs	HTPs: IQOS, glo, Ploom TECH	IQOS and other HTPs (brands not stated)
Sample size	W2: N=520 IQOS, 543 other HTPs W3: N=854 IQOS, 656 other HTPs	Year 3: N=2013 IQOS users Year 4: N=2000 IQOS users

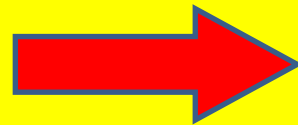
*ITC: people who currently and formerly smoked (<weekly cigarette use and former smoking, consumption of cigs = 0)

Analyses of the ITC Japan Survey data

- We recalibrated our weights to PMI's sex x age distribution in order to adjust the ITC data so that it was more comparable to the PMI data.
- Each Ploom TECH capsule x 4 to get number of equivalent HTP sticks

Cigarettes (CPD)+ HTPs (HPD) =
total consumption (TPD)

HPD/TPD = proportion of total
consumption from HTPs

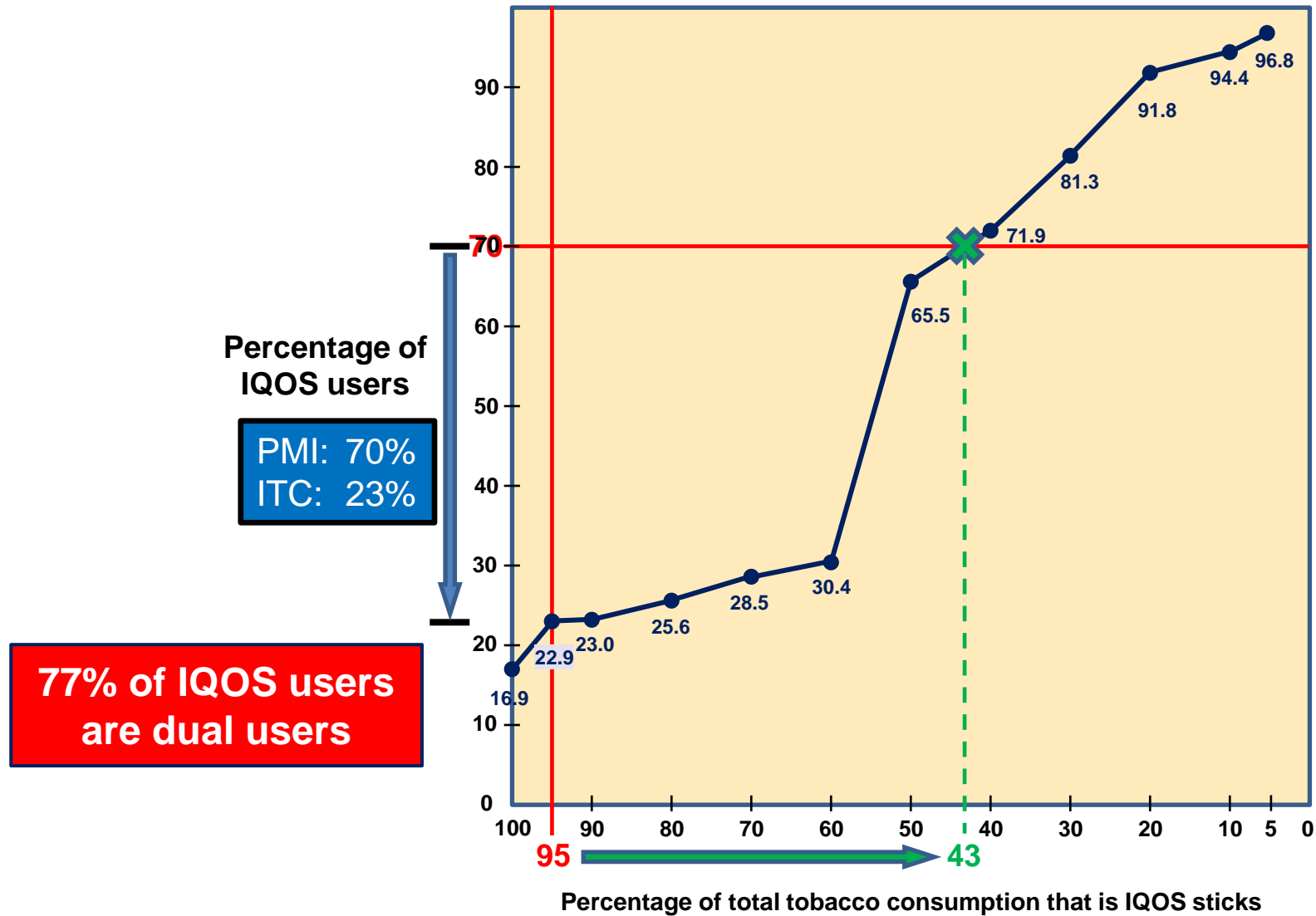


Create Cumulative distribution:

Highest (100% and 95%:
“completely transitioned”)

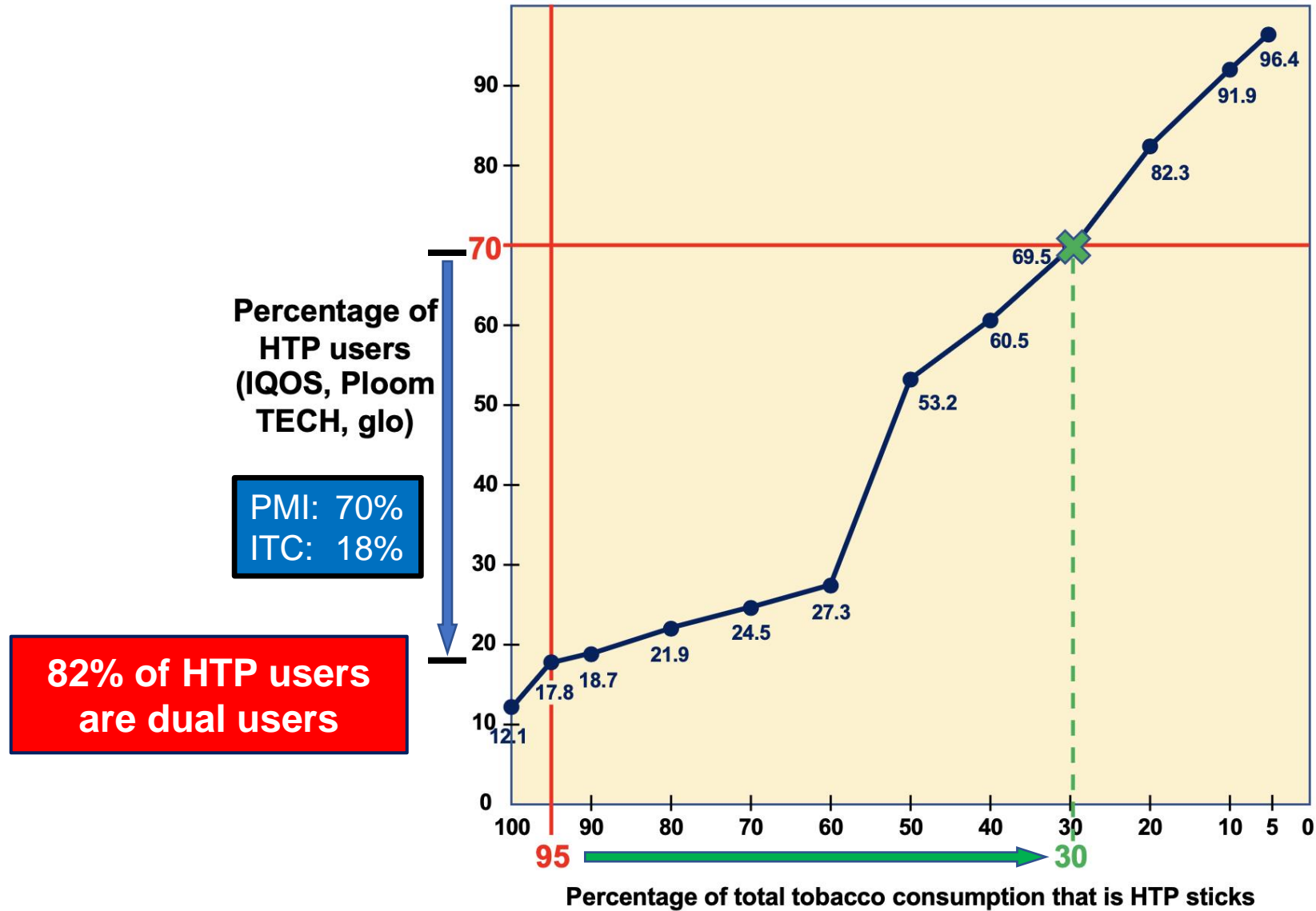
Lowest (5% and 0%:
exclusive smoking)

ITC Japan W2 (2018/19) vs. PMI (Q1 2019): ITC IQOS Consumers (N=520)



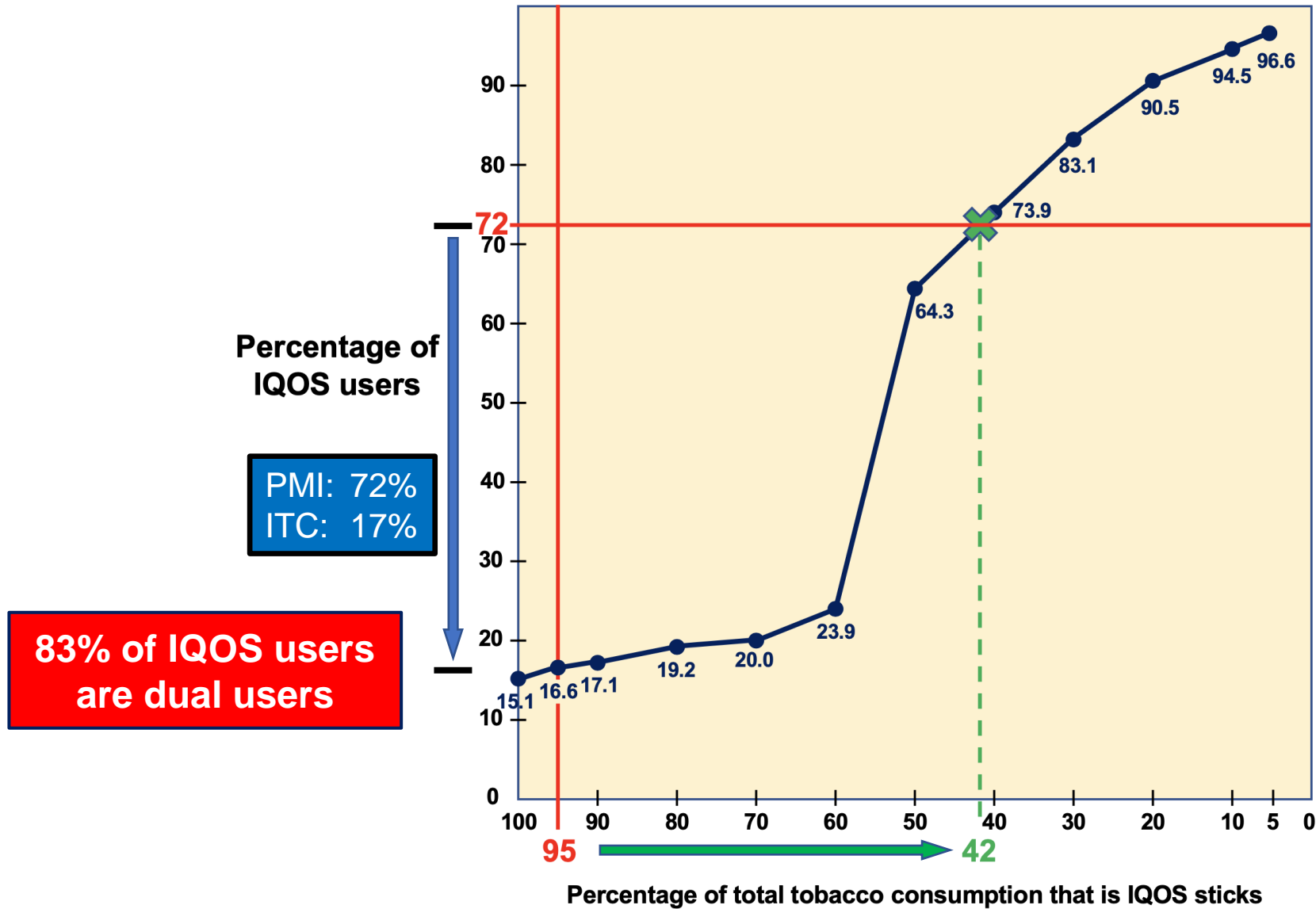
* Weighted to PMI age x sex distribution

ITC Japan W2 (2018/19) vs. PMI (Q1 2019): ITC **All HTP Consumers** (N=1063)



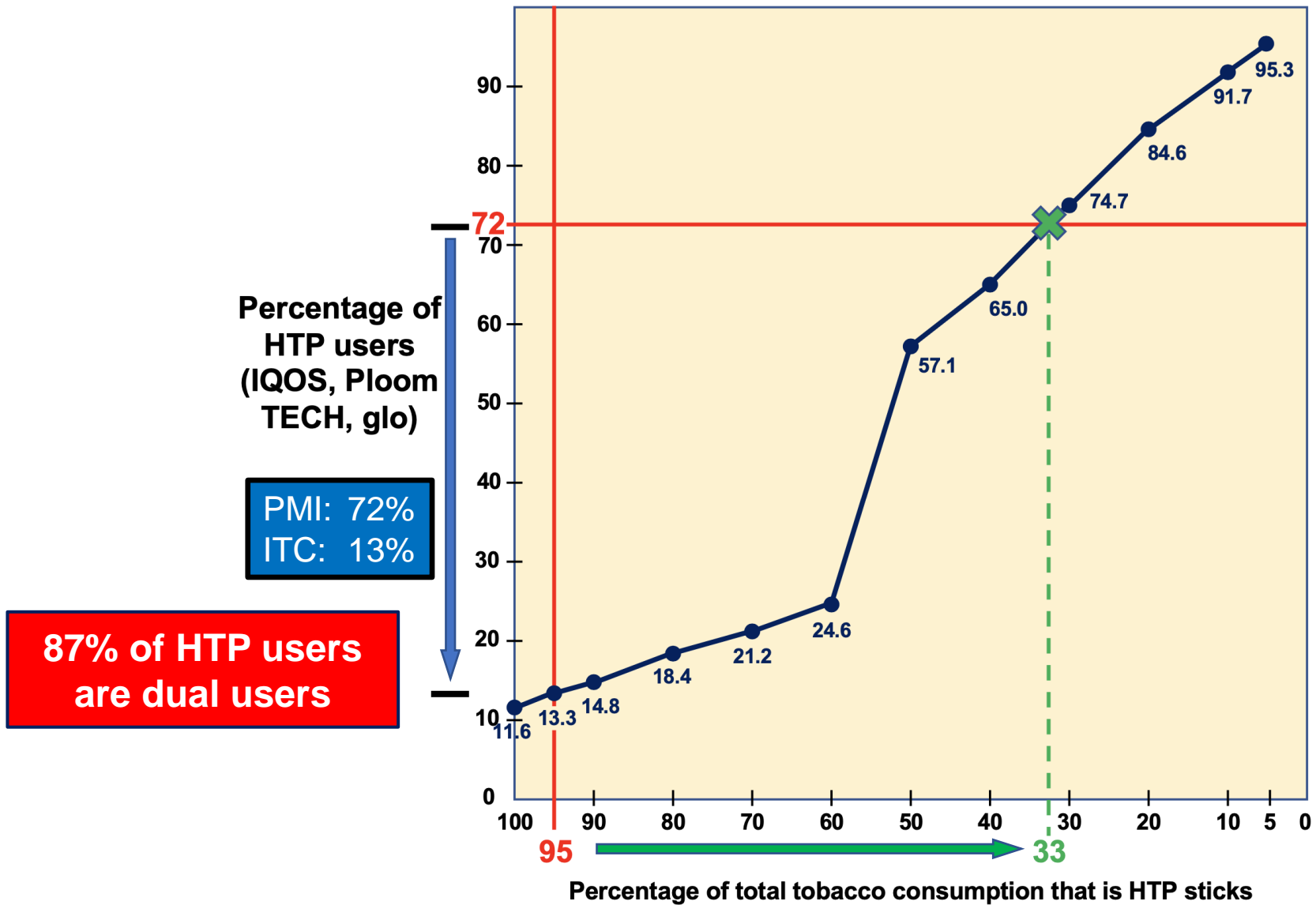
* Weighted to PMI age x sex distribution

ITC Japan W3 (2020) vs. PMI (Q2 2020): IQOS Consumers (N=854)



* Weighted to PMI age x sex distribution

ITC Japan W3 (2020) vs. PMI (Q2 2020): All HTP Consumers (N=1510)



* Weighted to PMI age x sex distribution

Summary

Data Source	% Dual Use	
	2019	2020
PMI Quarterly reports: from IQOS User Panel Survey, matched to time of ITC survey waves	30%	28%
ITC: IQOS Users	77%	83%
ITC: All HTP Users	82%	87%
ITC: among only exclusive smokers in 2018 who reported being IQOS users in 2019 / 2020	70%	73%
ITC: among only exclusive smokers in 2018 who reported being HTP users in 2019 / 2020	88%	83%

Summary and Conclusion

- Dual use is very high: over 70% among IQOS; over 80% among all HTPs
- Why do the IQOS User Surveys show such a high % no longer smoking?
 - The IQOS User Panel: Satisfaction/liking for the product is likely to be high.
 - For many HTP users, a top reason they give for using HTPs (including in PMI's own surveys): to quit cigarettes.
 - Thus, **the potential bias of the sample is directly related to the outcome measure (“completely transitioned” from smoking)**
- ITC Survey respondents: Those in the general population who use HTPs.
- Japan National Cancer Center Cohort: Dual use is about 50%.
- PMI's Japan General Population Adult Population (JGAP) Survey–Dual use:
2016-17: **66%**, 2017-18: **65%**, 2018-19: **57%**, 2019-20: **43%**, 2020-21: **41%**
- **“70% not smoking”**: does **NOT** mean that a smoker who takes up HTPs has a **70% chance of not smoking in the future!**

Transitions of Tobacco Product Use Among Adults Who Smoke Cigarettes and Adults Who Use Heated Tobacco Products (HTPs) in Japan: Initial Findings from Three Waves of the ITC Japan Cohort Survey (2018-20)

Geoffrey T. Fong^{1,2*}, Gang Meng¹, Shannon Gravely¹, Mary E. Thompson¹, Steve Shaowei Xu¹, Anne C. K. Quah¹, Janine Ouimet¹, Itsuro Yoshimi³, Kota Katanoda³, Takahiro Tabuchi⁴, K. Michael Cummings⁵, Andrew Hyland⁶

¹University of Waterloo, Canada; ²Ontario Institute for Cancer Research, Canada; ³Japan National Cancer Center, Japan;

⁴Osaka International Cancer Institute, Japan; ⁵Medical University of South Carolina, USA;

⁶Roswell Park Comprehensive Cancer Center, USA

Digging deeper: what is the interaction between cigarettes and HTPs at the individual level?

- The sales data are **consistent** with the idea that cigarettes are being substituted for HTPs, but these are **aggregate data**.
- It is important to understand the interplay between cigarettes and HTPs at the **individual level**:
 - When people who smoke take up HTPs, does this lead to quitting cigarettes, quitting HTPs and going back to cigarettes, or quitting both cigarettes and HTPs?
 - The proportions of these transitions are critically important for making assessments of the population-level effects.
 - What are the long-term use patterns for those who start using HTPs: long-term dual use or long-term exclusive HTP use?
 - These individual-level analyses are only possible with a longitudinal cohort design.

Transition tables of product use between waves

Wave 1		Wave 2				Total
		Cig only	Dual	HTP only	Neither Product	
Cig only	N	1478	483	41	100	2102
	%	69.6	22.5	1.8	6.1	
Dual	N	41	198	19	10	268
	%	18.7	71.7	6.4	3.3	
HTP only	N	2	14	42	4	62
	%	5.0	26.1	62.8	6.1	
Recent Quitter	N	11	4	1	25	41
	%	31.8	10.4	0.7	57.2	
Total		1532	699	103	139	2473

Challenges in drawing conclusions from the simple transition tables: It's not so simple

- The simple transition tables may be misleading: they over-represent the experience of individuals who have occupied initial Dual or HTP-only states for a longer period of time (**length biased sampling**).
- Another challenge: who were dual using who quit smoking prior to the recruitment into the survey are not included, but those who are dual using who haven't yet quit smoking (or have tried to quit but failed) are included. (**"treatment failure" issue**)
- Any survey (longitudinal or not) is taking a **snapshot of a movie**: the flow of individuals through a journey of product use, with some staying in a particular state for a long time, others for a short time.
- What can we do to do better measure and understand this process?

Improving our snapshots of the transition movie

- Don't start with those who dual use. Instead start with those who only smoke cigarettes and then follow them through their transition states. This deals with the “failed quitters” challenge.
- Distinguish between more transient, short-term states of use and more stable, longer-term states of use. That extends the timeframe of the snapshots that we are taking in our surveys. (iPhone “live” photo)
- Examine transitions over more than 2 waves.



Population cross-section proportions of different states of product use

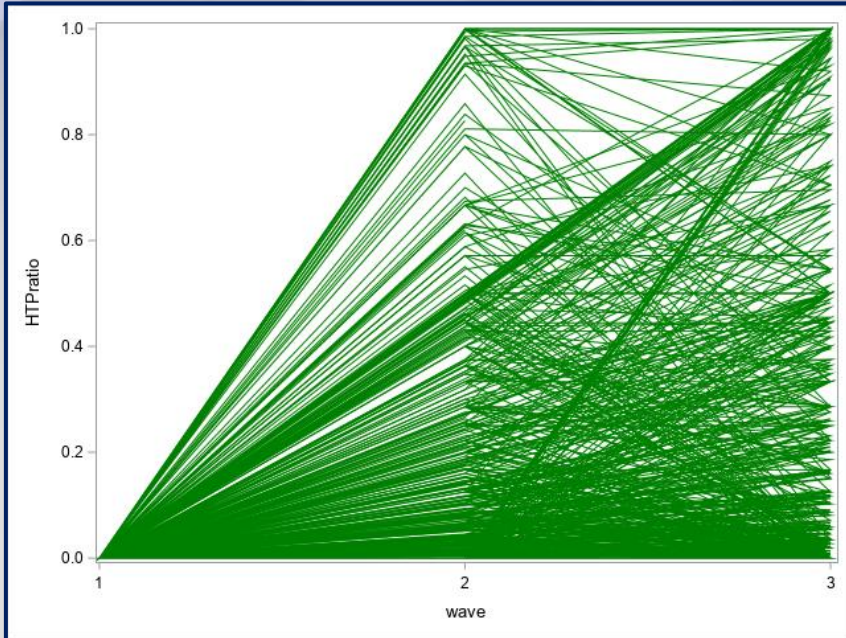
	Wave 1	Wave 2	Wave 3
Cig only & never regular HTP use	84.8%	53.5%	52.6%
Cig only & ever regular HTP use	4.9%	9.8%	20.6%
Short term dual (< 6 months)	2.9%	14.2%	4.6%
Long term dual (6 months or more)	2.5%	17.4%	19.9%
HTP only	4.8%	5.0%	2.3%
Total	100.0%	100.0%	100.0%

Key observations from this table:

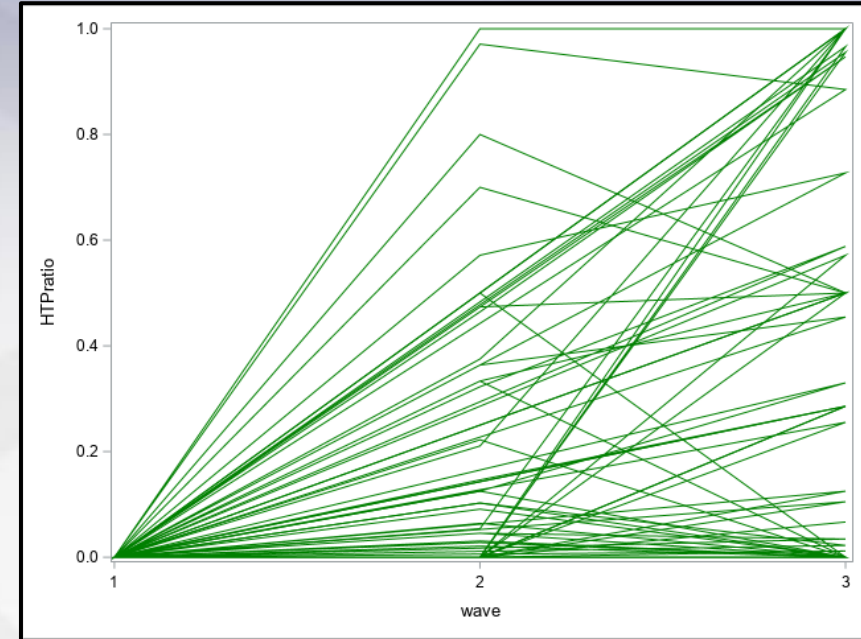
- a stable class of people who are engaging in long-term dual use
- HTP only use (completely transitioned smokers + very few never smokers) is very low and it is NOT increasing

Individual-Level Transitions at a Glance

Wave 1 cig only smokers who had NEVER used HTP



Wave 1 cig only smokers who HAD ever used HTP



- A lot of dual use (the points between the top and bottom)
- Transitions from dual use to exclusive smoking are more frequent (bottom) than to HTP only (top)
- A majority of respondents who picked up HTPs remained using a relatively lower amount of HTPs compared to cigarettes (greater density in the lower regions of the figure than the upper regions)
- Not many straight lines from Waves 2 to 3: not much stability over time. Lot of experimentation with HTPs.

Expanding the transition matrix: W1 to W2 and to W3

wave 1 (2018)	wave 2 (2019)																		
	cig only & never regular HTP use		cig only & ever regular HTP use		short-term dual		long-term dual		short-term HTP only		long-term HTP only		quitter ever used HTP		short-term quitter never used HTP		long-term quitter never used HTP		Total
	N=	%	N=	%	N=	%	N=	%	N=	%	N=	%	N=	%	N=	%	N=	%	N=
cig only & never regular HTP use	907	66.9	67	6.1	275	18.3	73	4.5	14	0.9	5	0.5	3	0.5	17	1.8	8	0.5	1369
cig only & ever regular HTP use			49	62.8	14	17.6	14	16.4	2	1.5	0	.	1	1.6					80
short-term dual (<6m)			15	19.2	11	16.3	64	62.2	0	.	2	2.3	0	.					92
long-term dual (6m+)			8	8.3	4	8.8	63	76.9	0	.	4	3.2	2	2.9					81
Total	907		139		304		214		16		11		6		17		8		1622

wave 1 (2018)	wave 3 (2020)																		
	cig only & never regular HTP use		cig only & ever regular HTP use		short-term dual		long-term dual		short-term HTP only		long-term HTP only		quitter ever used HTP		short-term quitter never used HTP		long-term quitter never used HTP		Total
	N=	%	N=	%	N=	%	N=	%	N=	%	N=	%	N=	%	N=	%	N=	%	N=
cig only & never regular HTP use	733	53.5	240	17.5	72	5.8	214	14.8	8	0.4	22	1.4	25	1.8	19	1.3	39	3.6	1372
cig only & ever regular HTP use			44	51.8	5	8.4	19	23.2	1	2.7	6	7.2	5	6.8					80
short-term dual (<6m)			28	31.0	6	5.8	47	52.5	2	1.7	7	8.6	1	0.5					91
long-term dual (6m+)			11	14.3	2	3.5	54	70.5	0	.	10	7.2	4	4.5					81
Total	733		323		85		334		11		45		35		19		39		1624

- Data are weighted but unadjusted. The difference in n for baseline cig only % never regular HTP user between the two tables is dual to missing HTP use durations.

- Transitioning from exclusive smoking to long-term dual was MUCH more likely (14.8%) than transitioning to HTP only (1.4%)
- Those who were long-term duals in 2018 stayed in that state (70.5%); more than half (52.5%) of short-term duals became long-term duals, showing that starting off in dual use leads to dual use as a stable state.

1. Is Long-Term HTP use associated with a greater likelihood of quitting cigarettes?

wave 1 (2018)	wave 3 (2020)												Difference (P-value)
	cig only & never regular HTP use		long-term quitter never used HTP		Long-term quit among never HTP users	long-term dual		long-term HTP only		Long-term quitter who ever long-term used HTP		Long-term quit among long-term HTP users	
	N=	%	N=	%	%	N=	%	N=	%	N=	%	%	
cig only & never regular HTP use	733	53.5	39	3.6	$3.6/(3.6+53.5) = 6.3$	214	14.8	22	1.4	1	0.1	$1.4+0.1/(1.4+0.1+14.8) = 9.2$	Diff=2.9% (p=0.34)

NO, although there is a non-significant (p=.34) trend

Long-term HTP users (N=237) = 9.2%

Never HTP users (N=772) = 6.3%

2. Is Long-Term HTP use associated with a greater likelihood of quitting cigarettes among daily smokers vs. non-dailys?

wave 1 (2018)		wave 3 (2020)												Difference (P-value)
		cig only & never regular HTP use		long-term quitter never used HTP		long-term quit among never HTP users	long-term dual		long-term HTP only		Long-term quitter who ever long-term used HTP		long-term quit among long-term HTP users	
		N=	%	N=	%	%	N=	%	N=	%	N=	%	%	
cig only & never regular HTP use	Daily smoker	704	53.4	35	3.5	$3.5/(3.5+53.4) = 6.2$	204	14.7	21	1.4	1	0.1	$(1.4+0.1)/(1.4+0.1+14.7) = 9.3$	Diff=3.1% (p=0.31)
	Non-daily smoker	29	53.8	4	5.9	$5.9/(5.9+53.8) = 9.9$	10	15.2	1	1.1	0	0	$1.1/(1.1+15.2) = 6.6$	Diff=-3.3% (p=0.70)

NO, although there is a non-significant trend (p=.31) for daily, but a non-significant trend in the opposite direction for non-daily (p=.70)

Daily

Long-term HTP (N=226) = 9.3%
 Never HTP (N=739) = 6.2%

Non-Daily

Long-term HTP (N=11) = 6.6%
 Never HTP (N=33) = 9.9%

3. Is long-term HTP use associated with a greater likelihood of daily smokers transitioning to non-daily smoking?

Non-daily smoking is a precursor for future quitting

wave 1 (2018)	wave 3 (2020)										Difference (P-value)
	daily cig only & never regular HTP		non-daily cig only & never regular HTP use		cig reduction among never HTP users	daily cig long-term dual		non-daily cig long-term dual		cig reduction among long-term HTP users	
	N=	%	N=	%	%	N=	%	N=	%	%	
Daily cig only & never regular HTP use	684	52.3	18	1.0	$1.0/(1.0+52.3) = 1.9$	186	13.5	11	0.8	$0.8/(0.8+13.5) = 5.4$	Diff=3.5% (p=0.08)

Maybe: A trend (p=.08) toward transitioning from daily to non-daily smoking
 Long-term HTP users (N=197) = 5.4%
 Never HTP users (N=702) = 1.9%

4. Association between ever-using HTPs and: (a) not smoking cigs, (b) using neither cigs nor HTPs

wave 1 (2018)	cig only & never regular HTP use		cig only & ever regular HTP use		short-term dual		long-term dual		short-term HTP only		long-term HTP only		quitter ever used HTP		short-term quitter never used HTP		long-term quitter never used HTP		Total
	N=	%	N=	%	N=	%	N=	%	N=	%	N=	%	N=	%	N=	%	N=	%	N=
	cig only & never regular HTP use	733	53.5	240	17.5	72	5.8	214	14.8	8	0.4	22	1.4	25	1.8	19	1.3	39	3.6

Cigarette free

	Denominator (%)	Numerator (%)	Not using any nicotine product at Wave 3(%)	Difference (P-value)
Ever-used HTPs	All groups that ever-used HTPs: 17.5 + 5.8 + 14.8 + 0.4 + 1.4 + 1.8 = 41.7	cig quitter ever used HTPs: 1.8 + 1.4 + 0.4 = 3.6	3.6/41.7 = 8.6%	Diff = 0.2% (p=0.92)
Never used HTPs	cig only & never regular HTP use + quitter never used HTPs: 53.5 + 1.3 + 3.6 = 58.4	cig quitter never used HTPs: 1.3 + 3.6 = 4.9	4.9/58.4 = 8.4%	

Tobacco free: Neither cigarettes nor HTPs

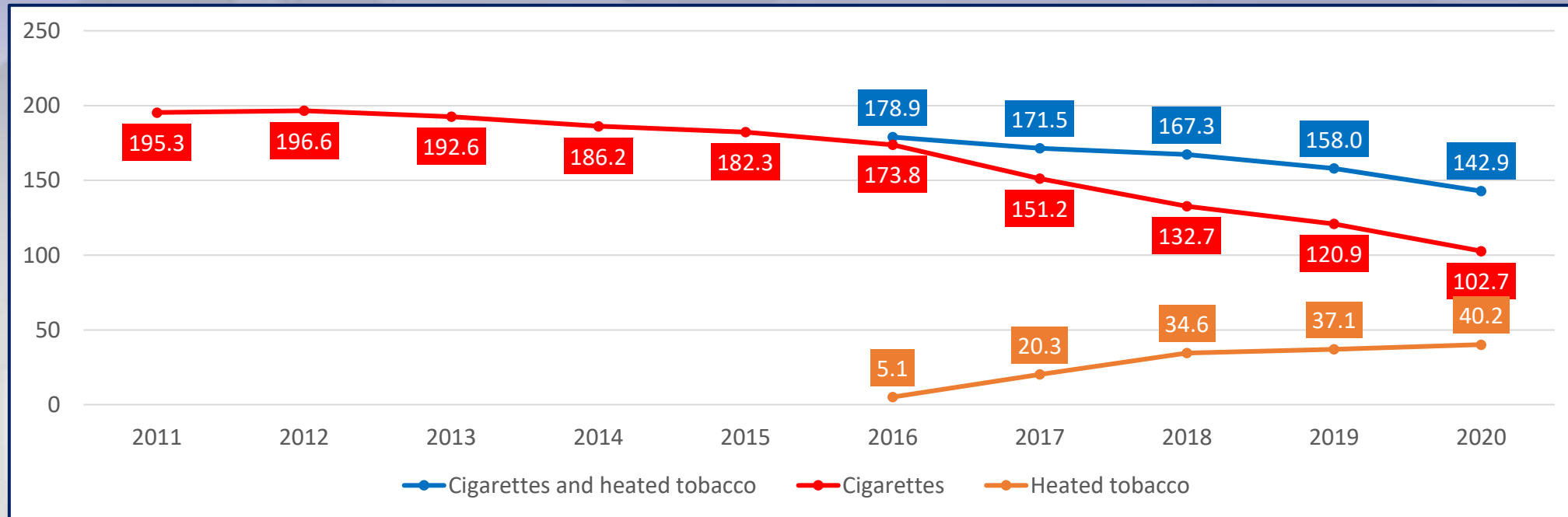
	Denominator (%)	Numerator (%)	Not using any nicotine product at Wave 3(%)	Difference (P-value)
Ever-used HTPs	All groups that ever-used HTPs: 17.5 + 5.8 + 14.8 + 0.4 + 1.4 + 1.8 = 41.7	quitter ever used HTP: 1.8	1.8/41.7 = 4.3%	Diff = -4.1% (p=0.02)
Never used HTPs	cig only & never regular HTP use + quitter never used HTPs: 53.5 + 1.3 + 3.6 = 58.4	quitter never used HTPs: 1.3+3.6 = 4.9	4.9/58.4 = 8.4%	

- **Cigarette Free:** no difference between ever-used HTPs (8.4%) and never-used HTPs (8.6%)
- **Tobacco Free:** those who ever-used HTPs from W1 to W3 were significantly **LESS LIKELY** (4.3%) than those who never-used HTPs (8.4%) (p=.02)

The journey of those who exclusively smoke at W1 (2018) over two years (W2: 2018-19 and W3: 2020)

1. Over time, there was a pattern of greater stability of those who take up HTPs, but this was NOT to quitting, but instead to long-term dual use.
2. Using HTPs for a longer period ($\geq 6M$) was not significantly associated with quitting cigarettes (but there was a trend).
3. Ever-trying HTPs and long-term HTP use were negatively associated with transitioning to using neither product.

How can we best interpret the trends in sales of cigarettes and HTPs in Japan?



The dramatic decrease in cigarette sales and the increase in HTP sales in Japan is likely due in large measure to partial substitution among smokers who are now duals, and likely to become long-term duals rather than due to smokers quitting or transitioning to using neither product.

Changes in Cigarette and Total Tobacco Consumption Among People Who Smoke Who Did and Did Not Initiate Heated Tobacco Products: Findings from the 2018-2021 ITC Japan Surveys

**Steve S. Xu^{1*}, Gang Meng¹, Shannon Gravely¹, Anne C. K. Quah¹, Janine Ouimet¹,
Itsuro Yoshimi², Kota Katanoda², Takahiro Tabuchi³, K. Michael Cummings⁴,
Andrew Hyland⁵, Geoffrey T. Fong^{1, 6}**

¹University of Waterloo, Canada; ²Japan National Cancer Center, Japan; ³Osaka International Cancer Institute, Japan; ⁴Medical University of South Carolina, USA; ⁶Roswell Park Comprehensive Cancer Center, USA;

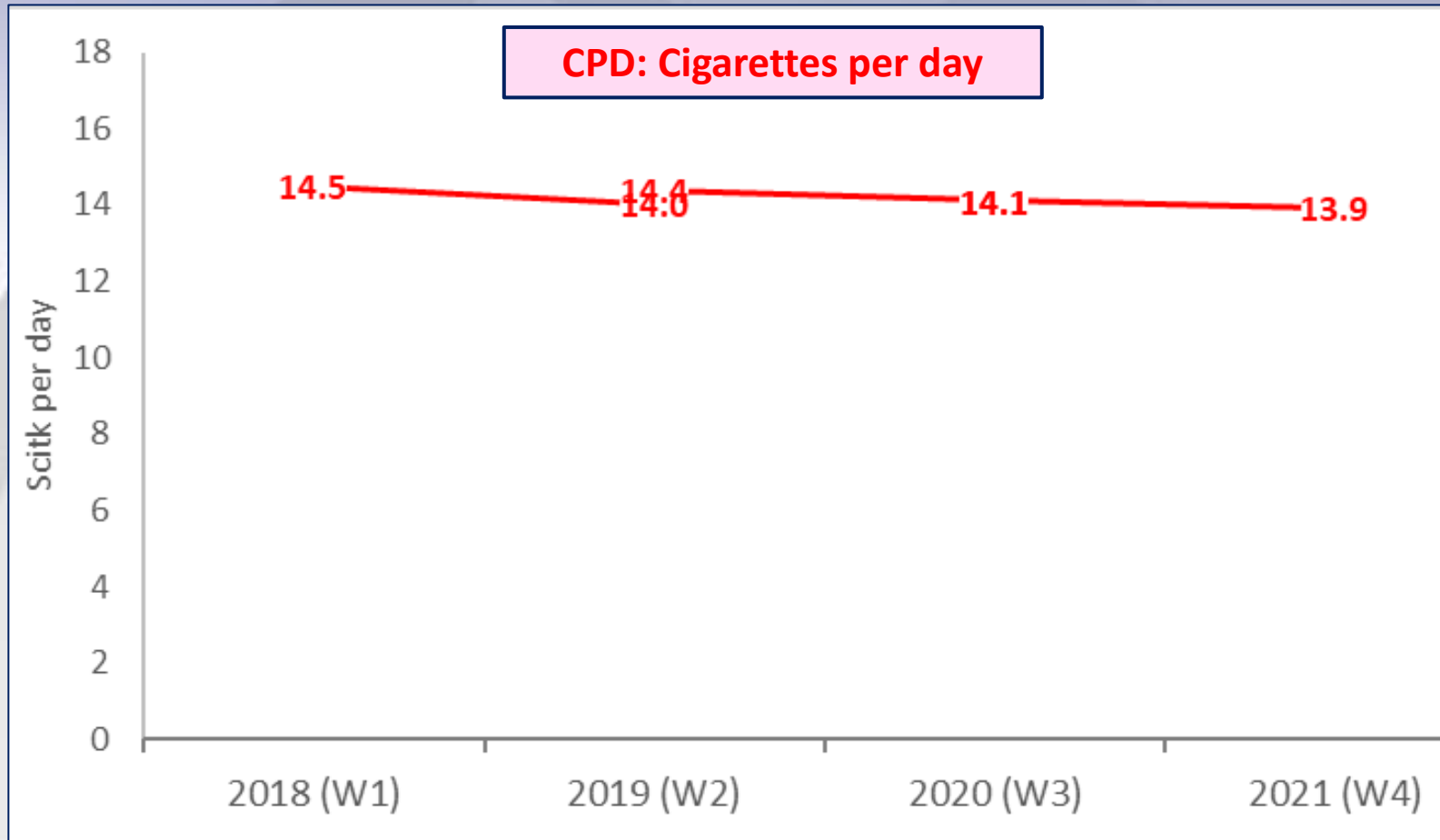
⁶Ontario Institute for Cancer Research, Canada

How does consumption change when people transition from (1) cig-only to dual, and (2) dual to cig-only & HTP-only?

Cigarettes: Cigarettes per day (**CPD**)
HTPs: HTP sticks per day (**HPD**)*
Total Tobacco: $CPD + HPD = TPD$

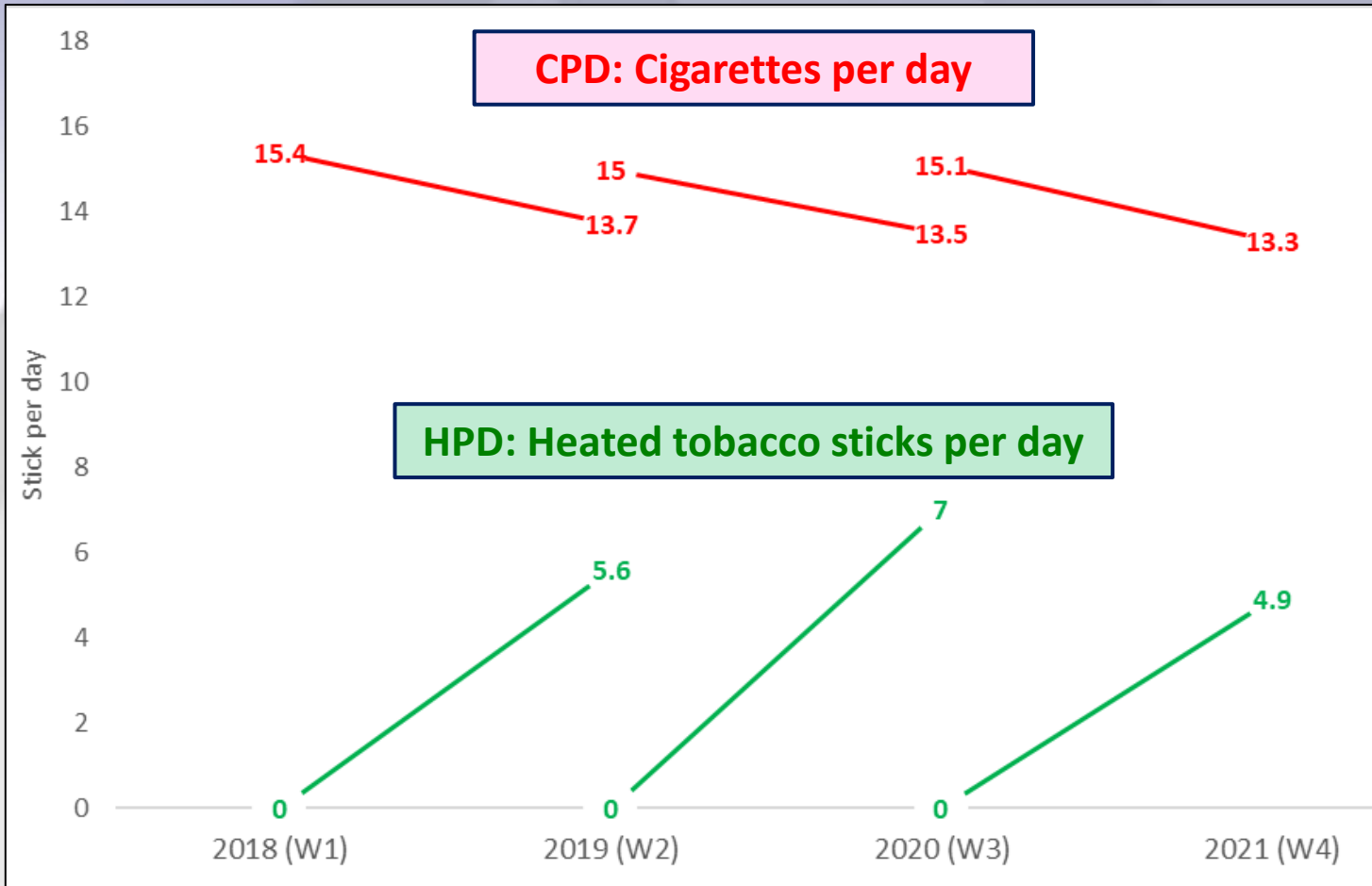
* For those who use Ploom TECH, one capsule = 4 HTP sticks

Cig-only → Cig-only



Year	Product	Difference (stick/%)
2018-2019	Cig	-0.5 (-3.4%)
	HTP	0
	Total	-0.5 (-3.4%)
2019-2020	Cig	-0.3 (-2.1%)
	HTP	0
	Total	-0.3 (-2.1%)
2020-2021	Cig	-0.2 (-1.4%)
	HTP	0
	Total	-0.2 (-1.4%)

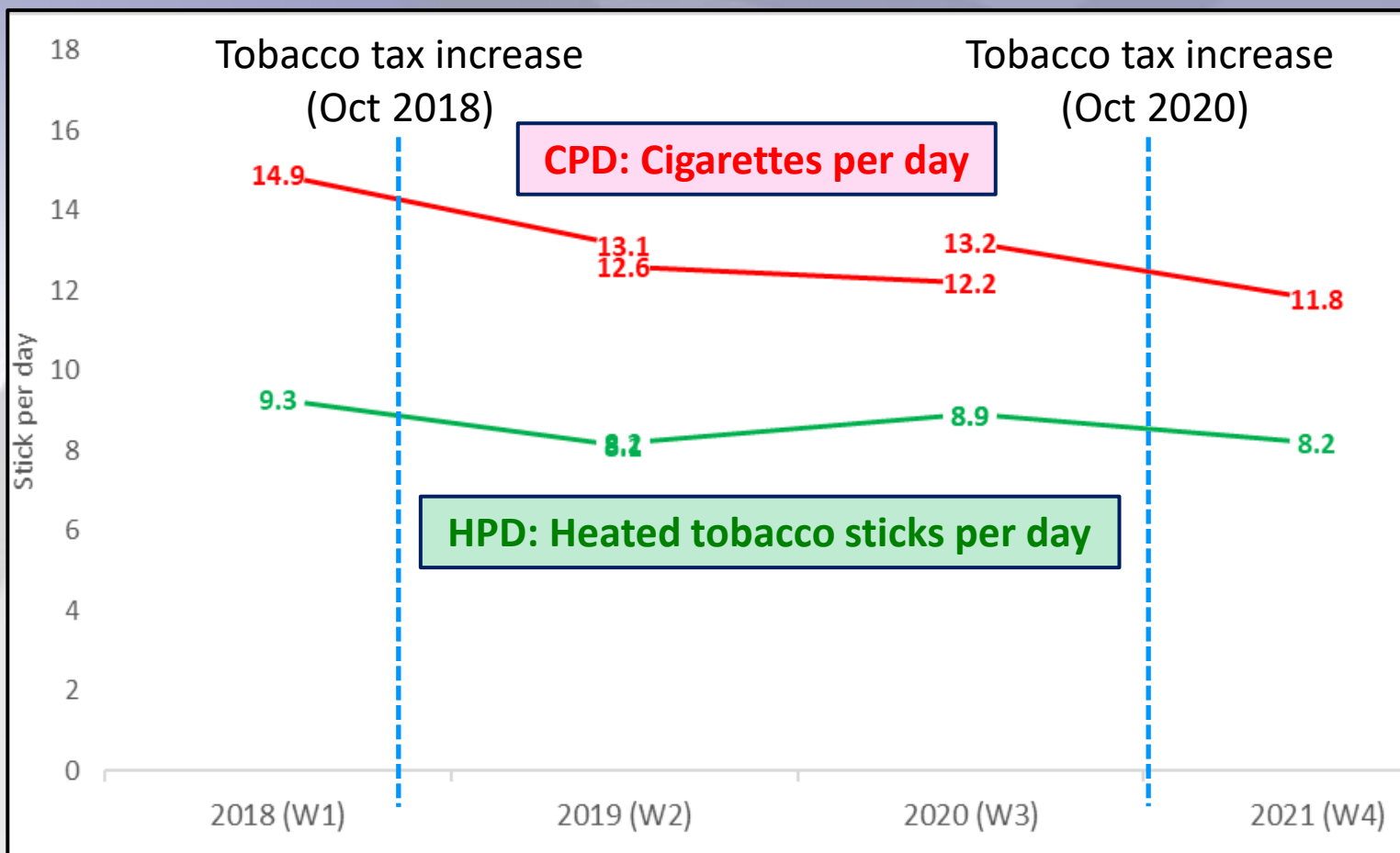
Cig-only → HTP+Cig



Year	Product	Difference (stick/%)
2018-2019	Cig	-1.7 (-11.0%) ***
	HTP	+5.6
	Total	+3.9 (+25.3%)
2019-2020	Cig	-1.5 (-10.0%) *
	HTP	+7.0
	Total	+5.5 (+33.3%)
2020-2021	Cig	-1.8 (-11.9%) ***
	HTP	+4.9
	Total	+3.1 (+20.5%)

* p<0.05 *** p<0.001

HTP+Cig → HTP+Cig

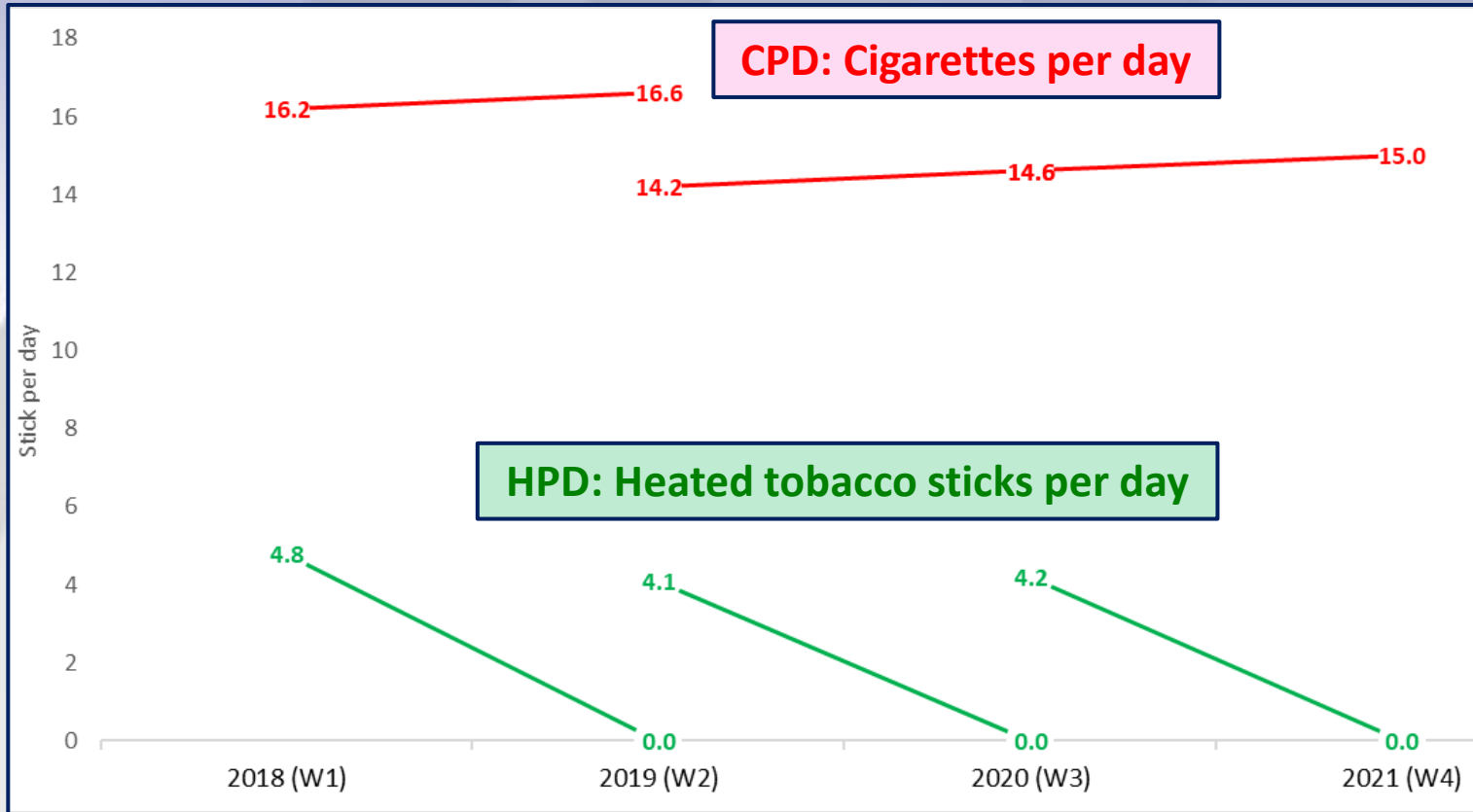


Year	Product	Difference (stick/%)
2018-2019	Cig	-1.8 (-12.1%) **
	HTP	-1.2 (-12.9%)
	Total	-3.0 (-12.4%) **
2019-2020	Cig	-0.4 (-3.1%)
	HTP	+0.7 (+8.5%)
	Total	+0.3 (+3.3%)
2020-2021	Cig	-1.4 (-10.6%) *
	HTP	-0.7 (-7.9%)
	Total	-2.3 (-10.3%) **

* p<0.05

** p<0.01

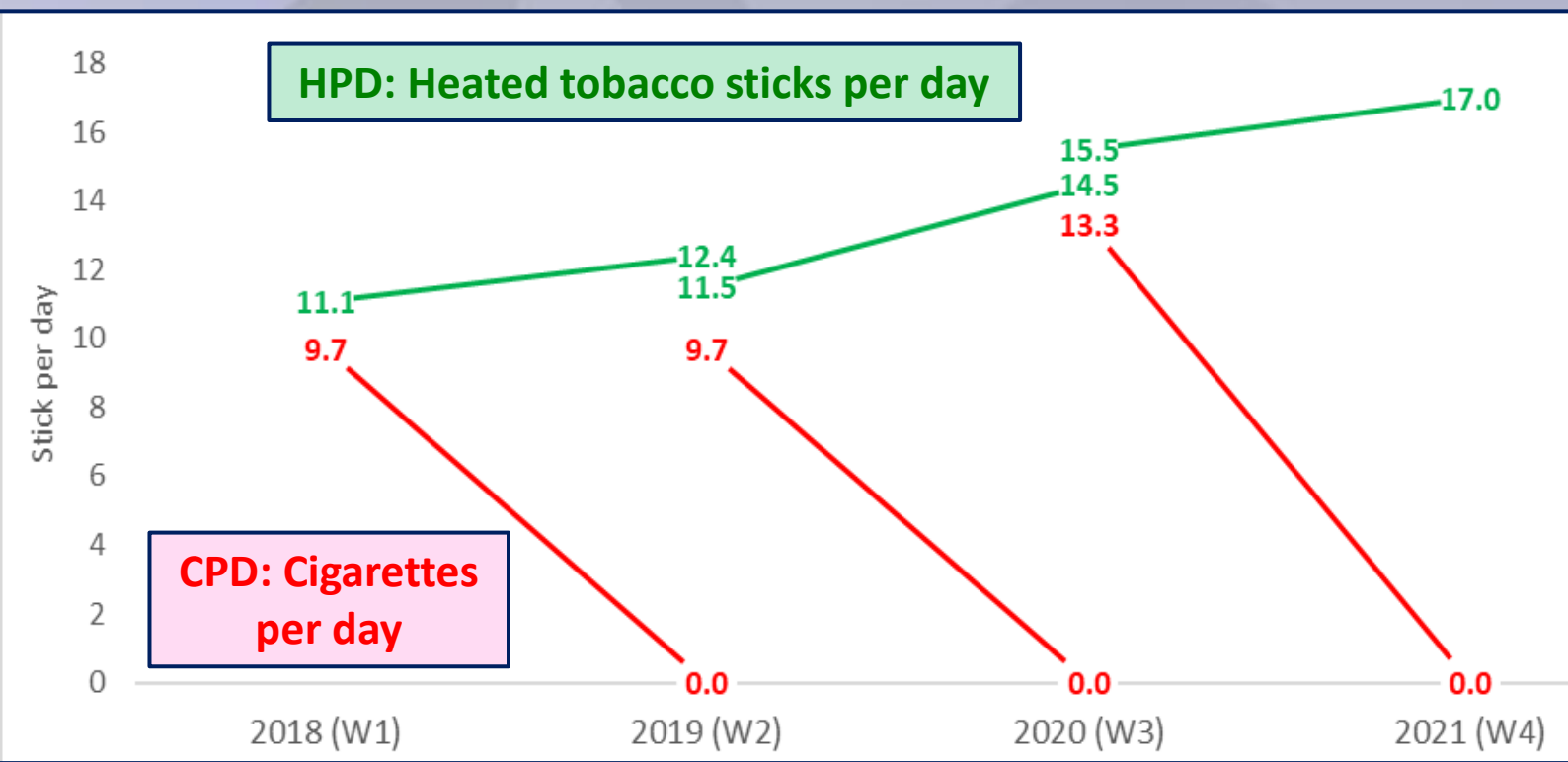
HTP+Cig → Cig-only



Year	Product	Difference (stick/%)
2018-2019	Cig	+0.4 (+2.4%)
	HTP	-4.8
	Total	-4.4 (-21.0%) **
2019-2020	Cig	+0.4 (+2.8%)
	HTP	-4.1
	Total	-3.7 (-20.2%)**
2020-2021	Cig	+0.4 (+2.7%)
	HTP	-4.2
	Total	-3.8 (-20.8%) **

* p<0.05 ** p<0.01

HTP+Cig → HTP-only



Year	Product	Difference (stick/%)
2018-2019	Cig	-9.7
	HTP	+1.3 (+11.7%) *
	Total	-8.4 (-40.4%) ***
2019-2020	Cig	-9.7
	HTP	+3.7 (+20.2%) ***
	Total	-6.9 (-31.1%) ***
2020-2021	Cig	-13.3
	HTP	+1.5 (+9.7%) ***
	Total	-11.6 (-40.3%) ***

* p<0.05 *** p<0.001

When people transition from cigarettes TO dual use:

...**26% increase in total consumption**

When people transition AWAY from dual use:

...**Back to cigarettes only (common): 21% decrease in total consumption.**

...**To HTPs only (rare): 37% decrease in total consumption.**

Business conclusion: Dual use is a substantial benefit for companies who produce both cigarettes and HTPs.

Potential public health consequences?

- Not clear because we are missing a key element: **the relative harmfulness of HTP sticks vs. cigarettes.**

- Consider the average consumption change for those transitioning from cig-only to cig+HTP:

Cigs: -1.7 sticks

HTPs: +5.8 sticks

HTP/cig ratio = $5.8/1.7 = 3.4$

- Simple heuristic^{**}: if the harmfulness of cigarettes relative to HTPs exceeds 3.4, then the decrease of 1.7 cigs may decrease risk more than the increase of 5.8 HTP sticks increases risk. The net effect would be a reduction in risk.

Year	Product	Difference (stick/%)
2018-2019	Cig	-1.7 (-11.0%) ***
	HTP	+5.6
	Total	+3.9 (+25.3%)
2019-2020	Cig	-1.5 (-10.0%) *
	HTP	+7.0
	Total	+5.5 (+33.3%)
2020-2021	Cig	-1.8 (-11.9%) ***
	HTP	+4.9
	Total	+3.1 (+20.5%)

* p<0.05 *** p<0.001

Public Health Conclusion: Transitioning from Cig-Only to Dual use may or may not constitute a less harmful state, depending on the relative harmfulness of HTPs vs. cigarettes.

^{**} Simple because there is certainly a non-linear (log) relationship between consumption and harmfulness.

Overall summary of ITC findings

- 1. Retrospective analysis:** Among those who use HTPs, dual use is very high (high dual use in other surveys, including PMI's General Population Survey).
- 2. Prospective analysis of product use transitions:**
 - When those who exclusively smoke cigarettes take up HTPs: long-term dual use is a state that seems to be increasing over time.
 - Initial evidence that long-term dual use may be associated with stopping smoking and increasing the likelihood that those who smoke daily will transition to non-daily smoking (but not statistically significant).
- 3. Prospective analysis of transitions of product use and consumption:**
 - **Dual use is an apex state:** transitioning **TO** dual increases total consumption by 26% and transitioning **AWAY** from dual decreases consumption by 21% and 37%.
 - Comparing gain/loss of cigarettes and HTP sticks is an **initial step** in assessing the harmfulness of dual use relative to exclusive cigarette smoking.

Major Support for the ITC Project



US National Cancer Institute
P01 CA200512



Canadian Institutes of Health Research
FDN-148477



Ontario Institute for Cancer Research
Senior Investigator Award (2007-2027)

ITC Project Research Organizations



ITC Project Research Support



iQOS-Health Effects and Toxicity

Aruni Bhatnagar, PhD

American Heart Association Tobacco Regulatory Science Center



EMISSIONS

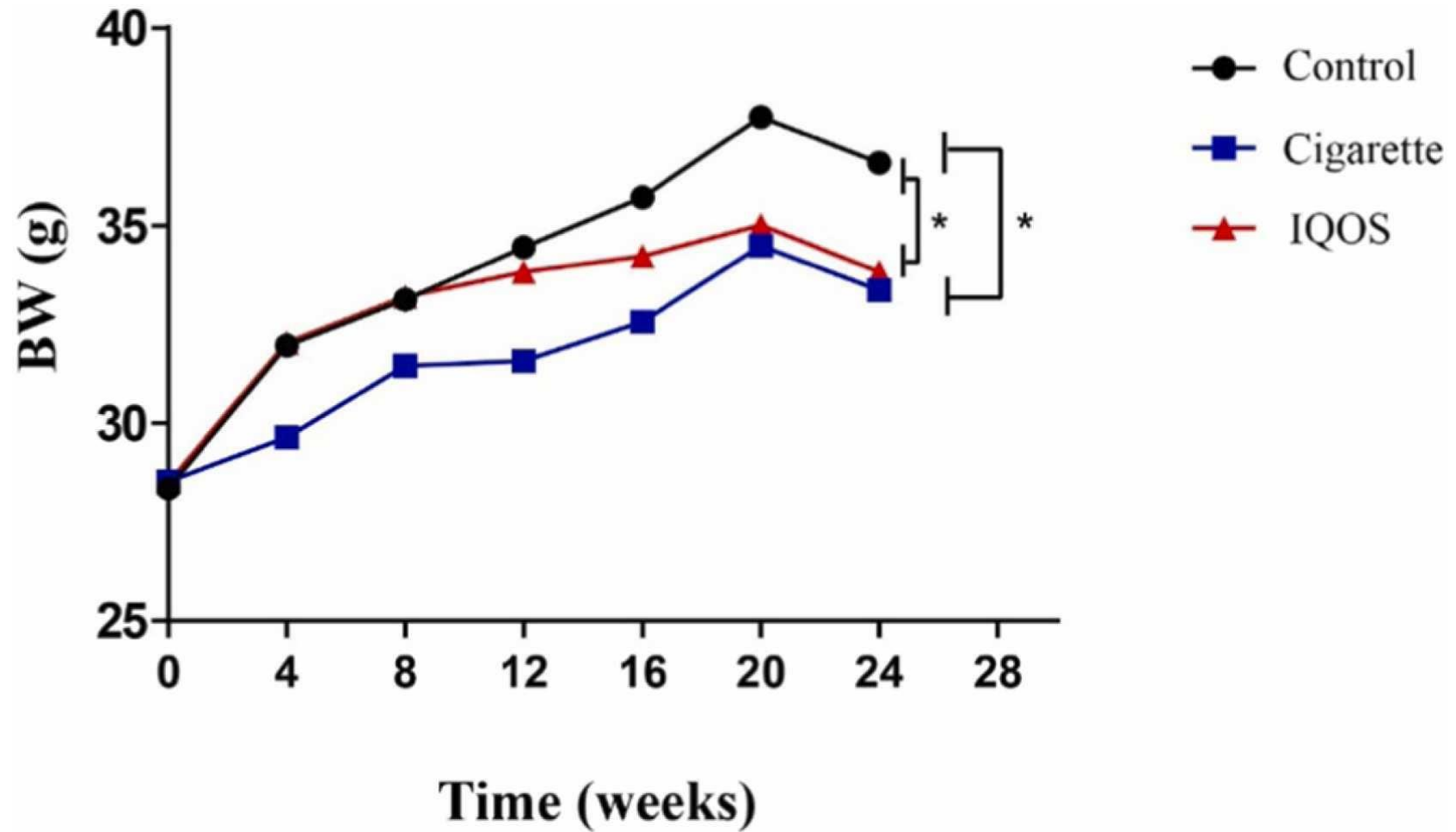


Table 2 Carbonyl emissions per mg nicotine yield for the products tested. Data presented as mean (standard deviation) from five repetitions.

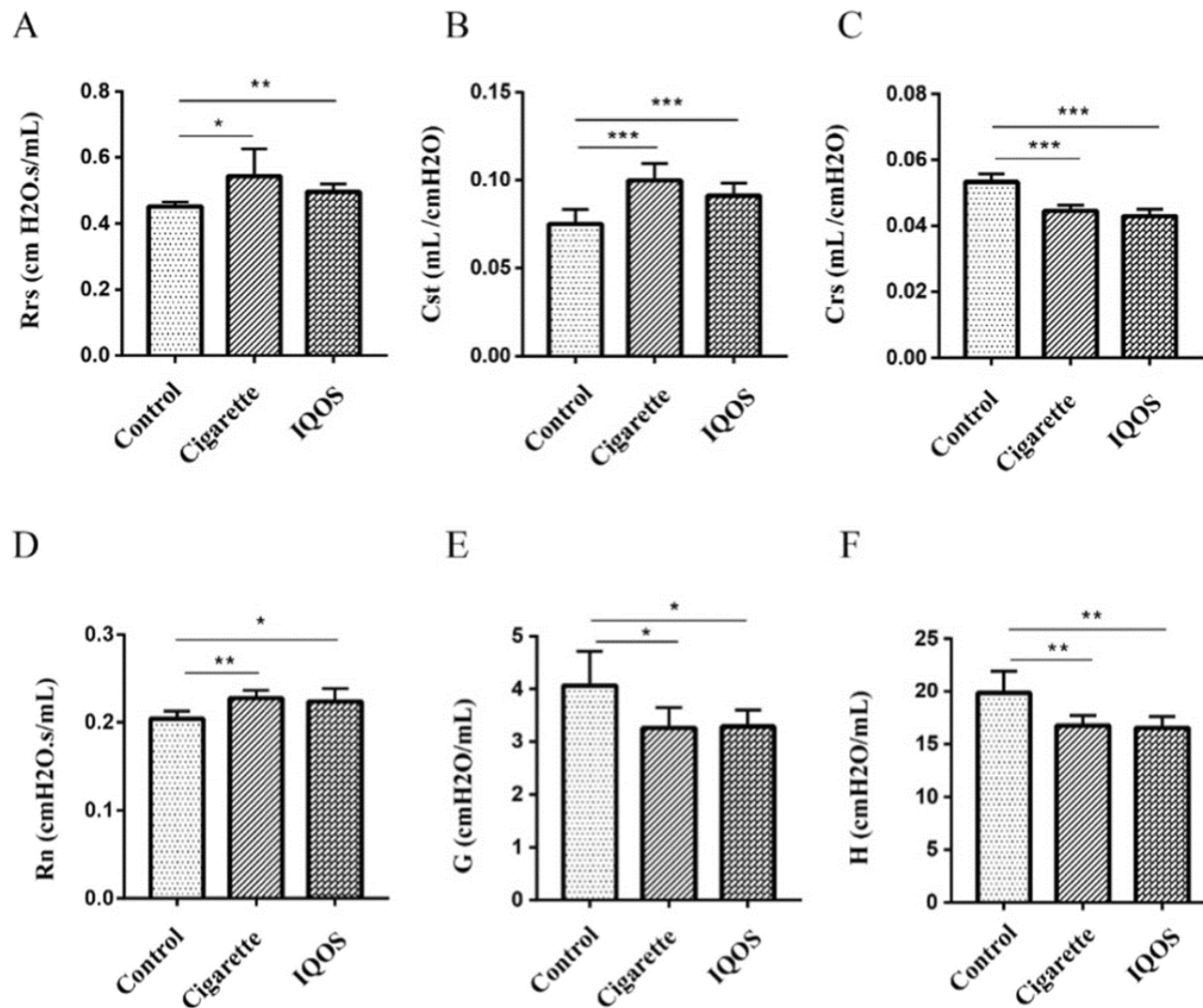
	<i>Formaldehyde</i>	<i>Acetaldehyde</i>	<i>Acrolein</i>	<i>Propionaldehyde</i>	<i>Crotonaldehyde</i>
	<i>µg/mg nicotine yield</i>				
PR1					
IQOS regular	5.3 (1.5)	120.1 (19.4)	9.0 (3.3)	10.7 (3.1)	1.6 (0.4)
IQOS menthol	4.1 (1.2)	147.3 (27.2)	8.6 (1.6)	9.2 (2.0)	1.6 (0.2)
E-cigarette 10 W	0.5 (0.2)	0.8 (0.3)	0.3 (0.1)	< LOD	< LOD
E-cigarette 14 W	0.6 (0.2)	0.9 (0.2)	0.3 (0.1)	< LOD	< LOD
Tobacco cigarette	36.7 (7.6)	580.4 (88.3)	61.6 (7.8)	59.4 (9.8)	22.5 (8.0)
PR2					
IQOS regular	7.0 (2.8)	112.9 (17.1)	6.3 (1.5)	6.8 (3.6)	1.1 (0.4)
IQOS menthol	10.4 (4.1)	144.5 (47.5)	8.2 (4.7)	10.2 (3.1)	1.9 (0.7)
E-cigarette 10 W	1.6 (0.5)	1.1 (0.3)	0.3 (0.2)	< LOD	< LOD
E-cigarette 14 W	1.3 (0.2)	0.8 (0.1)	0.4 (0.1)	< LOD	< LOD
Tobacco cigarette	35.9 (11.7)	663.2 (92.4)	75.7 (15.5)	54.9 (6.8)	31.7 (4.6)
PR3					
IQOS regular	10.7 (1.5)	103.2 (6.6)	6.5 (1.1)	7.4 (0.9)	1.9 (0.4)
IQOS menthol	13.3 (2.8)	110.0 (7.9)	7.7 (0.7)	8.0 (0.8)	1.9 (0.4)
E-cigarette 10 W	1.7 (0.8)	0.8 (0.2)	0.4 (0.1)	< LOD	< LOD
E-cigarette 14 W	1.2 (1.2)	0.9 (0.2)	0.4 (0.1)	< LOD	< LOD
Tobacco cigarette	29.4 (6.3)	499.0 (59.3)	66.2 (8.0)	48.2 (6.3)	16.7 (3.5)

IQOS = heated tobacco product; PR = puffing regime; LOD = limit of detection PR1: 2-s puff duration, 55-ml puff volume, 30-s interpuff interval. PR2: 3-s puff duration, 80-ml puff volume, 30-s interpuff interval. PR3: 3-s puff duration, 90-ml puff volume, 25-s interpuff interval.

Body Weight Decrease by cigarettes and IQOS

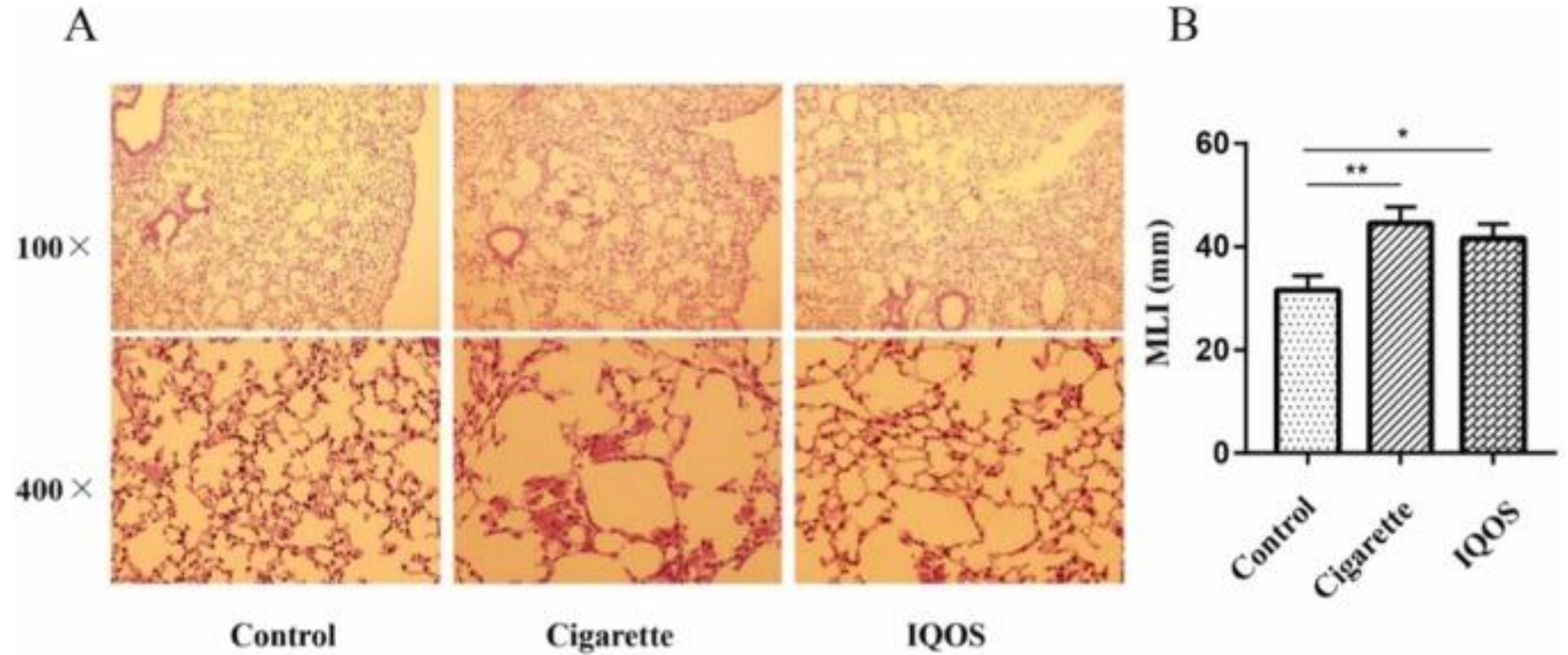


Airway resistance and compliance measured after IQOS and cigarette exposures

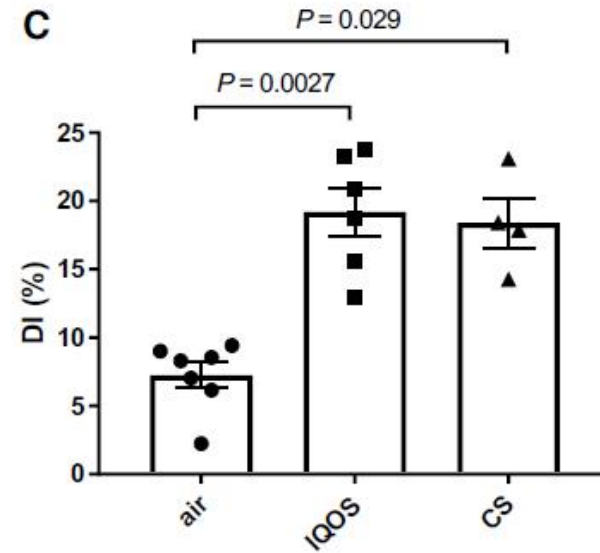
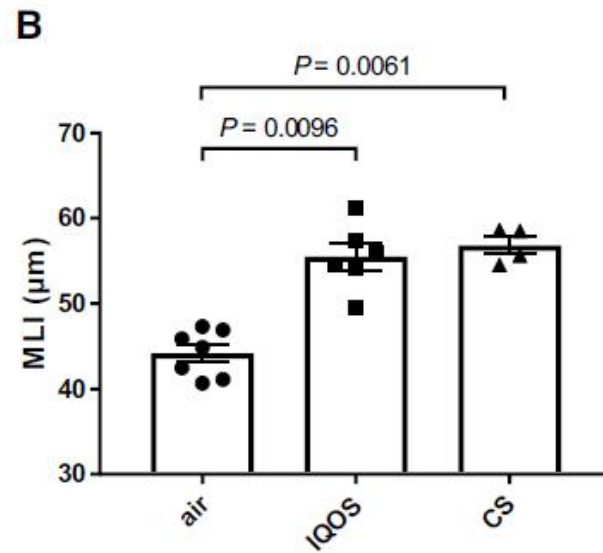
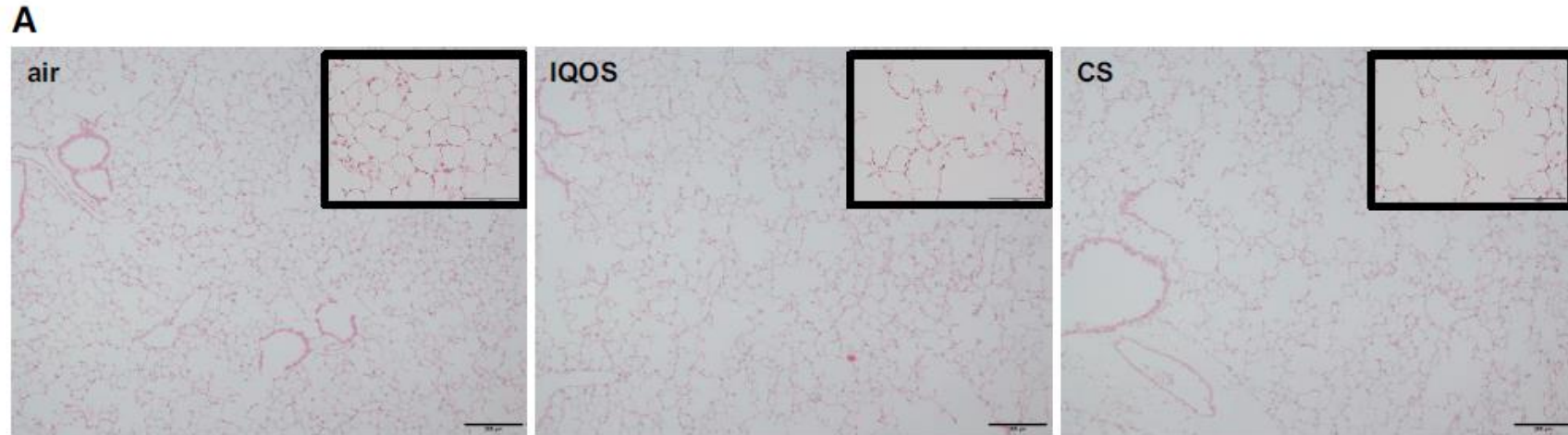


Airway resistance and compliance were measured by cigarette and IQOS aerosol exposure. A: Rrs: respiratory system resistance, B: Cst: quasi-static compliance, C: Crs: respiratory system compliance, D: central airway resistance (Rn), E: tissue damping(G), F: tissue elastance (H). Values are expressed as mean±SD (n = 8 mice); * $p < 0.05$, ** $P < 0.01$ and *** $P < 0.001$ vs control.

Lung histological changes after cigarette and IQOS aerosol exposure



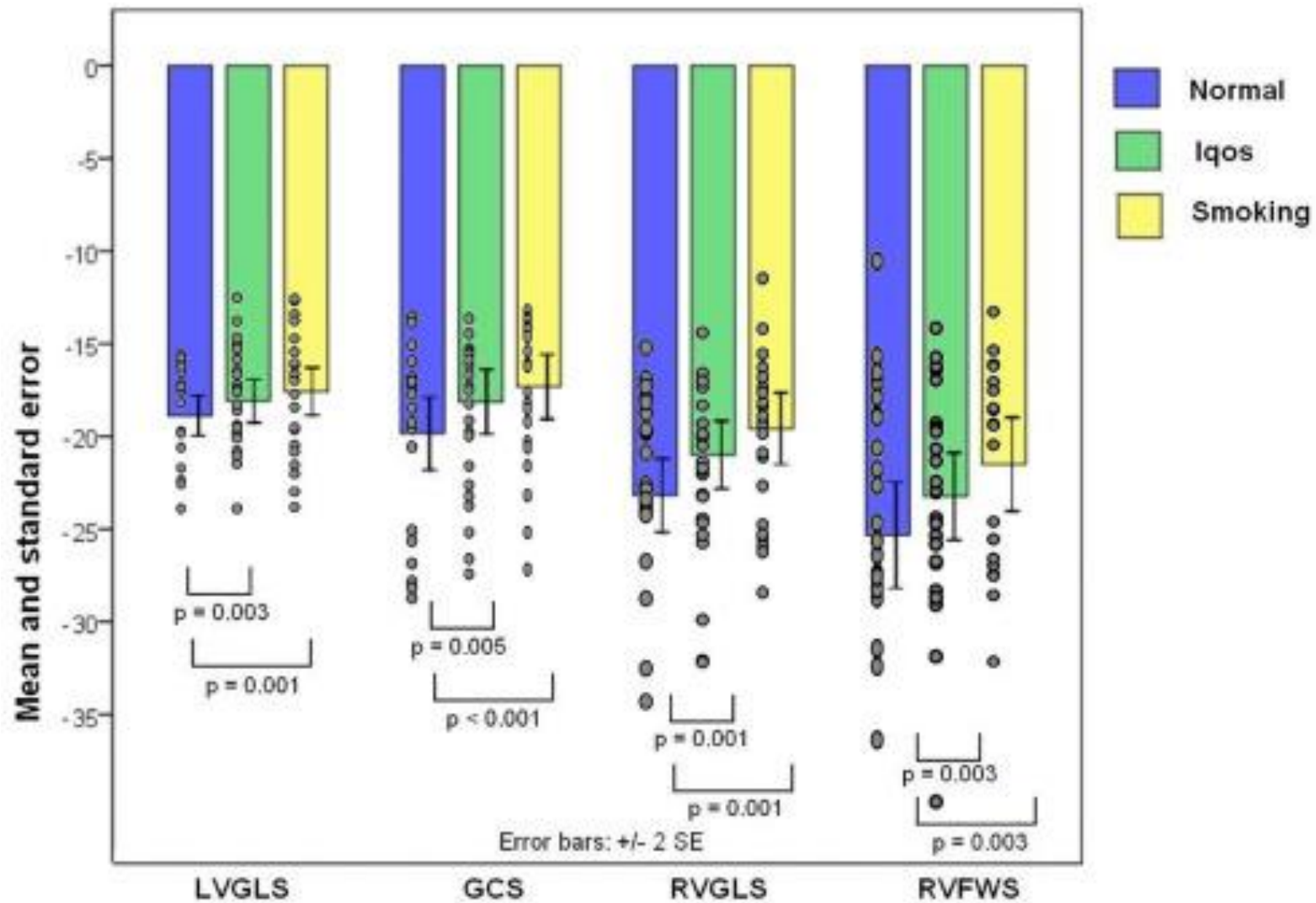
IQOS-induced lung emphysema in mice



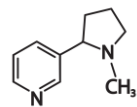
MLI – mean linear intercept – quantification of airspace enlargement

DI – destructive index

Myocardial deformation by IQOS



LVGLS – ventricular
global longitudinal
strain
GCS – LV
circumferential strain
RVGLS –RV global
longitudinal strain
RVFWS – RV free wall
strain

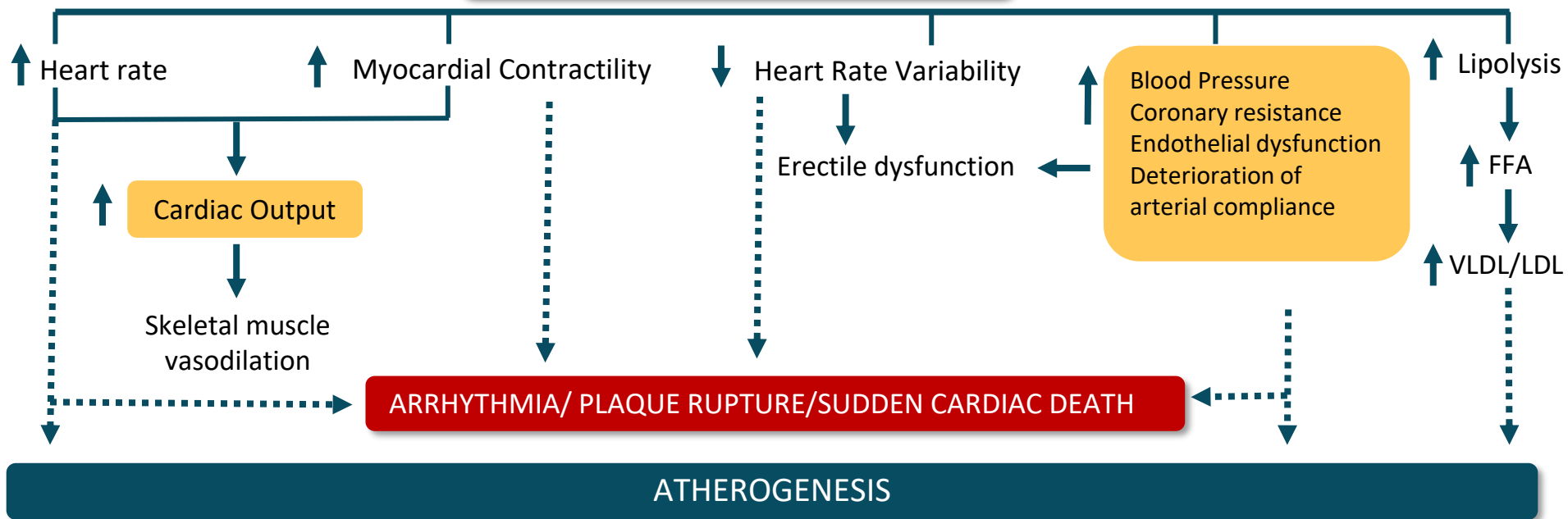


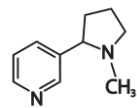
NICOTINE

Cholinergic Receptor

Brain, Autonomic Ganglia, Adrenals, Neuromuscular Junction

Sympathomimetic Effects



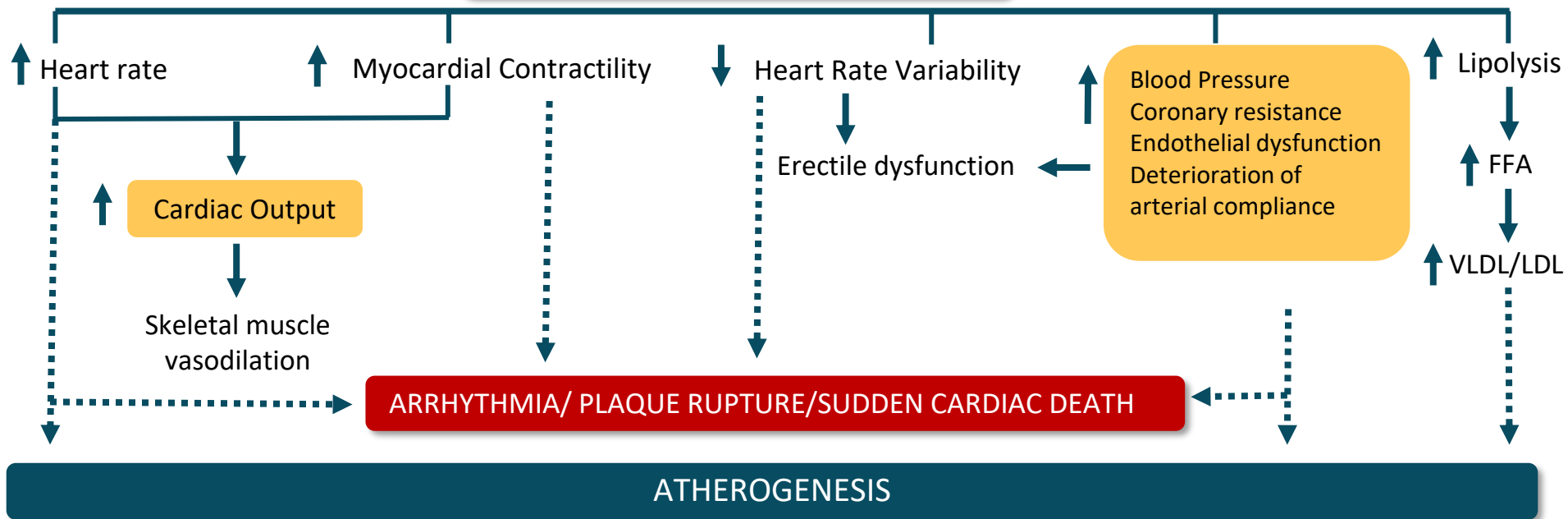


NICOTINE

Cholinergic Receptor

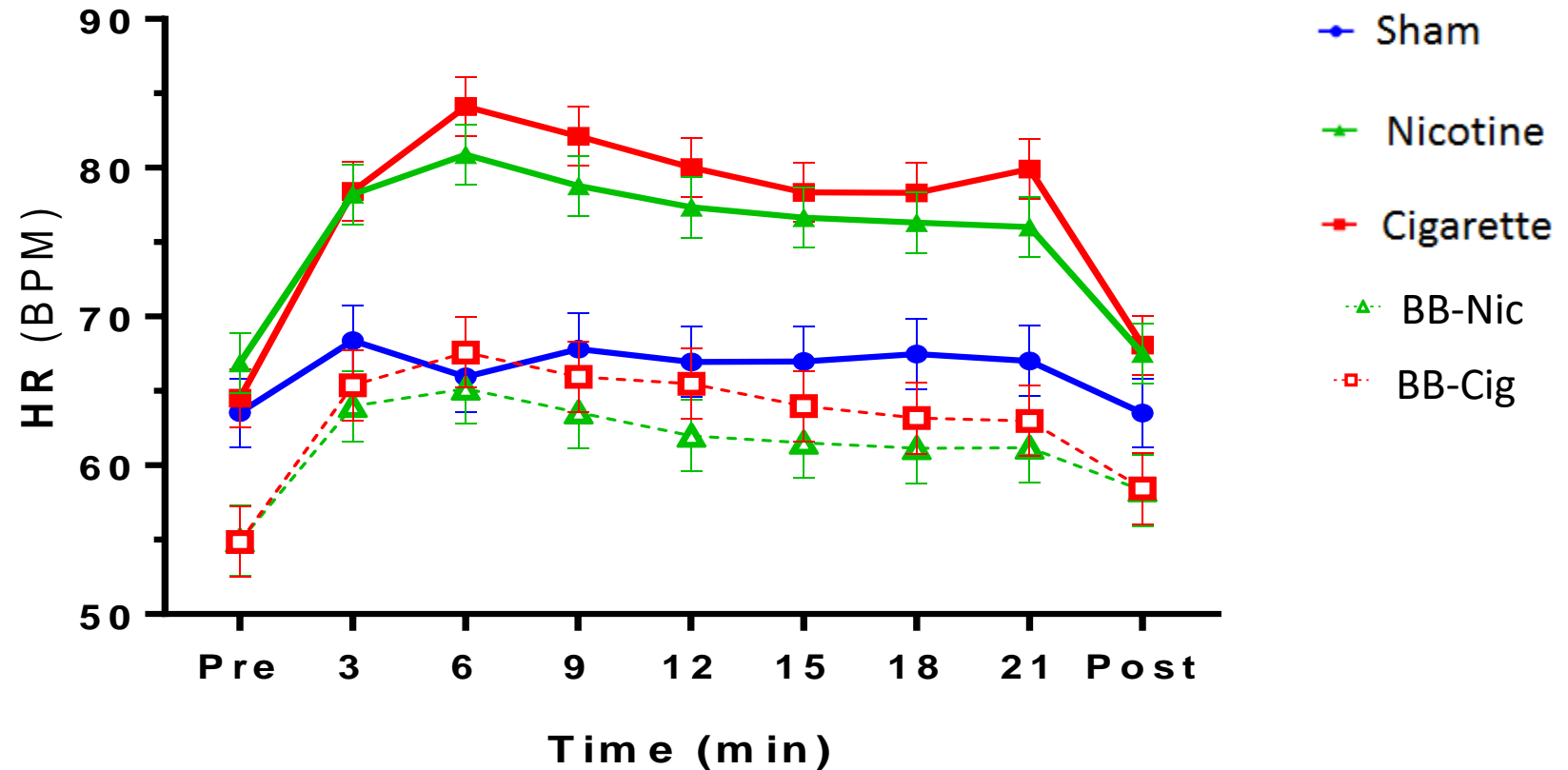
Brain, Autonomic Ganglia, Adrenals, Neuromuscular Junction

Sympathomimetic Effects



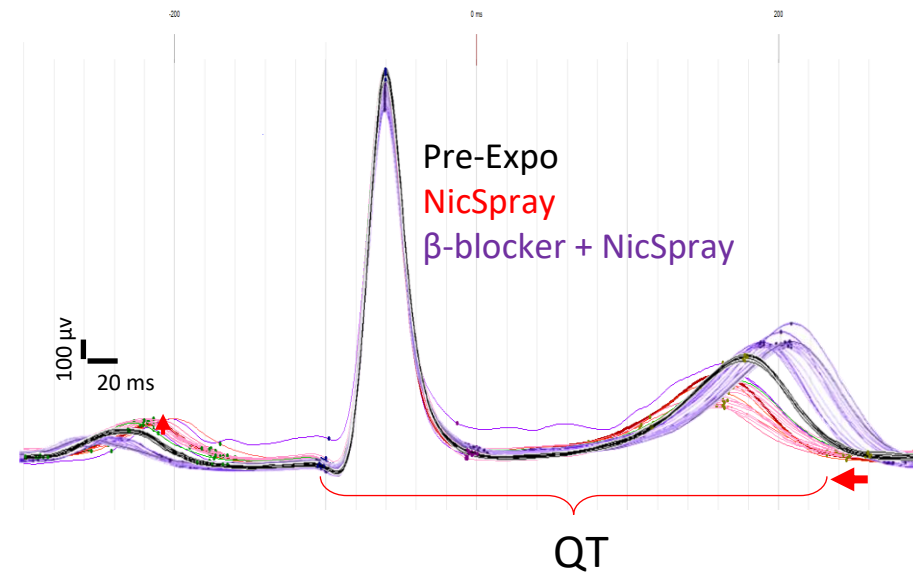
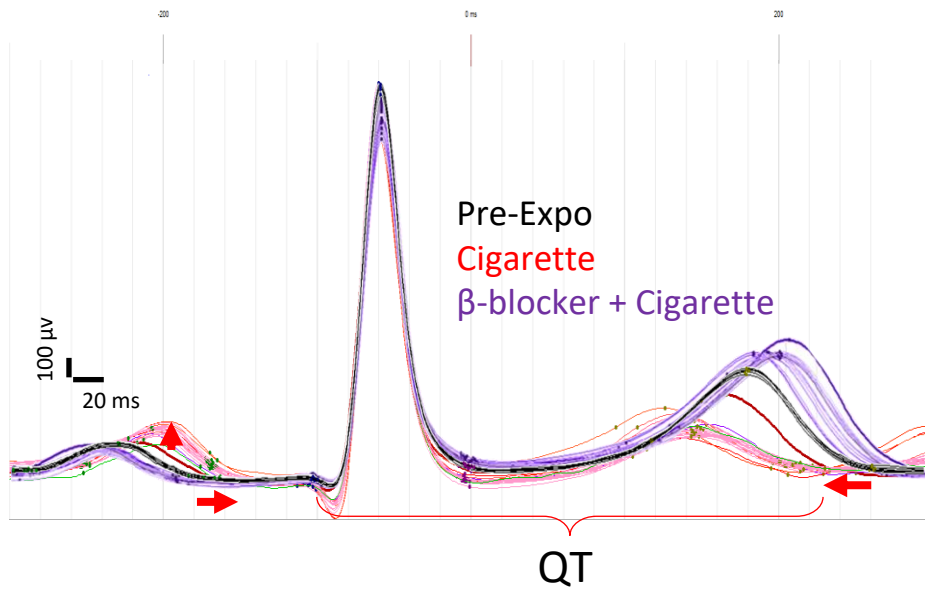
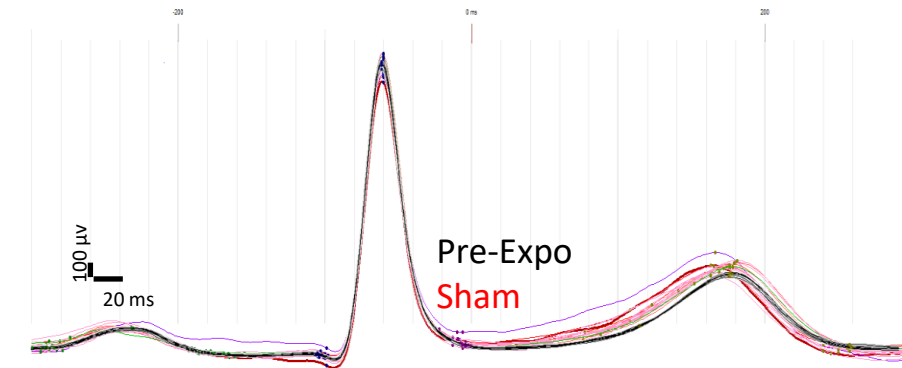
ATHEROGENESIS

Nicotine and Smoking Affect Heart Rate to the Same Extent

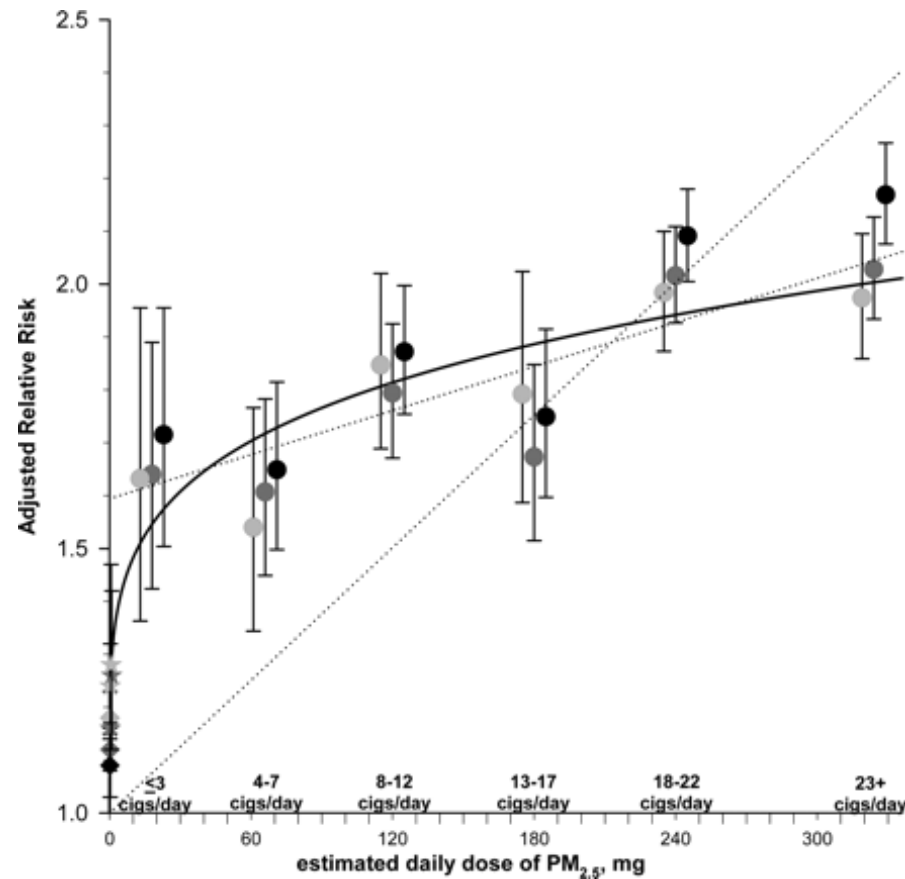


Participants (n=20) smoked a combustible cigarette or used nicotine spray \pm b-blocker propranolol

Smoking and Nicotine Shorten QT and PR (abolished by β -adrenergic blockade)



Reduced Exposure = Reduced Harm?



Harm depends on the level of exposure, which might increase with persistent e-cigarette use. For conventional cigarettes, the dose response for cardiovascular mortality is non-linear.

Most of the risk of smoking is at low doses. Smoking 3 cigarettes a day is associated with 80% of the harm due to smoking 2 packs a day

A 50 % less harmful device will be as harmful if used twice as often



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High-level overview of the most recent data from Japan

Angela van der Plas, Manager Real-World Evidence & Epidemiology

March 2023



PMI SCIENCE
PHILIP MORRIS INTERNATIONAL

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High-level overview of the most recent data from Japan

Angela van der Plas, Manager Real-World Evidence & Epidemiology

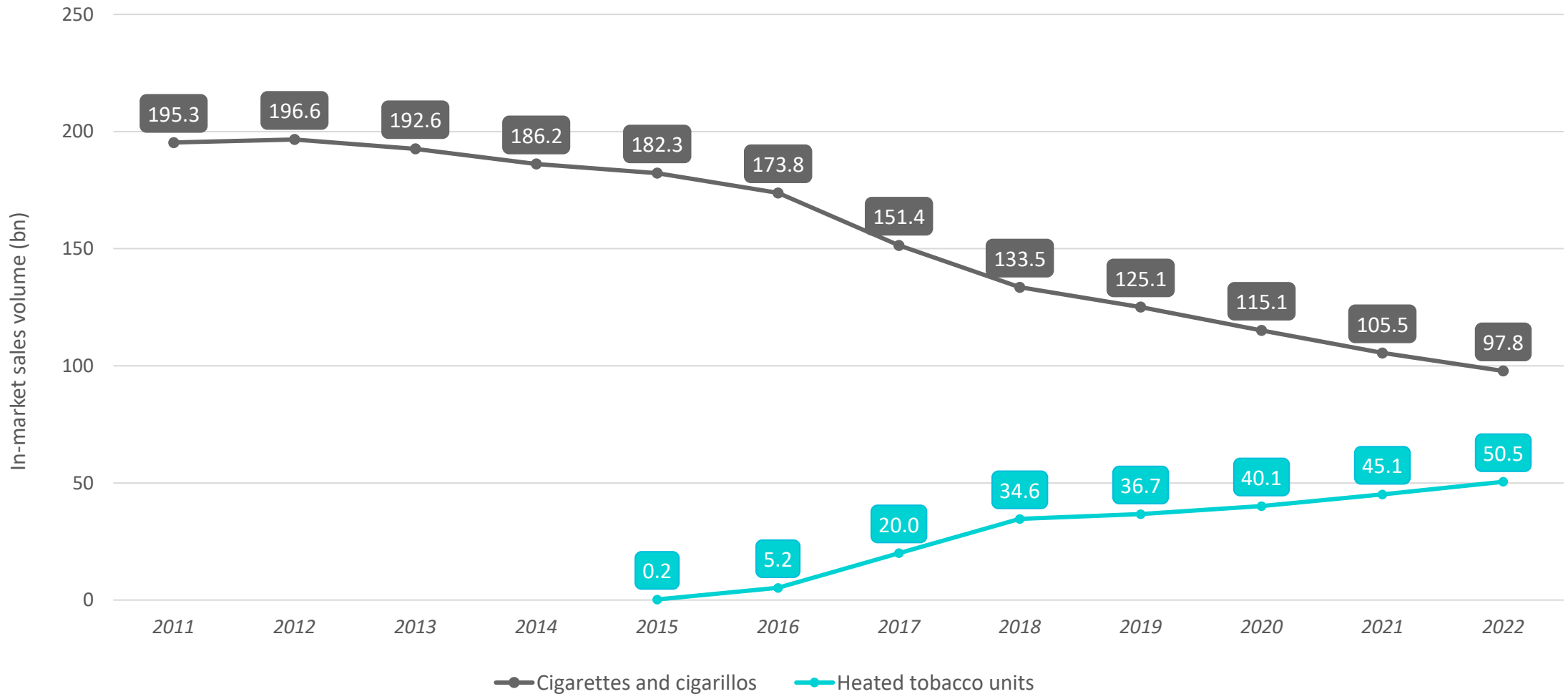
March 2023



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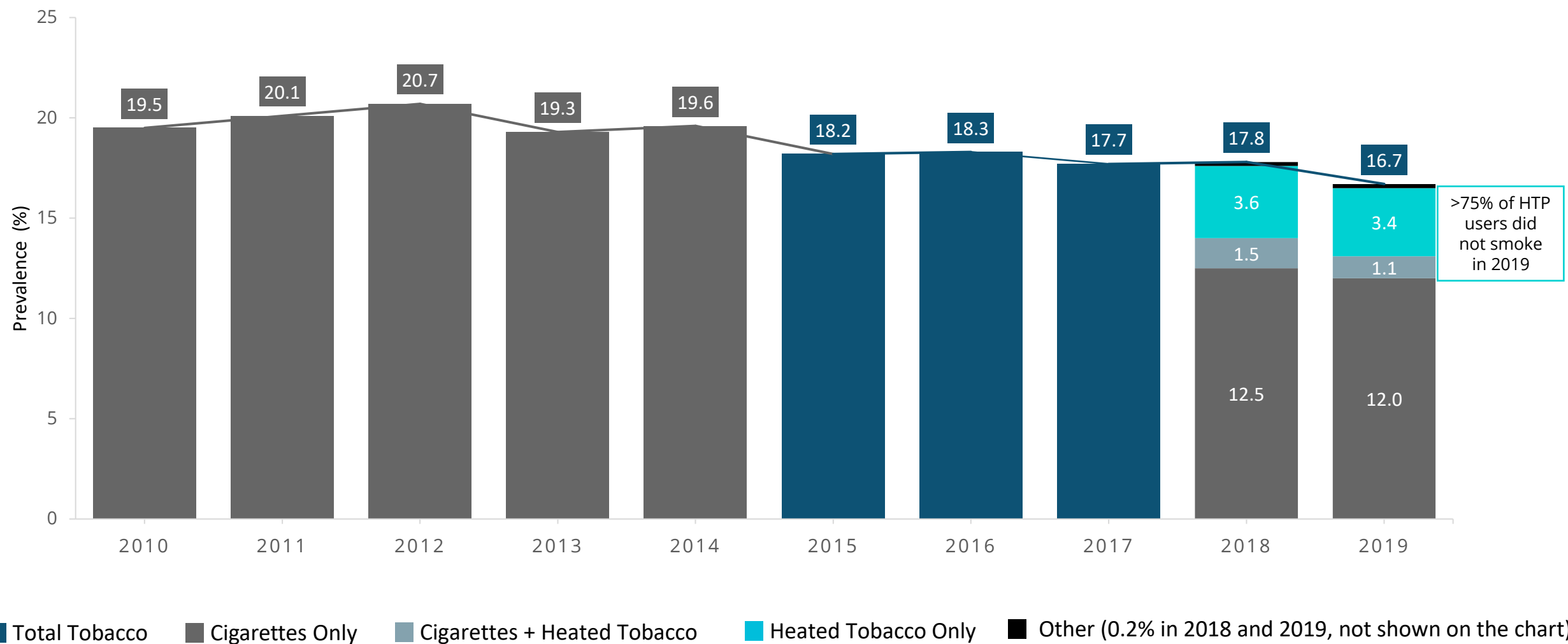


In-market sales volume of cigarettes, cigarillos, and HTUs in Japan



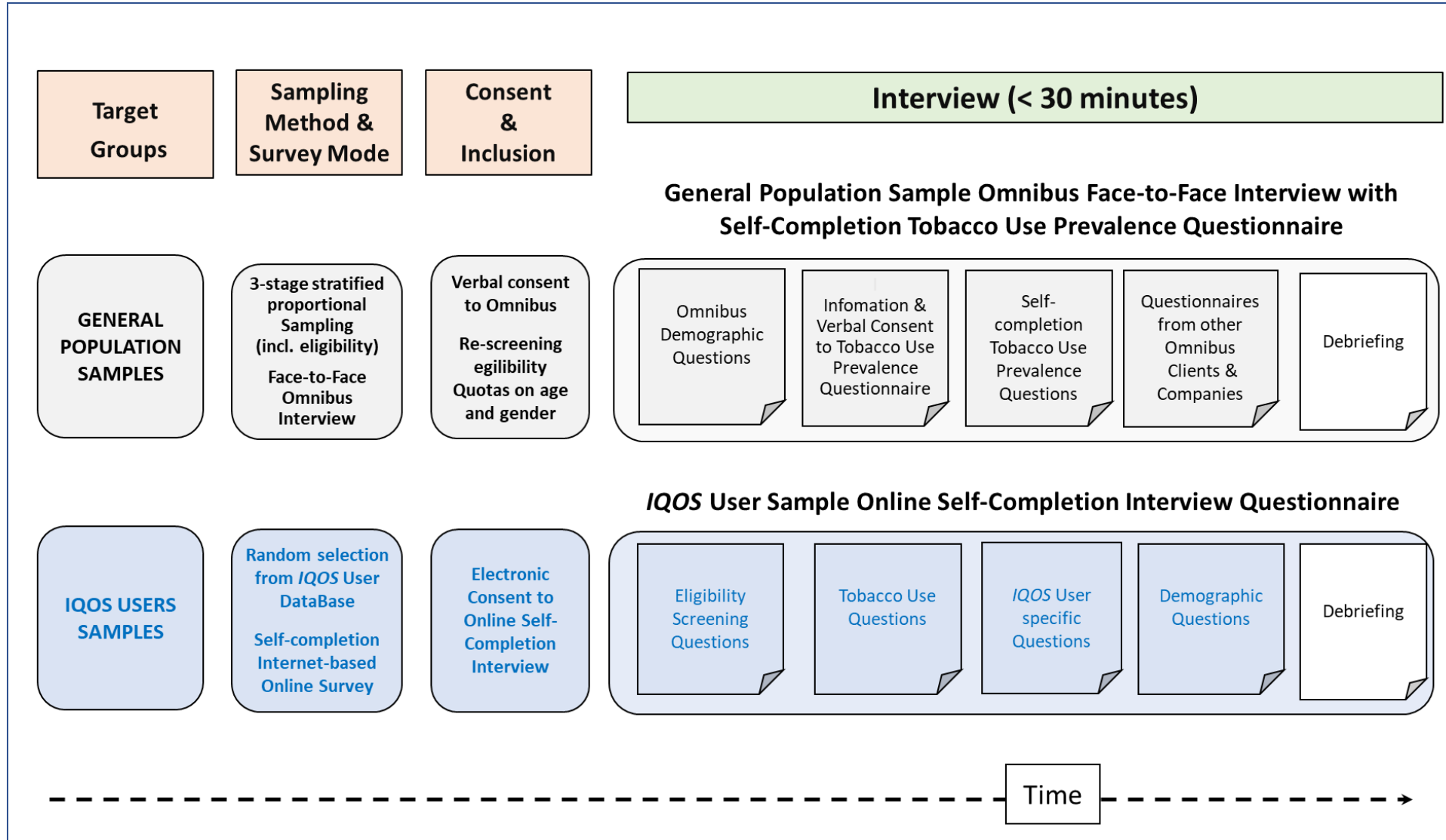
Adult (≥ 20 years) tobacco use prevalence in Japan

National Health and Nutrition Survey



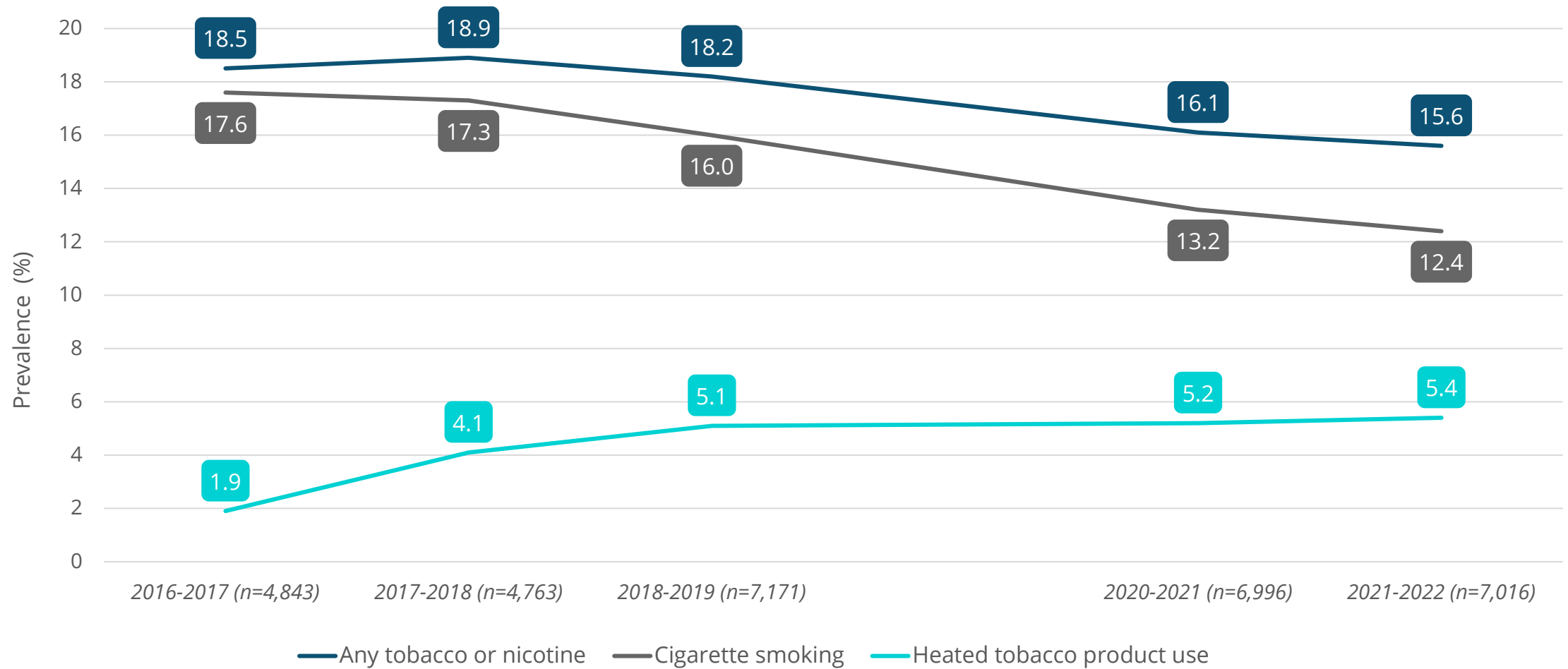


PMI's cross-sectional survey in Japan: Study design and plan



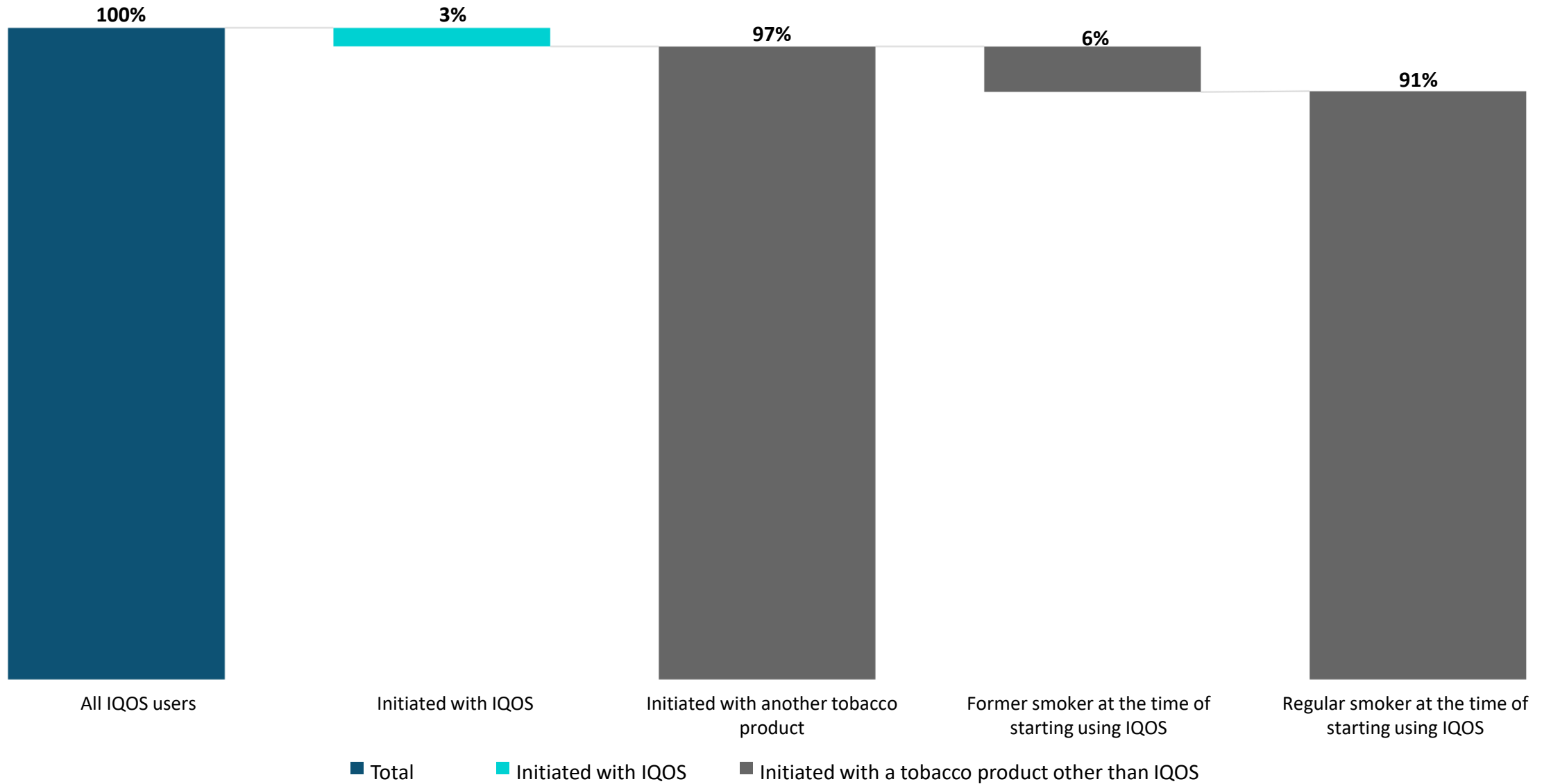


Adult tobacco use prevalence in Japanese adults



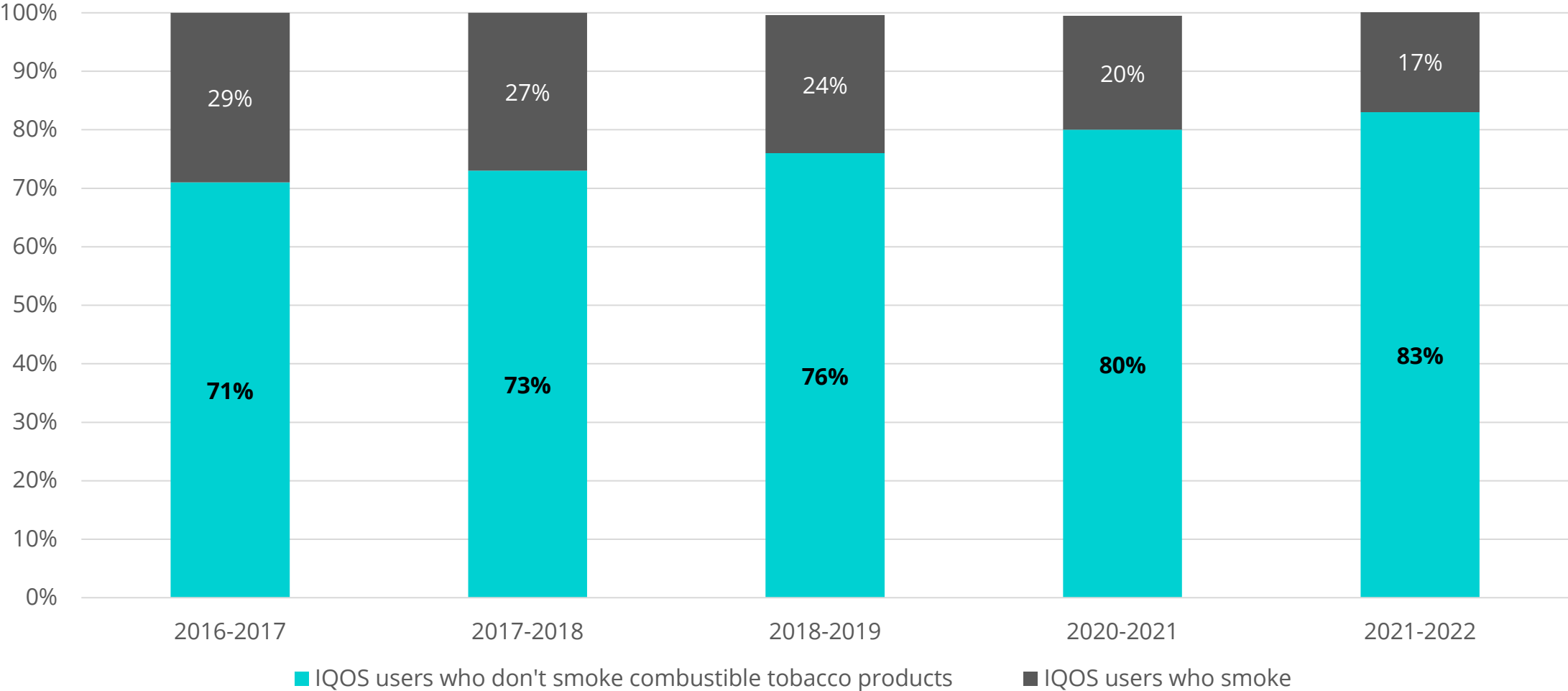


History of tobacco and nicotine use among adult IQOS users in Japan

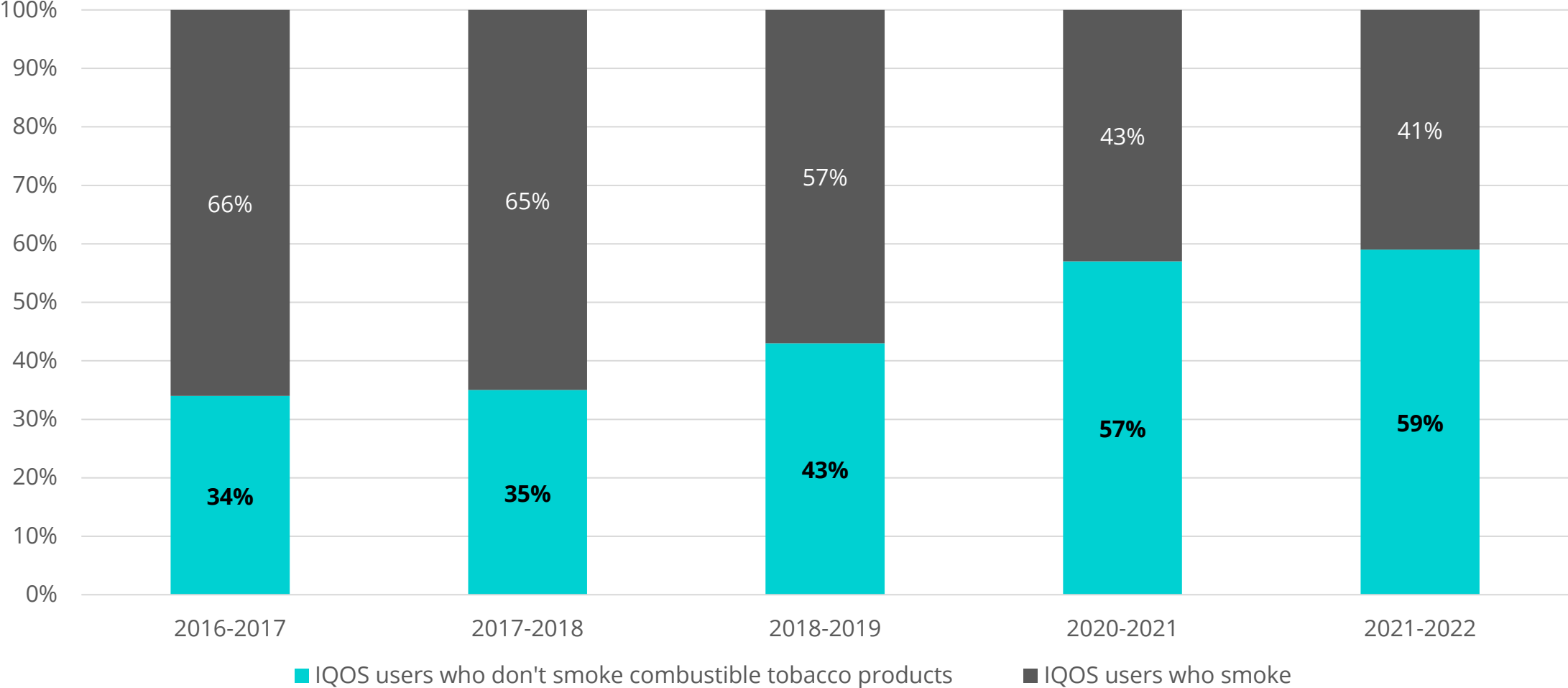




Patterns of use among adult IQOS users in Japan (IQOS user sample)



Patterns of use among adult IQOS users in Japan (general adult population sample)





Conclusions

- The prevalence data in Japan show that the overall tobacco use moderately declined following the introduction of heated tobacco products, with the share of tobacco users who smoke declining at an accelerated pace at the time the prevalence of heated tobacco product increased.
- These trends indicate that heated tobacco products may be successfully replacing cigarettes and have likely contributed to a decline in the prevalence of cigarette smoking in Japan.
- While the prevalence of cigarette smoking had plateaued at between 19-20% before 2015, the introduction and uptake of heated tobacco products coincided with an accelerated decrease of smoking prevalence to around 12% in 2022.
- The survey data also show that virtually all heated tobacco product users had a history of smoking before switching to heated tobacco products, and the majority of heated tobacco product users did not smoke combustible tobacco products.