

Characterization of Adult Cigarette Smokers' Behavior During Short- and Longer-Term Use of Reduced Nicotine Content Cigarettes

Andrea Rae Vansickel, Mingda Zhang, Jan Angel

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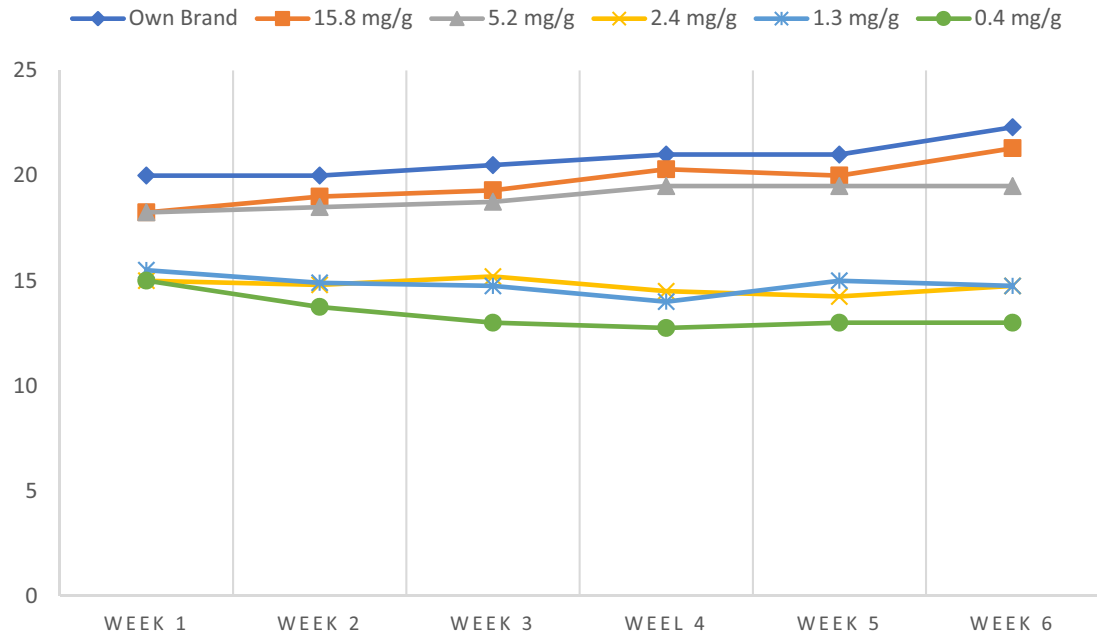
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Introduction

- FDA is considering a cigarette nicotine standard to make them “minimally or nonaddictive.”
- Recent research supporting this potential rule has centered around a single set of stimuli
- Switching to SPECTRUM[®] research cigarettes with reduced nicotine content results in fewer self-reported cigarettes per day (e.g. Donny et al., 2015; Hatsukami et al., 2018).
- However the SPECTRUM[®] research cigarettes are not acceptable to many smokers (e.g. Mercincavage, 2017; Hatsukami et al. 2013) evidenced further by high non-compliance rates (e.g. Donny et al. 2015)

Previous Work Demonstrates Fewer Self-Reported CPD With Reduced Nicotine SPECTRUM[®] Cigarettes

STUDY CIGARETTES (REDRAWN: DONNY ET AL., 2015)



73 to 81% of participants reported **non-study cigarette use** on **24 to 35% of days** in the 5.2 mg/g and less conditions (Donny et al., 2015)

Non-study CPD Estimates Exceeded Self-Reported CPD Reductions Based on Biomarker Data



The average under-reported CPD estimates are higher than the corresponding self-reported CPD reductions after switching to VLNC for six weeks, with 15.8 mg/g CNC as the reference (Donny et al. 2015). Therefore, when the magnitude of under-reporting is taken into consideration, there was no reduction in the total number of CPD for any VLNC group in the study compared to the reference group. The red line indicates the baseline CPD. (Zhang et al., 2019)



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Study Objectives

- Characterize differences in CPD and willingness to use the product again between the test prototype cigarettes (reduced nicotine content (RNC, 1.3 mg/g nicotine in tobacco filler) and normal nicotine content (NNC, 15.3 mg/g nicotine in tobacco filler)) and usual brand cigarette smoking under short-term conditions.
- Characterize the effect of longer-term (17 days), at-home use of RNC cigarettes on number of cigarettes per day relative to NNC cigarettes.
 - Capture and closely examine self-reported non-compliance

Study Products

RNC Test Cigarette (A)	NNC Test Cigarette (B)	Own Brand Cigarette (C)
<ul style="list-style-type: none">• 1.3 mg nicotine per gram tobacco filler (1.3 mg/g)• 10 mg Tar• King Size• Menthol and Non-Menthol• Unbranded• Test-Test	<ul style="list-style-type: none">• 15.3 mg nicotine per gram tobacco filler (15.3 mg/g)• 10 mg Tar• King Size• Menthol and Non-Menthol• Unbranded• Internal Control	<ul style="list-style-type: none">• Any market brand• Mid to Low Tar• King Size• Menthol and Non-Menthol• Branded – Free of charge• Positive Control

Summary of Findings

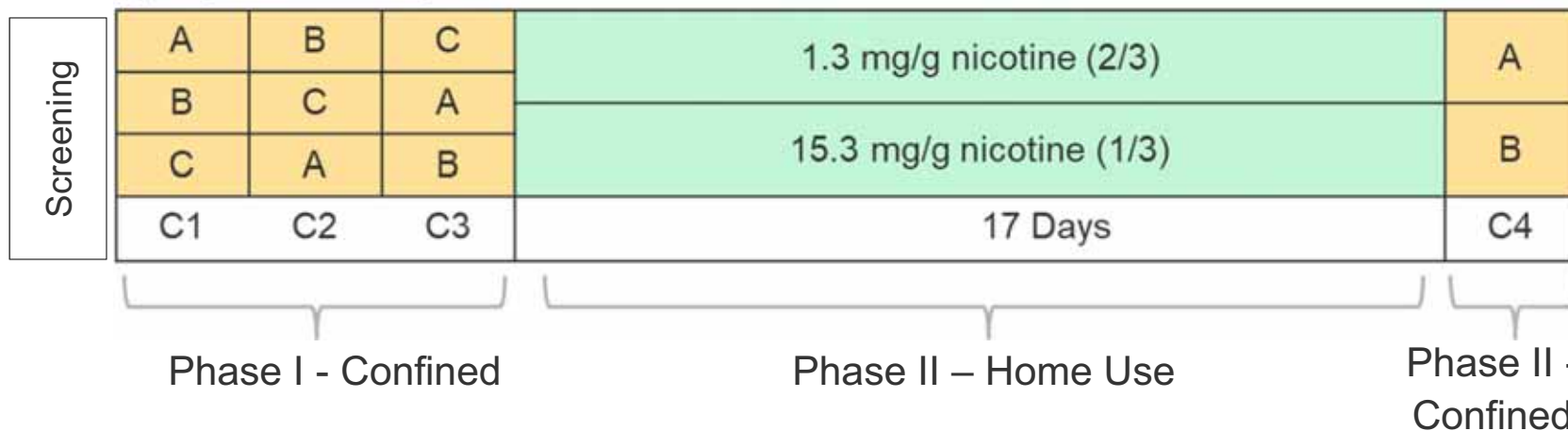
- Our findings diverge from a previous study with SPECTRUM[®] cigarettes (Donny et al., 2015)
- We observed no difference in cigarettes per day between the 1.3 and 15.3 mg/g cigarette during 17-days of home use
- Relatively low self-reported non-compliance rates observed for both conditions (0 to 9% on any given day)

Unique Study Design

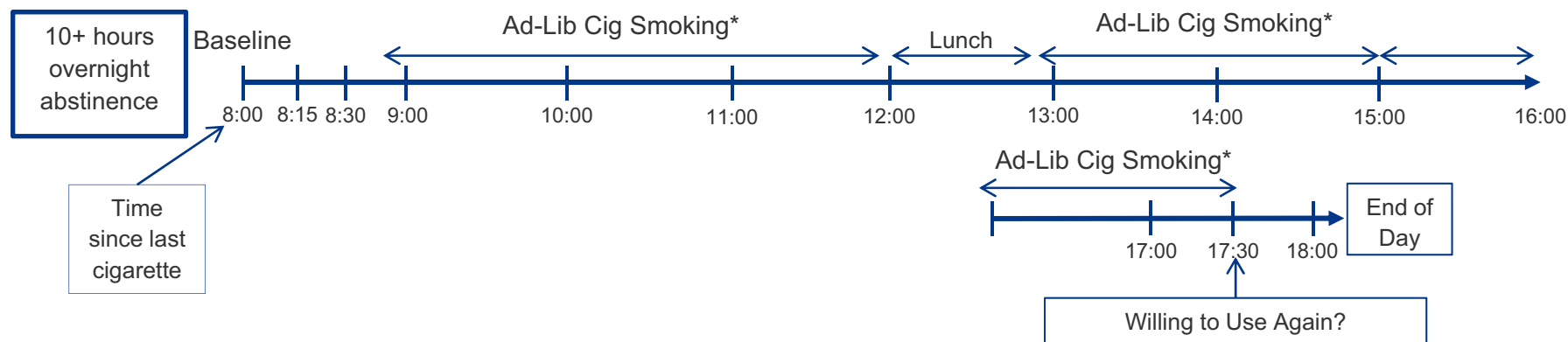
Study Overview:

Random Assignment to Product Order

Random Assignment to Test Cigarette, Daily
Electronic Diaries



Confined Study Days:



*Staff-Allocated; Personal Ash Trays & Butt Collection



Participant Demographics

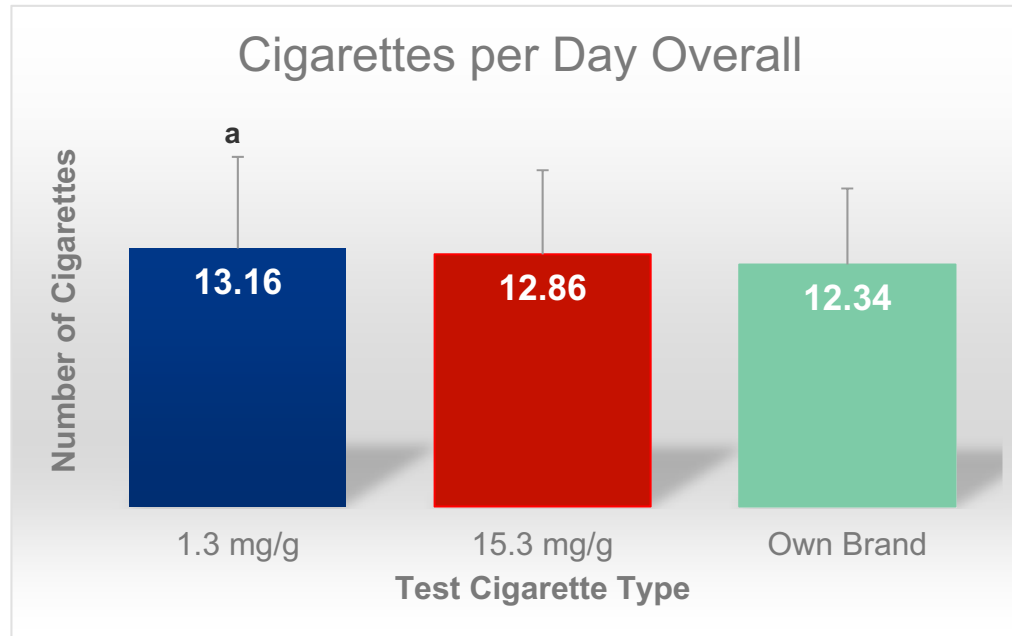
Characteristic	Menthol Group	Non-Menthol Group	Total Sample
Gender	20 Female 15 Male	16 Female 19 Male	36 Female 34 Male
Age ¹	46 (\pm 11.9)	42.5 (\pm 11.8)	44.3 (\pm 11.9)
Cigarettes per Day (CPD) ¹	14.9 (\pm 7.6)	19 (\pm 7.2)	16.9 (\pm 7.6)
Employed Full Time	34%	37%	36%
Education – Some College	25.7%	24.3%	25%

¹ Average \pm S.D.

Phase I Results

Confined, 3-Way Crossover

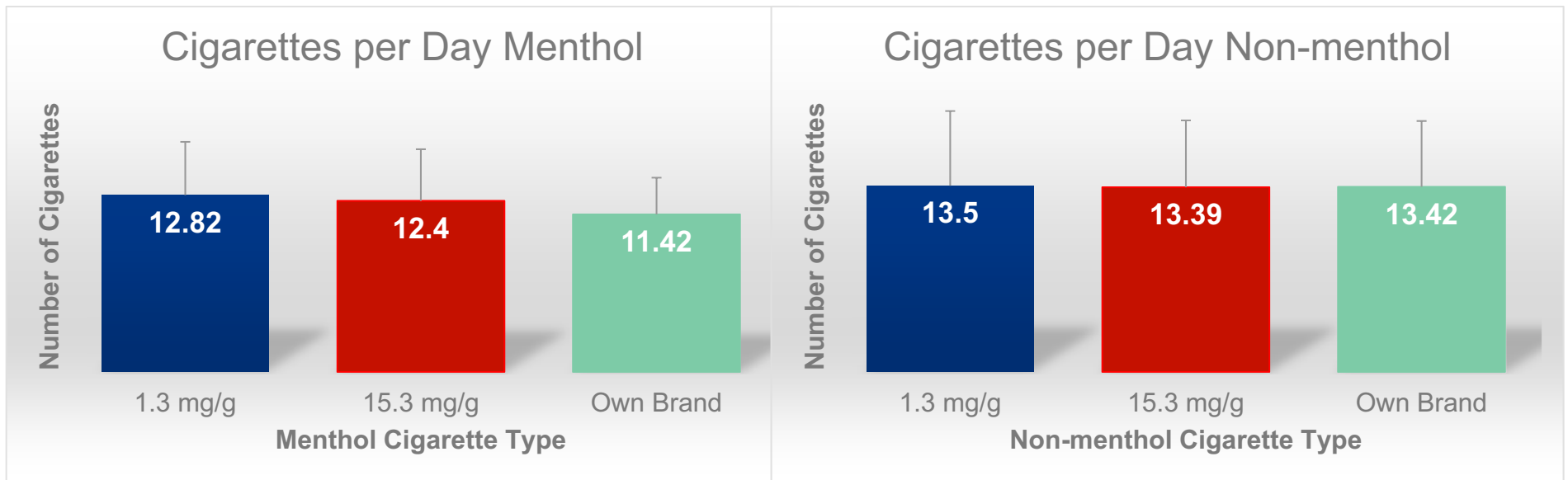
Phase I - Confined: Marginally Greater CPD With the 1.3 mg/g Test Cigarette Relative to Own Brand



^a Marginal difference between 1.3 and Own Brand $p = 0.05$

Screening Average CPD: 16.9, N = 70

Phase I - Confined: No Difference in CPD When Broken Out by Menthol/Non-Menthol Subgroups



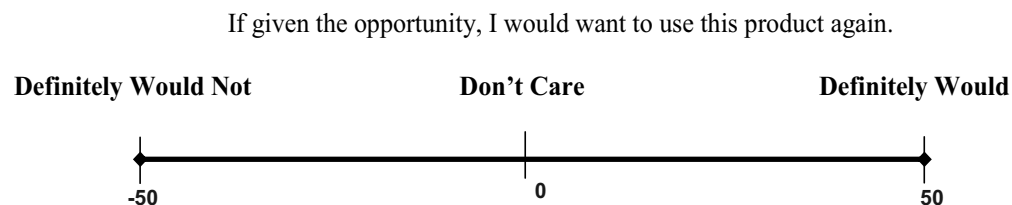
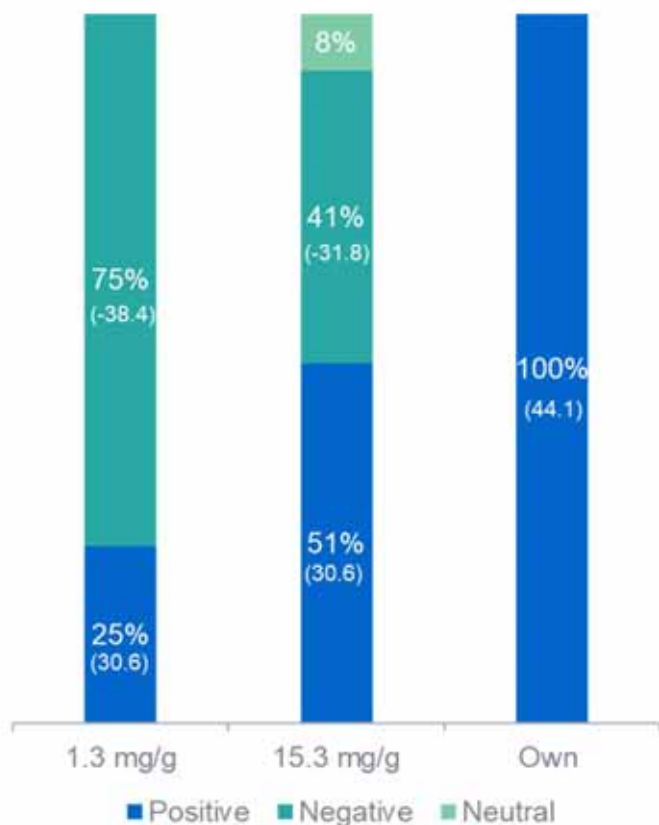
Screening Average CPD: 14.9, N = 35

Screening Average CPD: 19, N = 35



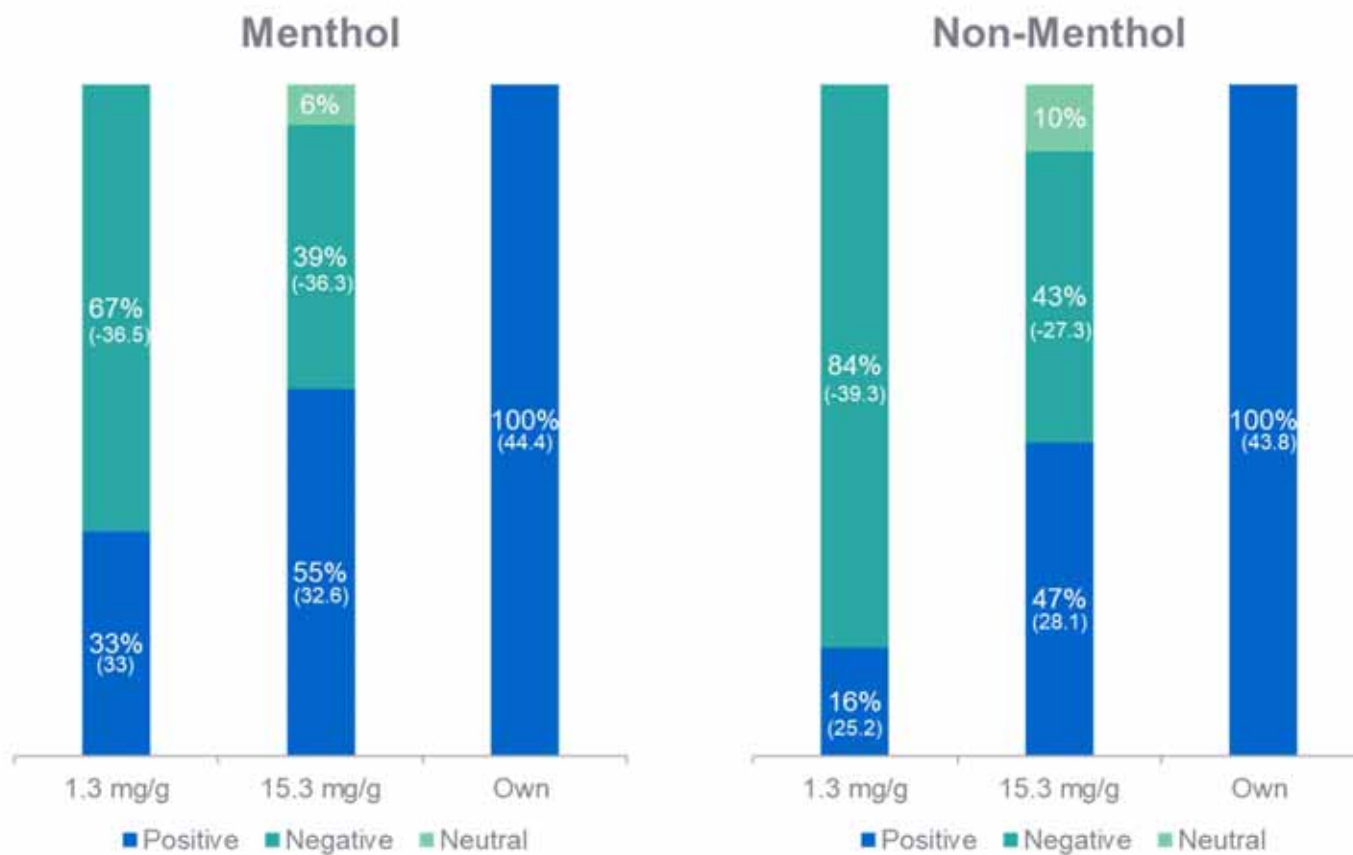
Phase I - Willingness to Use Differed by Product

OVERALL



Significant difference between 15.3 mg/g and 1.3 mg/g: Fisher's Exact Test (two-sided; $p < 0.001$)

Phase I - Willingness to Use by Menthol Preference



Significant difference between 15.3 mg/g and 1.3 mg/g: Fisher's Exact Test (two-sided; $p < 0.05$)

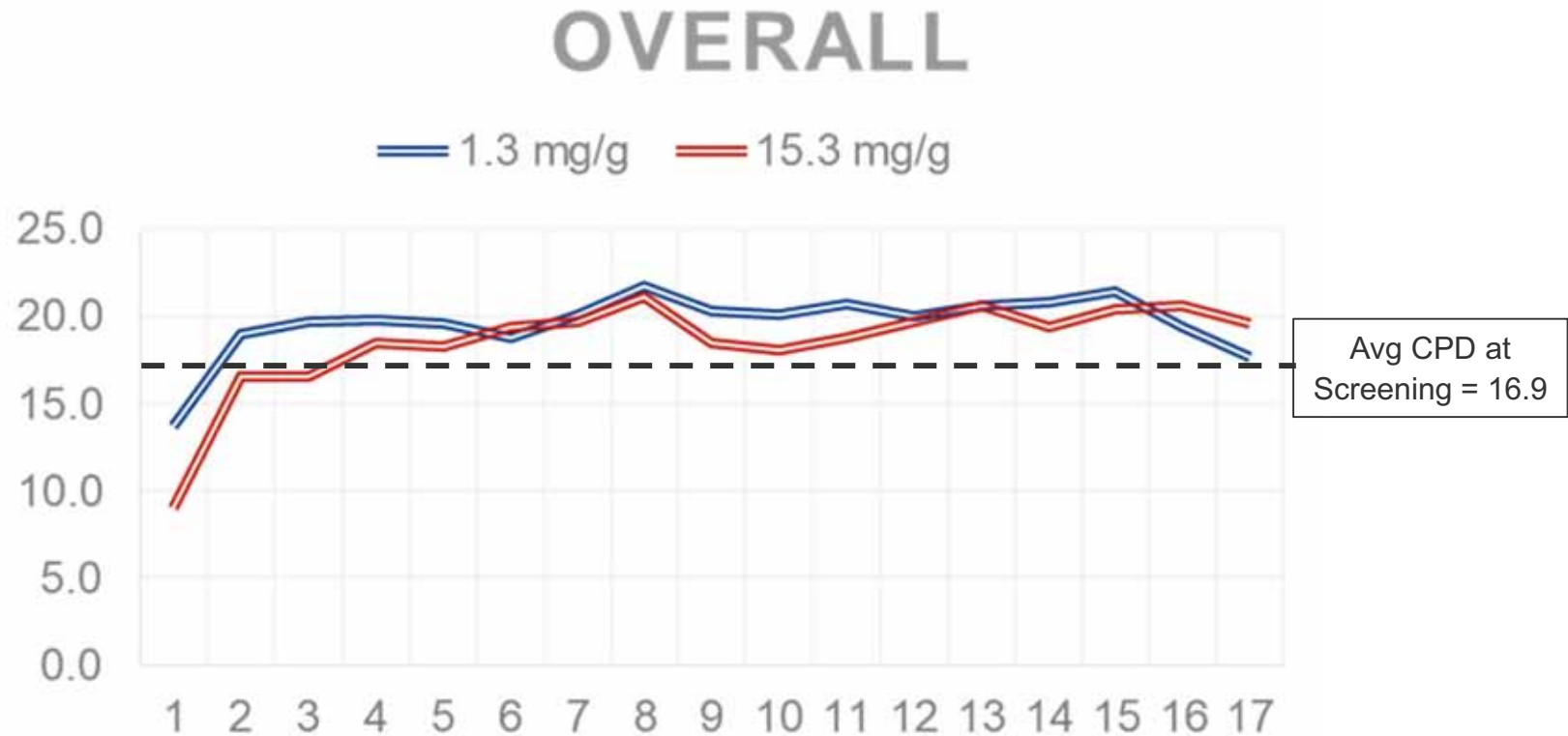
Significant difference between 15.3 mg/g and 1.3 mg/g: Fisher's Exact Test (two-sided; $p < 0.01$)



Phase II Results

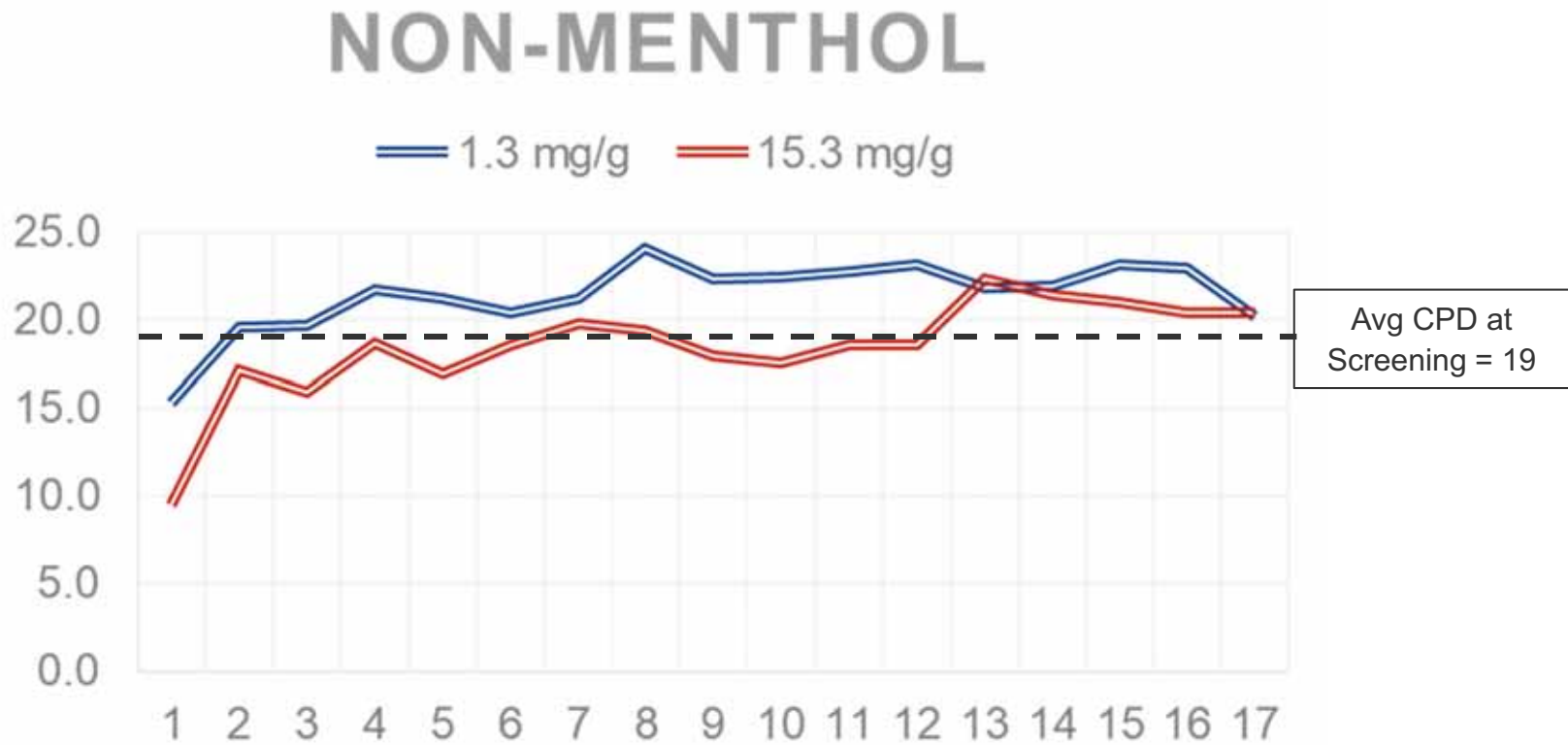
17-Day At-Home Use

Phase II – Home Use: Overall CPD was Similar between 1.3 and 15.3 mg/g Test Cigarettes



1.3 mg/g N = 43; 15.3 mg/g N = 22

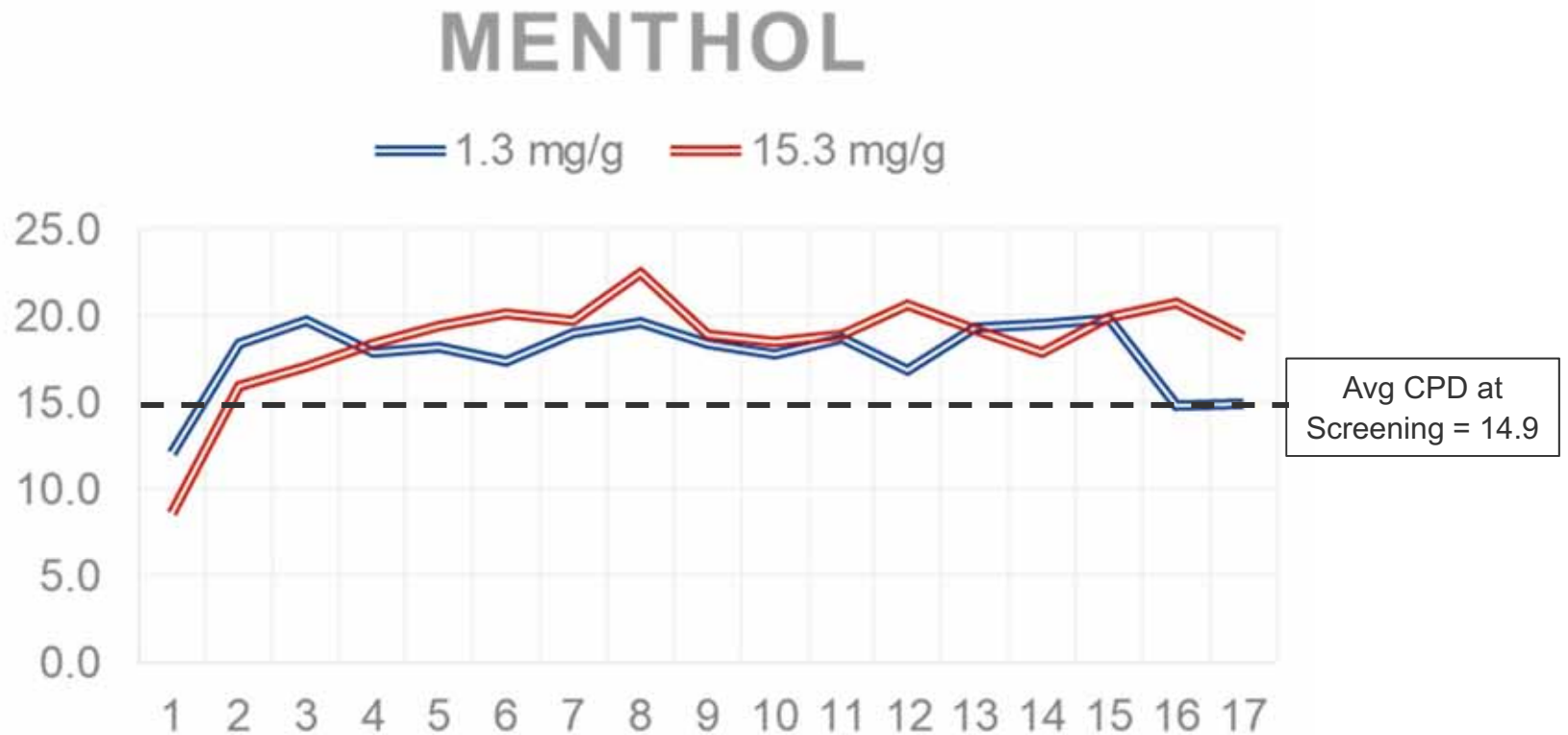
Phase II – Home Use: Non-Menthol Smokers' CPD Tended to be Higher in the 1.3 mg/g Test Condition Relative to 15.3 mg/g



1.3 mg/g N = 21; 15.3 mg/g N = 10



Phase II – Home Use: Menthol Smokers’ CPD was Similar Between 1.3 and 15.3 mg/g Test Cigarettes

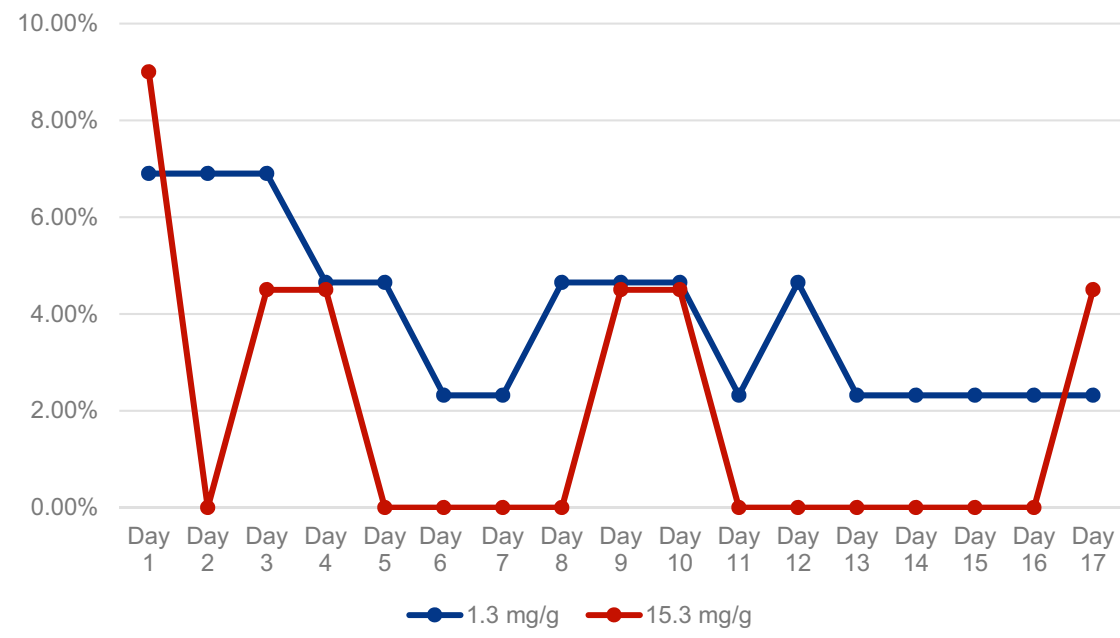


1.3 mg/g N = 22; 15.3 mg/g N = 12



Phase II – Home Use: Self-Reported Non-Compliance Among the Study Population was Low

Percent of Participants Reporting Non-Study Cigarette Smoking



	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Day 15	Day 16	Day 17
1.3 mg/g; N =	3	3	3	2	2	1	1	2	2	2	1	2	1	1	1	1	1
15.3 mg/g; N =	2	0	1	1	0	0	0	0	0	1	1	0	0	0	0	0	1

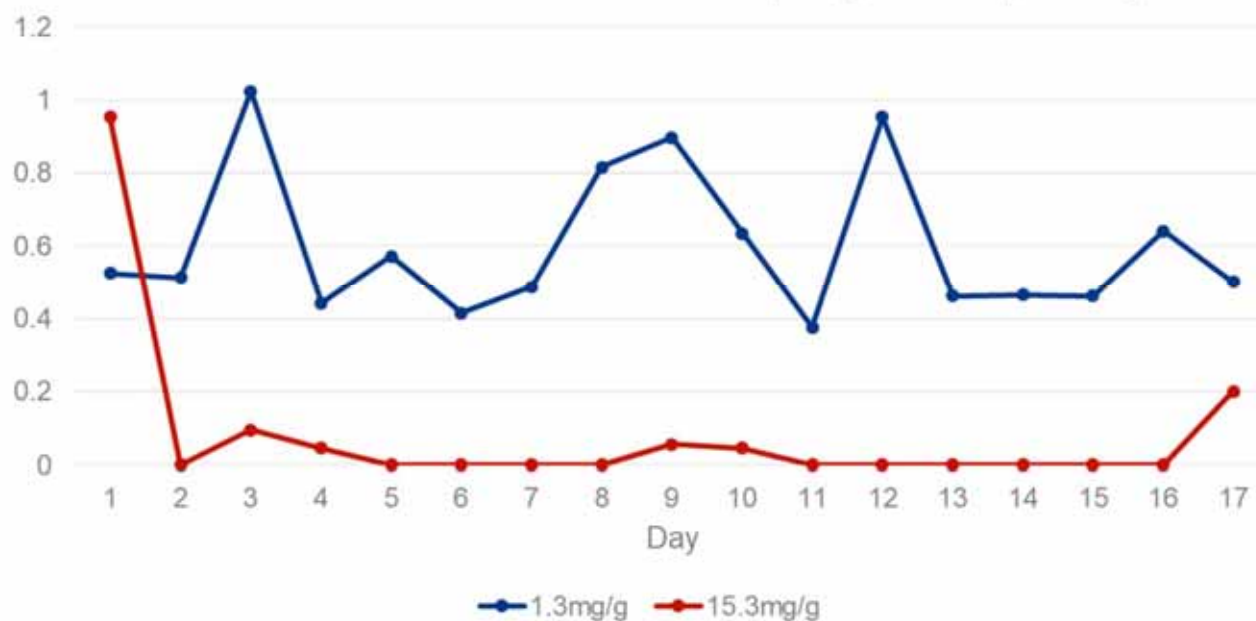
- 57 to 81% of Donny et al. self-reported non-compliance with SPECTRUM®
- 27.3% (15.3 mg/g) and 16.7% (1.3 mg/g) reported non-compliance on at least one day in this study
- Shorter observation period



Phase II – Home Use: The Denominator Matters When Reporting Non-Study Cigarette Use

Overall Sample as Denominator

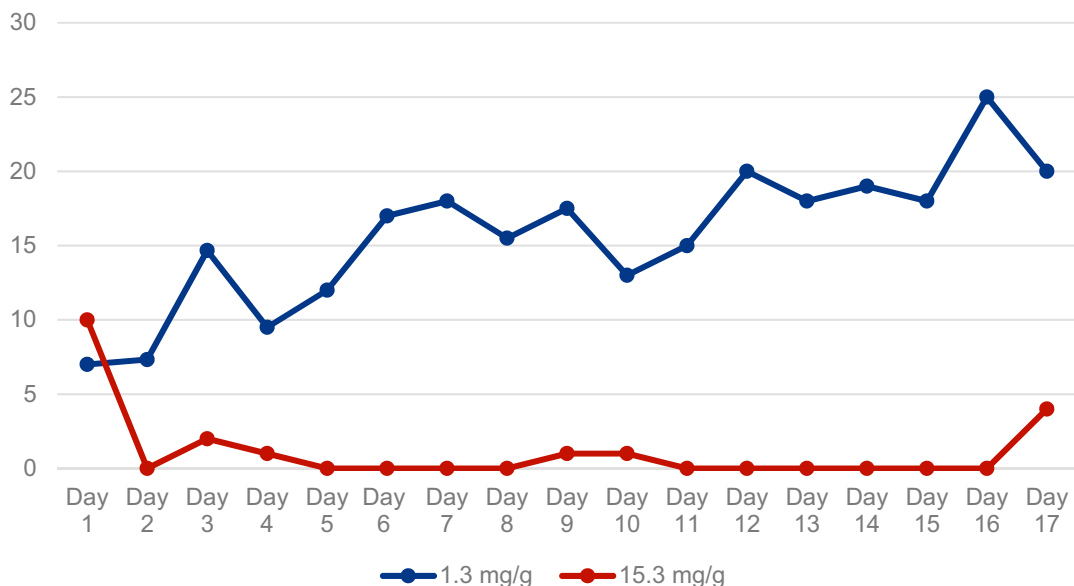
Mean Number of Non-study Cigarettes per day



Phase II – Home Use: The Denominator Matters When Reporting Non-Study Cigarette Use

Non-Compliant Number as Denominator

Mean Number of Non-Study Cigarettes per Day Among Participants Reporting Noncompliance



	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Day 15	Day 16	Day 17
1.3 mg/g; N =	3	3	3	2	2	1	1	2	2	2	1	2	1	1	1	1	1
15.3 mg/g; N =	2	0	1	1	0	0	0	0	0	1	1	0	0	0	0	0	1



Summary

- Marginally greater number of 1.3 mg/g cigarettes smoked relative to Own Brand in Phase I
- Proportions willing to use the product again: Own Brand > 15.3 mg/g > 1.3 mg/g in Phase I
 - 51% (15.3 mg/g) and 25% (1.3 mg/g) positive willingness to use the product again
- Similar cigarettes per day between the 1.3 and 15.3 mg/g cigarette conditions, overall during Phase II
- Relatively low self-reported non-compliance rates observed in Phase II for both conditions

Limitations

- Limitations of this study include small sample size, short observation period, self-reported cigarette consumption and no biochemical verification of compliance.
- A common limitation of this study as well as other studies is the use of cigarettes at different nicotine levels that are also different in sensory performance and construction.
 - This common limitation makes it difficult to determine the contribution of nicotine reduction to changes in smoking behavior vs. sensory performance issues

Conclusions

- Our findings indicated similar consumption of the 1.3 mg/g and 15.3 mg/g test cigarettes and low self-reported non-compliance during the 17-day home use period
 - These findings diverge from a previous study, which showed fewer self-reported CPD with SPECTRUM[®] RNC (1.3 mg/g) relative to NNC (15.8 mg/g) after a similar duration of home use and higher self-reported non-compliance rates (Donny et al., 2015)
- Analyses and interpretation of results from behavioral studies should differentiate the contribution of nicotine level versus other sensory attributes on behavioral outcomes

References

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- Hatsukami, Luo, Jensen et al. Effect of immediate versus gradual reduction in nicotine content of cigarettes on biomarkers of smoke exposure: a randomized clinical trial. *JAMA* 2018, 320(9): 880-891
- Zhang M, Edmiston J, Karles G, McKinney W, Smith D: Method for Estimating Non-study Cigarette Use Among Switchers to Very Low Nicotine Content (VLNC) Cigarettes in Ambulatory Clinical Trials. In: *SRNT 2019*. San Francisco, CA; 2019: Poster #55.