Estimating the extent to which nicotine vaping increases cannabis initiation risk in the presence of positivity violations

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BACKGROUND

- Numerous studies found that nicotine vaping increases cannabis initiation risk.
- The extent to which the studies satisfied positivity, a causal identification assumption, is unknown.
- Positivity is the nonzero probability that there are observations at all exposure levels in causal contrast within observed covariate strata.
- Failure to satisfy positivity could lead to invalid inference that nicotine vaping causes cannabis initiation.

AIM

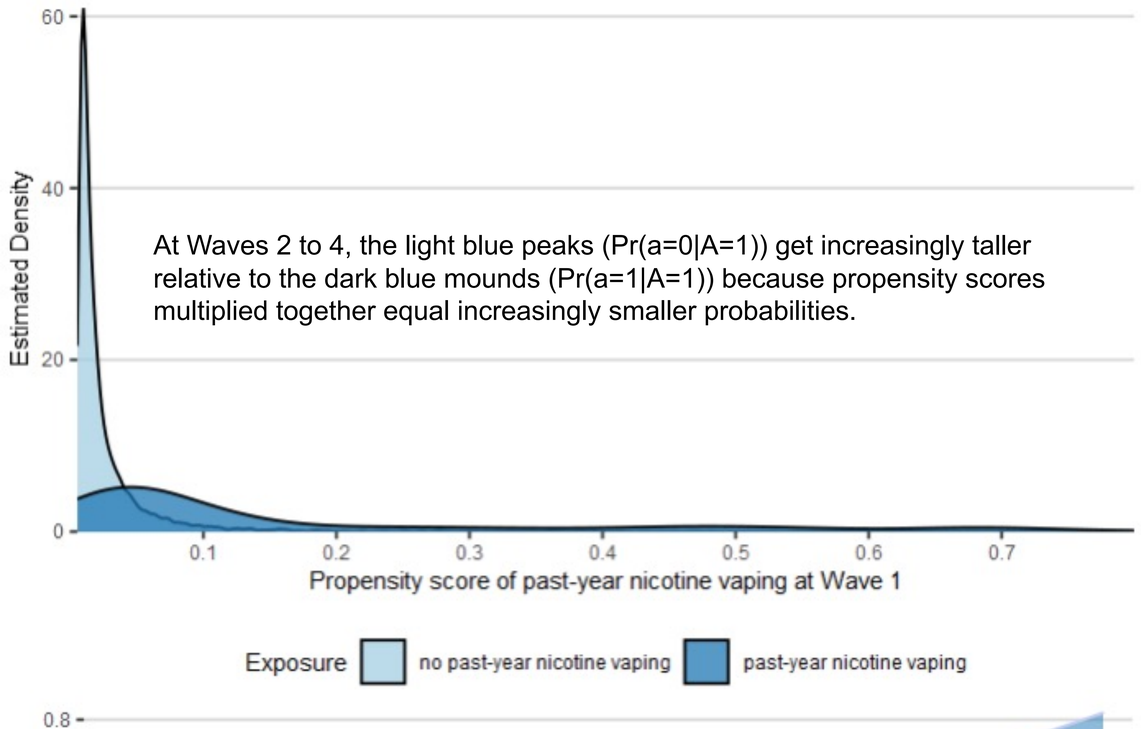
- To estimate the extent to which nicotine vaping affects the risk of cannabis initiation.

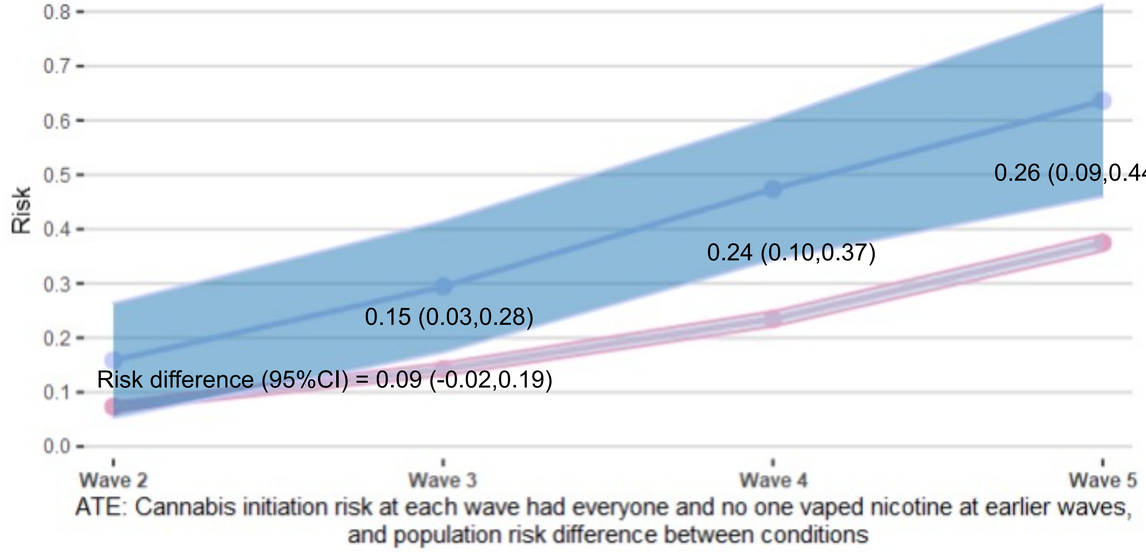
METHODS

- **Data**: Population Assessment of Tobacco & Health, Waves 1 (2013-14), 2 (14-15), 3 (15-16), 4 (16-18), and 5 (18-19) / N=9,571 baseline participants aged 12-16 years old.
- **Outcome**: Past-year cannabis initiation.
- **Exposure**: Past-year nicotine vaping at previous waves.
- **Covariates**: Socio-demographics, other substance use, family and friends' influences on substance use, psychopathology, school factors, and others.
- **Analyses**:

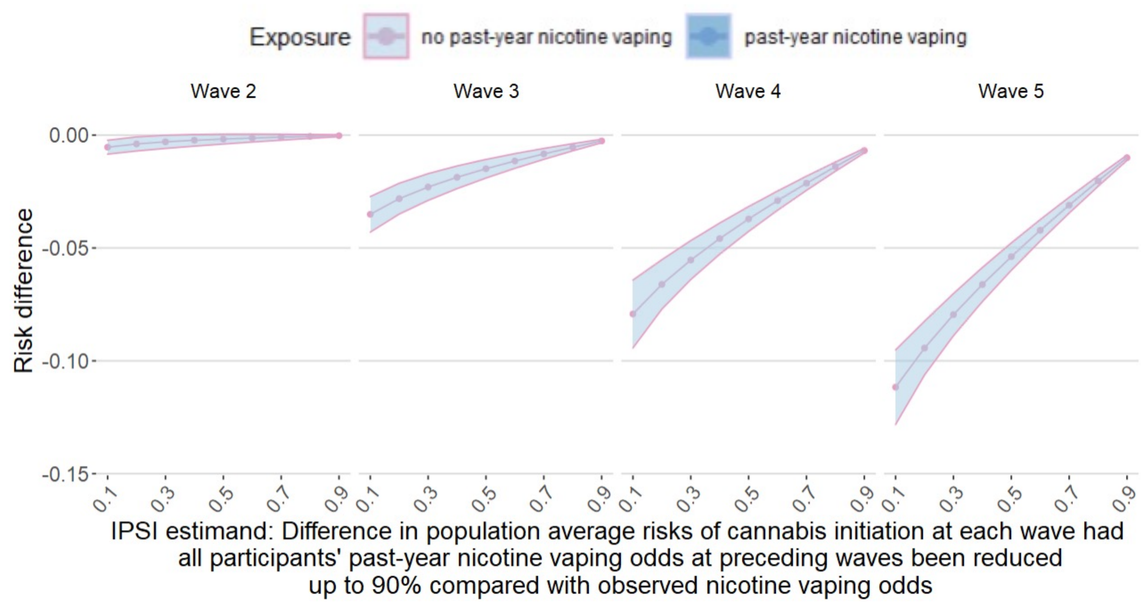
1. Nicotine vaping propensity score density at Waves 1, 2, 3, and 4 (with first imputed data set of 15).
2. *Average treatment effect (ATE)*: population average difference in cannabis initiation risk had everyone versus no one vaped nicotine in the past-year in preceding waves / estimated with longitudinal targeted minimum loss-based estimation (LTMLE).
3. *Incremental propensity score intervention (IPSI)* estimand: difference in cannabis initiation risks had everyone's past-year nicotine vaping odds reduced up to 90% compared with observed nicotine vaping odds in preceding waves / estimated with nonparametric efficient estimator described in Kennedy *et al.*, 2019.

RESULTS





ATE: Cannabis initiation risk at each wave had everyone and no one vaped nicotine at earlier waves, and population risk difference between conditions



IPSI estimand: Difference in population average risks of cannabis initiation at each wave had all participants' past-year nicotine vaping odds at preceding waves been reduced up to 90% compared with observed nicotine vaping odds

RESULTS (cont.)

PATH Wave	0th percentile/Median/100th percentile N Pr(a=1|A=1)	0th percentile/Median/100th percentile N Pr(a=1|A=0)
WAVE 1	0.008 / 0.071 / 0.810 304	0.006 / 0.015 / 0.073 9,267
WAVES 1-2	0.008 / 0.304 / 0.813 244	0.007 / 0.014 / 0.68 9,327
WAVES 1-3	0.005 / 0.064 / 0.871 176	0.004 / 0.008 / 0.786 9,395
WAVES 1-4	0.003 / 0.047 / 0.788 96	0.002 / 0.004 / 0.687 9,475

Discussion

- The positivity assumption was violated as early as Wave 1 (through 2014) when prevalence of nicotine vaping was low.
  - 100th percentile of propensity score was 0.810 and 0.073 for participants reporting and not reporting nicotine vaping, respectively.
- Compromise between interpretation and flexibility.
  - ATE interpreted as outcome difference had everyone versus no one vaped nicotine.
  - IPSI estimand interpreted as outcome difference if everyone's vaping odds were shifted versus not shifted.
- Estimation with LTMLE and proposed IPSI estimator both show that nicotine vaping is harmful but ATE was not identified.

- Key takeaways:
  - Lower (greater) nicotine vaping odds associated with decreased (increased) cannabis initiation risk.
  - Check positivity assumption, especially when using longitudinal observational data with rare exposures and estimating ATE.
  - Consider using shift estimand when positivity is unsatisfied.

References:
Perlmutter, AP. Does current evidence support harmful effects of nicotine vaping on cannabis and prohibited substance use risks? A systematic review. In Preparation.
Kennedy EH. Nonparametric Causal Effects Based on Incremental Propensity Score Interventions. *J Am Stat Assoc.* 2019;114(526):645-656.
Naimi AI, Rudolph JE, Kennedy EH, et al. Incremental Propensity Score Effects for Time-fixed Exposures. *Epidemiology (Cambridge, Mass).* 2021;32(2):202-208.
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