Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about the work.

Supplementary Appendix

Cannabis legalization and the presence of tetrahydrocannabinol in moderately injured drivers.

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Table S1: Prevalence of substances detected in injured drivers (n=4409).

Substance	Number (prevalence)
Cannabis	
THC = 0	3,923 (89.0%)
THC > 0 ng/mL	486 (11.0%)
0 < THC < 2 ng/mL	277 (6.3%)
2 ≤ THC < 5 ng/mL	140 (3.2%)
THC ≥ 2 ng/mL	209 (4.7%)
THC ≥ 5 ng/mL	69 (1.6%)
Alcohol	
BAC = 0	3,912 (88.7%)
BAC > 0	497 (11.3%)
0 < BAC < .05%	62 (1.4%)
.05 ≤ BAC < .08%	37 (0.8%)
BAC ≥ .08%	399 (9.0%)
Cannabis and Alcohol	
THC > 0 & BAC > 0	103 (2.3%)
THC ≥ 2.5 ng/mL & BAC ≥ 0.05%	24 (0.5%)
Stimulants*	342 (7.8%)
Sedating medications**	873 (19.8%)
Opiates detected***	280 (6.4%)
Any substance detected	1,741 (39.5%)

* This category includes cocaine, amphetamines

** This category excludes opioids but includes benzodiazepines and Z-drugs, antihistamines, antidepressants, anticonvulsants, antipsychotics

*** Includes prescription and non-prescription opioids

Table S2: Count (percent) of moderately injured drivers involved in MVCs testing positive for substances before and after cannabis legalization, including month of legalization.

	Entire study period Jan 2013 – Mar 2020	Pre legalization Jan 2013 – Sep 2018	Month of legalization Oct 2018	Post legalization Nov 2018 – Mar 2020	Crude Legalization PR (95%CI)[1,3]	Adjusted Legalization PR (95%CI)[2,3]
Total drivers	4,409 (100%)	3,550 (100%)	70 (100%)	789 (100%)		
Cannabis						
THC = 0	3,923 (89.0%)	3,225 (90.8%)	50 (71.4%)	648 (82.1%)		
THC > 0 ng/mL	486 (11.0%)	325 (9.2%)	20 (28.6%)	141 (17.9%)	1.95 (1.63, 2.34)	1.33 (1.05, 1.68)
THC ≥ 2 ng/mL	209 (4.7%)	136 (3.8%)	5 (7.1%)	68 (8.6%)	2.25 (1.70, 2.98)	2.29 (1.52, 3.45)
THC ≥ 5 ng/mL	69 (1.6%)	38 (1.1%)	< 5	28 (3.5%)	3.32 (2.05, 5.37)	2.05 (1.00, 4.18)
Alcohol						
BAC = 0	3,912 (88.7%)	3,141 (88.5%)	59 (84.3%)	712 (90.2%)		
BAC > 0	497 (11.3%)	409 (11.5%)	11 (15.7%)	77 (9.8%)	0.85 (0.67, 1.07)	0.90 (0.71, 1.14)
BAC ≥ .08%	399 (9.0%)	331 (9.3%)	< 5	64 (8.1%)	0.87 (0.67, 1.12)	0.98 (0.74, 1.30)
Cannabis and Alcohol						
THC > 0 & BAC > 0	103 (2.3%)	75 (2.1%)	< 5	24 (3.0%)	1.44 (0.92, 2.27)	0.84 (0.49, 1.45)
THC ≥ 2.5 ng/mL & BAC ≥ 0.05%	24 (0.5%)	17 (0.5%)	0	7 (0.9%)	1.85 (0.77, 4.45)	2.88 (0.76, 10.9)

1. Wald confidence interval (excluding month of legalization)

2. Obtained from log-binomial regression model adjusted for Annual trend (year), Season (Spring, Summer, Fall, Winter), Sex (Male, Female), Age group (<30, 30-49, ≥50 years), Health Authority (VCH, FA, IHA, VIHA), Injury severity (Admitted, Discharged), Time of collision (Daytime, Night-time), and Type of collision (Single-vehicle, Multi-vehicle)

3. Confidence intervals have not been adjusted for multiplicity. No statistical inferences may be drawn.

Table S3: Count (percent) of moderately injured drivers testing positive for THC before and after cannabis legalization by subgroup.

	Entire study period Jan 2013 - Mar 2020	Pre-legalization Jan 2013 - Sep 2018	Post-legalization Nov 2018 - Mar 2020	Crude Legalization PR (95%CI)[1,3]	Adjusted Legalization PR (95%CI)[2,3]
All drivers	4,409 (100%)	3,550 (100%)	789 (100%)		
THC > 0	486 (11.0%)	325 (9.2%)	141 (17.9%)	1.95 (1.63, 2.34)	1.33 (1.05, 1.68)
THC ≥ 2 ng/mL	209 (4.7%)	136 (3.8%)	68 (8.6%)	2.25 (1.70, 2.98)	2.29 (1.52, 3.45)
THC ≥ 5 ng/mL	69 (1.6%)	38 (1.1%)	28 (3.5%)	3.32 (2.05, 5.37)	2.05 (1.00, 4.18)
Male	2,728 (100%)	2,182 (100%)	499 (100%)		
THC > 0	384 (14.1%)	248 (11.4%)	120 (24.0%)	2.12 (1.74, 2.57)	1.39 (1.09, 1.78)
THC ≥ 2 ng/mL	163 (6.0%)	101 (4.6%)	57 (11.4%)	2.47 (1.81, 3.36)	2.44 (1.60, 3.74)
THC ≥ 5 ng/mL	54 (2.0%)	28 (1.3%)	23 (4.6%)	3.59 (2.09, 6.18)	2.22 (1.05, 4.71)
Female	1,681 (100%)	1,368 (100%)	290 (100%)		
THC > 0	102 (6.1%)	77 (5.6%)	21 (7.2%)	1.29 (0.81, 2.05)	0.98 (0.60, 1.61)
THC ≥ 2 ng/mL	46 (2.7%)	35 (2.6%)	11 (3.8%)	1.48 (0.76, 2.88)	1.68 (0.80, 3.50)
THC ≥ 5 ng/mL	15 (0.9%)	10 (0.7%)	5 (1.7%)	2.36 (0.81, 6.85)	1.45 (0.44, 4.82)
Age < 30 years	1,106 (100%)	906 (100%)	192 (100%)		
THC > 0	224 (20.3%)	162 (17.9%)	58 (30.2%)	1.69 (1.31, 2.18)	1.45 (1.03, 2.05)
THC ≥ 2 ng/mL	112 (10.1%)	81 (8.9%)	28 (14.6%)	1.63 (1.09, 2.43)	2.52 (1.40, 4.56)
THC ≥ 5 ng/mL	39 (3.5%)	26 (2.9%)	12 (6.2%)	2.18 (1.12, 4.24)	2.59 (0.85, 7.90)
Age 30-49 years	1,559 (100%)	1,240 (100%)	291 (100%)		
THC > 0	164 (10.5%)	106 (8.5%)	51 (17.5%)	2.05 (1.51, 2.79)	1.18 (0.88, 1.58)
THC ≥ 2 ng/mL	62 (4.0%)	39 (3.1%)	22 (7.6%)	2.40 (1.45, 3.99)	1.73 (1.05, 2.84)
THC ≥ 5 ng/mL	17 (1.1%)	< 10	8 (2.7%)	4.26 (1.61, 11.3)	1.41 (0.61, 3.28)
Age ≥ 50 years	1,744 (100%)	1,404 (100%)	306 (100%)		
THC > 0	98 (5.6%)	57 (4.1%)	32 (10.5%)	2.58 (1.70, 3.90)	1.74 (1.12, 2.72)
THC ≥ 2 ng/mL	35 (2.0%)	16 (1.1%)	18 (5.9%)	5.16 (2.66, 10.0)	5.18 (2.49, 10.8)
THC ≥ 5 ng/mL	13 (0.7%)	< 5	8 (2.6%)	9.18 (2.78, 30.3)	5.31 (1.42, 19.8)
Admitted	962 (100%)	781 (100%)	167 (100%)		
THC > 0	139 (14.4%)	90 (11.5%)	48 (28.7%)	2.49 (1.83, 3.39)	1.42 (1.02, 1.98)
THC ≥ 2 ng/mL	56 (5.8%)	34 (4.4%)	22 (13.2%)	3.03 (1.82, 5.04)	2.74 (1.55, 4.86)
THC ≥ 5 ng/mL	15 (1.6%)	7 (0.9%)	8 (4.8%)	5.34 (1.97, 14.5)	3.04 (1.01, 9.17)
Single-vehicle collision	1,322 (100%)	1,064 (100%)	234 (100%)		
THC > 0	203 (15.4%)	138 (13.0%)	56 (23.9%)	1.85 (1.40, 2.43)	1.27 (0.93, 1.73)
THC ≥ 2 ng/mL	89 (6.7%)	56 (5.3%)	29 (12.4%)	2.35 (1.54, 3.60)	2.52 (1.50, 4.23)
THC ≥ 5 ng/mL	32 (2.4%)	17 (1.6%)	13 (5.6%)	3.48 (1.71, 7.06)	2.26 (0.93, 5.50)
Night-time collision	1,541 (100%)	1,243 (100%)	280 (100%)		
THC > 0	189 (12.3%)	124 (10.0%)	56 (20.0%)	2.00 (1.50, 2.67)	1.40 (1.02, 1.92)
THC ≥ 2 ng/mL	79 (5.1%)	48 (3.9%)	27 (9.6%)	2.50 (1.59, 3.93)	2.73 (1.61, 4.66)
THC ≥ 5 ng/mL	30 (1.9%)	17 (1.4%)	11 (3.9%)	2.87 (1.36, 6.06)	1.78 (0.71, 4.44)

1. Wald confidence interval (excluding month of legalization)

2. Obtained from log-binomial regression model adjusted for Annual trend (year), Season (Spring, Summer, Fall, Winter), Sex (Male, Female), Age group (<30, 30-49, ≥50 years), Health Authority (VCH, FA, IHA, VIHA), Injury severity (Admitted, Discharged), Time of collision (Daytime, Night-time), and Type of collision (Single-vehicle, Multi-vehicle). Estimates for specific subgroups were derived from models that also included an interaction between Legalization and the subgroup.

3. Confidence intervals have not been adjusted for multiplicity. No statistical inferences may be drawn.

Table S4: Adjusted prevalence ratios (aPR) and 95% confidence intervals (CI) obtained from log-binomial regression models. Each column represents a separate model where the outcome is whether the substance was detected at the specified level and the explanatory variables are Legalization (Pre, Post), Annual trend (year), Season (Spring, Summer, Fall, Winter), Sex (Male, Female), Age group (<30, 30-49, ≥50 years), Health Authority (VCH, FA, IHA, VIHA), Injury severity (Admitted, Discharged), Time of collision (Daytime, Night-time), and Type of collision (Single-vehicle, Multi-vehicle). Model coefficients were exponentiated so that they may be interpreted as adjusted prevalence ratios. The rows indicate the aPR (relative to reference value) for each covariate. For example, after adjustment for all other covariates (including legalization), the prevalence of THC > 0 among drivers 50 years or older is 51% smaller than that of drivers aged 30 – 49 years (aPR = 0.49).

	THC > 0	THC ≥ 2 ng/mL	THC ≥ 5 ng/mL	BAC > 0	BAC ≥ 0.08%	THC ≥ 2.5 ng/mL & BAC ≥ 0.05%
Count (%) above substance threshold[1]	466/4339 (10.7%)	204/4339 (4.7%)	66/4339 (1.5%)	486/4339 (11.2%)	395/4339 (9.1%)	24/4339 (0.6%)
	aPR (95% CI)[2]					
Post-legalization (ref = Pre-legalization)	1.33 (1.05, 1.68)	2.29 (1.52, 3.45)	2.05 (1.00, 4.18)	0.90 (0.71, 1.14)	0.98 (0.74, 1.30)	2.88 (0.76, 10.9)
Annual trend (year)	1.14 (1.07, 1.21)	1.00 (0.90, 1.11)	1.20 (0.98, 1.47)	1.00 (0.95, 1.04)	0.97 (0.92, 1.03)	0.93 (0.69, 1.24)
Season (ref = Fall)						
Spring	1.07 (0.83, 1.36)	1.06 (0.71, 1.59)	0.97 (0.49, 1.90)	1.08 (0.88, 1.31)	1.10 (0.87, 1.39)	1.07 (0.35, 3.27)
Summer	1.11 (0.87, 1.42)	1.21 (0.82, 1.78)	0.85 (0.43, 1.69)	0.98 (0.79, 1.20)	0.97 (0.76, 1.24)	0.94 (0.29, 3.09)
Winter	0.98 (0.76, 1.28)	1.13 (0.75, 1.70)	0.83 (0.40, 1.69)	1.07 (0.87, 1.32)	1.15 (0.91, 1.45)	0.89 (0.27, 2.99)
Male (ref = Female)	2.01 (1.62, 2.49)	1.86 (1.34, 2.57)	1.75 (0.98, 3.13)	1.42 (1.17, 1.71)	1.30 (1.05, 1.60)	1.13 (0.42, 3.06)
Age group (ref = 30-49)						
< 30 years	1.70 (1.41, 2.04)	2.28 (1.69, 3.10)	3.10 (1.73, 5.56)	1.06 (0.91, 1.23)	1.05 (0.88, 1.25)	4.24 (1.44, 12.5)
≥ 50 years	0.49 (0.38, 0.62)	0.48 (0.32, 0.72)	0.66 (0.32, 1.40)	0.55 (0.45, 0.68)	0.50 (0.39, 0.64)	0.52 (0.10, 2.85)
Health Authority (ref = VCH)						
FHA	1.33 (1.07, 1.66)	1.12 (0.78, 1.60)	0.64 (0.32, 1.25)	0.95 (0.77, 1.17)	0.93 (0.74, 1.17)	Insufficient data[3]
IHA	2.22 (1.74, 2.85)	1.76 (1.16, 2.68)	0.71 (0.25, 1.98)	1.41 (1.15, 1.73)	1.34 (1.06, 1.69)	1.43 (0.46, 4.43)
VIHA	2.27 (1.82, 2.83)	2.12 (1.49, 3.02)	1.54 (0.80, 2.94)	1.49 (1.25, 1.79)	1.33 (1.08, 1.64)	1.82 (0.75, 4.45)
Admitted (ref = Discharged from ED)	1.16 (0.97, 1.39)	1.16 (0.86, 1.56)	0.94 (0.52, 1.68)	1.42 (1.23, 1.63)	1.34 (1.14, 1.58)	1.26 (0.54, 2.90)
Night-time collision (ref = Daytime)	0.94 (0.80, 1.12)	0.84 (0.63, 1.11)	1.01 (0.62, 1.66)	3.51 (2.91, 4.23)	3.76 (3.03, 4.66)	4.54 (1.54, 13.4)
Single-vehicle collision (ref = Multi-vehicle)	1.17 (0.99, 1.39)	1.23 (0.92, 1.63)	1.60 (0.96, 2.65)	3.07 (2.55, 3.68)	4.57 (3.66, 5.70)	29.4 (3.87, 224)

1. Counts are reported for all moderately injured drivers during entire study period, excluding 70 drivers injured in an MVC during the month of legalization.
2. Confidence intervals have not been adjusted for multiplicity. No statistical inferences may be drawn.
3. Insufficient data: zero drivers tested positive in the pre and/or post legalization period in this subgroup

Table S5: Adjusted prevalence ratios (aPR) and 95% confidence intervals (CI) obtained from log-binomial regression models with interaction. The first row in the table represents aPRs for cannabis legalization effect from adjusted log-binomial regression models without interaction (i.e Post-legalization aPR estimates from Table S2). Subsequent rows show aPRs for legalization in specific subgroups obtained from models that also include an interaction term with Legalization and the specified covariate.

	THC > 0	THC ≥ 2 ng/mL	THC ≥ 5 ng/mL	BAC > 0	BAC ≥ 0.08%	THC ≥ 2.5 ng/mL & BAC ≥ 0.05%
Count (%) above substance threshold[1]	466/4339 (10.7%)	204/4339 (4.7%)	66/4339 (1.5%)	486/4339 (11.2%)	395/4339 (9.1%)	24/4339 (0.6%)
			Legalization aPR (95% CI)[2]			
Overall (models without interaction)	1.33 (1.05, 1.68)	2.29 (1.52, 3.45)	2.05 (1.00, 4.18)	0.90 (0.71, 1.14)	0.98 (0.74, 1.30)	2.88 (0.76, 10.9)
Models including interaction with Legalization and:[3]						
Age group						
< 30 years	1.45 (1.03, 2.05)	2.52 (1.40, 4.56)	2.59 (0.85, 7.90)	1.15 (0.85, 1.55)	1.15 (0.79, 1.67)	2.19 (0.19, 25.9)
30-49 years	1.18 (0.88, 1.58)	1.73 (1.05, 2.84)	1.41 (0.61, 3.28)	0.76 (0.53, 1.09)	0.91 (0.62, 1.34)	2.83 (0.69, 11.7)[4]
≥ 50 years	1.74 (1.12, 2.72)	5.18 (2.49, 10.8)	5.31 (1.42, 19.8)[4]	0.74 (0.44, 1.24)	0.77 (0.41, 1.44)	5.22 (0.28, 97.8)[4]
Sex						
Female	0.98 (0.60, 1.61)	1.68 (0.80, 3.50)	1.45 (0.44, 4.82)	0.98 (0.60, 1.61)	1.12 (0.66, 1.90)	Insufficient data[5]
Male	1.39 (1.09, 1.78)	2.44 (1.60, 3.74)	2.22 (1.05, 4.71)	0.88 (0.68, 1.14)	0.95 (0.70, 1.29)	3.69 (0.95, 14.4)
Injury severity						
Treated and released	1.26 (0.96, 1.66)	2.10 (1.33, 3.32)	1.78 (0.82, 3.88)	0.91 (0.68, 1.23)	1.04 (0.75, 1.45)	3.24 (0.75, 14.1)
Admitted	1.42 (1.02, 1.98)	2.74 (1.55, 4.86)	3.04 (1.01, 9.17)	0.89 (0.64, 1.22)	0.89 (0.60, 1.34)	2.27 (0.38, 13.6)[4]
Time of day						
Daytime collision	1.28 (0.97, 1.69)	2.07 (1.30, 3.30)	2.26 (0.99, 5.13)	0.89 (0.56, 1.41)	0.98 (0.57, 1.68)	2.74 (0.23, 32.2)[4]
Night-time collision	1.40 (1.02, 1.92)	2.73 (1.61, 4.66)	1.78 (0.71, 4.44)	0.90 (0.70, 1.17)	0.98 (0.73, 1.33)	2.91 (0.74, 11.5
Type of collision						
Multi-vehicle collision	1.37 (1.03, 1.81)	2.14 (1.34, 3.43)	1.88 (0.82, 4.35)	0.68 (0.43, 1.09)	0.97 (0.56, 1.66)	Insufficient data[5]
Single-vehicle collision	1.27 (0.93, 1.73)	2.52 (1.50, 4.23)	2.26 (0.93, 5.50)	0.97 (0.75, 1.25)	0.99 (0.73, 1.33)	3.08 (0.81, 11.7)
Health authority						
VCH	2.15 (1.57, 2.94)	3.88 (2.36, 6.40)	3.18 (1.39, 7.28)	0.82 (0.58, 1.16)	0.98 (0.68, 1.43)	4.09 (0.89, 18.8)
FHA	1.02 (0.69, 1.53)	1.60 (0.82, 3.15)	0.91 (0.23, 3.66)[4]	0.84 (0.52, 1.35)	0.84 (0.49, 1.44)	Insufficient data[5]
VIHA	0.93 (0.54, 1.58)	1.46 (0.54, 3.95)	4.02 (0.53, 30.6)[4]	0.70 (0.36, 1.38)	0.95 (0.48, 1.88)	2.52 (0.21, 30.0)[4]
IHA	1.07 (0.70, 1.64)	1.20 (0.54, 2.71)	0.75 (0.16, 3.65)[4]	1.13 (0.90, 1.41)	1.17 (0.76, 1.82)	1.41 (0.16, 12.7)[4]

1. Counts are reported for all moderately injured drivers during entire study period, excluding 70 drivers injured in an MVC during the month of legalization.
2. Confidence intervals have not been adjusted for multiplicity. No statistical inferences may be drawn.
3. Estimates are derived from models including an interaction term between legalization and the specified subgroup, as well as all explanatory variables listed in Table S2.
4. Unreliable estimate: fewer than 5 drivers tested positive in the pre and/or post legalization period in this subgroup
5. Insufficient data: zero drivers tested positive in the pre and/or post legalization period in this subgroup

S6: Missing Data Assumptions.

We assume that availability of excess blood is covariate-dependent only (*i.e.,* availability of excess blood is not related to whether a driver would test positive for THC AND availability of blood depends only on measured confounders that are included in our model). This assumption is justified because the reason excess blood is missing is related to laboratory processes, not clinical presentation. Excess blood is unavailable when the blood obtained is fully consumed as part of hospital analysis (i.e. an insufficient volume of blood remains for toxicology analysis) or if the lab disposes of blood samples before the research assistants are able to obtain them. Note that laboratory procedures did not change following legalization.

When missing data is covariate-dependent only, a complete-case analysis that includes all covariates in a regression model produces asymptotically unbiased estimates, assuming the model is correctly specified.[1]

Note that the availability of excess blood in our study differs by hospital site (one of the measured confounders included in our model), but that this missingness is related to hospital laboratory protocols (how quickly blood is disposed of) and not driver impairment.

Note that we treated cases without blood available as exclusions and, prior to 2018, did not capture any data on those cases; since 2018 we capture minimal data (age, sex, ambulance arrival). As such, we have insufficient data to perform statistical techniques for missingness. However, we confirm that driver characteristics collected since 2018 for cases with missing blood samples do not differ significantly from cases with excess blood available.

	Blood available (since Jan 2018)	Excess blood unavailable (since Jan 2018)	P-value
Total number	1770	337	
Male (%)	65.0%	64.4%	0.8325*
Ambulance arrival (%)	89.7%	91.5%	0.3439*
Mean ± SD age (years)	44.4 ± 17.6 years	43.8 ± 17.9 years	0.6008**

*Two sample z test of proportions

**Two sample t test

1. Jonathan W, Bartlett JW, Harel O, Carpenter JR. Asymptotically Unbiased Estimation of Exposure Odds Ratios in Complete Records Logistic Regression. American Journal of Epidemiology. 2015;182(8):730-736. https://doi.org/10.1093/aje/kwv114