

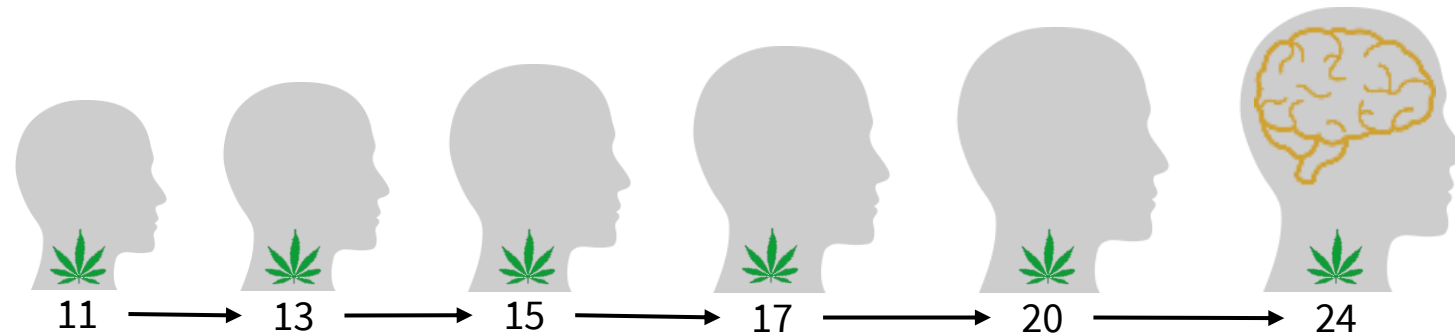
A Longitudinal Study of Adolescent Cannabis Use on Cognitive Performance in Young Adulthood: Associations and Trajectories

Clarissa Janousch, Urs Grob, Lukas Eggenberger, Lydia Johnson-Ferguson, Denis Ribeaud, Manuel Eisner, Lilly Shanahan, Boris B. Quednow

zIReN Meeting 05 - 07 September 2024, Bari

Session 3: Substance use, cognition, and psychopathology

05 September 2024



Background

Substance use in adolescence and young adulthood

- Heightened brain plasticity and sensitivity, marked by significant neural development (Casey et al., 2017; Gogtay et al., 2004; Fuhrmann et al., 2015)
- Enhanced sensitivity to rewarding effects of substances (Doremus-Fitzwater et al., 2010)
- Increased risk of substance use disorders (Chen et al., 2009; Jordan et al., 2017)
- In general, substance use is highly prevalent among adolescents and young adults (Degenhardt et al., 2013; Gmel et al., 2017; Shanahan et al., 2021; Quednow et al., 2022), with cannabis as one of the most used (illegal) substances (United Nations Office on Drugs and Crime, 2023)

Cannabis

- Δ^9 -tetrahydrocannabinol (THC) as the main psychoactive compound in cannabis
- THC has a long elimination half-life, staying in the body longer than most substances (Musshoff & Madea, 2006)

Background – effects of cannabis use on cognitive development

Animals:

- Memory deficits and brain changes (Miller et al., 2019; Salmanzadeh et al., 2020; Spear, 2015)

Adolescence:

- Earlier onset linked to worse cognitive outcomes (Jacobus et al., 2015; Meier et al., 2012; 2022)
- Affecting memory, executive functions, and IQ (Jacobus et al., 2015; Meier et al., 2012; 2018; 2022; Morin et al., 2019; Pacheco-Colón et al., 2022)
- Effects may decrease with abstinence (Bourque & Potvin, 2021; Scott et al., 2018)
- Neurodevelopmental changes observed (Albaugh et al., 2021)

Adulthood:

- Acute: Small to moderate cognitive impairments (Zhornitsky et al., 2021)
- Chronic: Effects on executive functions, attention, and memory (Figueiredo et al., 2020; Lovell et al., 2020)

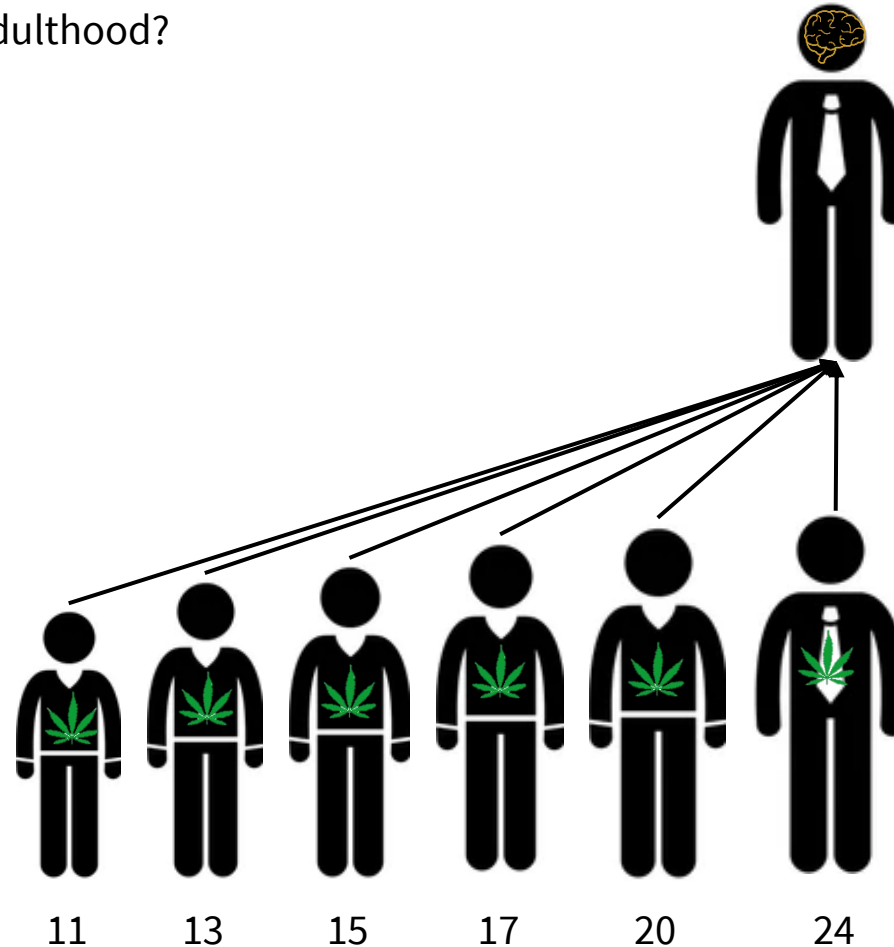
Research gap

Extensive research, yet critical gaps remain:

- Inconsistent findings across studies (e.g., Meier et al., 2012; 2018; 2022; Morin et al., 2019; Pacheco-Colón et al., 2022)
- Limited longitudinal data on long-term associations (e.g., Meier et al., 2012; 2022)
- Focus on specific (highly selective) samples
- Focus on older participants (e.g., Lovell et al., 2020)
- Methodological variations (e.g., Miller et al., 2019; Salmanzadeh et al., 2020; Spear, 2015)
- Insufficient control for confounding factors (e.g., sociodemographic variables, mental health, other substance use; e.g., Albaugh et al., 2021; Bourque & Potvin, 2021; Scott et al., 2018)
- Addressing heterogeneity

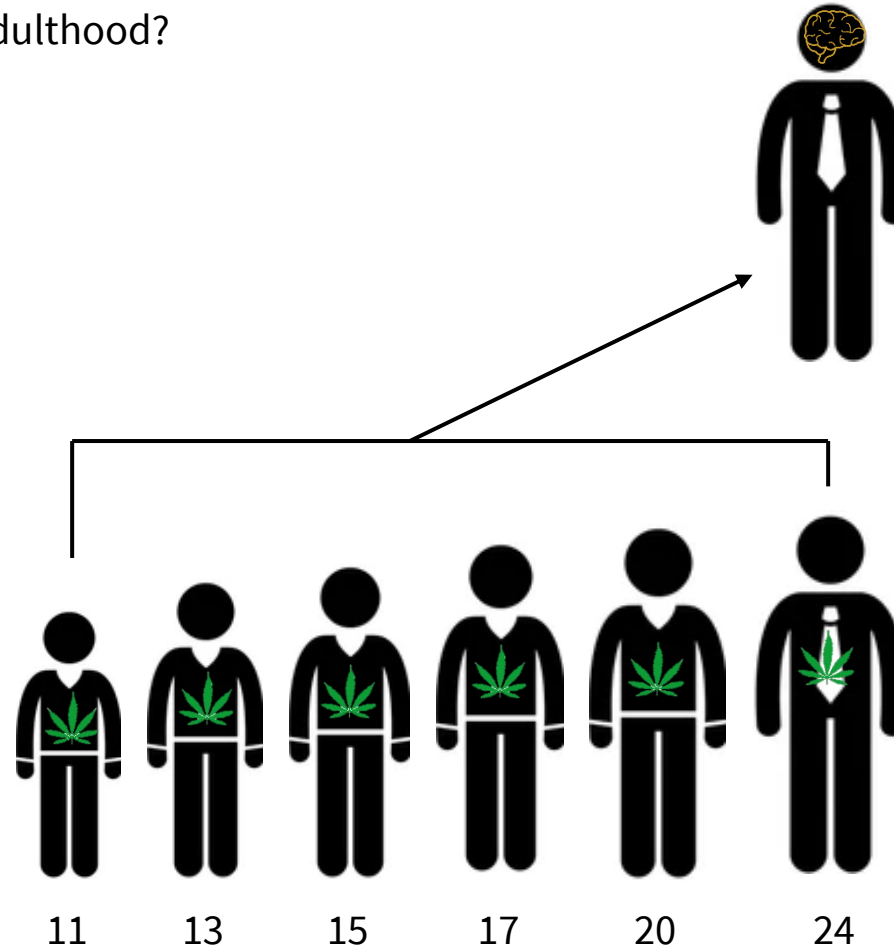
Research questions – associations

1. What are the associations between self-reported cannabis use in adolescence and cognitive performance as measured by the CANTAB tasks PAL, RVP & SWM in young adulthood?



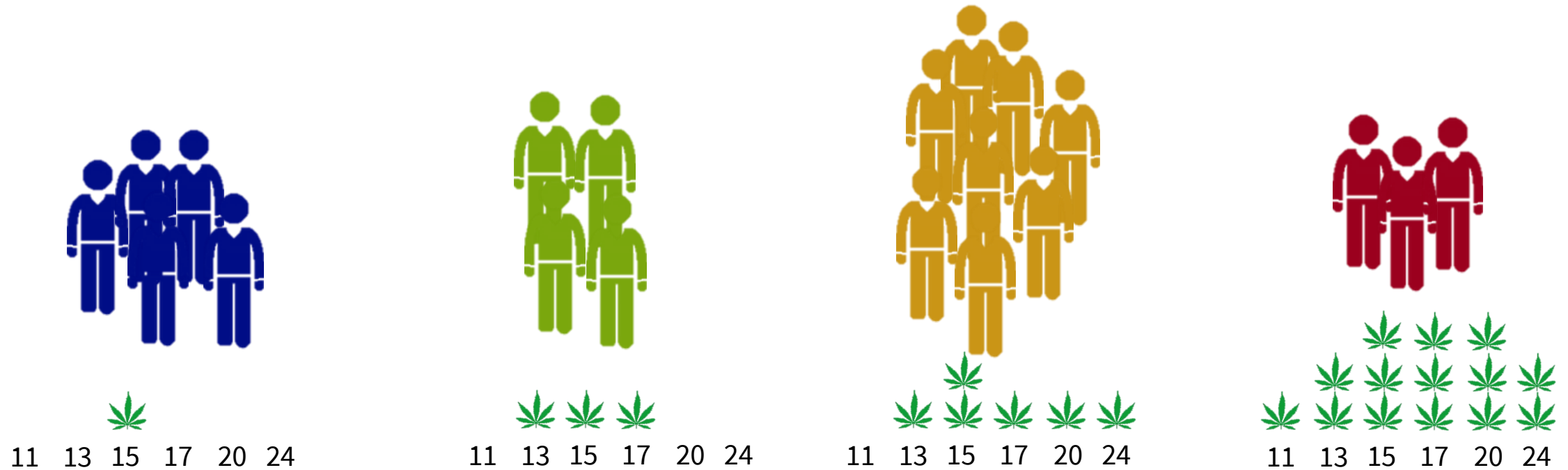
Research questions – associations

1. What are the associations between self-reported cannabis use in adolescence and cognitive performance as measured by the CANTAB tasks PAL, RVP & SWM in young adulthood?



Research questions – trajectories

2. What distinct latent subgroups of cannabis use trajectories can be identified?

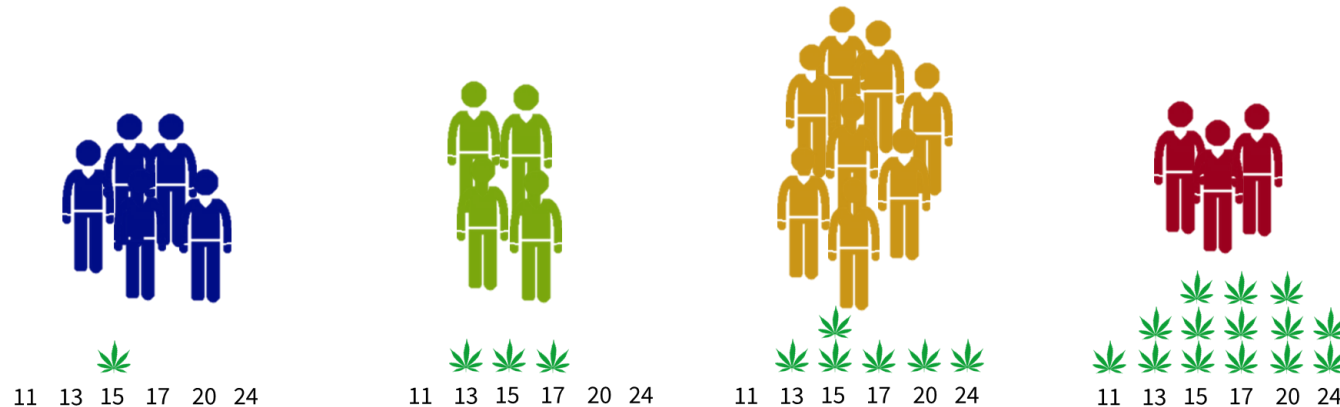
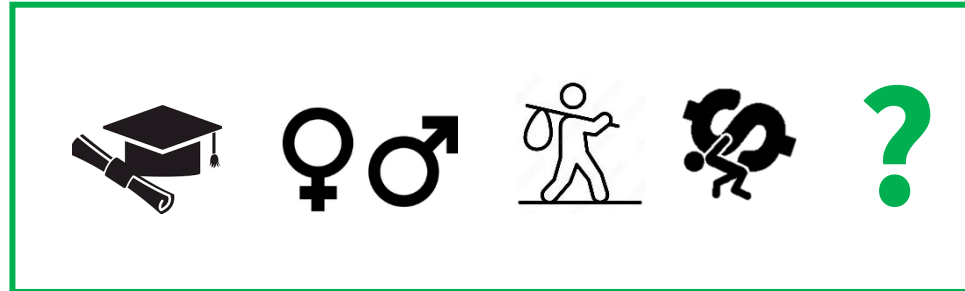


Research questions – trajectories

2.1 How are these latent subgroups of cannabis use associated with sociodemographic variables?

2.2 How are these latent subgroups of cannabis use associated with cognitive performance on the CANTAB?

2.3 How are these latent subgroups of cannabis use associated with cognitive performance on the CANTAB while controlling for sociodemographic variables?

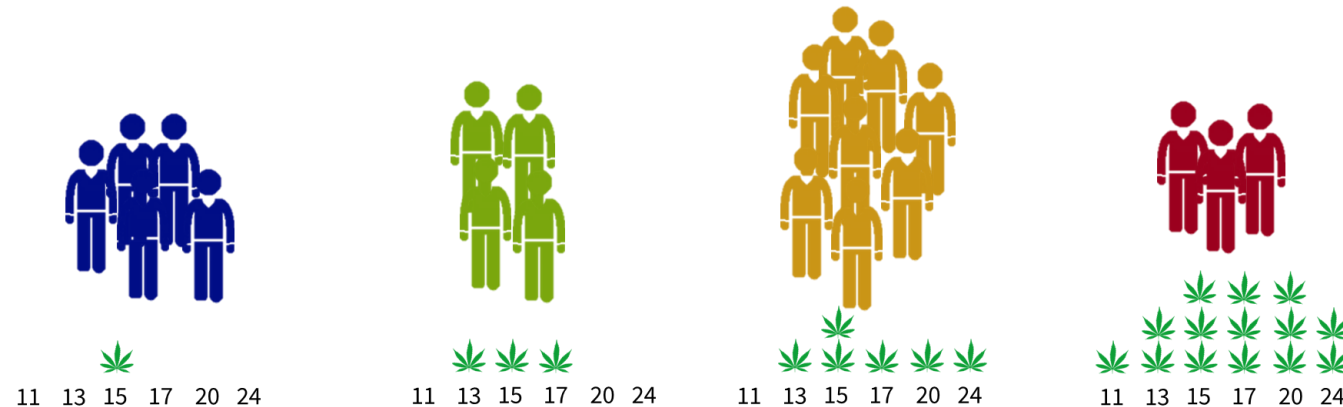
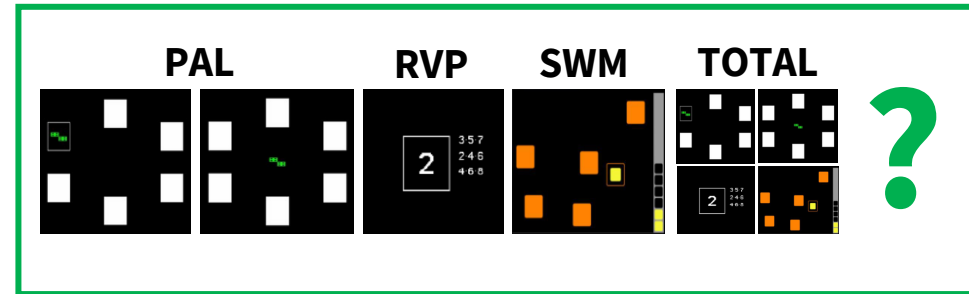


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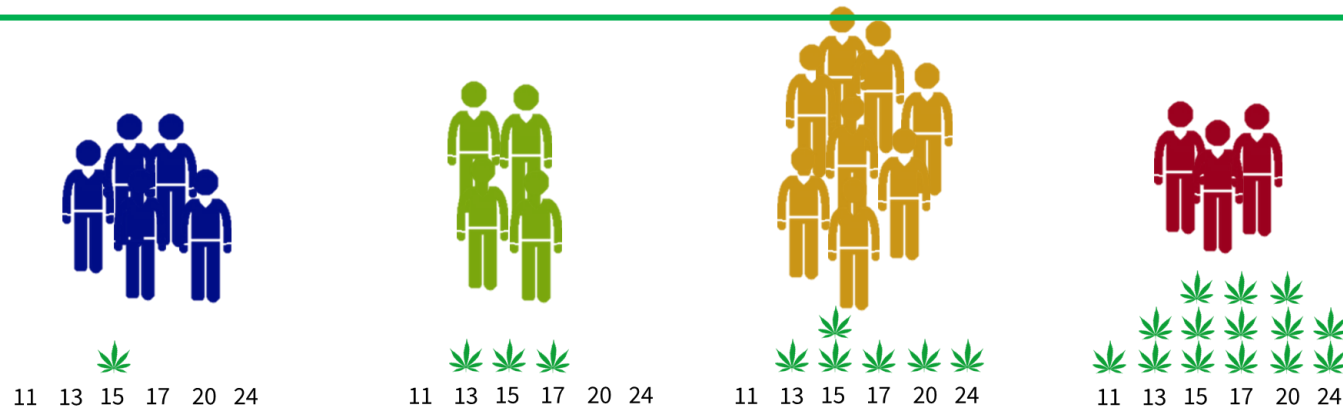
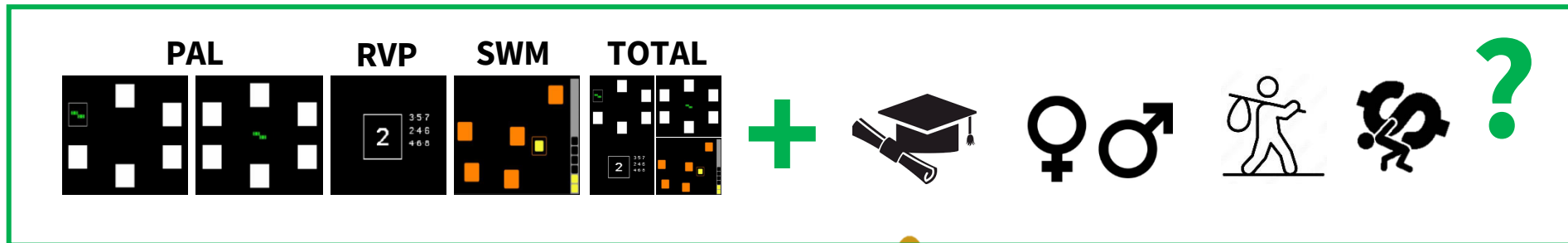


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Methods – participants & measures

Participants:





z-proso (Ribeaud et al., 2022): $n = 1,522$ (at least one available value for cannabis use)

Measures: (z-proso Project Team, 2024)

Cannabis use:

- W4 –9: Number of times of cannabis use in the last 12 months
- Categories: 1 = never, 2 = once, 3 = 2-5 times, 4 = monthly, 5 = weekly, 6 = (almost) daily

Sociodemographic variables:

-  Education (3 dummies)
-  Sex (0/1)
-  ISEI (16-90)
-  Migration background (0/1)

Cambridge Neuropsychological Test Automated Battery

(CANTAB; Strauss et al., 2006) :



Total Errors Adjusted (PAL)



Vigilance (RVP)



Working Memory Total (SWM)

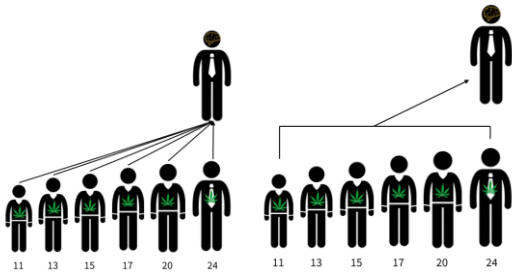


Total (summed up score)

Further covariates:

- Anxiety/depression self-reported at wave 9 (Murray et al., 2019; Tremblay et al., 1991)
- Cocaine measured in hair at wave 9 (Scholz et al., 2021)

Methods – statistical analyses



1. Regression analyses
2. Graphical representation of use across time
3. Helmert contrast analyses (average across time vs. single time points)

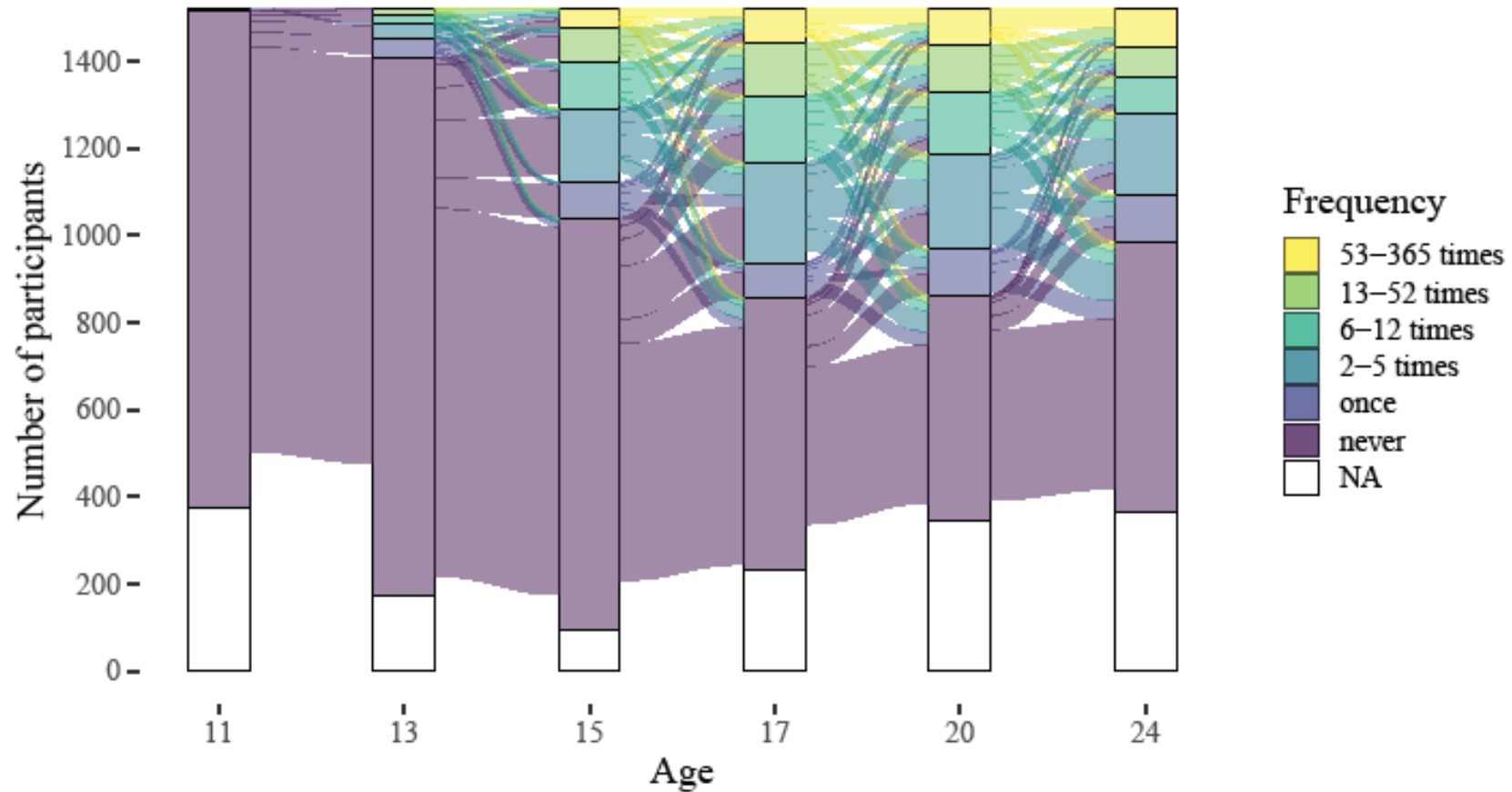


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4. Latent Class Growth Analyses (& regressions)

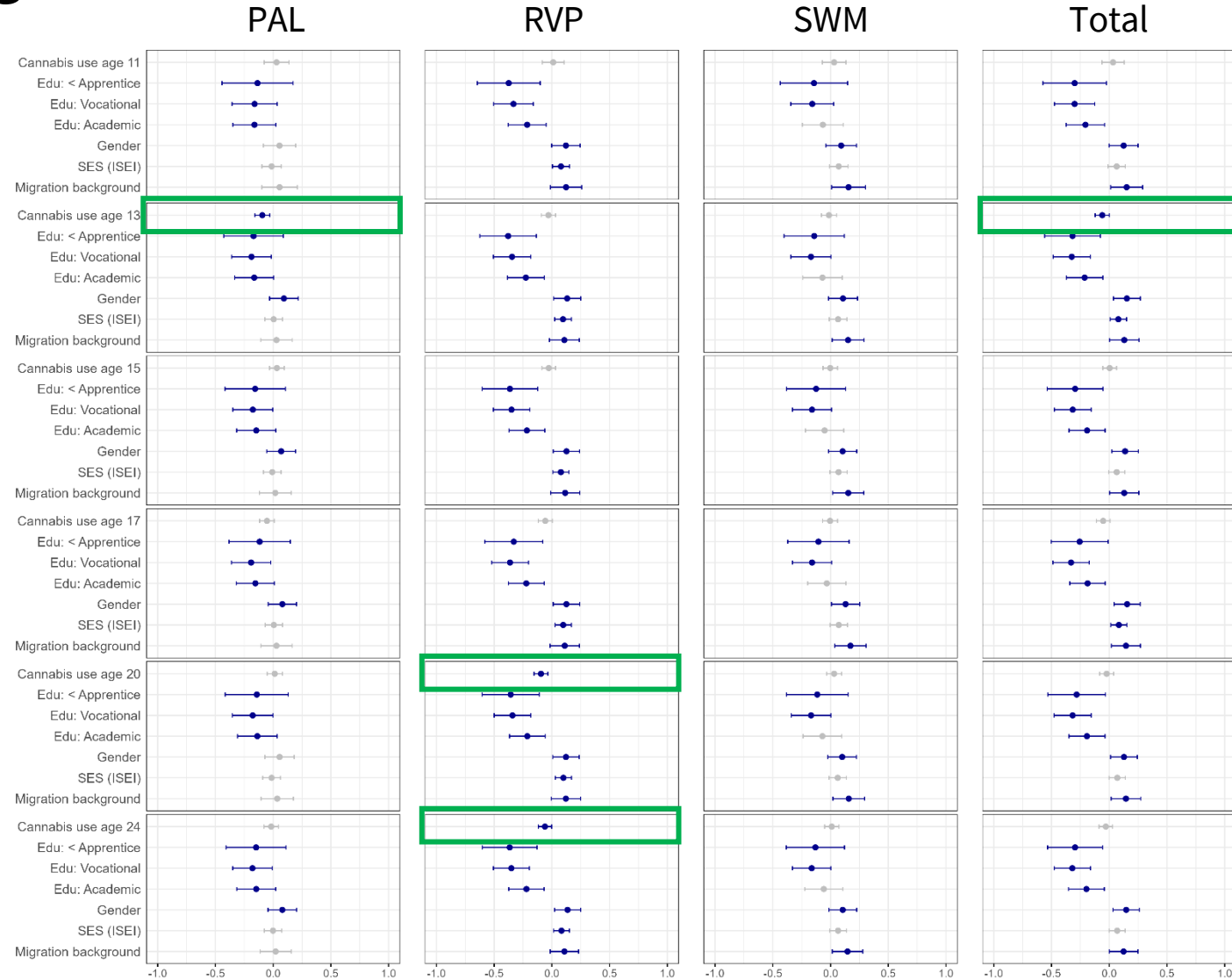


Results – descriptives

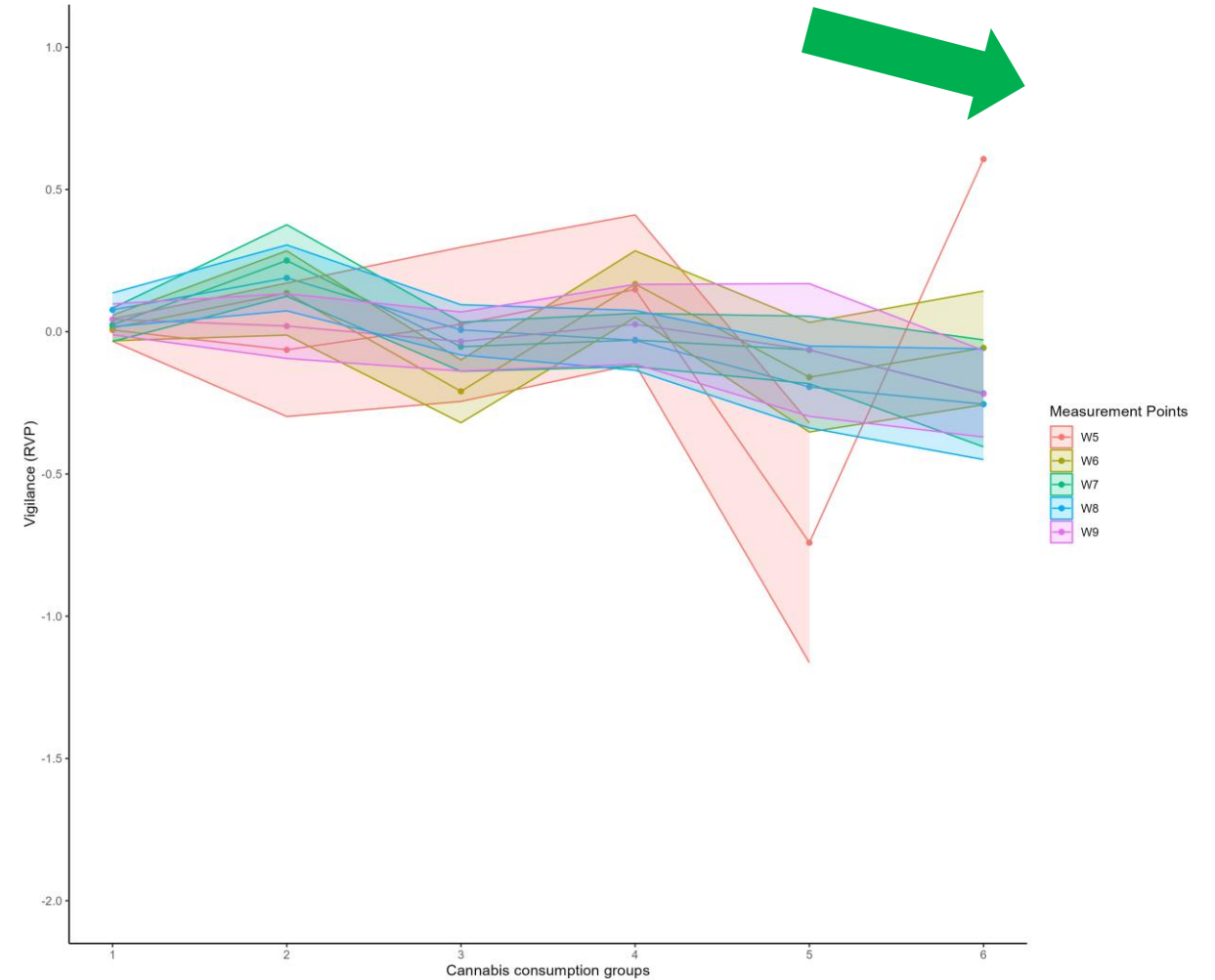
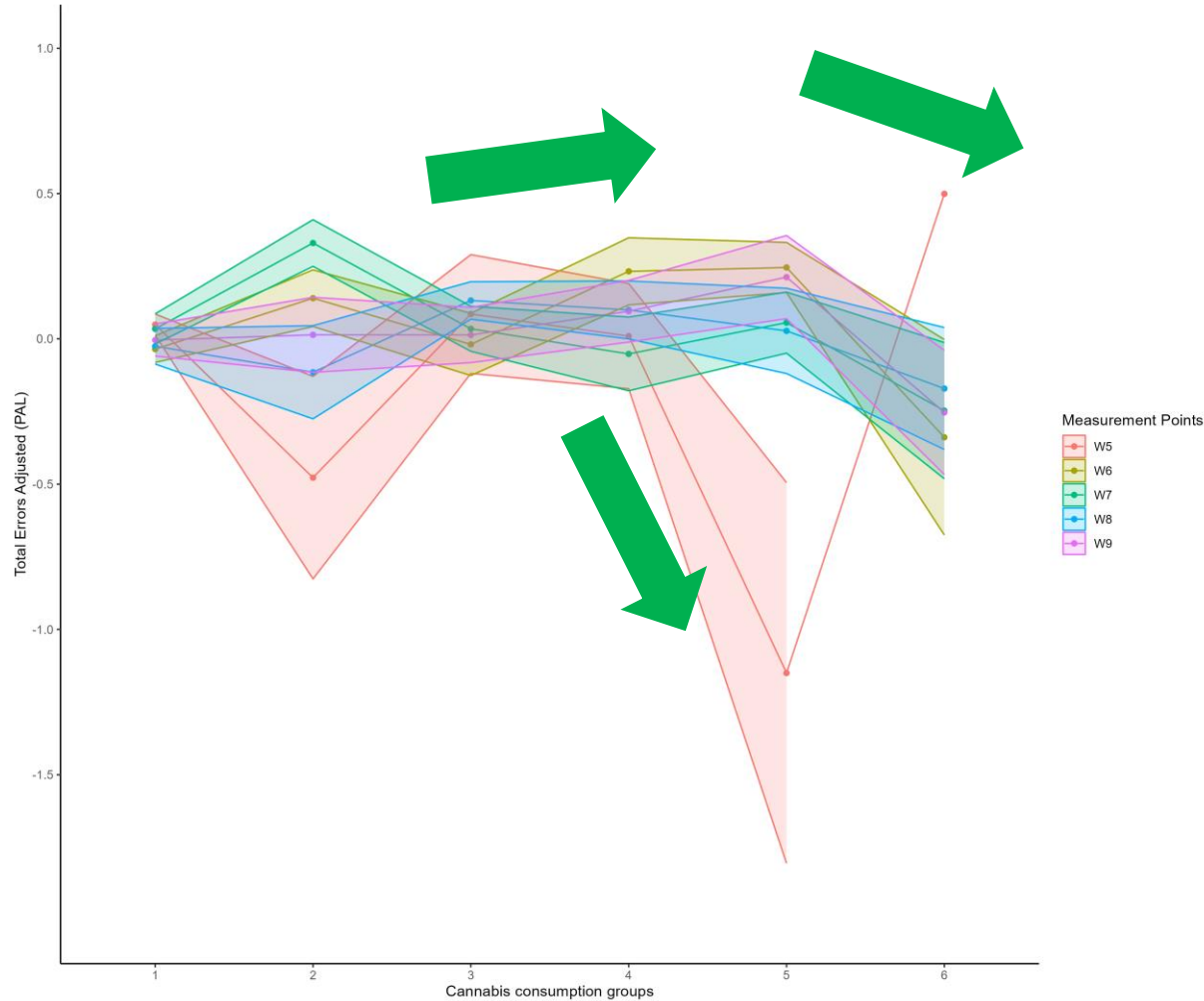
Cannabis use ($n = 1,522$)



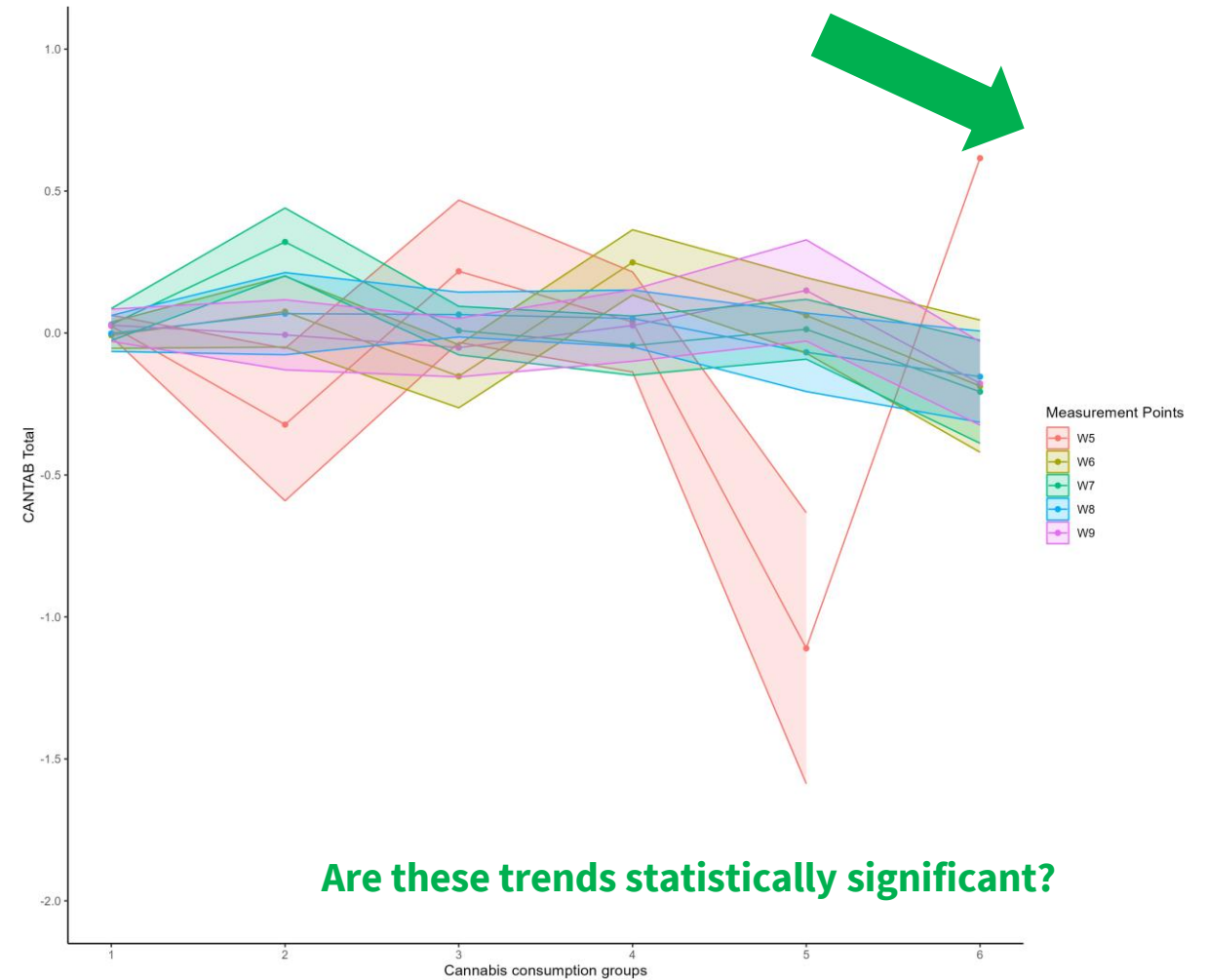
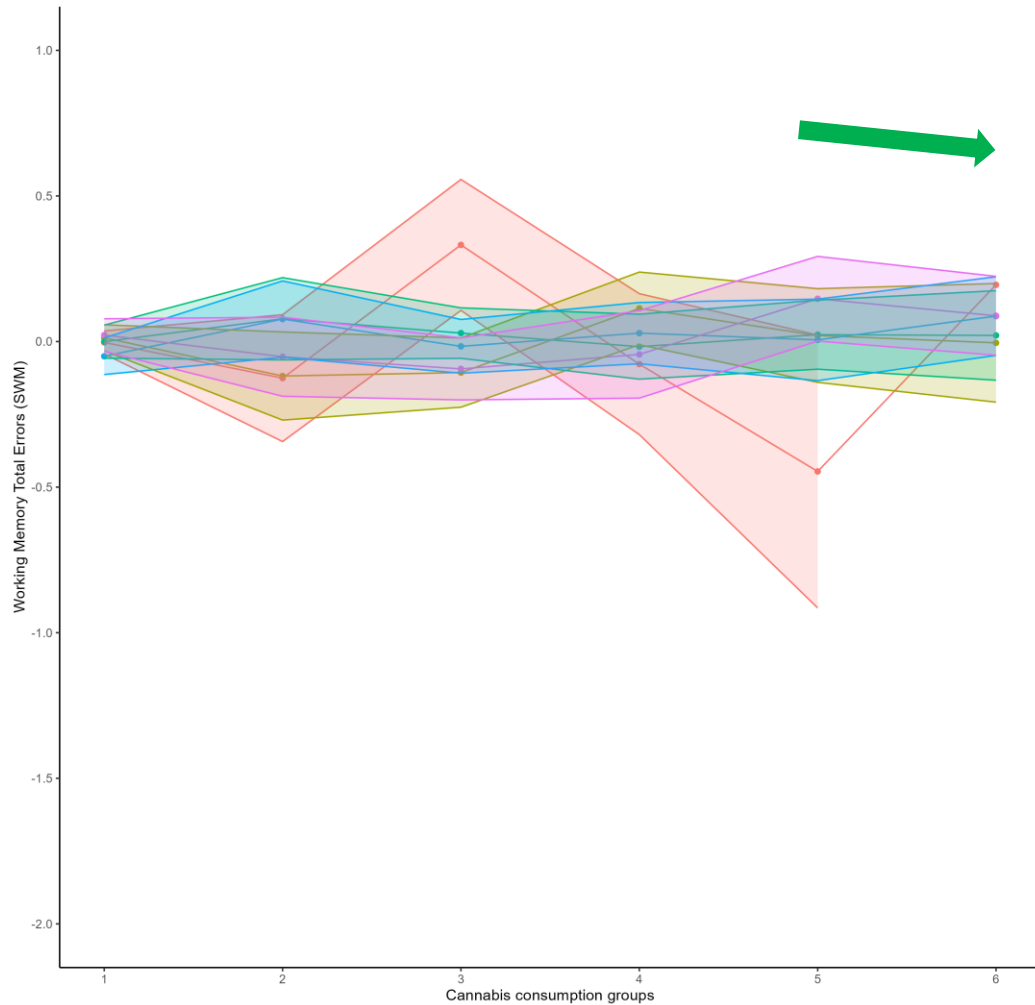
Results – linear regressions



Results – graphical representation of cannabis use and cognitive performance



Results – graphical representation of cannabis use and cognitive performance



Results – Helmert contrasts

ANOVA Table for Total Errors Adjusted (PAL)

Term	Estimate	SE	t	p	95% CI
Intercept	-0.005	0.021	-0.242	.809	[-0.05, 0.04]
Category 2 vs. 1	0.001	0.029	0.039	.969	[-0.06, 0.06]
Category 3 vs. 2+1	0.014	0.016	0.854	.393	[-0.02, 0.04]
Category 4 vs. 3+2+1	0.012	0.014	0.884	.377	[-0.01, 0.04]
Category 5 vs. 4+3+2+1	0.007	0.013	0.550	.582	[-0.02, 0.03]
Category 6 vs. 5+4+3+2+1	-0.047	0.012	-4.041	< .001***	[-0.07, -0.02]

ANOVA Table for Vigilance (RVP)

Term	Estimate	SE	t	p	95% CI
Intercept	-0.039	0.021	-1.850	.064	[-0.08, 0.00]
Category 2 vs. 1	0.043	0.029	1.481	.139	[-0.01, 0.10]
Category 3 vs. 2+1	-0.042	0.016	-2.612	.009**	[-0.07, -0.01]
Category 4 vs. 3+2+1	-0.001	0.014	-0.057	.954	[-0.03, 0.03]
Category 5 vs. 4+3+2+1	-0.034	0.013	-2.614	.009**	[-0.06, -0.01]
Category 6 vs. 5+4+3+2+1	-0.032	0.012	-2.756	.006**	[-0.06, -0.01]

Results – Helmert contrasts

ANOVA Table for Working Memory Total Errors (SWM)

Term	Estimate	SE	t	p	95% CI
Intercept	0.009	0.021	0.407	.684	[-0.03, 0.05]
Category 2 vs. 1	-0.009	0.029	-0.295	.768	[-0.07, 0.05]
Category 3 vs. 2+1	-0.006	0.016	-0.380	.704	[-0.04, 0.03]
Category 4 vs. 3+2+1	0.007	0.014	0.507	.612	[-0.02, 0.04]
Category 5 vs. 4+3+2+1	0.007	0.013	0.539	.590	[-0.02, 0.03]
Category 6 vs. 5+4+3+2+1	0.010	0.012	0.861	.390	[-0.01, 0.03]

ANOVA Table for Total CANTAB

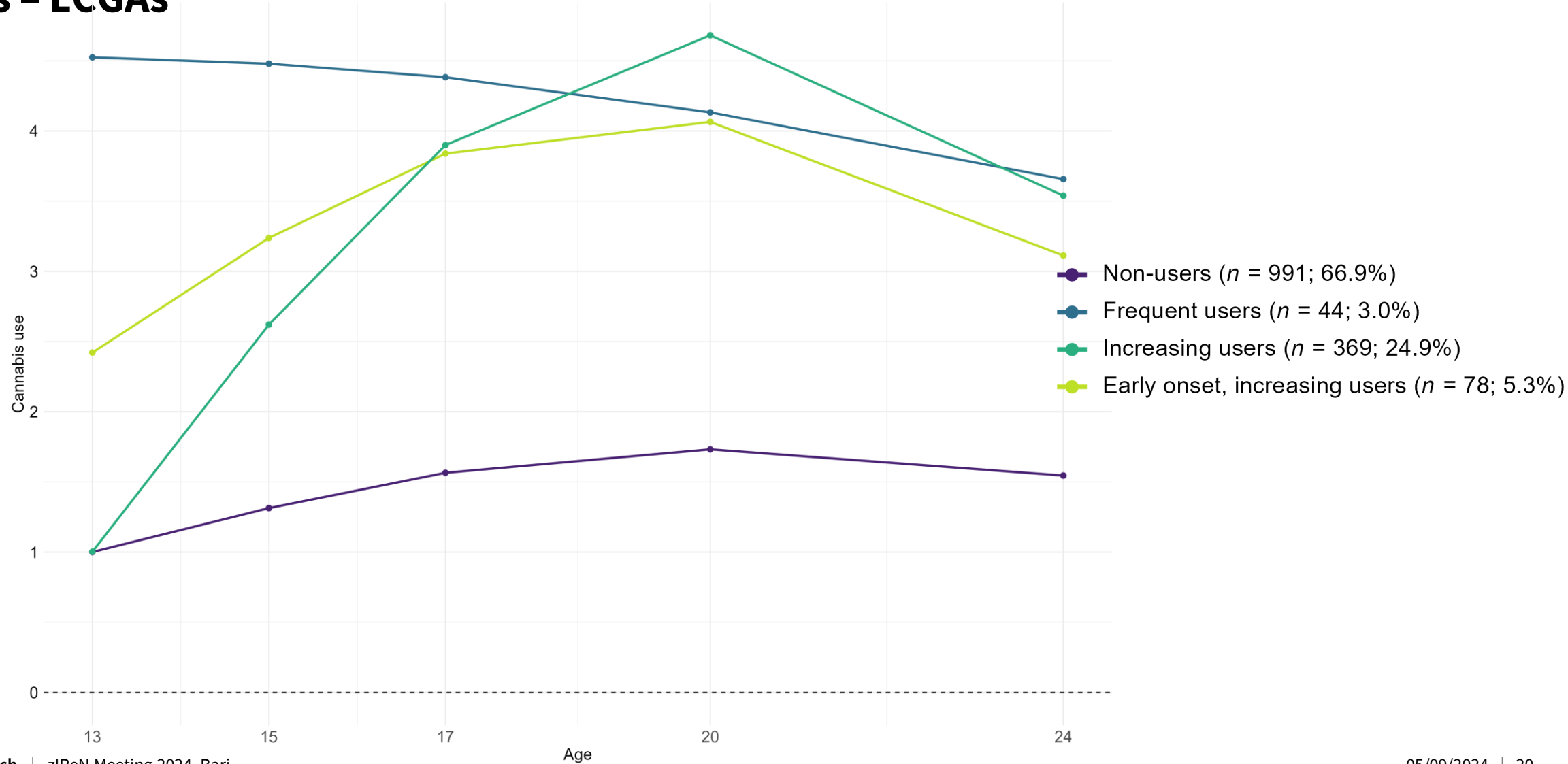
Term	Estimate	SE	t	p	95% CI
Intercept	-0.014	0.021	-0.650	.516	[-0.05, 0.03]
Category 2 vs. 1	0.018	0.029	0.617	.537	[-0.04, 0.07]
Category 3 vs. 2+1	-0.015	0.016	-0.919	.358	[-0.05, 0.02]
Category 4 vs. 3+2+1	0.009	0.014	0.627	.531	[-0.02, 0.04]
Category 5 vs. 4+3+2+1	-0.008	0.013	-0.629	.530	[-0.03, 0.02]
Category 6 vs. 5+4+3+2+1	-0.032	0.012	-2.793	.005**	[-0.06, -0.01]

Results – Helmert contrasts for each time point

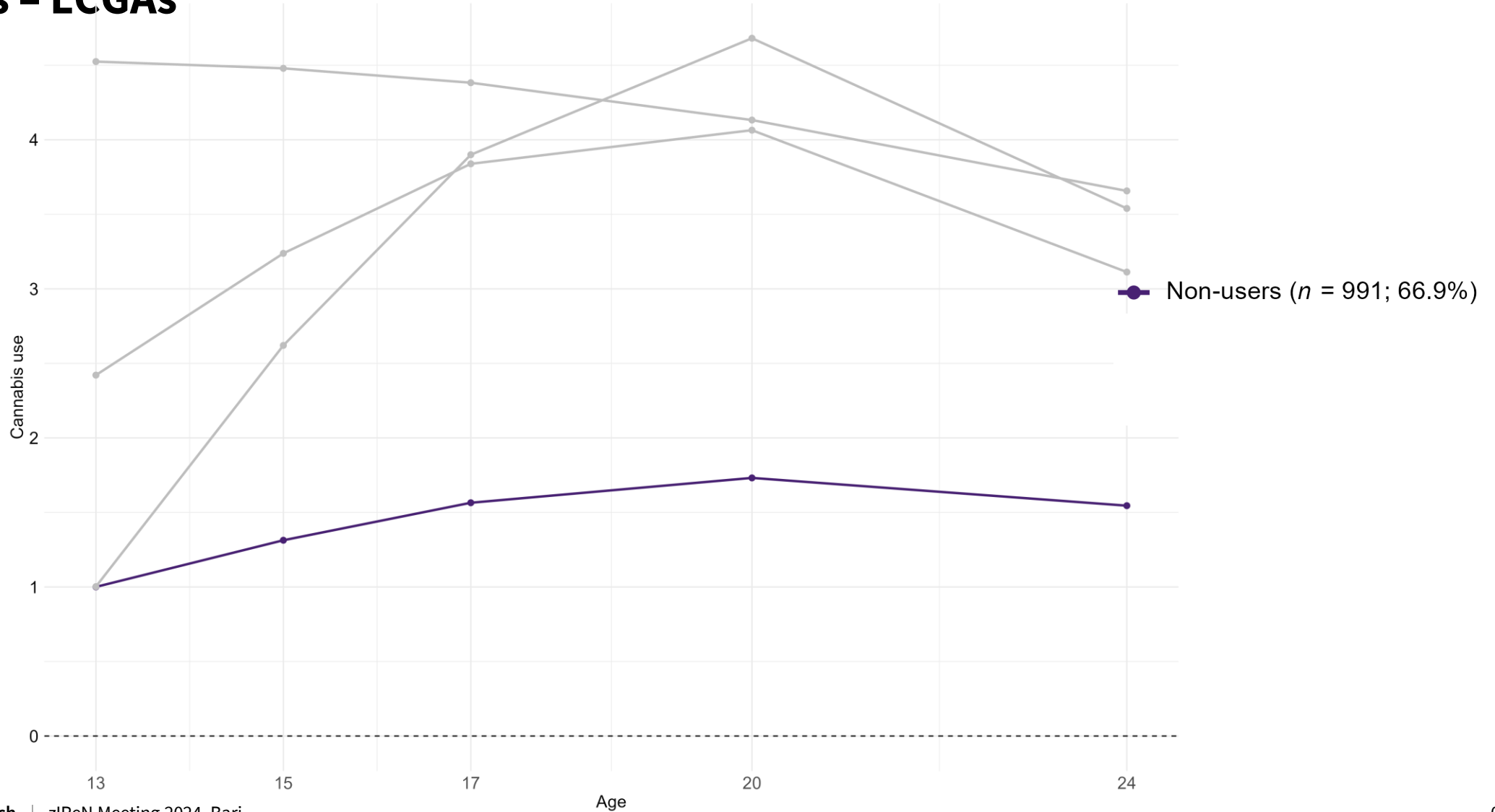
Overview of Helmert contrasts for each time point separately.

Term	PAL					RVP					SWM					Total				
	W5	W6	W7	W8	W9	W5	W6	W7	W8	W9	W5	W6	W7	W8	W9	W5	W6	W7	W8	W9
Intercept																				
Category 2 vs. 1																				
Category 3 vs. 2+1	█		█					█												
Category 4 vs. 3+2+1				█		█												█		
Category 5 vs. 4+3+2+1	█								█							█				
Category 6 vs. 5+4+3+2+1		█	█		█															

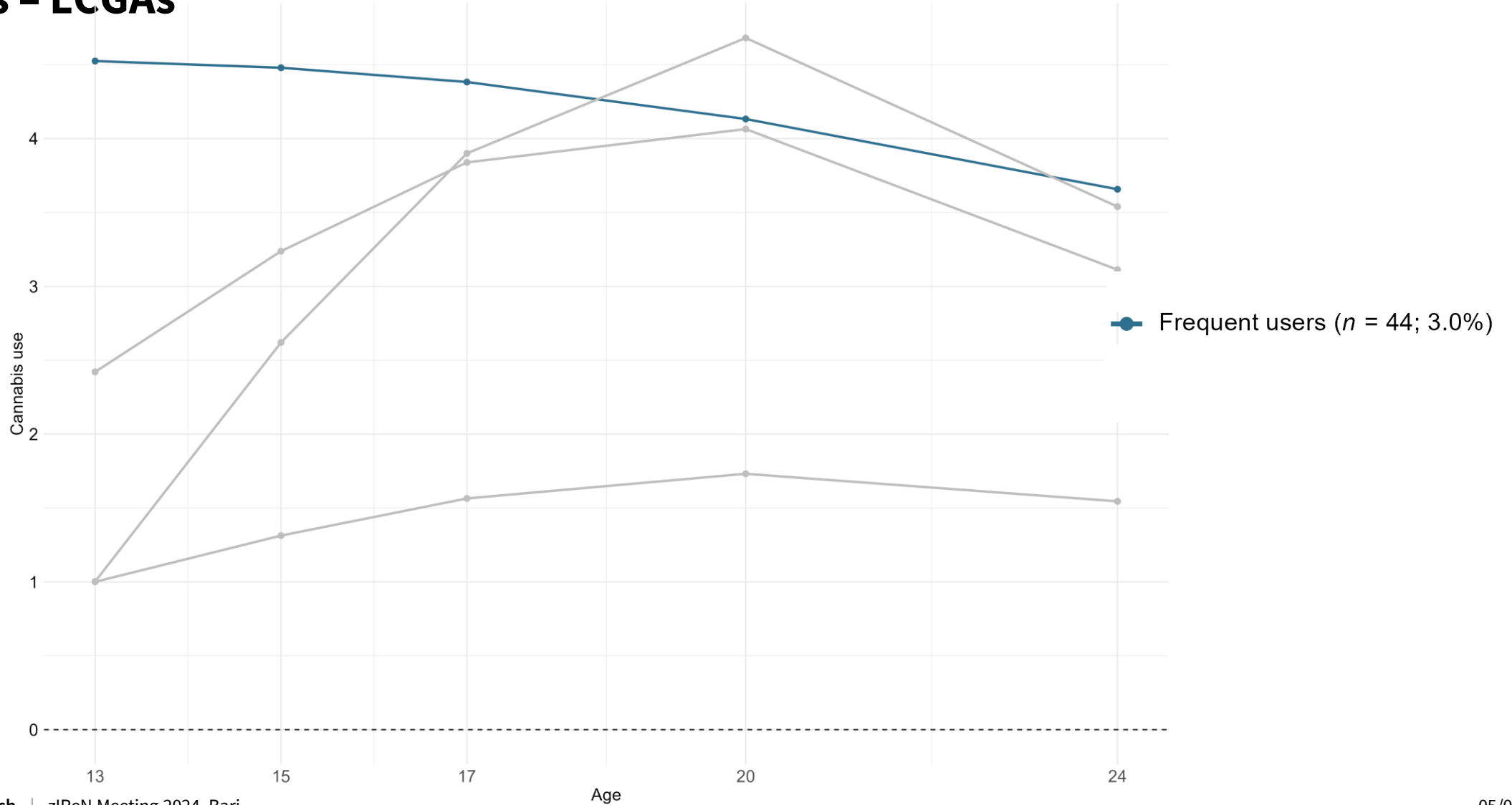
Results – LCGAs



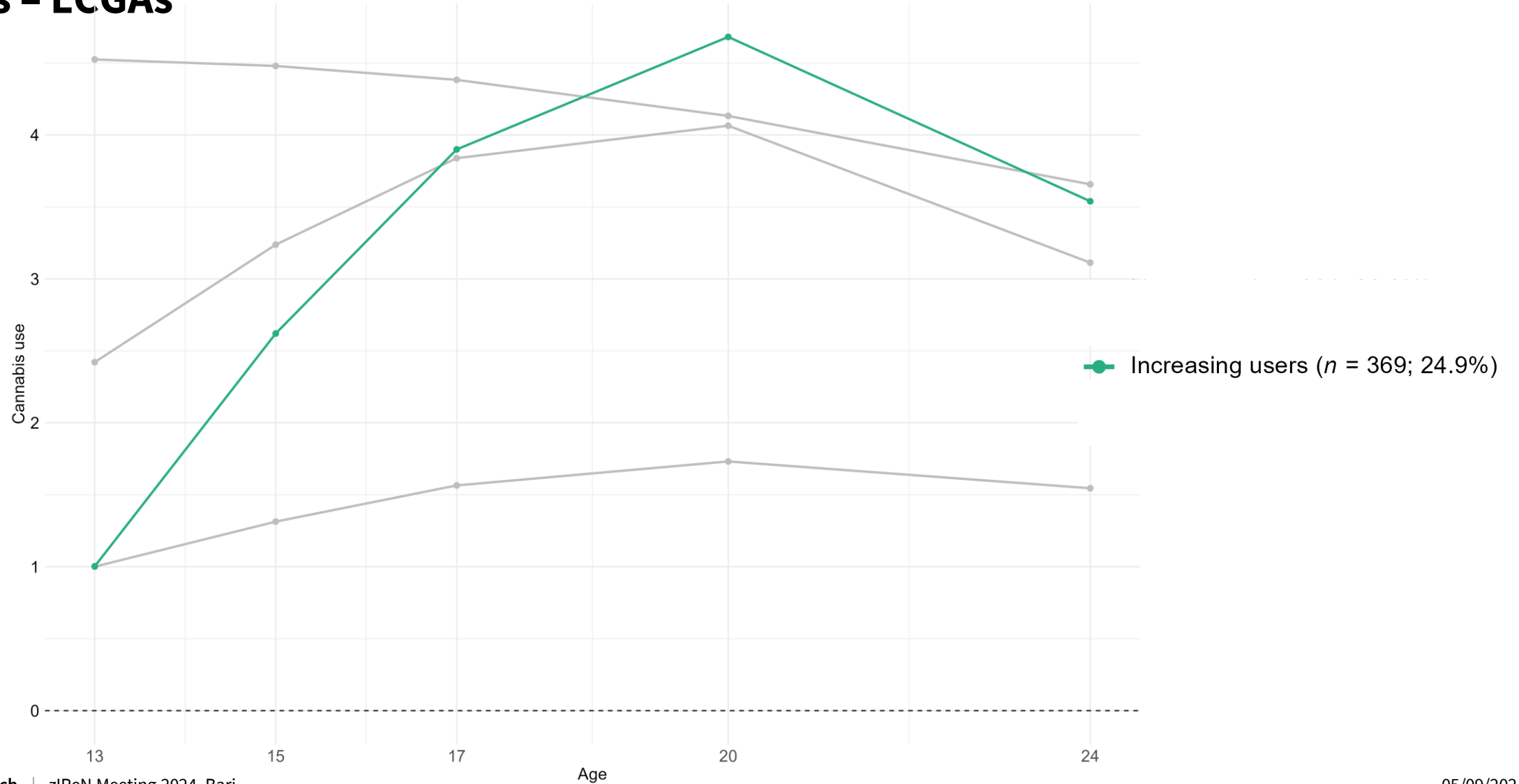
Results – LCGAs



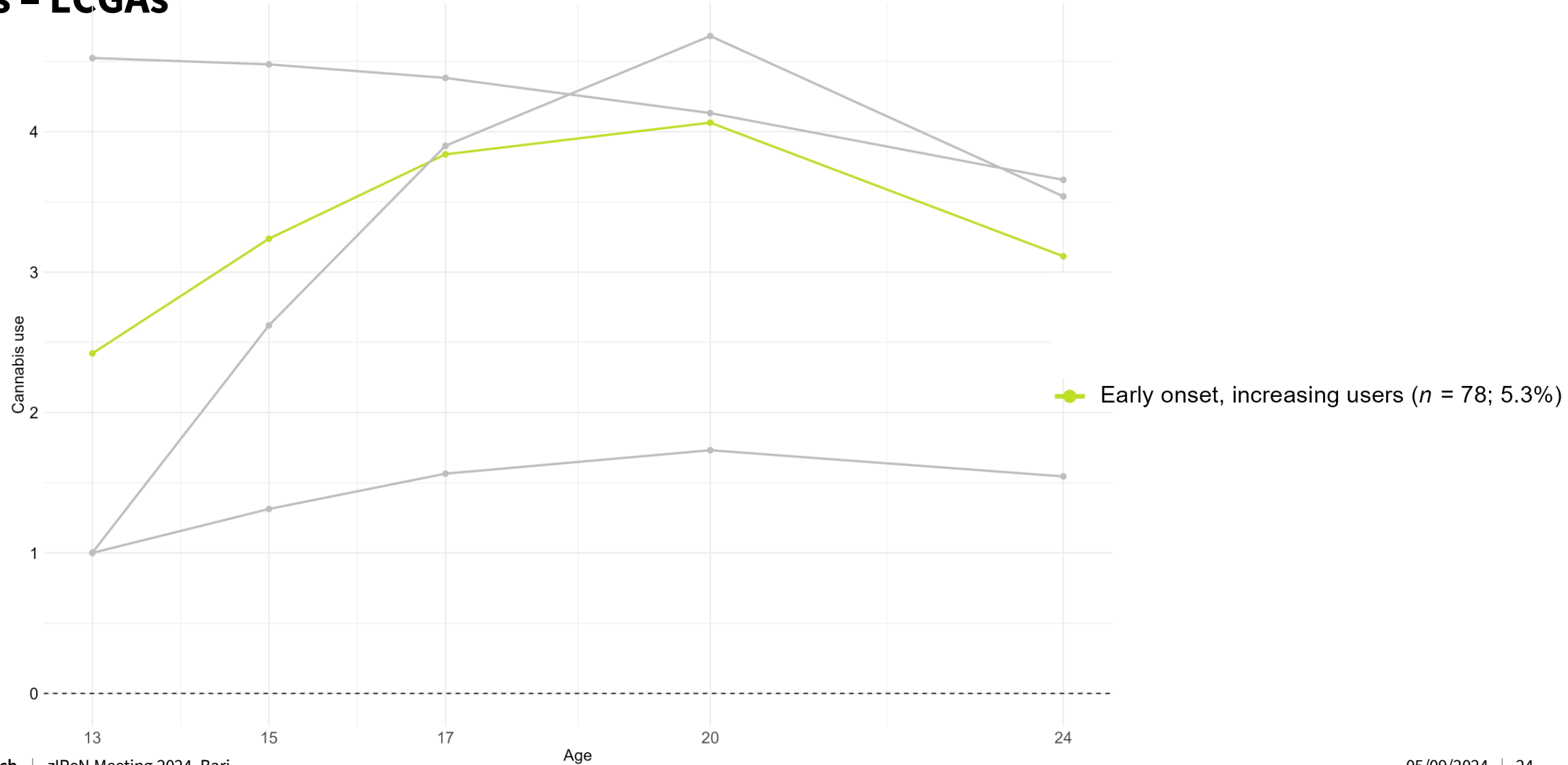
Results – LCGAs



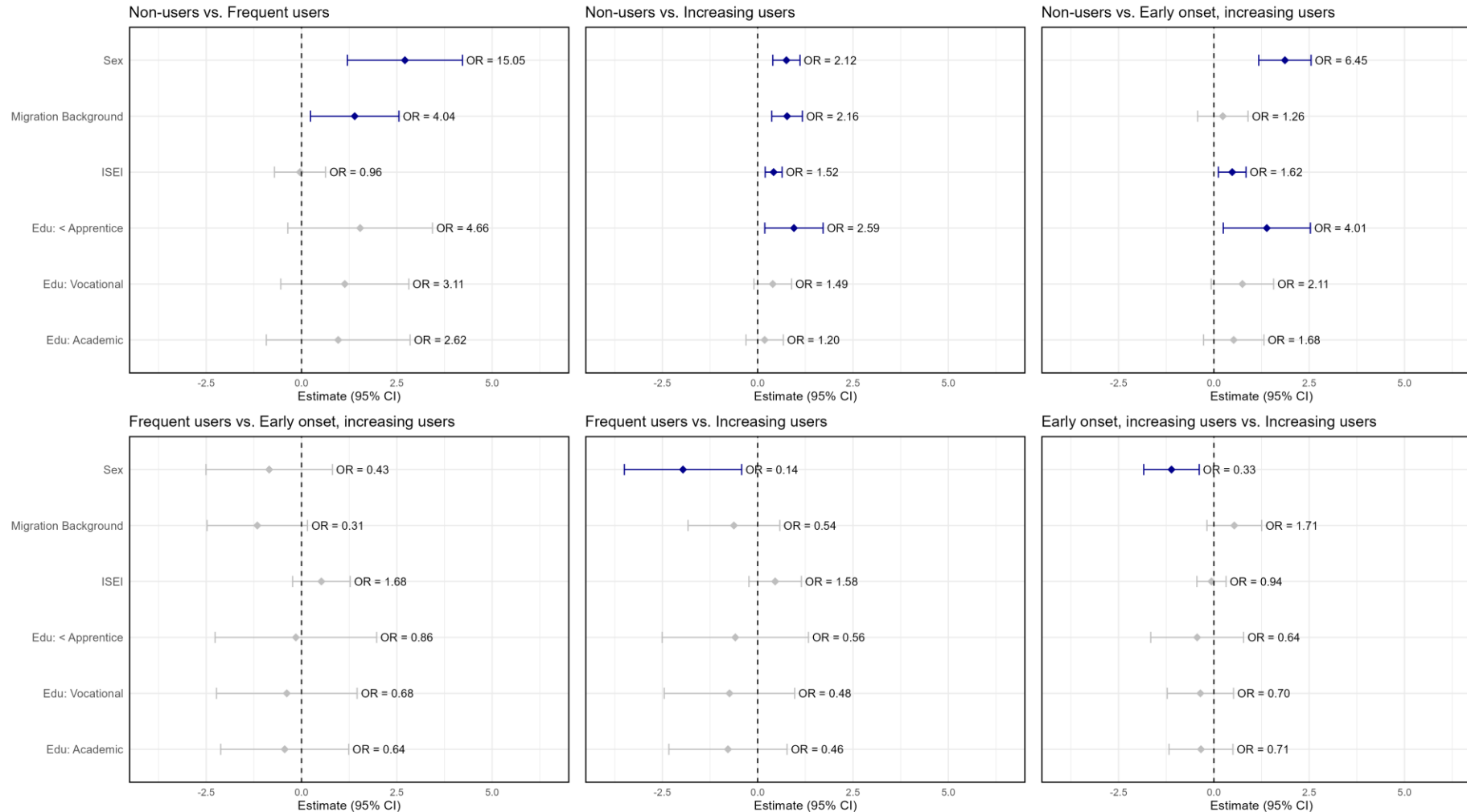
Results – LCGAs



Results – LCGAs

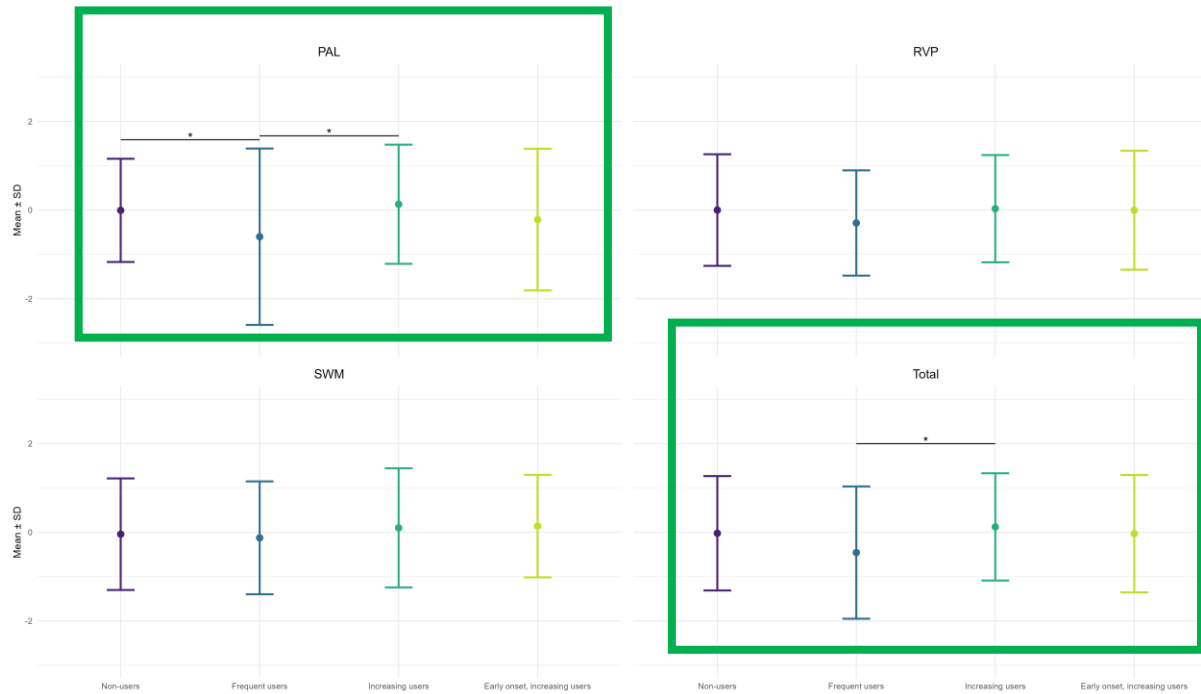


Results – LCGAs sociodemographic variables

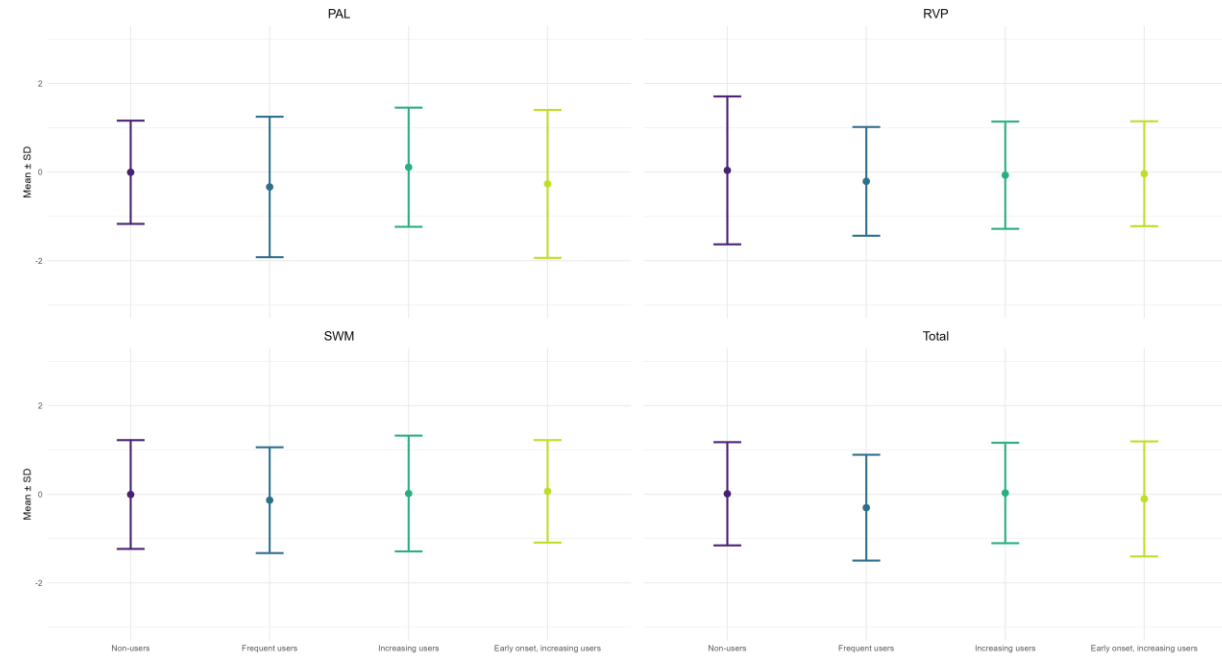


Results – LCGAs incl. sociodemographic & CANTAB variables

Without sociodemographic variables



With sociodemographic variables partialized out



Discussion

Summary

- Nuanced results: No straightforward relationship between cannabis use and cognitive performance, but a tendency for higher use being associated with lower performance
- Specific cognitive domains: Associations between cannabis use and PAL, RVP, and CANTAB total score.
- Latent subgroups: Significant relationship between group membership and sociodemographic variables
- Sociodemographic factors: Highly influential

Methodological considerations

- Only one time point for cognitive performance
- Ordered cannabis use responses and only self-reports (Steinhoff et al., 2023)
- No information on the THC potency

➤ Caution when interpreting

Discussion

Future directions

- Performance changes in CANTAB
- Moderating/mediating factors
- Further substances

Thank you!



... also to the entire z-proso project team,

... to the Experimental Pharmacopsychology and Psychological Addiction Research team,

... and to the Risk and Resilience team!

Contact

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Literature (IV)

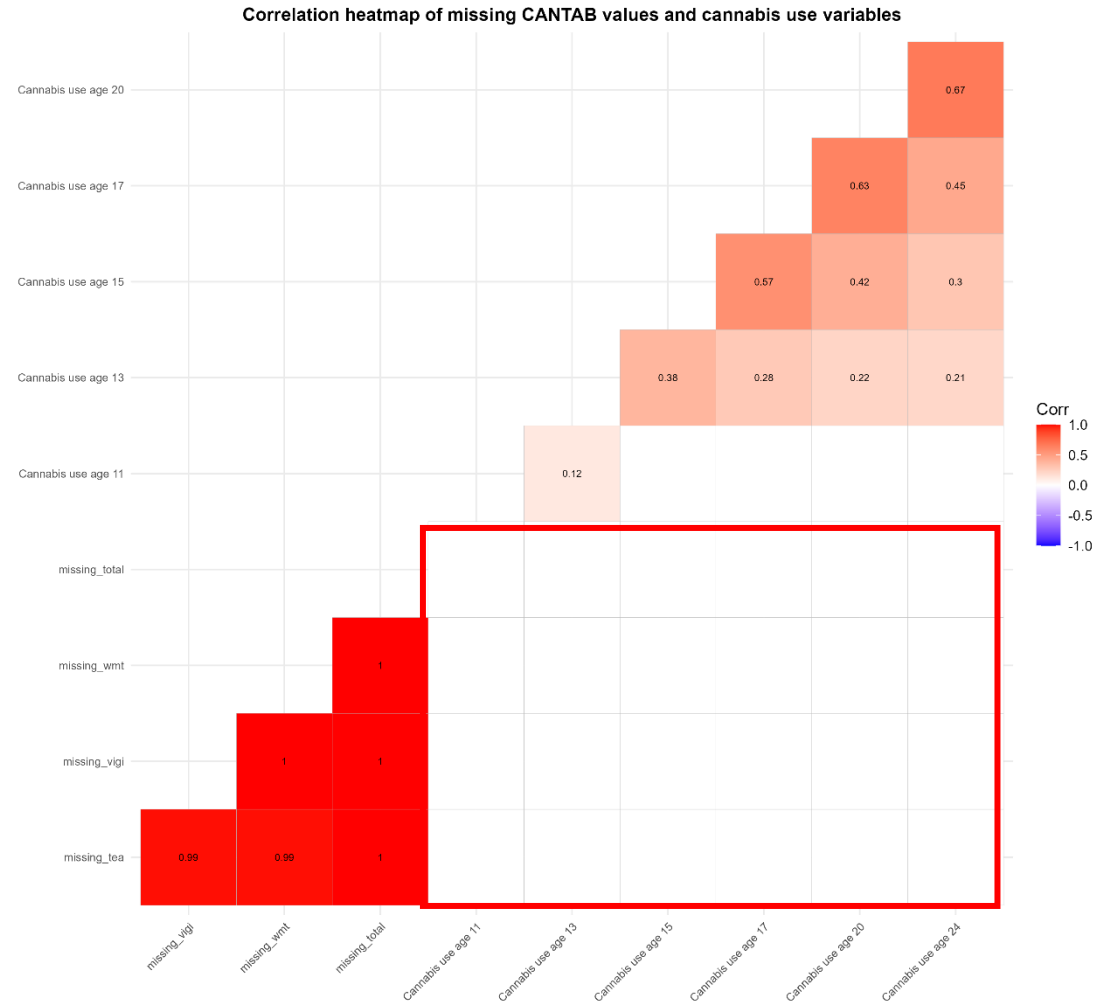
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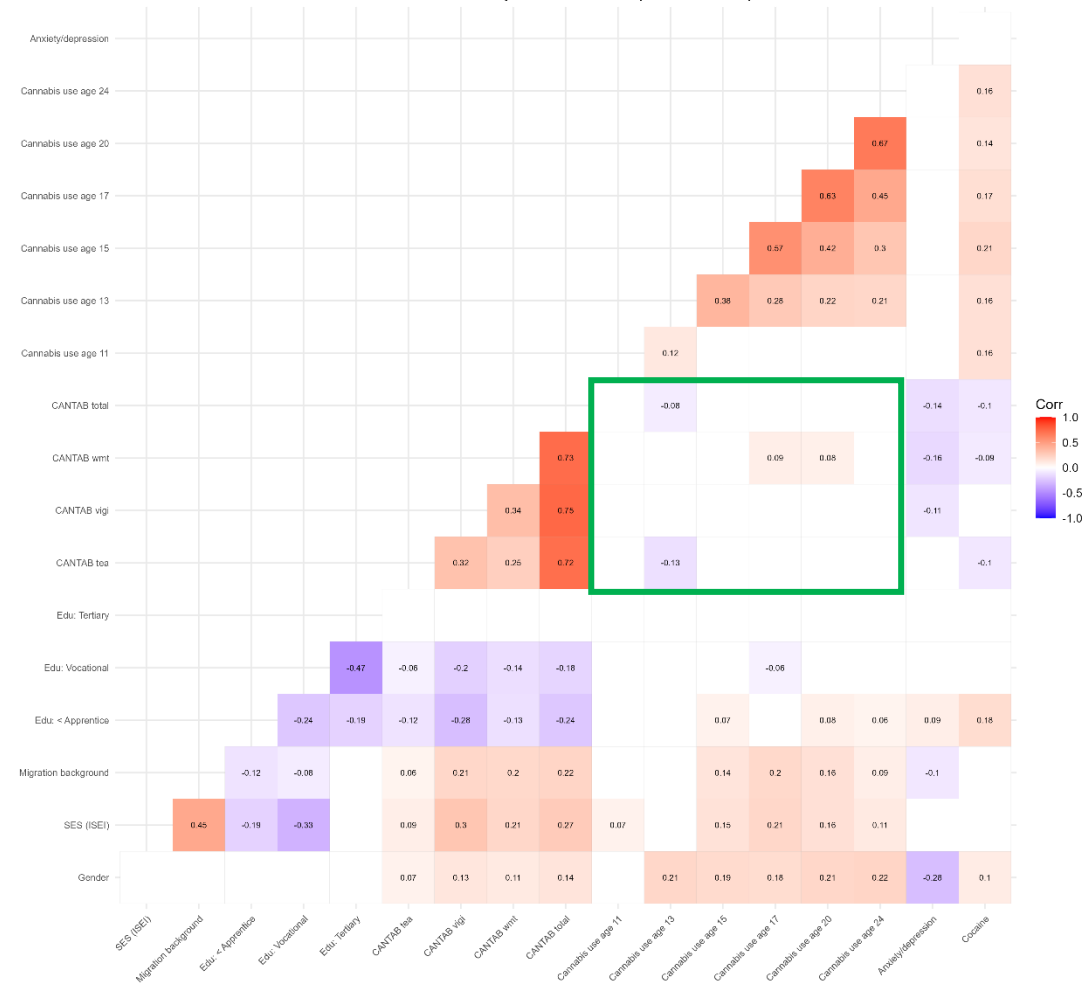
Backup

Results – missingness analysis

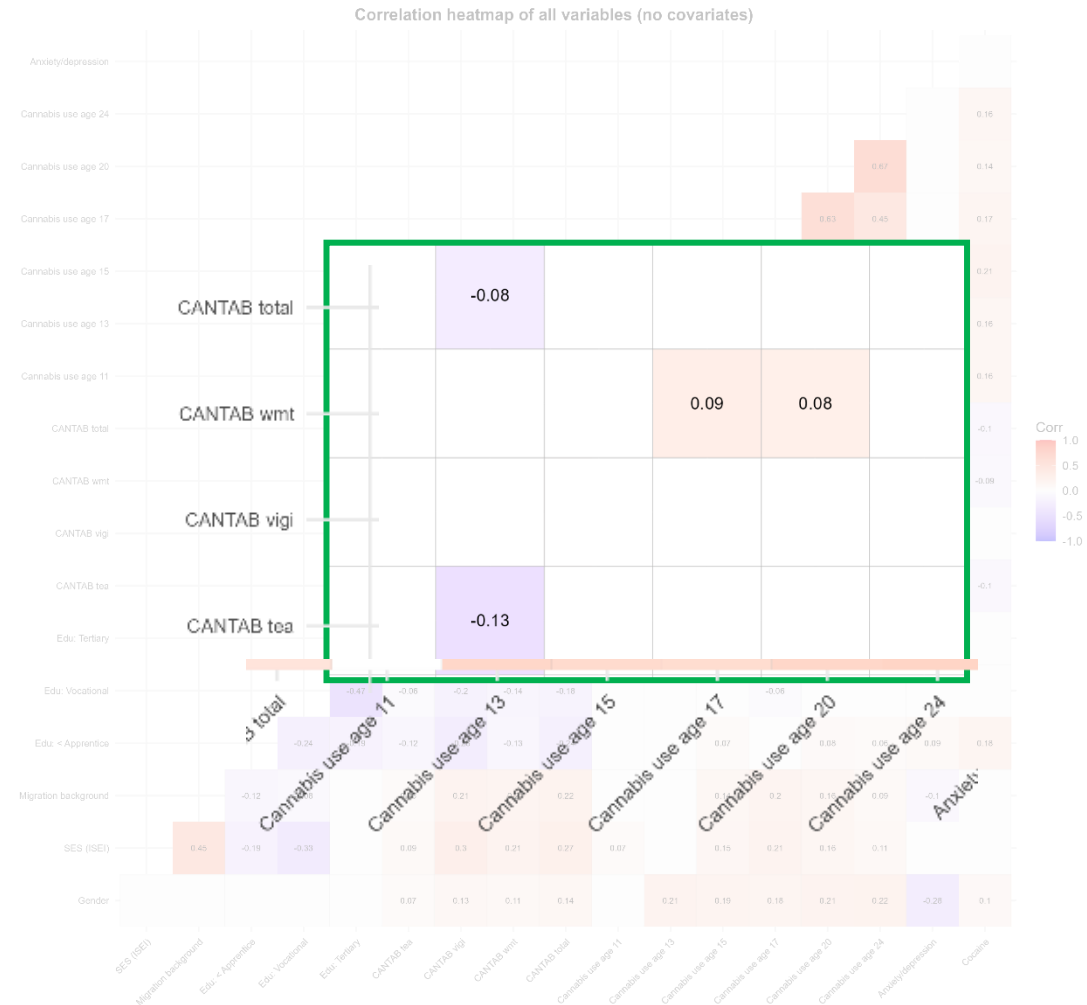


Results – correlations

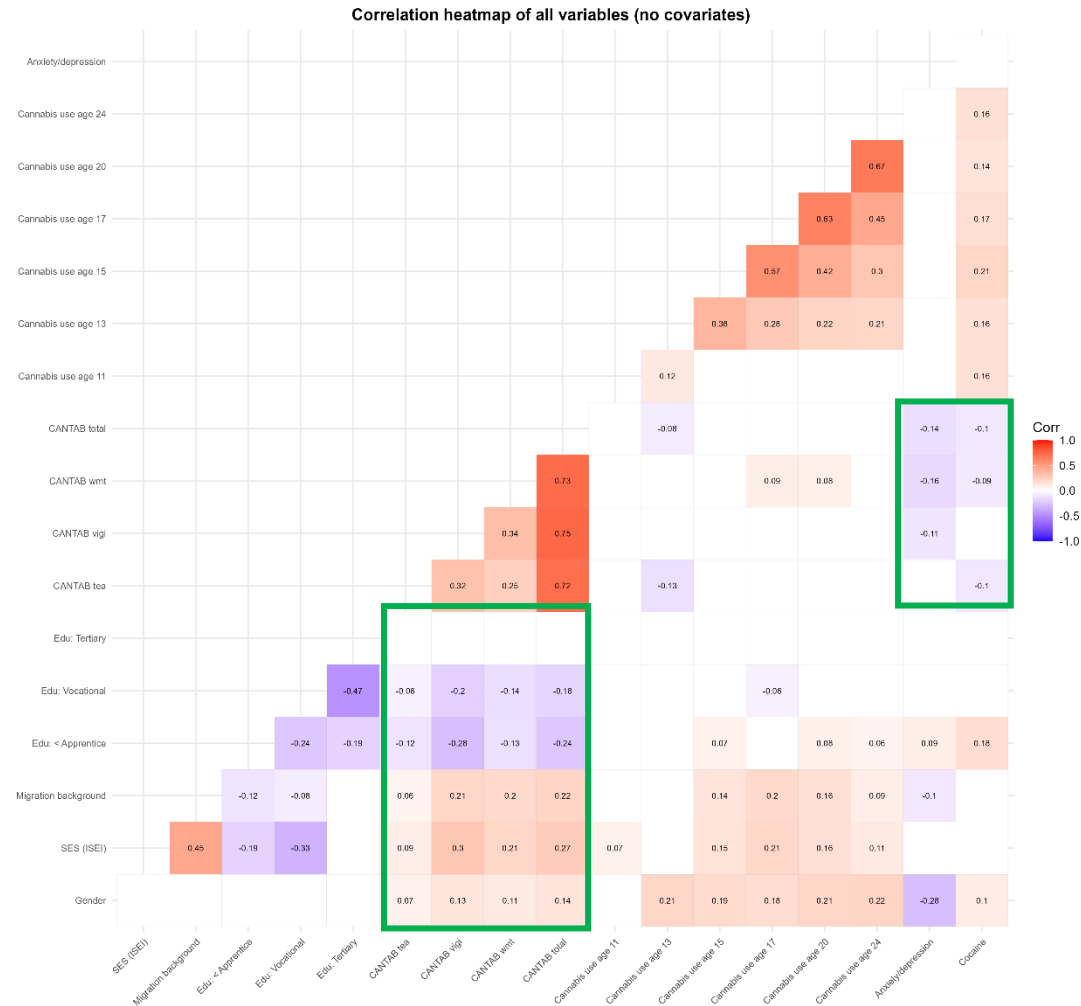
Correlation heatmap of all variables (no covariates)



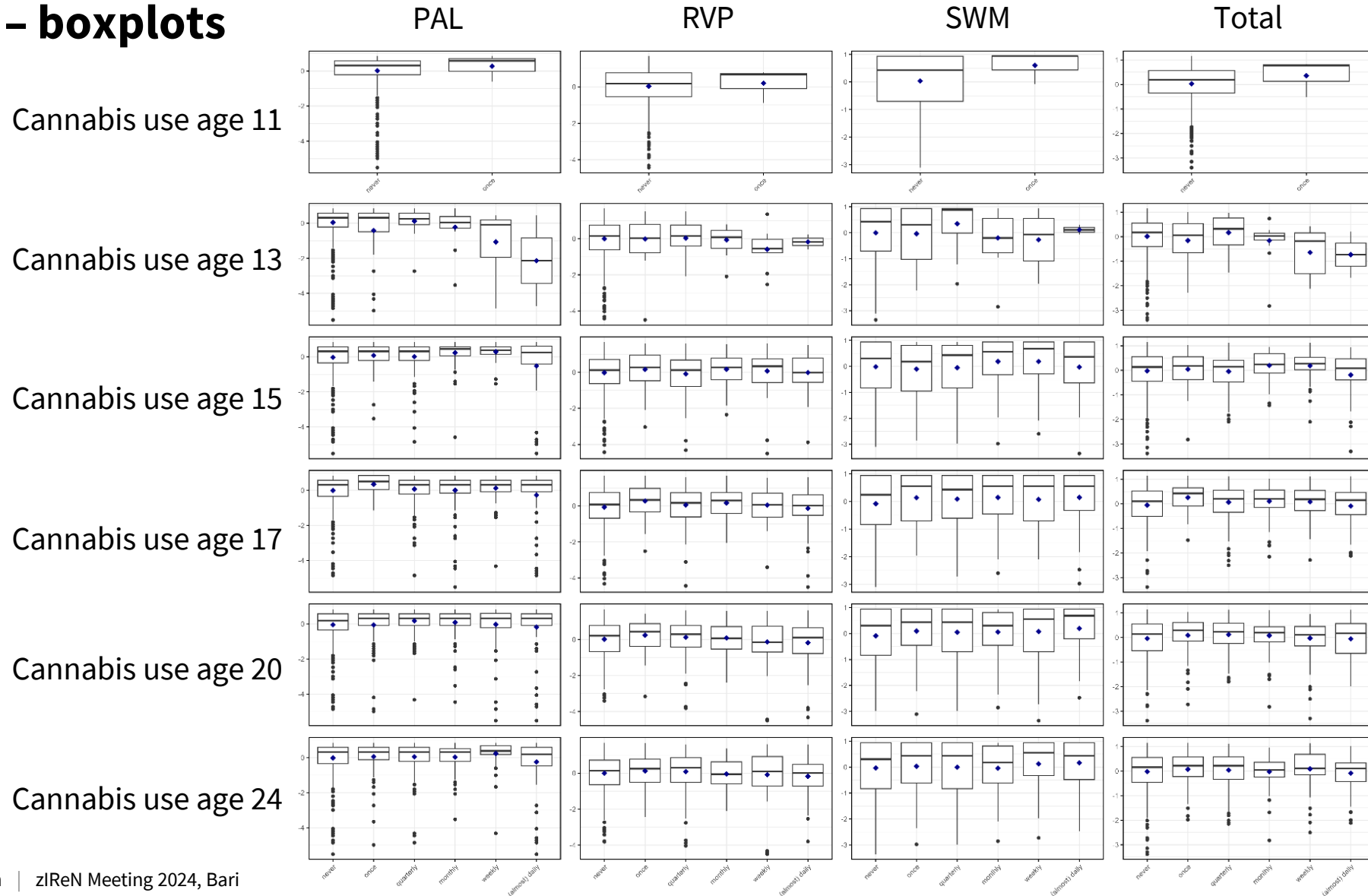
Results – correlations



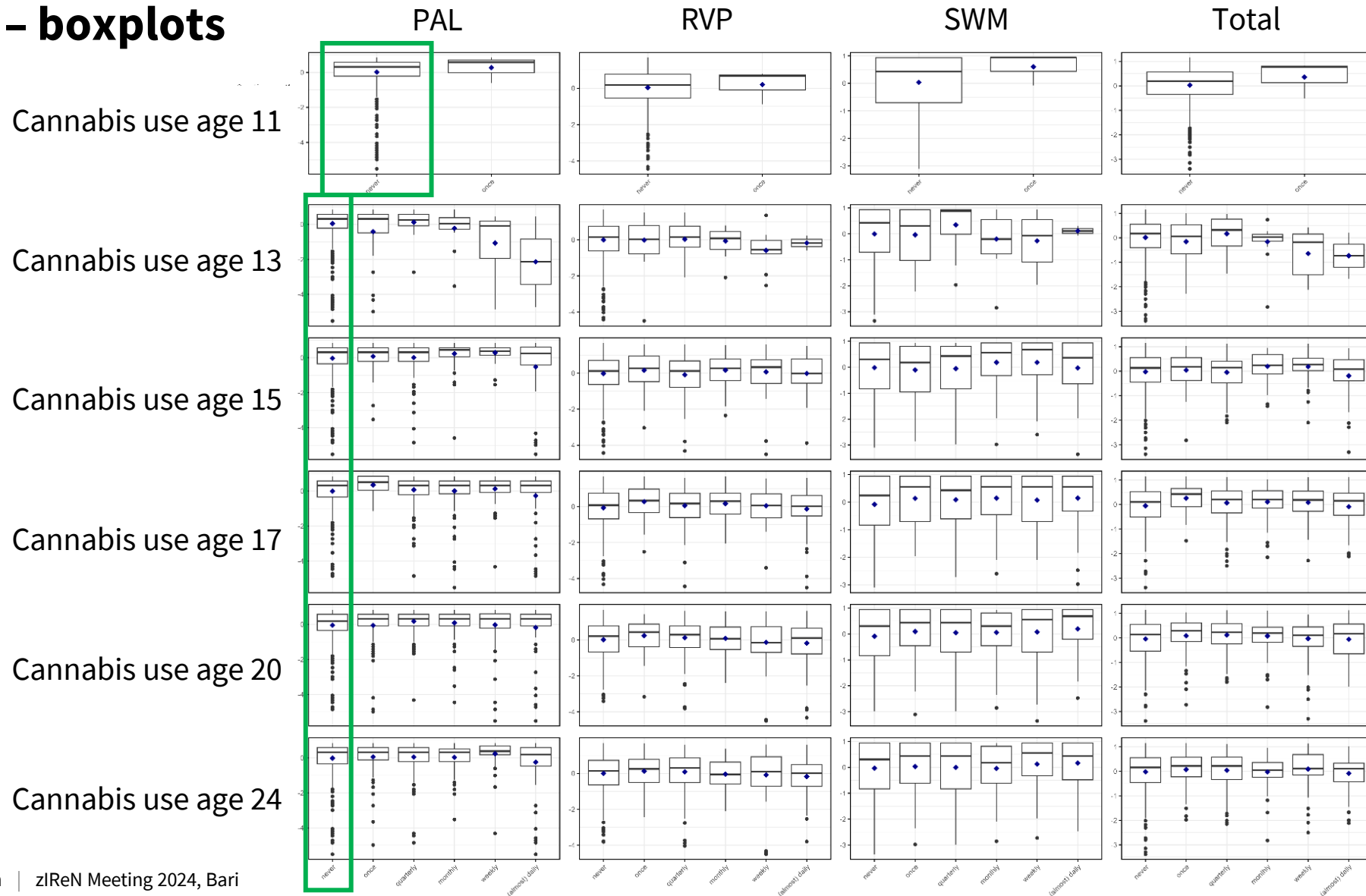
Results – correlations



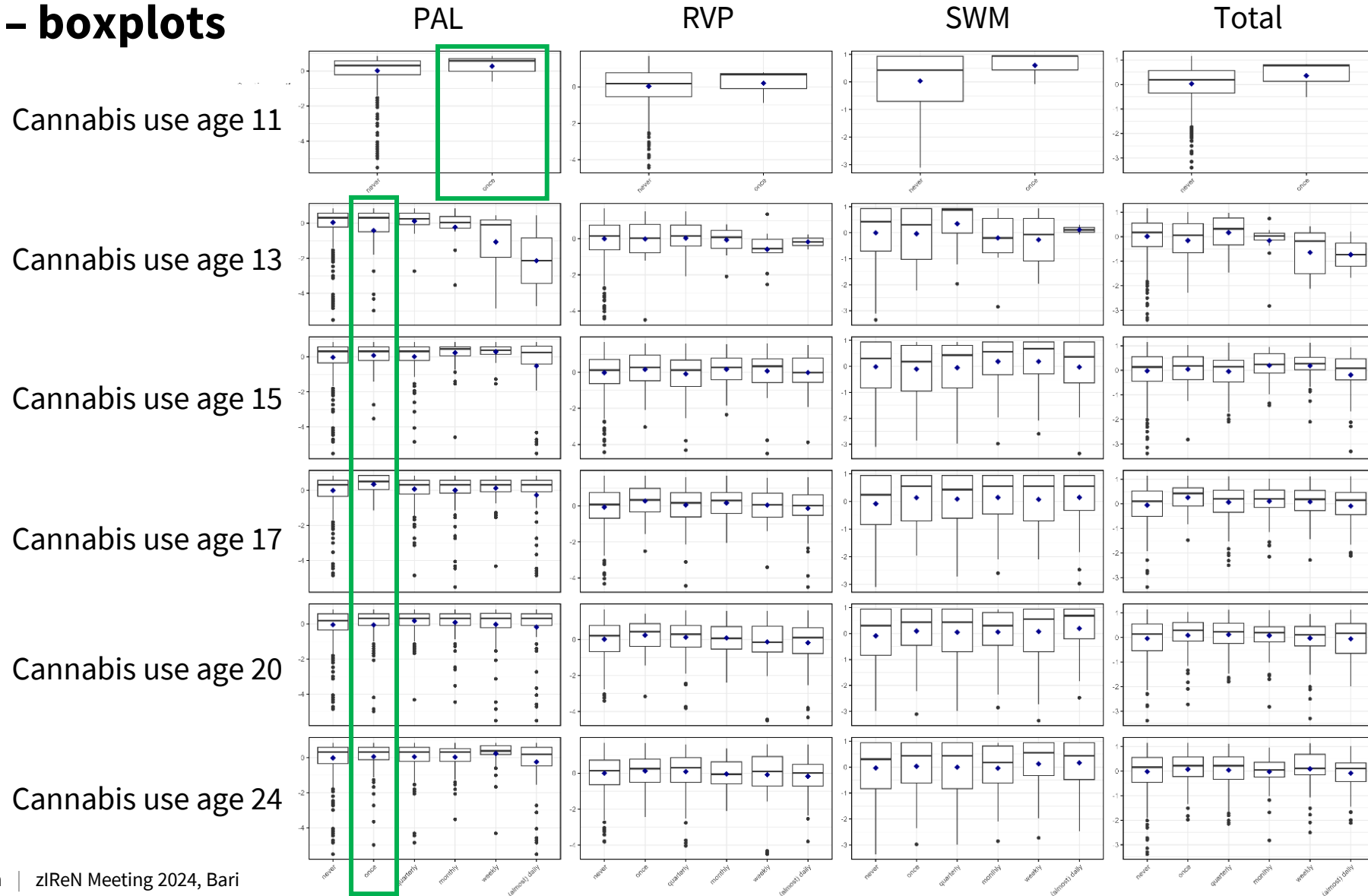
Results – boxplots



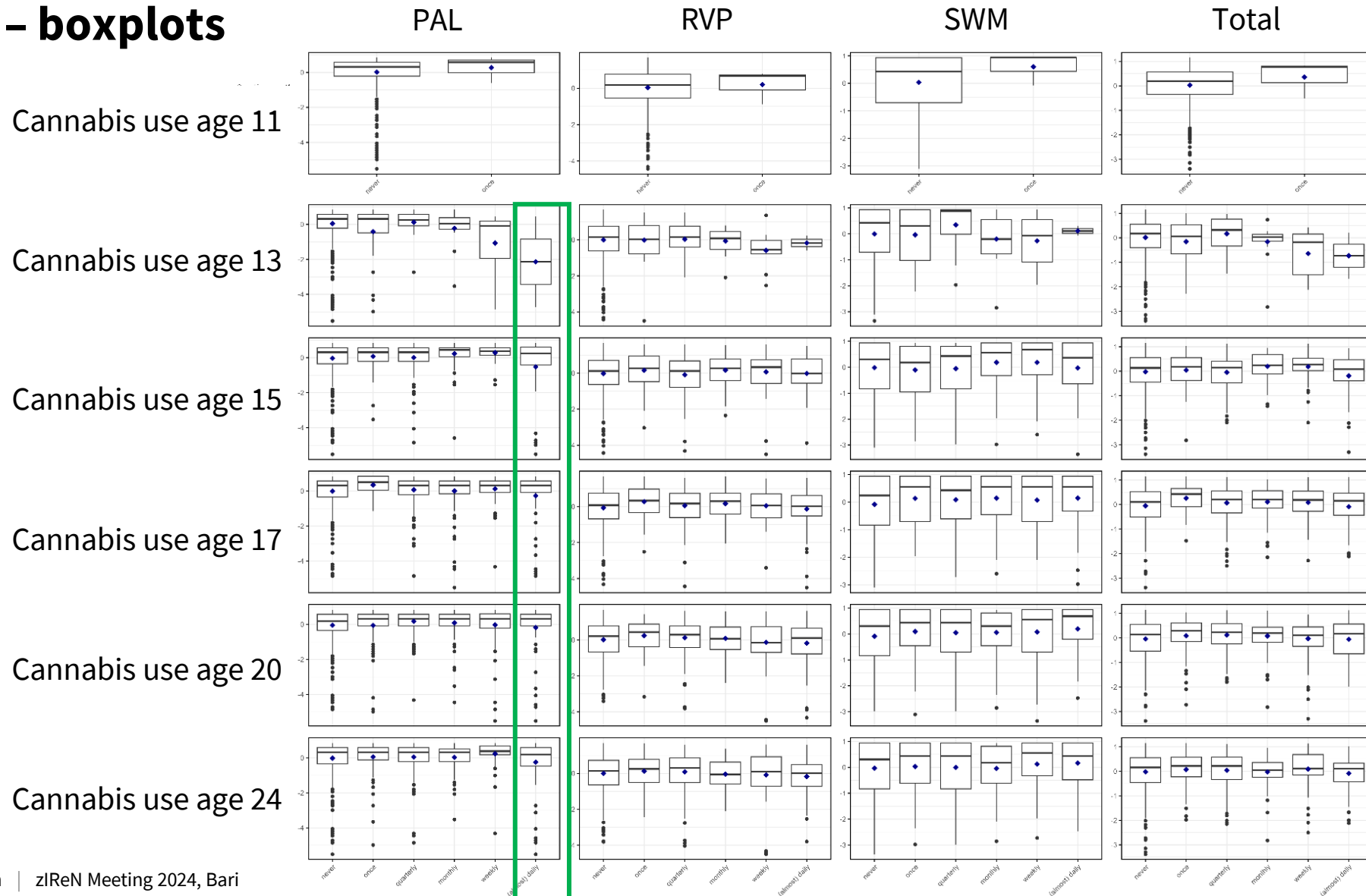
Results – boxplots



Results – boxplots

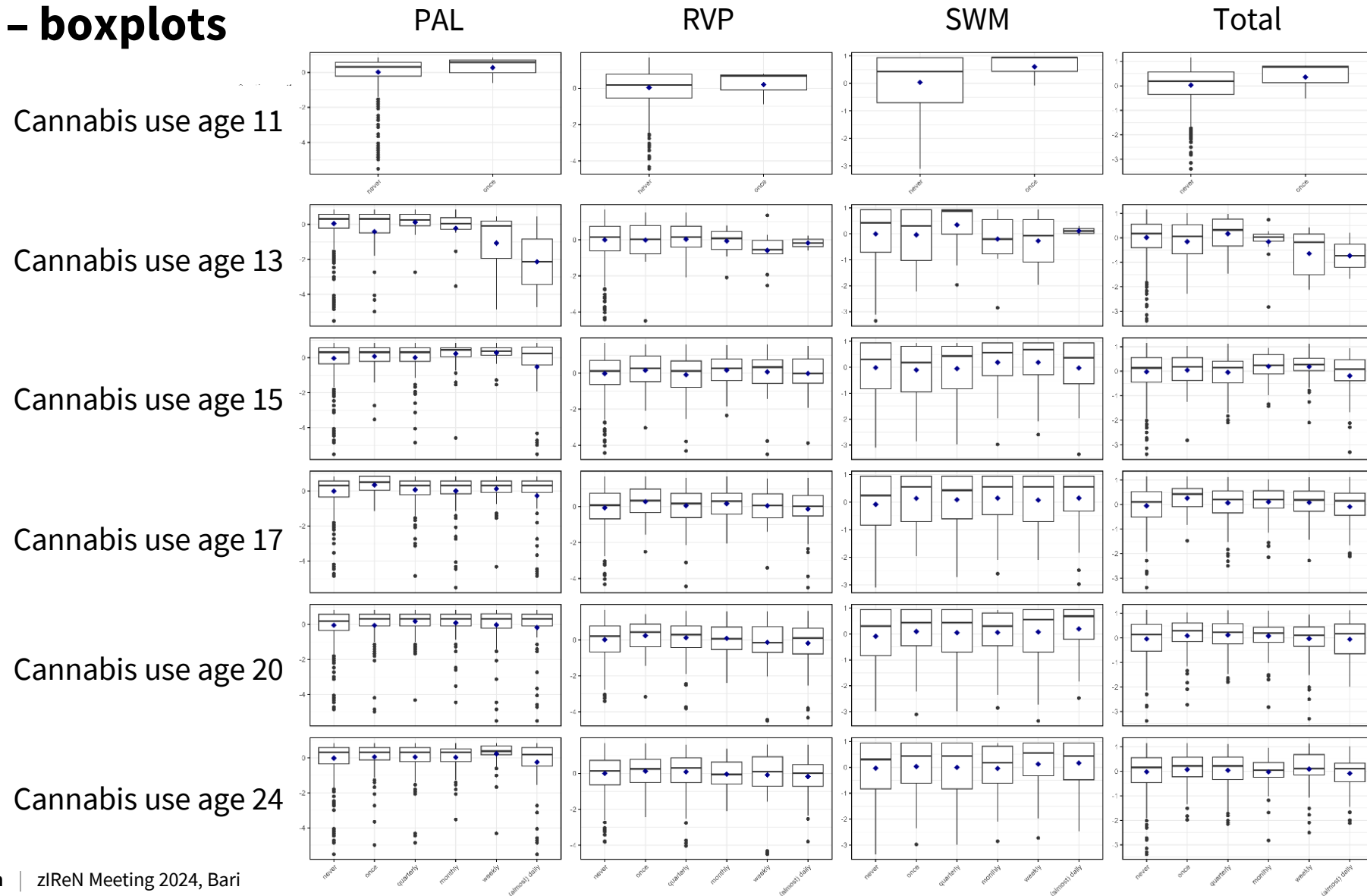


Results – boxplots



(almost) daily

Results – boxplots



Results – ANOVAs

Overview of group comparisons (ANOVAs).

Categories	PAL					RVP					SWM					Total					
	W5	W6	W7	W8	W9	W5	W6	W7	W8	W9	W5	W6	W7	W8	W9	W5	W6	W7	W8	W9	
V1	never/once vs. occasional								Yellow	Green									Green		
	never/once vs. frequent	Green																			
	occasional vs. frequent																				
V2	never/once vs. occasional								Yellow												
	never/once vs. frequent									Yellow	Yellow										
	occasional vs. frequent									Yellow											

Note: Categories in version 1 (V1) were: never/once = 1/2, occasional = 3/4, frequent = 5/6. Categories in version 2 (V2) were: never/once = 1/2, occasional = 3/4/5, frequent = 6.

Results – LCGAs incl. sociodemographic & CANTAB variables

Multinomial logistic regression model results for sex, migration background, ISEI, and education (R3STEP).

Predictor	Non-users vs. Frequent users		Non-users vs. Early onset, increasing users		Non-users vs. Increasing users		Frequent users vs. Early onset, increasing users		Frequent users vs. Increasing users		Early onset, increasing users vs. Increasing users	
	Estimate (SE)	OR	Estimate (SE)	OR	Estimate (SE)	OR	Estimate (SE)	OR	Estimate (SE)	OR	Estimate (SE)	OR
Sex ¹	2.712*** (0.770)	15.055	1.864*** (0.350)	6.449	0.753 *** (0.182)	2.124	-0.848 (0.846)	0.428	-1.959* (0.785)	0.141	-1.111** (0.371)	0.329
Migration Background ²	1.395* (0.592)	4.035	0.235 (0.337)	1.265	0.771*** (0.205)	2.162	-1.160 (0.672)	0.314	-0.624 (0.614)	0.536	0.536 (0.366)	1.709
ISEI ³	-0.040 (0.342)	0.961	0.481** (0.185)	1.618	0.418*** (0.113)	1.519	0.521 (0.385)	1.683	0.458 (0.351)	1.580	-0.063 (0.195)	0.939
Edu: < Apprenticeship ⁴	1.538 (0.968)	4.658	1.389* (0.583)	4.011	0.951* (0.390)	2.588	-0.149 (1.081)	0.861	-0.587 (0.979)	0.556	-0.438 (0.621)	0.645
Edu: Vocational	1.135 (0.857)	3.111	0.749 (0.418)	2.114	0.396 (0.252)	1.485	-0.386 (0.941)	0.680	-0.739 (0.873)	0.477	-0.353 (0.444)	0.702
Edu: Academic	0.962 (0.781)	2.617	0.521 (0.404)	1.683	0.183 (0.250)	1.201	-0.441 (0.857)	0.643	-0.779 (0.791)	0.459	-0.338 (0.428)	0.713

Note. Estimate = β from R3STEP analysis; *** $p < .001$; ** $p < .01$; * $p < .05$. ¹: 0 = female, 1 = male; ²: 0 = migration background, 1 = at least one parent born in Switzerland; ³: ISEI range 16-90 z-standardized; ⁴: reference category = below apprenticeship.

Results – LCGAs incl. sociodemographic & CANTAB variables

Mean values of the CANTAB tests for each latent subgroup.

	Tests	Non-users		Frequent users		Increasing users		Early onset, increasing users	
		<i>M</i>	<i>SE</i>	<i>M</i>	<i>SE</i>	<i>M</i>	<i>SE</i>	<i>M</i>	<i>SE</i>
Without sociodemographic variables	Total Errors Adjusted (PAL)	-0.006	0.037	-0.601	0.300	0.132	0.070	-0.214	0.181
	Vigilance (RVP)	0.001	0.040	-0.291	0.179	0.032	0.068	-0.002	0.152
	Working Memory Total (SWM)	-0.044	0.040	-0.126	0.192	0.099	0.070	0.139	0.131
	CANTAB (total)	-0.023	0.041	-0.459	0.225	0.121	0.063	-0.032	0.150
With partialized out sociodemographic variables	Total Errors Adjusted (PAL)	-0.004	0.037	-0.335	0.239	0.110	0.070	-0.266	0.189
	Vigilance (RVP)	0.039	0.036	-0.209	0.185	-0.070	0.063	-0.037	0.134
	Working Memory Total (SWM)	-0.006	0.039	-0.134	0.180	0.017	0.068	0.066	0.131
	CANTAB (total)	0.011	0.037	-0.303	0.180	0.029	0.059	-0.105	0.147

Results – LCGAs incl. sociodemographic & CANTAB variables

Equality tests of means across classes (BCH).

Predictor	Overall test		Non-users vs. Frequent users		Non-users vs. Increasing users		Non-users vs. Early onset, increasing users		Frequent users vs. Increasing users		Frequent users vs. Early onset, increasing users		Increasing users vs. Early onset, increasing users		
	Chi-Square	<i>p</i>	Chi-Square	<i>p</i>	Chi-Square	<i>p</i>	Chi-Square	<i>p</i>	Chi-Square	<i>p</i>	Chi-Square	<i>p</i>	Chi-Square	<i>p</i>	
Without sociodemographic variables	Total Errors Adjusted (PAL)	8.271	.041*	3.889	.049*	2.735	.098	1.264	.261	5.530	.019*	1.209	.272	3.086	.079
	Vigilance (RVP)	2.802	.423	2.529	.112	0.138	.711	0.000	.986	2.758	.097	1.485	.223	0.040	.842
	Working Memory Total (SWM)	4.405	.221	0.173	.678	2.825	.093	1.793	.181	1.175	.278	1.281	.258	0.073	.787
	CANTAB total	7.543	.056	3.632	.057	3.343	.067	0.003	.955	6.008	.014*	2.461	.117	0.869	.351
With partialized out sociodemographic variables	Total Errors Adjusted (PAL)	5.954	.114	1.873	.171	1.832	.176	1.858	.173	3.094	.079	0.050	.822	3.372	.066
	Vigilance (RVP)	3.627	.305	1.732	.188	2.020	.155	0.298	.585	0.489	.484	0.560	.454	0.050	.824
	Working Memory Total (SWM)	0.873	.832	0.483	.487	0.080	.777	0.281	.596	0.602	.438	0.798	.372	0.108	.743
	CANTAB total	3.667	.300	2.944	.086	0.060	.807	0.585	.445	3.007	.083	0.718	.397	0.692	.406