Cumulative distribution of cases diagnosed with MDD
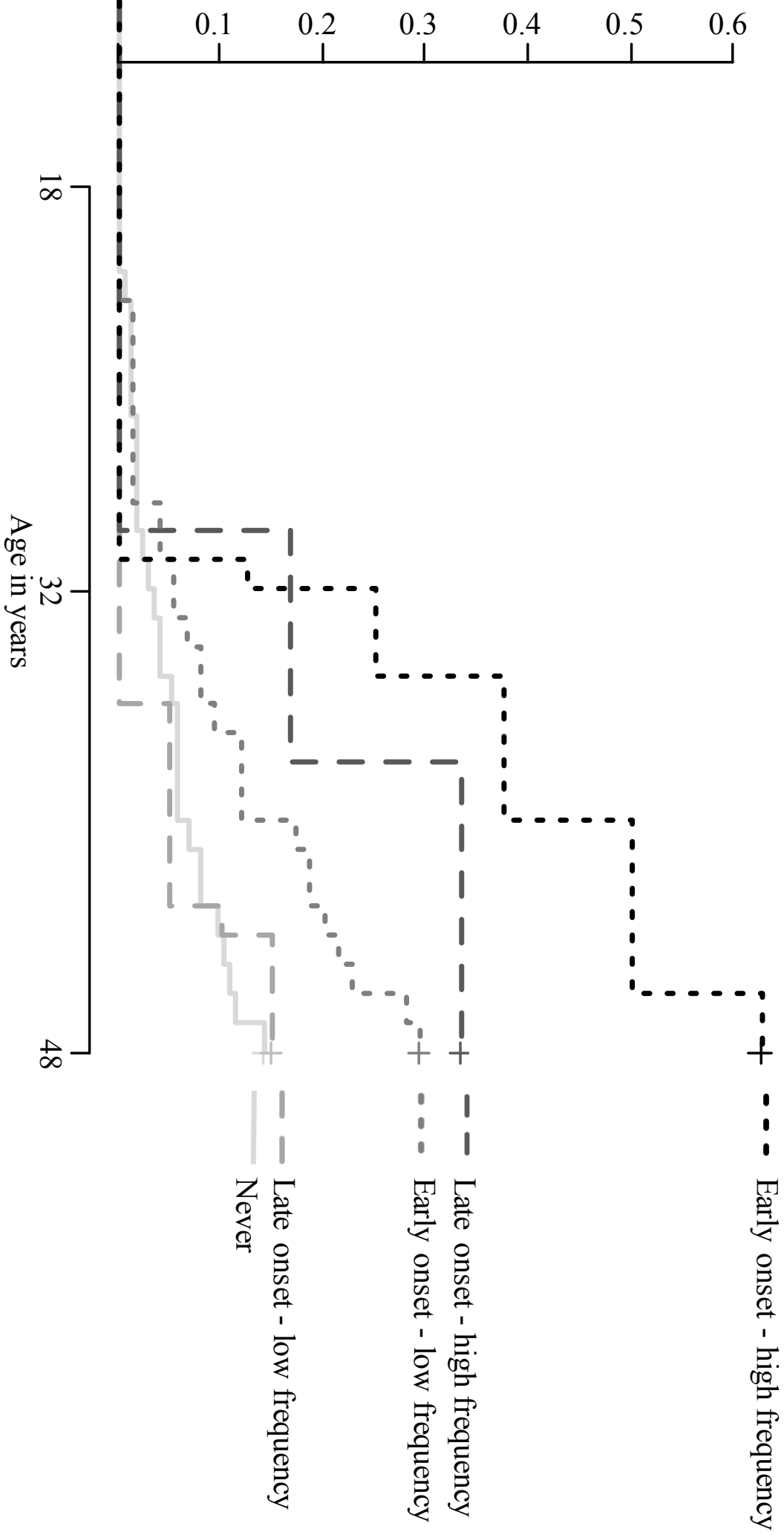
0.1 0.2 0.3 0.4 0.5 0.6

Age in years

18 32 48

Never

Late onset - low frequency

Early onset - low frequency

Late onset - high frequency

Early onset - high frequency

Table 1. Cannabis and depression trajectories (N=285)

Age of onset MDD	Mean in years (SD)	38.57 (7.13)
Diagnosis of MDD	Ever diagnosed (yes) (n)	20.4% (58)
	Before 18 (n)	0% (0)
	Between 18-32 (n)	22.4% (13)
	Between 33-48 (n)	77.6% (45)
Cannabis use trajectory	Ever used (yes)	38.2% (109)
	Onset up to 14 (n)	0% (0)
	Onset between 15-18 (n)	76.1% (83)
	Onset between 27-32 (n)	13.8% (15)
	Onset between 43-48 (n)	10.1% (11)
Cannabis use pattern	Never used (n)	61.8% (176)
	Late onset – low frequency (n)	7.7% (22)
	Late onset – high frequency (n)	1.4% (4)
	Early onset – low frequency (n)	27.4% (78)
	Early onset – high frequency (n)	1.75% (5)
Cannabis-Depression Trajectory	Cannabis → MDD	11.3% (32)
	Cannabis → no MDD	26.3% (75)
	Never cannabis, no MDD	53.3% (152)
	Never cannabis → MDD	8.8% (25)
	MDD → Cannabis	0.4% (1)

Note. MDD = Diagnosis of Major Depression Disorder based on Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I)

Table 2. Cannabis profiles and risk of subsequent MDD: Logistic regression analyses*

Simple logistic regression (N=284)	OR	95% CI	p
Cannabis late onset – low frequency	0.71	0.11 – 2.69	0.66
Cannabis late onset – high frequency	3.02	0.40 – 16.34	0.22
Cannabis early onset – low frequency	2.67	1.39 – 5.12	**0.003**
Cannabis early onset – high frequency	10.07	2.33 – 51.61	**0.002**
Multiple logistic regression (N=284)	**OR**	**95% CI**	**p**
Cannabis late onset – low frequency	0.68	0.10 - 2.65	0.63
Cannabis late onset – high frequency	2.23	0.26 - 14.94	0.42
Cannabis early onset – low frequency	2.41	1.22 - 4.76	**0.01**
Cannabis early onset – high frequency	8.83	1.29 - 70.79	**0.03**
Other mental illness (yes)	2.18	1.15 - 4.14	**0.02**
Other illicit drug use (yes)	1.10	0.28 - 3.75	0.88
Employment status (unemployed)	2.34	1.19 - 4.53	**0.01**

Note. Reference group = never cannabis users; Early onset = Cannabis use at age 18 or before; High frequency = $\geq$ 450 cumulative number of times used across time points (ages 18, 32, 48)

*n=1 cases excluded since MDD was diagnosed prior to cannabis use

Table 3. Cannabis profiles and time until subsequent MDD: Hazard ratios (HR)*

Simple Cox Regression (N=284)	HR	95% CI	*p*
Cannabis late onset – low frequency	1.05	0.32-3.49	0.93
Cannabis late onset – high frequency	2.90	0.69-12.25	0.15
Cannabis early onset – low frequency	2.26	1.27-4.01	**0.005**
Cannabis early onset – high frequency	6.65	2.54-17.41	**0.0001**
Multiple Cox Regression (N=284)	**HR**	**95% CI**	***p***
Cannabis late onset – low frequency	1.06	0.32-3.54	0.92
Cannabis late onset – high frequency	2.77	0.61-12.51	0.19
Cannabis early onset – low frequency	2.09	1.16-3.74	**0.01**
Cannabis early onset – high frequency	8.69	2.07-36.52	**0.003**
Other mental illness (yes)	1.78	1.05-3.03	**0.03**
Other illicit drug use (yes)	0.73	0.25-2.15	0.56
Employment status (unemployed)	1.97	1.14-3.41	**0.02**

Note. Reference group = never cannabis users; Early onset = Cannabis use at age 18 or before; High frequency = ≥ 450 cumulative number of times used across time points (ages 18, 32, 48)

*n=1 cases excluded since MDD was diagnosed prior to cannabis use

Table 4. Fixed effects regression analysis

	Univariate			Multivariate*		
	OR	**95% CI**	**p**	**OR**	**95% CI**	**p**
Effect of Cannabis frequency on MDD in young adolescence (age 18 – 32)						
Cannabis frequency (age 14 - 18)	1.08	(1.04 – 1.13)	**0.0002**	1.08	(1.03 – 1.12)	**0.0008**
Cannabis frequency (age 18 - 32)	1.02	(1.00 – 1.05)	0.07	1.01	(0.99 – 1.05)	0.32
Effect of Cannabis frequency on MDD in adulthood (age 32 – 48)						
Cannabis frequency (age 14 - 18)	1.22	(1.12 – 1.33)	**<0.0001**	1.20	(1.10 – 1.31)	**<0.0001**
Cannabis frequency (age 18 - 32)	1.07	(1.02 – 1.13)	**0.007**	1.05	(0.99 – 1.11)	0.10
Cannabis frequency (age 32 - 48)	1.04	(0.99 – 1.09)	0.17	1.01	(0.95 – 1.07)	0.76
	Univariate			Multivariate*		
	Est.	**95% CI**		**Est.**	**95% CI**	
Effect of MDD on cannabis frequency in adulthood (age 32 – 48)						
MDD (age 18 - 32)	0.77	(0.59 – 0.99)	**0.05**	0.72	(0.57 – 0.92)	**0.009**
MDD (age 32 - 48)	1.07	(0.94 – 1.21)	0.33	1.02	(0.90 – 1.15)	0.77

Note. Increase in frequency = increase in one unit [(0) non-user; (1) low frequency user; (2) high frequency user]

*Controlled for random effects, including (1) other psychiatric illness and (2) other illicit drug use, (3) employment status at age 48