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Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

METHAMPHETAMINE USE DISORDER: TREATMENT UPDATE

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project ECHO

SPEAKER DISCLOSURES

✓ No Conflicts of Interest

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OBJECTIVES

1

Review basics of MeUD

2

Discuss 3 RCT's used for MeUD

3

Outline 3 large reviews of agonist-therapy for MeUD.

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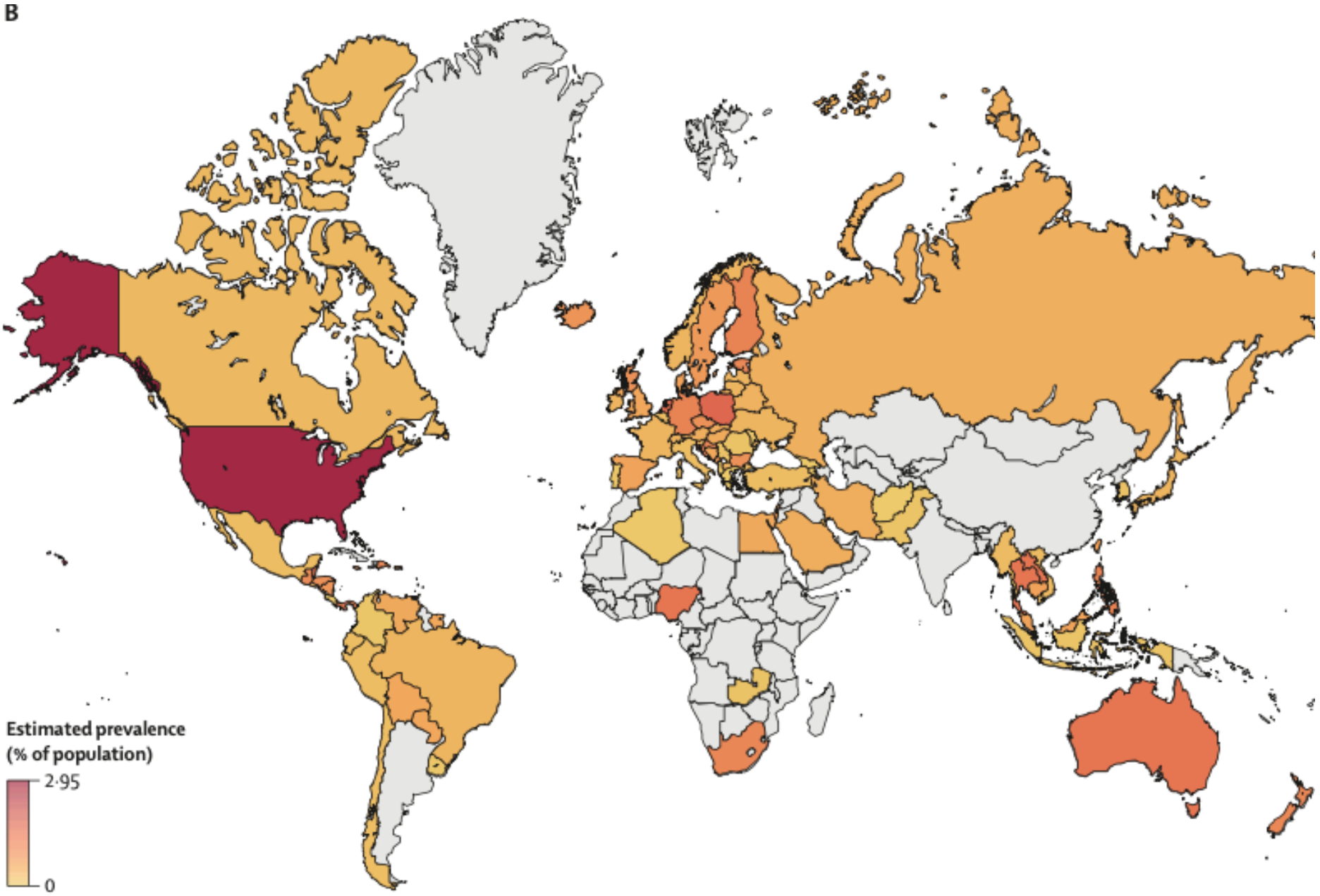
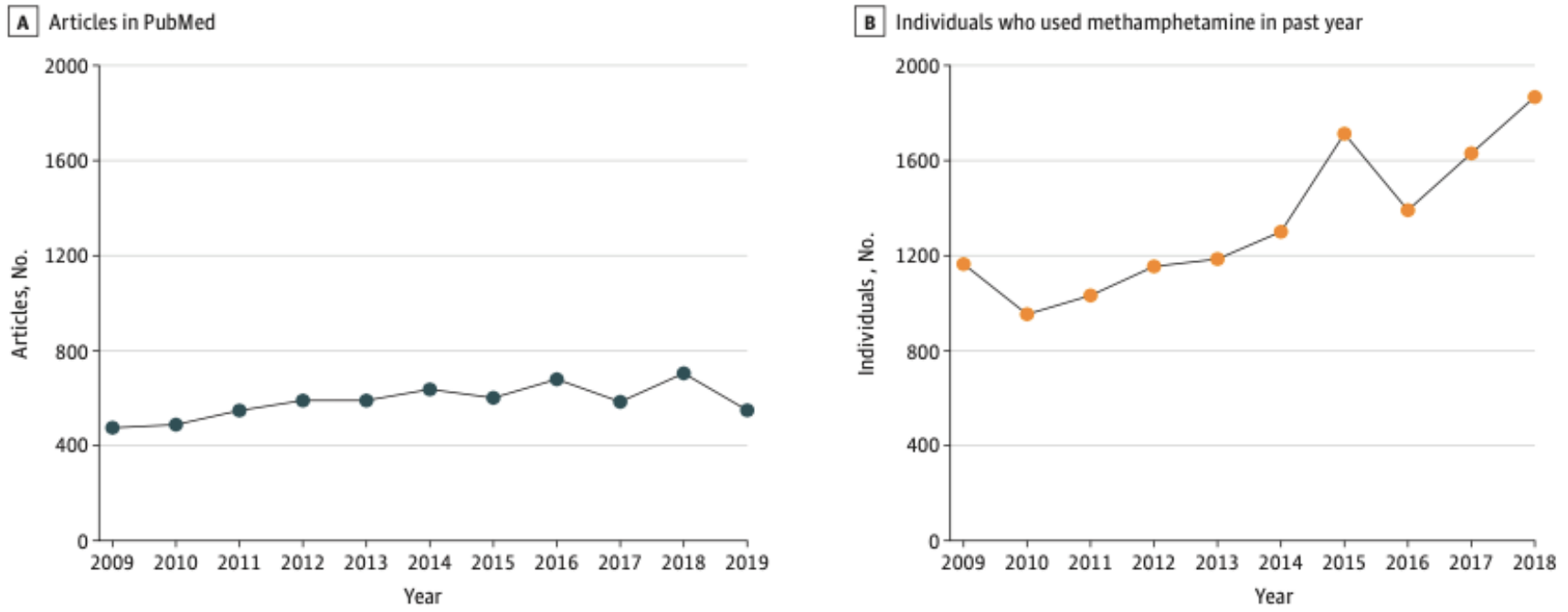
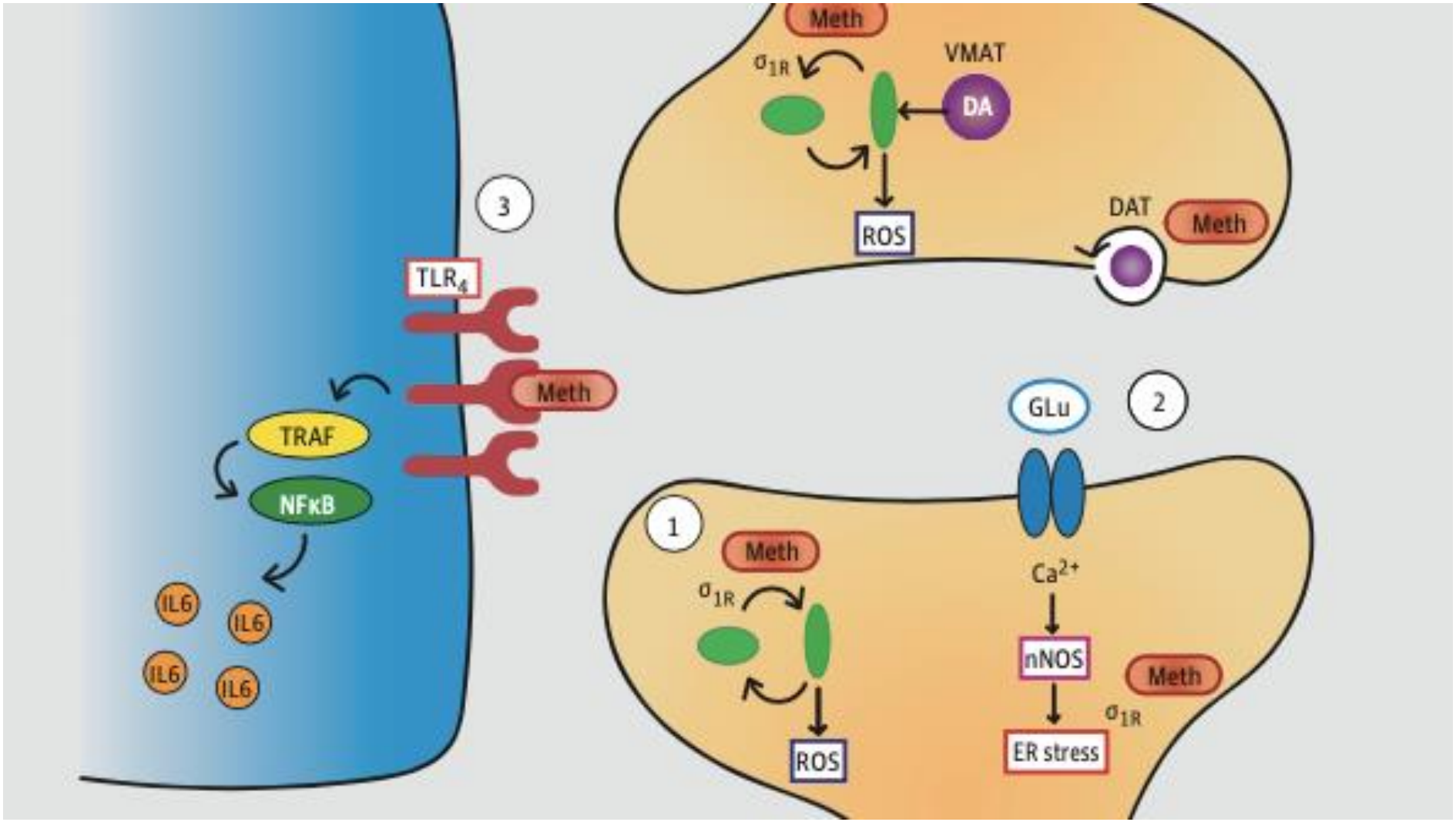


(Farrell et al. 2019)

Figure 1. Summary Statistics of Articles Published Mentioning Methamphetamine and Past-Year Methamphetamine Use From 2009 to 2019



Paulus, et al 2020



Paulus, et al 2020

Table 2
List (modified) of medications tested for treatment of cocaine dependence by the U.S. NIH, National Institute on Drug Abuse, Division of Research and Development; courtesy of Ivan Montoya, MD

Medications tested for cocaine/stimulant abuse and dependence (*N*=42)			
Amantadine	Dextroamphetamine	L-dopa/carbidopa	Naltrexone depot
Aripiprazole	Dextropmetrophan	Lofexidine	Progesterone
Atomoxetine	Disulfiram	LY544344	Propanolol
Baclofen	Divalproex	Mecamylamine	Selegiline
Buprenophine	Dronabinol	Memantine	Sertraline
Bup/Naloxone	Fluoxetine	Methamphetamine	Tiagabine
Buproprion	Gabapentin	Methylphenidate	Topiramate
Clonidine	GBR12909	Methadone	Venlafaxine
Cocaine-Vaccine	GCP44352	Modafinil	Yohimbine
Desipramine	Hydromorphone	*N*-acetyl-aspartate	
	LAAM	Naltrexone	

Grabowski, et al. 2004

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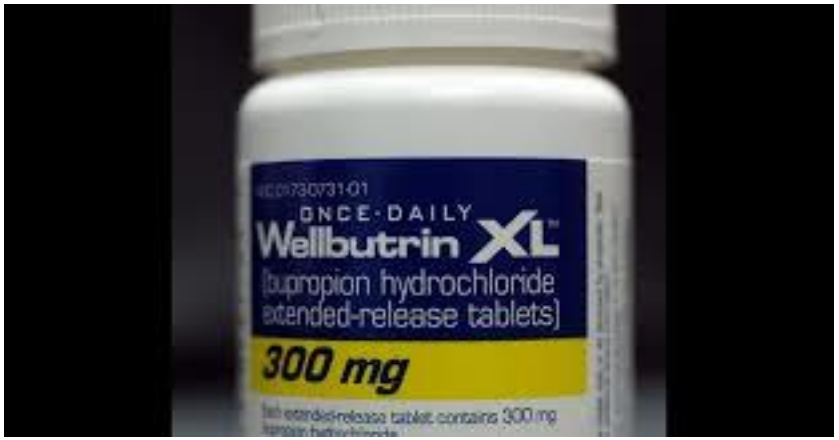
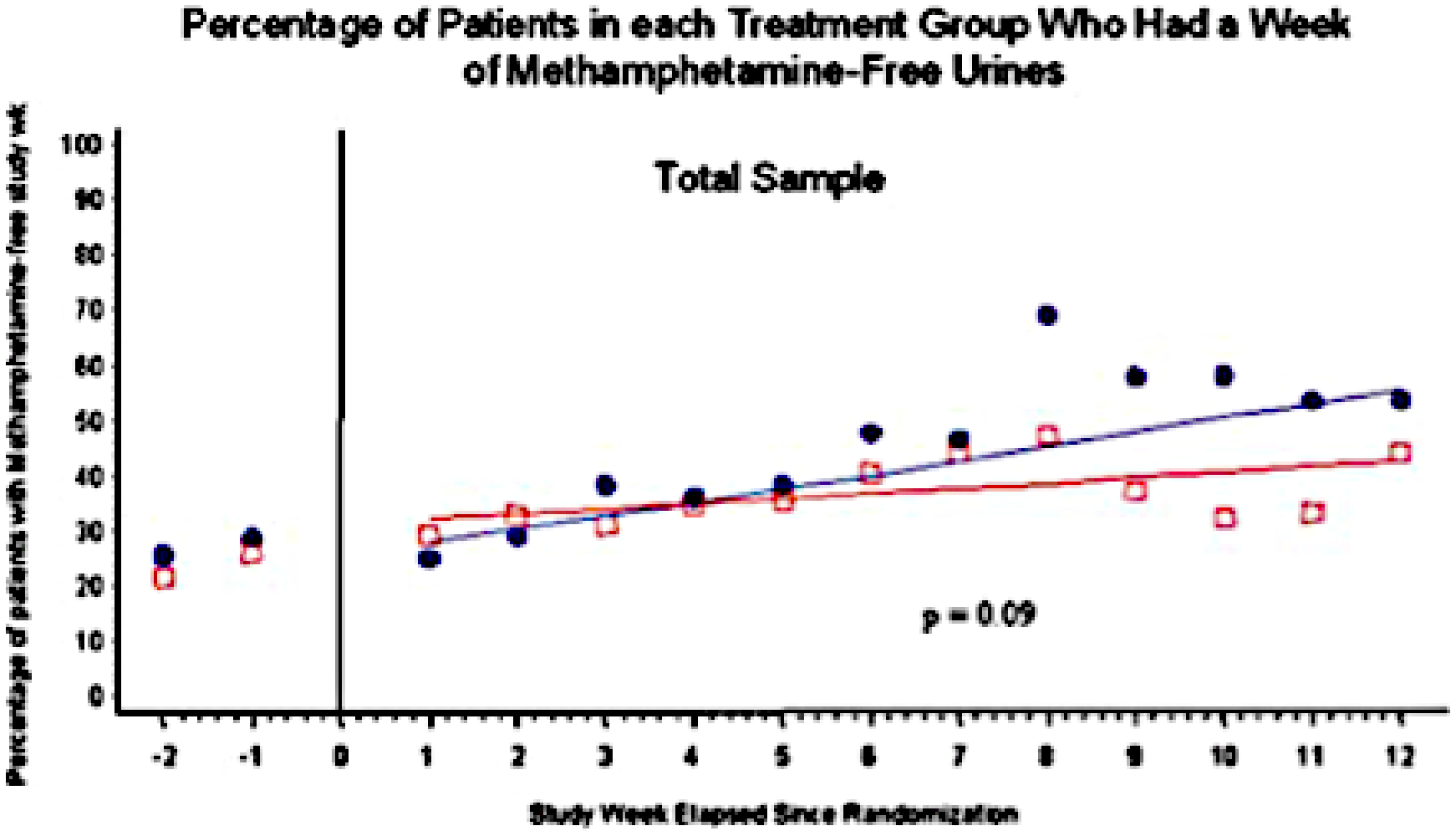


Vivitrol®

(naltrexone for extended-release injectable suspension)



Elkashef, et al 2008

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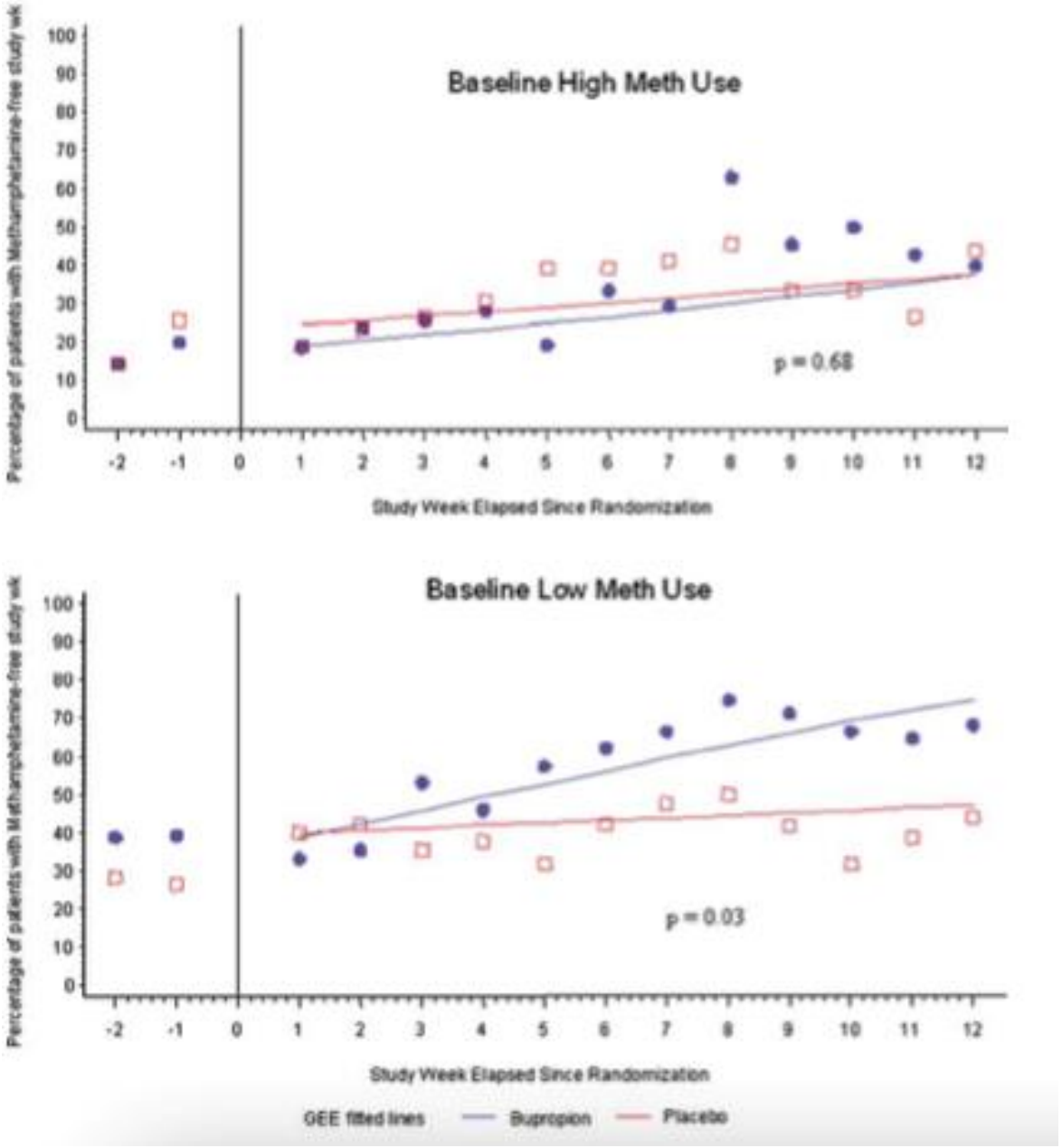
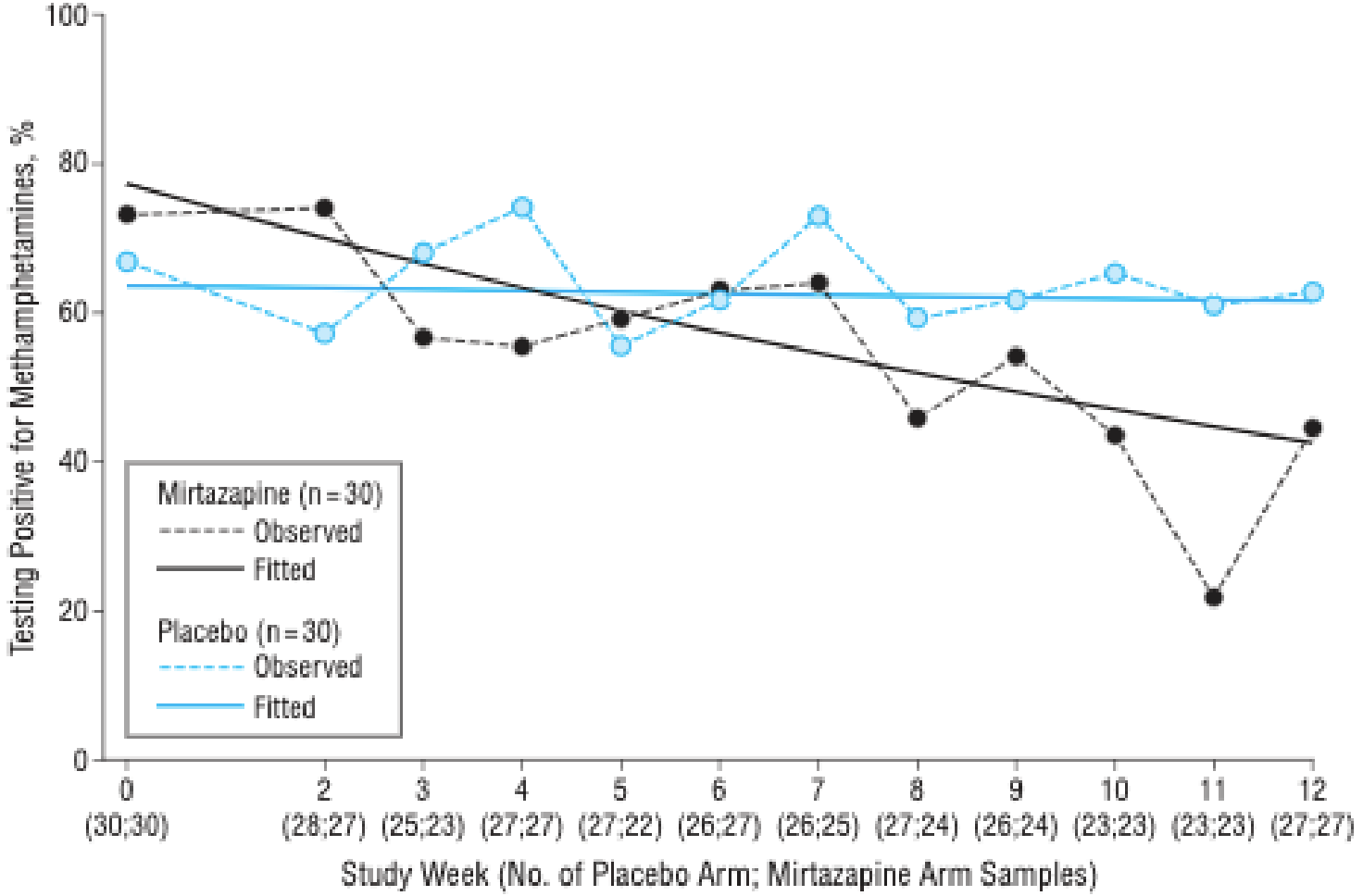
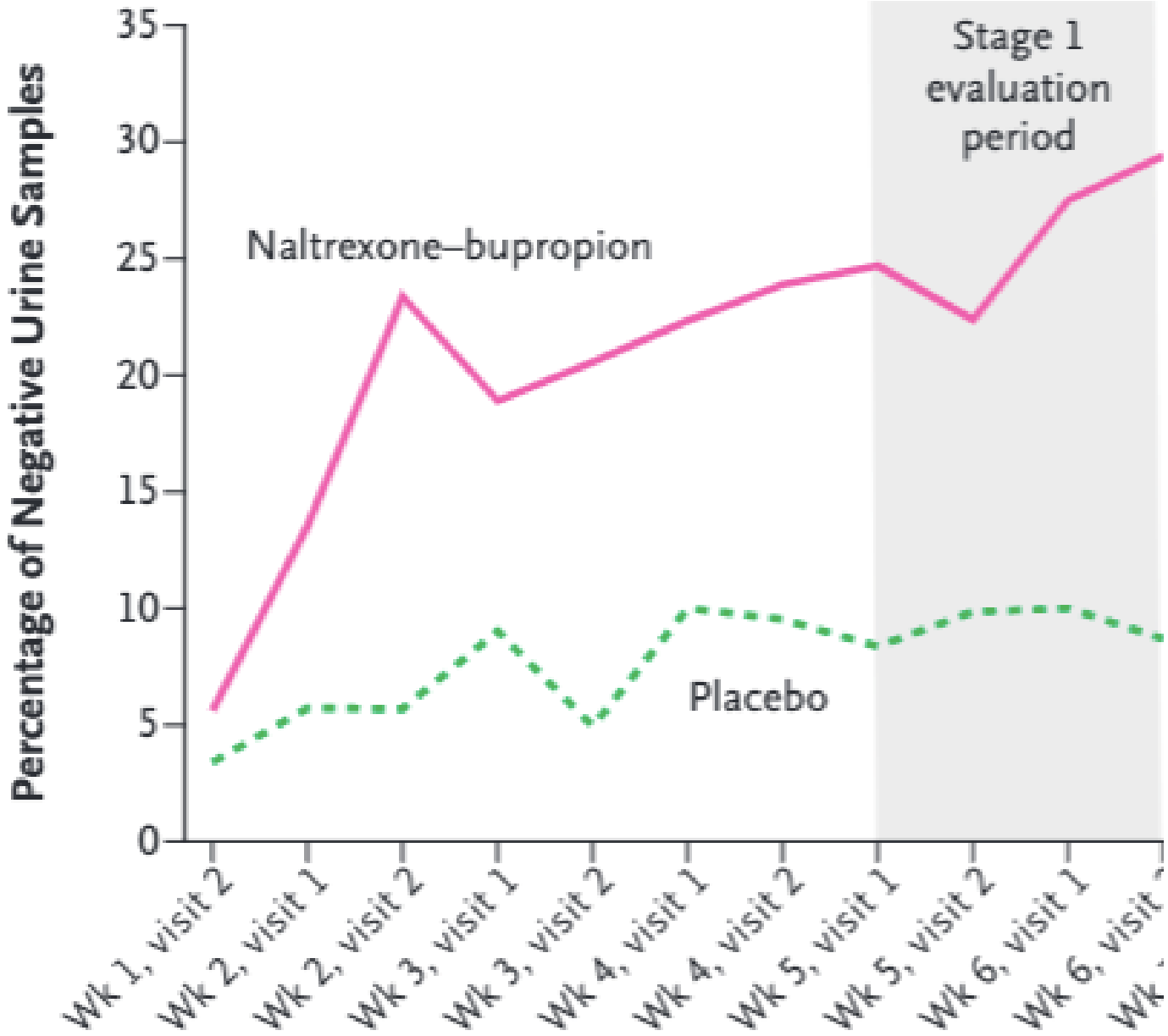


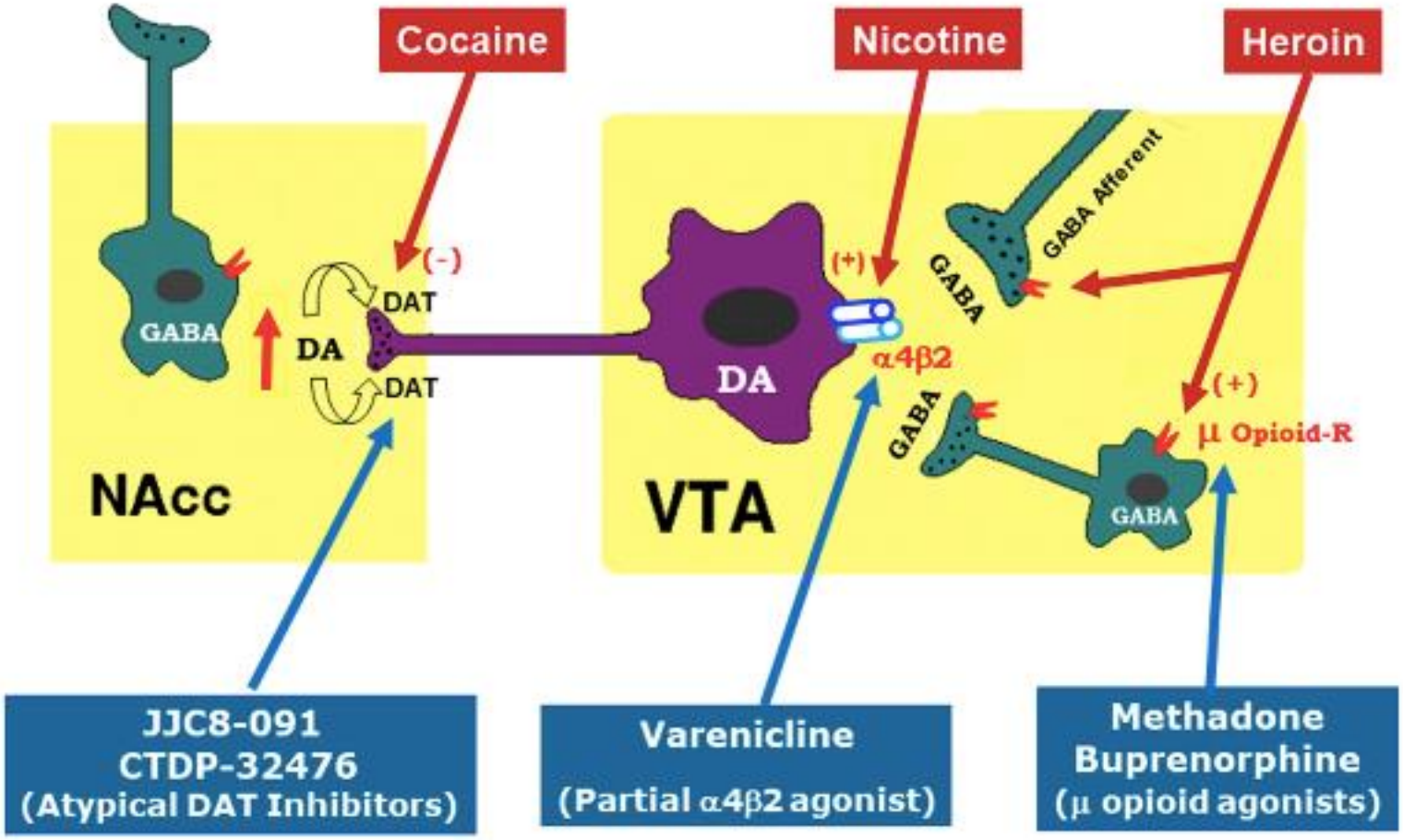
Elkashef, et al 2008



Colfax et al, 2011



Trivedi et al, 2021



Jorden et al, 2019

Psychostimulants for amphetamine abuse or dependence

Patient or population: Amphetamine abuse or dependence
Settings: Outpatients
Intervention: Psychostimulants

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Psychostimulants				
Amphetamine use (UA) Negative urinalyses across the study Follow-up: 8-12 weeks	The mean of the proportion of amphetamine-negative UA ranged in the control groups from 0.56 to 33.1	The mean of the proportion of amphetamine-negative UA ranged in the intervention groups from 0.33 to 36.85		473 (7 studies)	⊕◯◯◯ **very low**[1,2,3,4,5]	**MD -0.26** (-0.85 to 0.33)
Sustained abstinence Negative urinalyses for at least 3 consecutive weeks Follow-up: mean 8-12 weeks	**Study population**		**RR 1.12** (0.84 to 1.49)	559 (6 studies)	⊕◯◯◯ **very low**[1,2,3,4,5]	
	220 per 1000	**247 per 1000** (185 to 328)				
	Moderate					
	285 per 1000	**319 per 1000** (239 to 425)				
Retention to treatment Number of participants who competed treatment Follow-up: 8-20 weeks	**Study population**		**RR 1.01** (0.9 to 1.14)	791 (11 studies)	⊕⊕◯◯ **low**[2,3,4,5,6]	
	489 per 1000	**494 per 1000** (440 to 557)				

Perez-Mana et al. 2013

Table 3 Brief summary of findings.

	Abstinence	Use	Retention	Harms
All Antidepressants	★★	Ø	★★	★
Aminoketone: Bupropion	★	★	★★	Ø
Atypical Antidepressant: Mirtazapine	NA	Ø	Ø	Ø
SSRI: Sertraline	Ø	NA	Ø	NA
Atypical Antipsychotics: Aripiprazole	Ø	★	Ø	Ø
Psychostimulants and Other Medications for ADHD				
All Psychostimulants: Modafinil, Dexamphetamine, Methylphenidate	★	Ø	★	NA
Methylphenidate	NA	★	★	NA
Atomoxetine	NA	Ø	Ø	Ø
All Anticonvulsant and Muscle Relaxants: Baclofen, Gabapentin, Topiramate	Ø	Ø	Ø	Ø
Topiramate	NA	★	★	★
Medications used for other substance use disorders				
Naltrexone	Ø	★	★	★★
Varenicline	NA	Ø	Ø	Ø

Shading represents the direction of effect:

(No color)	Unclear
Grey	No difference
Green	Evidence of benefit
Red	Favors placebo

Symbols represent the strength of the evidence:

NA	No evidence or not applicable
Ø	Insufficient
★	Low
★★	Moderate
★★★	High

Chan et al. 2019

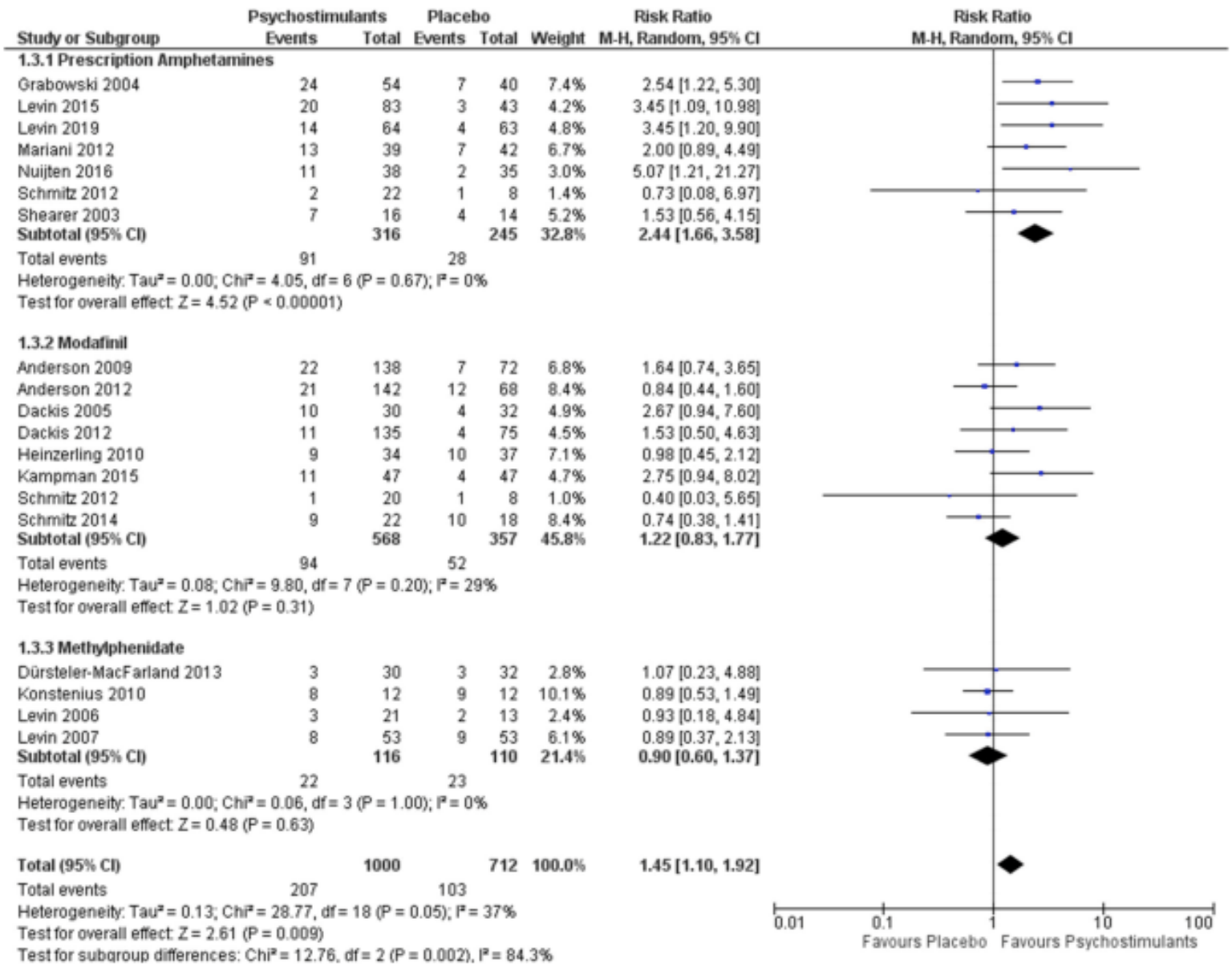


Fig. 3. Overall and by treatment drug effect of prescription psychostimulants compared to placebo for outcome sustained abstinence

Tardelli et al. 2020

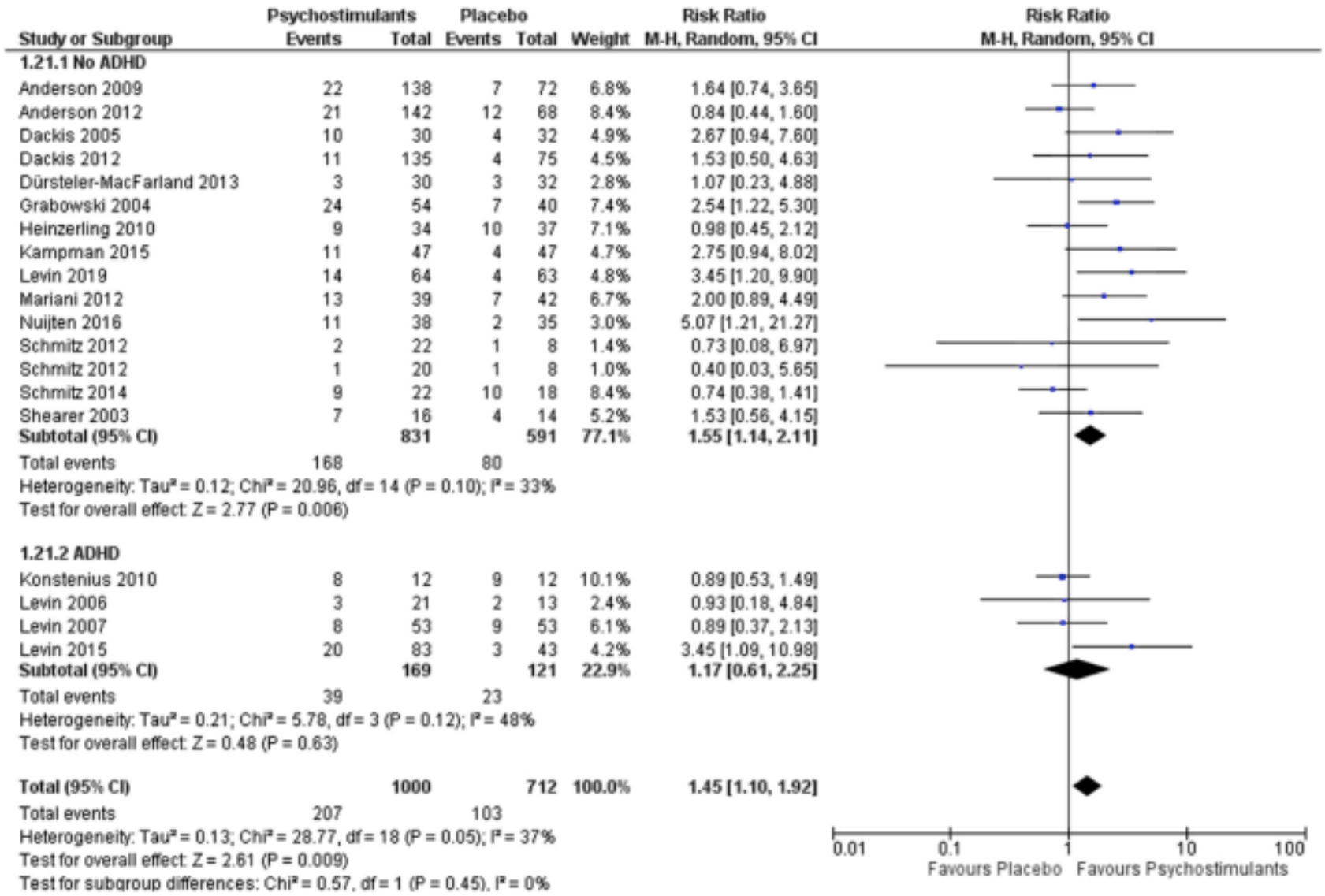


Fig. 4. Overall and by ADHD status effect of prescription psychostimulants compared to placebo for outcome sustained abstinence

Tardelli et al. 2020

Study or Subgroup	Psychostimulants Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.23.1 No comorbid Dependence						
Anderson 2009	22	138	7	72	6.8%	1.64 [0.74, 3.65]
Anderson 2012	21	142	12	68	8.4%	0.84 [0.44, 1.60]
Dackis 2005	10	30	4	32	4.9%	2.67 [0.94, 7.60]
Dackis 2012	11	135	4	75	4.5%	1.53 [0.50, 4.63]
Heinzerling 2010	9	34	10	37	7.1%	0.98 [0.45, 2.12]
Kampman 2015	11	47	4	47	4.7%	2.75 [0.94, 8.02]
Konstenius 2010	8	12	9	12	10.1%	0.89 [0.53, 1.49]
Levin 2007	8	53	9	53	6.1%	0.89 [0.37, 2.13]
Levin 2015	20	83	3	43	4.2%	3.45 [1.09, 10.98]
Levin 2019	14	64	4	63	4.8%	3.45 [1.20, 9.90]
Mariani 2012	13	39	7	42	6.7%	2.00 [0.89, 4.49]
Schmitz 2012	1	20	1	8	1.0%	0.40 [0.03, 5.65]
Schmitz 2012	2	22	1	8	1.4%	0.73 [0.08, 6.97]
Schmitz 2014	9	22	10	18	8.4%	0.74 [0.38, 1.41]
Subtotal (95% CI)		**841**		**578**	**79.2%**	**1.34 [0.98, 1.83]**
Total events	159		85			
Heterogeneity: $Tau^2 = 0.13$; $Chi^2 = 21.44$, df = 13 (P = 0.06); $I^2 = 39\%$						
Test for overall effect: Z = 1.83 (P = 0.07)						
1.23.2 Comorbid Heroin Dependence						
Dürsteler-MacFarland 2013	3	30	3	32	2.8%	1.07 [0.23, 4.88]
Grabowski 2004	24	54	7	40	7.4%	2.54 [1.22, 5.30]
Levin 2006	3	21	2	13	2.4%	0.93 [0.18, 4.84]
Nuijten 2016	11	38	2	35	3.0%	5.07 [1.21, 21.27]
Shearer 2003	7	16	4	14	5.2%	1.53 [0.56, 4.15]
Subtotal (95% CI)		**159**		**134**	**20.8%**	**2.03 [1.24, 3.33]**
Total events	48		18			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.84$, df = 4 (P = 0.43); $I^2 = 0\%$						
Test for overall effect: Z = 2.83 (P = 0.005)						
Total (95% CI)		**1000**		**712**	**100.0%**	**1.45 [1.10, 1.92]**
Total events	207		103			
Heterogeneity: $Tau^2 = 0.13$; $Chi^2 = 28.77$, df = 18 (P = 0.05); $I^2 = 37\%$						
Test for overall effect: Z = 2.61 (P = 0.009)						
Test for subgroup differences: $Chi^2 = 1.99$, df = 1 (P = 0.16), $I^2 = 49.7\%$						

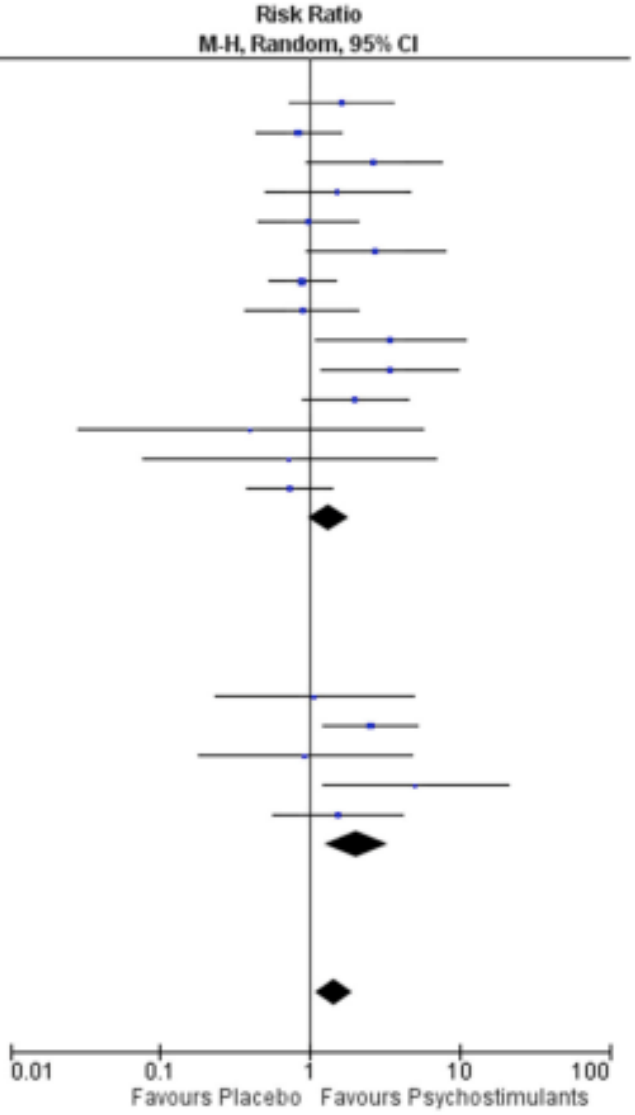


Fig. 5. Overall and by comorbid dependence status effect of prescription psychostimulants compared to placebo for outcome sustained abstinence

Tardelli et al. 2020

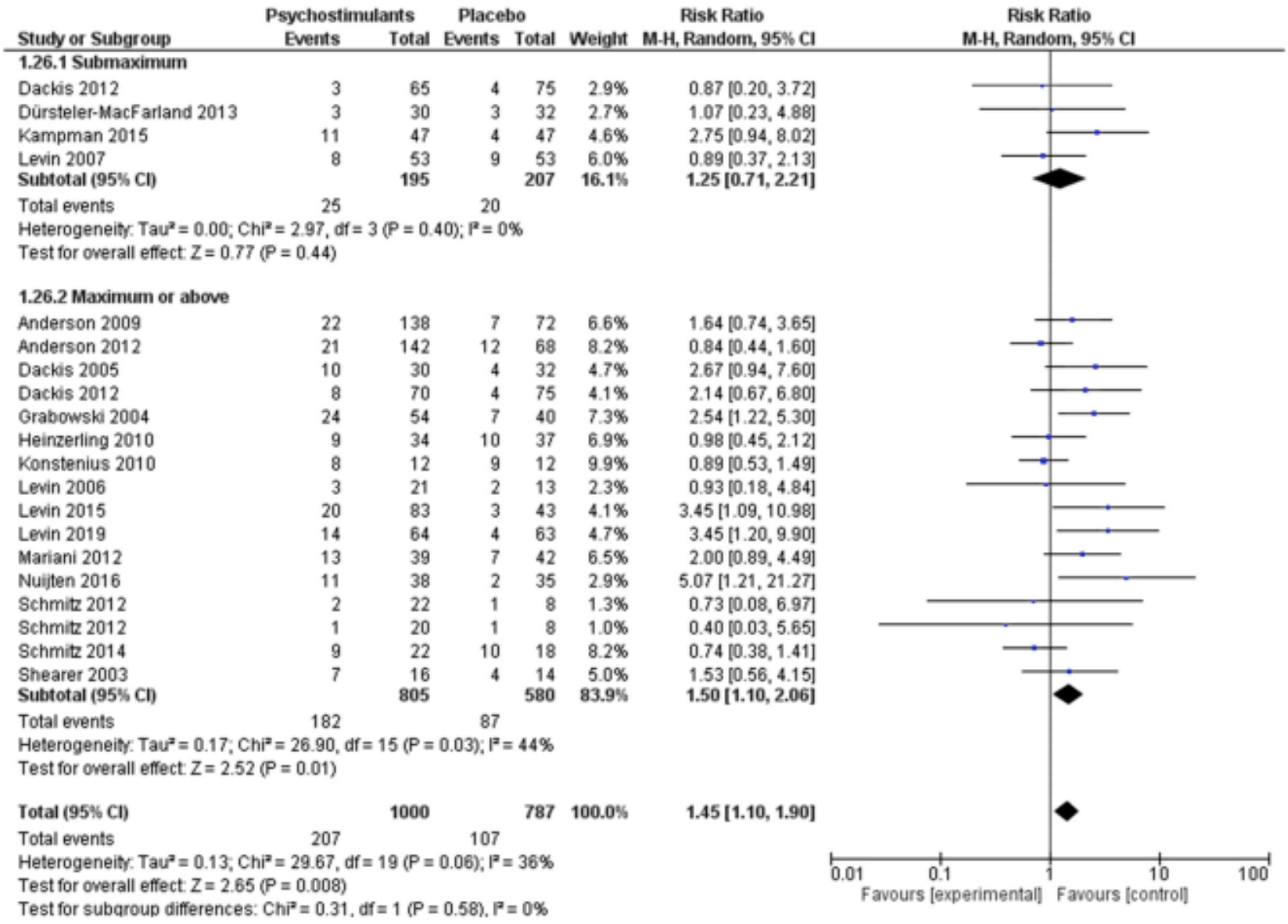


Fig. 6. Overall and by dose effect of prescription psychostimulants compared to placebo on outcome sustained abstinence—overall PSUD

Tardelli et al. 2020

SUMMARY

- Weak evidence for reduced meth + UA
  - bupropion (low-use, 16% reduction) ,
  - mirtazapine (19% reduction) and
  - vivitrol/bupropion (18% reduction)
- Poor evidence using psychostimulants as agonist;
  - Cochrane review, 2013
  - Chan, 2019
- Possible benefit when using prescription stimulants, among co-using methadone patients at higher doses
  - Tardelli, 2020

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