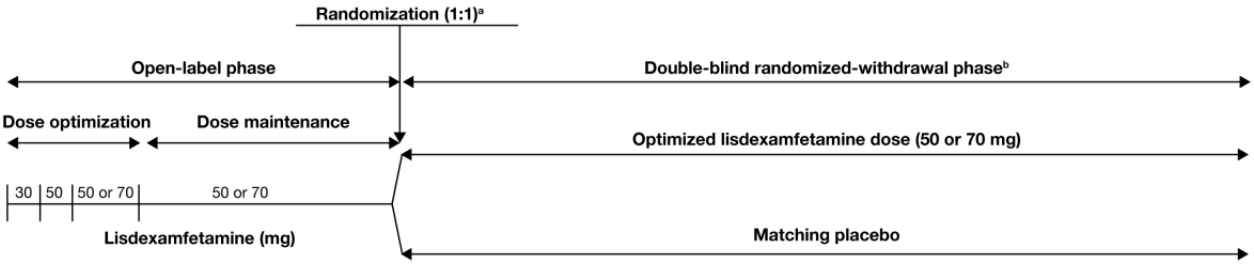
Supplementary Online Content

Hudson JI, McElroy SL, Ferreira-Cornwell MC, Radewonuk J, Gasior M. Efficacy of lisdexamfetamine in adults with moderate to severe binge-eating disorder: a randomized clinical trial. *JAMA Psychiatry*. Published online July 12, 2017. doi:10.1001/jamapsychiatry.2017.1889

This supplementary material has been provided by the authors to give readers additional information about their work.



eFigure. Study Design

[a]Only protocol-defined lisdexamfetamine responders (those reporting ≤1 binge eating day/week for the last 4 consecutive weeks [28 days] with a Clinical Global Impressions-Severity score ≤2) were randomized.
[b]Lisdexamfetamine responders meeting relapse criteria (≥2 binge eating days/week for 2 consecutive weeks [14 days] before the visit and a ≥2-point Clinical Global Impressions-Severity score increase from randomized-withdrawal baseline) were discontinued.

eMethods. Study Exclusion Criteria

1. Current diagnosis of bulimia nervosa or anorexia nervosa, as defined by the Structured Clinical Interview for the *Diagnostic and Statistical Manual of Mental Disorders, 4th edition – text revision* (*DSM-IV-TR*) Axis I Disorders eating disorders module
2. Receiving psychotherapy or weight loss support for binge eating disorder (BED) that began within the 3 months prior to screening; those receiving psychotherapy or weight loss support that was initiated ≥3 months before screening could continue to receive treatment if no changes were made during the study
3. Having used psychostimulants to facilitate fasting or dieting as a part of their BED within the 6 months of screening
4. Having a current comorbid Axis I or Axis II psychiatric disorder that was either controlled with prohibited medications or was uncontrolled and associated with significant symptoms; those with mild mood or anxiety symptoms that did not meet criteria for Axis I disorder, did not require treatment based on the investigator's assessment, and did not confound efficacy or safety assessments in the opinion of the investigator could be included.
5. Having a lifetime history of psychosis, mania, hypomania, dementia, or attention-deficit/hyper activity disorder
6. Having other symptomatic manifestations that contraindicated treatment with lisdexamfetamine or confounded efficacy or safety assessments in the opinion of the investigator
7. Having Montgomery-Åsberg Depression Rating Scale total score ≥18 at screening
8. Being considered a suicide risk in the opinion of the investigator, having previously made a suicide attempt, or currently demonstrating active suicidal ideation; those with intermittent

passive suicidal ideation were not necessarily excluded based on the assessment of the investigator

9. Having a concurrent chronic or acute illness, disability, or other condition that might have confounded the results of safety assessments or that might have increased participant risk
10. Having a history of seizures (other than infantile febrile seizures), any tic disorder, or a current diagnosis and/or a known family history of Tourette's Disorder, serious neurological disease, history of significant head trauma, dementia, cerebrovascular disease, Parkinson's disease, or intracranial lesions
11. Having a known history of symptomatic cardiovascular disease, advanced arteriosclerosis, structural cardiac abnormality, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious cardiac problems that may have placed the participant at increased vulnerability to the sympathomimetic effects of a psychostimulant
12. Having a known family history of sudden cardiac death or ventricular arrhythmia
13. Having any clinically significant electrocardiogram before open-label baseline
14. Having any clinically significant laboratory abnormality before open-label baseline; participants with hypokalemia at screening and before open-label baseline were excluded
15. Having current abnormal thyroid function (defined as abnormal thyroid stimulating hormone and T4 at screening); treatment with a stable dose of thyroid medication for at least 3 months before screening was permitted
16. Having initiated treatment with a lipid lowering medication within the past 3 months; treatment with a stable dose of lipid lowering medication for at least 3 months before screening was permitted

17. Having a history of moderate or severe hypertension, a resting average sitting systolic blood pressure >139 mmHg or average diastolic blood pressure >89 mmHg at screening and/or open-label baseline; those with mild, well-controlled hypertension on a stable antihypertensive treatment regimen (defined as having maintained the current dose for at least 3 months at the time of screening) were eligible
18. Having taken any medication prohibited by the protocol, including sedatives/hypnotics, benzodiazepines, anxiolytics, antipsychotics, antidepressants, monoamine oxidase inhibitors, clonidine, guanfacine, atomoxetine, over-the-counter or prescription weight loss therapies, or narcotics (within 30 days of screening), sedating antihistamines, herbal preparations, or melatonin (within 7 days of screening), or sympathomimetics or appetite suppressants (within 6 months of screening).
19. Having a known or suspected intolerance or hypersensitivity to lisdexamfetamine, closely related compounds, or any of the stated ingredients
20. Having a history of suspected substance abuse or dependence disorder based on *DSM-IV-TR* criteria within the past 6 months or a lifetime history of amphetamine, cocaine, or other stimulant abuse and/or dependence; nicotine dependence was not exclusionary
21. Having a positive drug result at screening, unless it could be verified that the positive result was attributed to a prescribed medication. In such cases, the medication was discontinued and verified by a negative drug result before open-label baseline
22. Having glaucoma
23. Having taken medications with central nervous system effects or that could affect performance, such as chronic use of sedating antihistamines and decongestant

sympathomimetics, within 7 days of screening; stable use of bronchodilator inhalers was not exclusionary

24. Being pregnant or nursing.
25. Having had bariatric surgery, lap bands, duodenal stents, or other procedures for weight loss
26. Having participated in an investigational or observational study within 30 days of screening or any previous participation in a clinical study involving lisdexamfetamine
27. Having previously completed, discontinued, or withdrawn from the current study

eTable 1. Life-Table for the Estimated Proportion of Participants Relapsing Following Randomization by Treatment Group, Full Analysis Set[a]

	Placebo (n=131)				Lisdexamfetamine (n=136)			
Days to Relapse[b]	Number at Risk[c]	Number of Relapses	Number Censored[d]	Estimated Proportion Relapsed (95% CI)[e]	Number at Risk[c]	Number of Relapses	Number Censored[d]	Estimated Proportion Relapsed (95% CI)[e]
0	131	0	0	—	136	0	0	—
15	116	12	3	0.09 (0.04, 0.14)	133	2	1	0.01 (–0.01, 0.03)
30	99	26	6	0.20 (0.13, 0.27)	127	3	6	0.02 (–0.00, 0.05)
45	87	31	13	0.25 (0.17, 0.32)	124	3	9	0.02 (–0.00, 0.05)
60	76	34	21	0.27 (0.19, 0.35)	123	3	10	0.02 (–0.00, 0.05)
90	66	38	27	0.31 (0.23, 0.40)	116	4	16	0.03 (0.00, 0.06)
120	58	41	32	0.35 (0.26, 0.43)	115	4	17	0.03 (0.00, 0.06)
150	55	41	35	0.35 (0.26, 0.43)	110	5	21	0.04 (0.01, 0.07)
180	49	42	40	0.36 (0.27, 0.45)	104	5	27	0.04 (0.01, 0.07)

[a]Randomized participants taking ≥1 study drug dose during the randomized-withdrawal phase and having ≥1 postrandomization CGI-S assessment.
[b]Days from the date of randomization.
[c]Participants who had not had relapse or had not been censored by the end of the specified day.
[d]Participants censored on or before the specified day; participants who did not relapse were censored on the date of discontinuation or the final visit, whichever occurred later.
[e]Estimates are derived using Kaplan-Meier method with 95% CI based on Greenwood formula.

eTable 2. Summary of Secondary Efficacy Outcome Variables, Full Analysis Set

	Placebo		Lisdexamfetamine	
Binge eating days/week				
Mean (SD) number at randomized-withdrawal baseline	0.13 (0.274)	n=131	0.12 (0.262)	n=136
Mean (SD) number at wk 37 and 38	0.26 (0.465)	n=50	0.08 (0.239)	n=102
LS mean (SEM) change from randomized-withdrawal baseline[a]	0.63 (0.076)	n=50	0.02 (0.061)	n=102
LS mean (95% CI) treatment difference[b]; nominal *P* value[c]	–0.61 (–0.81, –0.42); <0.001			
CGI-S				
Scores at randomized-withdrawal baseline				
Normal, not at all, n/N (%)	98/131 (74.8)		114/136 (83.8)	
Borderline ill, n/N (%)	33/131 (25.2)		22/136 (16.2)	
Scores at week 38/ET				
Normal, not at all, n/N (%)	59/131 (45.0)		111/136 (81.6)	
Borderline ill, n/N (%)	14/131 (10.7)		16/136 (11.8)	
Mildly ill, n/N (%)	19/131 (14.5)		3/136 (2.2)	
Moderately ill, n/N (%)	29/131 (22.1)		3/136 (2.2)	
Severely ill, n/N (%)	9/131 (6.9)		3/136 (2.2)	
Markedly ill, n/N (%)	0/131 (0)		0/136 (0)	
Among the most extremely ill, n/N (%)	1/131 (0.8)		0/136 (0)	
Nominal *P* value[d]	<0.001			
Y-BOCS-BE total score				
Mean (SD) total score at randomized-withdrawal baseline	2.4 (3.25)	n=131	1.9 (2.97)	n=136
Mean (SD) total score at week 38	4.5 (5.94)	n=54	1.6 (3.48)	n=107
LS mean (SEM) change from randomized-withdrawal baseline[a]	5.5 (0.66)	n=54	−0.0 (0.52)	n=107
LS mean (95% CI) treatment difference[b]; nominal *P* value[c]	−5.6 (−7.2, −3.9); <0.001			

CGI-S=Clinical Global Impressions−Severity; df=degrees of freedom; ET=early termination; LS=least squares; Y-BOCS-BE=Yale-Brown Obsessive Compulsive Scale Modified for Binge Eating.

[a]Negative scores indicate improvement.

[b]Based on lisdexamfetamine–placebo (negative scores indicate greater score increases with placebo).

[c]Based on mixed-effects model for repeated measures over all post-randomization visits during the double-blind randomized-withdrawal phase, with change from randomized-withdrawal baseline as the outcome variable, treatment, visit, and their interaction as factors, and randomization value as a covariate with its interaction with visit included in the model.

[d]Based on a covariate-adjusted Cochran-Mantel-Haenszel test with a modified ridit score, adjusting for Clinical Global Impressions-Severity score at week 12 as the covariate.

