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Supplementary Material

Article Title: Sleep-Associated Adverse Events During the Methylphenidate Treatment of Attention-Deficit/Hyperactivity Disorder: A Meta-Analysis

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Appendix 1: Search Strategy

The search strategy/syntax for Pubmed.gov was:

((ADHD OR attention deficit OR attention-deficit OR attention deficit hyperactivity disorder OR hyperkinetic syndrome OR hyperkinetic disorder OR hyperactivity disorder OR hyperactive child syndrome) AND (stimulant* OR psychostimulant* OR Methylphenidate OR Aptensio OR Biphentin OR Rubifen OR Focalin OR Methylin OR Cotempla OR Ritalin OR Metadate OR Equasym OR Medikinet OR Concerta OR Daytrana OR Quillivant OR NWP06 OR Quillichew OR HLD200 OR PRC-063) AND (Randomized OR randomised OR random* OR cross-over OR crossover OR parallel OR classroom)) OR ((ADHD OR attention deficit OR attention-deficit OR attention deficit hyperactivity disorder OR hyperkinetic syndrome OR hyperkinetic disorder OR hyperactivity disorder OR hyperactive child syndrome) AND (stimulant* OR psychostimulant* OR Methylphenidate OR Aptensio OR Biphentin OR Rubifen OR Focalin OR Methylin OR Cotempla OR Ritalin OR Metadate OR Equasym OR Medikinet OR Concerta OR Daytrana OR Quillivant OR NWP06 OR Quillichew OR HLD200 OR PRC-063) AND (sleep OR insomnia)).

The search strategy for OVID databases OVID databases (PsycInfo, EMBASE+EMBASE classic, OVID Medline) was:

((ADHD OR attention deficit OR attention-deficit OR attention deficit hyperactivity disorder OR attention-deficit/hyperactivity disorder OR hyperkinetic syndrome OR hyperkinetic disorder OR hyperactivity disorder OR hyperactive child syndrome) AND (stimulant* OR psychostimulant* OR Methylphenidate OR Aptensio OR Biphentin OR Rubifen OR Focalin OR Methylin OR Cotempla OR Ritalin OR Metadate OR Equasym OR Medikinet OR Concerta OR Daytrana OR Quillivant OR NWP06 OR Quillichew OR HLD200 OR PRC-063) AND

(Randomized OR randomised OR random* OR cross-over OR crossover OR parallel OR classroom)) OR ((ADHD OR attention deficit OR attention-deficit OR attention deficit hyperactivity disorder OR attention-deficit/hyperactivity disorder OR hyperkinetic syndrome OR hyperkinetic disorder OR hyperactivity disorder OR hyperactive child syndrome) AND (stimulant* OR psychostimulant* OR Methylphenidate OR Aptensio OR Biphentin OR Rubifen OR Focalin OR Methylin OR Cotempla OR Ritalin OR Metadate OR Equasym OR Medikinet OR Concerta OR Daytrana OR Quillivant OR NWP06 OR Quillichew OR HLD200 OR PRC-063) AND (sleep OR insomnia)).

The search strategies for Web of Knowledge (Web of Science [Science Citation Index Expanded], Biological Abstracts, BIOSIS, Food Science and Technology Abstracts) was:

Search 1: (ADHD OR attention deficit OR attention-deficit OR attention deficit hyperactivity disorder OR attention-deficit/hyperactivity disorder OR hyperkinetic syndrome OR hyperkinetic disorder OR hyperactivity disorder OR hyperactive child syndrome) AND (stimulant* OR psychostimulant* OR Methylphenidate OR Aptensio OR Biphentin OR Rubifen OR Focalin OR Methylin OR Cotempla OR Ritalin OR Metadate OR Equasym OR Medikinet OR Concerta OR Daytrana OR Quillivant OR NWP06 OR Quillichew OR HLD200 OR PRC-063) AND (Randomized OR randomised OR random* OR cross-over OR crossover OR parallel OR classroom).

Search 2: (ADHD OR attention deficit OR attention-deficit OR attention deficit hyperactivity disorder OR attention-deficit/hyperactivity disorder OR hyperkinetic syndrome OR hyperkinetic disorder OR hyperactivity disorder OR hyperactive child syndrome) AND (stimulant* OR psychostimulant* OR Methylphenidate OR Aptensio OR Biphentin OR Rubifen OR Focalin OR Methylin OR Cotempla OR Ritalin OR Metadate OR Equasym OR Medikinet

OR Concerta OR Daytrana OR Quillivant OR NWP06 OR Quillichew OR HLD200 OR PRC-063) AND (sleep OR insomnia).

The search strategy for ClinicalTrials.gov was: Condition: ADHD; Other terms: methylphenidate OR dexamethylphenidate; Status-> Studies: Completed.

Supplementary Table 1: Study Assessment Methodology

Study	Drug	Rater	Methodology
Pliszka 2017	DR/ER-MPH	Clinician	Solicited by Direct query – MedDRA version 18.0
Greenhill 2002	MPH CD	Clinician	Spontaneous – COSTART 3 rd edition
		Parent	Solicited by PSERS
Findling 2006	MPH CD	Clinician	Spontaneous – Coding system not specified
	MPH IR		
Pearson 2013	MPH LA	Parent	Solicited by a checklist of sleep items
		Teacher	
Biederman 2003	MPH LA	Clinician	Spontaneous – Coding system not specified
Simonoff 2013	MPH IR	Parent	Solicited by AE questionnaire
Lee 2011	MPH IR	Parent	Solicited by SERS
Rapport 2008	MPH IR	Self-report	Solicited by STESS
		Parent	
Daviss 2008	MPH IR	Clinician	Spontaneous – Coding system not specified
		Parent	Solicited by PSERS
		Teacher	
Pelham 1999	MPH IR	Parent	Solicited by PSERS
Stein 1996	MPH IR	Parent	Solicited by SERS
Buitelaar 1996	MPH IR	Parent	Solicited by SERS
Ahman 1993	MPH IR	Parent	Solicited by SERS
Barkley 1990	MPH IR	Parent	Solicited by SERS
		Teacher	
Ramtvedt 2014	MPH IR	Parent	Solicited by SERS
Arnold 2005	MPH IR	Clinician	Spontaneous – COSTART version not specified
Klorman 1990	MPH IR	Self-report	Solicited by STESS
		Parent	
FIU 2002	MPH IR	Parent	Solicited by PSERS
Pelham 1990	MPH-IR	Parent	Solicited by SSEC
	MPH-SR		
Wigal 2015	MPH MLR	Clinician	Spontaneous – MedDRA version not specified
Findling 2010	MTS	Clinician	Spontaneous – MedDRA version 7.0
Wilens 2010	MTS	Clinician	Spontaneous – Coding system not specified
Findling 2008	MTS	Clinician	Spontaneous – MedDRA version 7.0
			Solicited by CSHQ
	OROS MPH		Spontaneous – MedDRA version 7.0
			Solicited by CSHQ
Becker 2016	OROS MPH	Parent	Solicited by PSERS
CHMC 2010	OROS MPH	Parent	Solicited by systematic assessment of AEs
Coghill 2013	OROS MPH	Clinician	Spontaneous – MedDRA version 11.1
Stein 2003	OROS MPH	Parent	Solicited by SERS
Wilens 2006	OROS MPH	Clinician	Spontaneous – Coding system not specified
Lin 2014	OROS MPH	Clinician	Spontaneous – Coding system not specified
Newcorn 2008	OROS MPH	Clinician	Spontaneous – MedDRA version 5.1
Riggs 2012	OROS MPH	Clinician	Spontaneous – Coding system not specified
Kollins 2016	PRC-063	Clinician	Spontaneous – Coding system not specified
Childress 2009	d-MPH-ER	Clinician	Spontaneous – MedDRA version not specified
Greenhill 2006	d-MPH-ER	Clinician	Spontaneous – MedDRA version not specified
Stein 2011	d-MPH-ER	Parent	Solicited by SERS

Supplementary Table 2: Confounding Variables			
Variable	Relative risk for Sleep AEs	Association with	
Subject Features		Relative Risk	Drug
Mean Age			
8-8.7	2.5		
8.8-9.2	3.3		
9.3-10.0	2.7	0.003	<0.0001
10.2-10.9	6.2		
11.0-16.5	3.6		
% Males in Sample			
64-70	4.1		
72-75	5.5		
76-80	2.9	<0.0001	<0.0001
81-88	4.1		
89-100	1.8		
Stimulant responder (%)			
0	6.3		
64	2.1	<0.0001	<0.0001
100	3.6		
Drug Features			
Release type			
Immediate release	1.9	0.03	<0.0001
Extended release	4.8		
Dosing frequency			
Once-daily	4.6		
Twice-daily	1.7	<0.0001	<0.0001
Thrice-daily	2.5		
Missing	1.2		
Study Design Features			
Year			
1990-1999	1.9		
2002-2006	3.3		
2008-2010	3.8	0.03	<0.0001
2011-2014	4.8		
2015-2017	4.8		
Method of Diagnosis			
DSM	3.7	<0.0001	0.58
Other	2.0		
Number of Sites			
1	2.5		
2-15	2.6		
16-31	5.3	0.0003	<0.0001
32-48	5.3		
Missing	4.0		
Dosing methods			
Stabilized & optimized / Not forced	4.8	<0.0001	0.05

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Neither stabilized nor optimized / Forced	4.6		
Neither stabilized nor optimized / Not forced	3.0		
Missing	8.5		
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Rater of AEs			
Clinician/Investigator	5.3		
Self-reporter	0.9		
Parent	2.5	<0.0001	<0.0001
Teacher	1.6		
Missing	1.3		
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Rating scale elicited AEs			
No	5.0		
Yes	2.3	0.02	<0.0001