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Supplementary Material

Article Title: Effect of Continuing and Discontinuing Medications on Quality of Life After Symptomatic Remission in Attention-Deficit/Hyperactivity Disorder: A Systematic Review and Meta-Analysis

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Supplementary Table 1: Search syntax for PubMed

| # | Search terms | Number of references |
|-----|--|----------------------|
| #1 | (Attention Deficit Disorder with Hyperactivity/drug therapy[MH] OR ADHD[TIAB] OR AD/HD[TIAB] OR AD-HD[TIAB] OR ADDH[TIAB] OR attention def* [TIAB] OR "brain dysfunction"[TIAB]) | 34810 |
| #2 | Withholding Treatment[MH:NoExp] OR Placebo Effect[MH] | 14982 |
| #3 | (drug*[TIAB] OR Pharmacotherap*[TIAB] OR medication*[TIAB] OR "Central Nervous System Stimulants"[MH] OR stimulant[TIAB] OR "non-stimulant"[TIAB] OR "Adrenergic alpha-Agonists"[MH] OR "alpha adrenergic agonist"[TIAB] OR "alpha adrenergic receptor"[TIAB] OR "Dopamine Uptake Inhibitors"[MH] OR "dopamine reuptake inhibitor" [TIAB] OR "norepinephrine reuptake inhibitor"[TIAB] OR "dopamine releaser"[TIAB] OR "Amphetamine"[MH] OR Amphetamine*[TIAB] OR "Atomoxetine Hydrochloride"[MH] OR atomoxetine[TIAB] OR Clonidine[TW] OR Methylphenidate[MH] OR Methylphenidate[TIAB] OR Dexmethylphenidate[TIAB] OR lisdexamfetamine[TW] OR guanfacine[TW]) | 1758504 |
| #4 | (withdr*[TIAB] OR discontinu*[TIAB] OR abstinence[TIAB] OR avoid*[TIAB] OR ceas*[TIAB] OR cessation*[TIAB] OR remov*[TIAB] OR stop*[TIAB] OR Withhold*[TIAB] OR continu*[TIAB] OR maintenance*[TIAB]) | 2306248 |
| #5 | #3 AND #4 | 266642 |
| #6 | #2 OR #5 | 280599 |
| #7 | #1 AND #6 | 2084 |
| #8 | #7 AND (randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[TIAB] OR placebo[TIAB] OR drug therapy[sh] OR randomly[TIAB] OR trial[TIAB] OR groups[TIAB]) | |
| #9 | #7 AND (randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [TIAB] OR placebo [TIAB] OR clinical trials as topic [MH: noexp] OR randomly [TIAB] OR trial [ti]) NOT (animals [mh] NOT humans [mh]) | 621 |
| #10 | #7 AND (Meta-Analysis[ptyp] OR systematic[sb]) | |

Supplementary Table 2: Search syntax for Cochrane Library

| # | Search terms | Number of references |
|-----|---|----------------------|
| #1 | [mh "Attention Deficit Disorder with Hyperactivity"/DT] | 1327 |
| #2 | ADHD:ti,ab,kw | 3292 |
| #3 | AD-HD:ti,ab,kw | 39 |
| #4 | ADDH:ti,ab,kw | 24 |
| #5 | attention def*:ti,ab,kw | 8470 |
| #6 | brain dysfunction:ti,ab,kw | 215 |
| #7 | #1 or #2 or #3 or #4 or #5 or #6 | 8942 |
| #8 | [mh ^"Withholding Treatment"] | 334 |
| #9 | [mh "Placebo Effect"] | 1418 |
| #10 | #8 or #9 | 1751 |
| #11 | drug*:ti,ab,kw | 375119 |
| #12 | Pharmacotherap*:ti,ab,kw | 6971 |
| #13 | medication*:ti,ab,kw | 66035 |
| #14 | [mh "Central Nervous System Stimulants"] | 2249 |
| #15 | stimulant:ti,ab,kw | 2199 |
| #16 | non-stimulant:ti,ab,kw | 52 |
| #17 | [mh "Adrenergic alpha-Agonists"] | 1095 |
| #18 | alpha adrenergic agonist:ti,ab,kw | 46 |
| #19 | alpha adrenergic receptor:ti,ab,kw | 590 |
| #20 | [mh "Dopamine Uptake Inhibitors"] | 309 |
| #21 | dopamine reuptake inhibitor:ti,ab,kw | 31 |
| #22 | norepinephrine reuptake inhibitor:ti,ab,kw | 329 |
| #23 | dopamine releaser:ti,ab,kw | 2 |
| #24 | [mh Amphetamine] | 897 |
| #25 | Amphetamine*:ti,ab,kw | 1625 |
| #26 | [mh "Atomoxetine Hydrochloride"] | 306 |
| #27 | [mh Clonidine] | 1845 |
| #28 | Clonidine:ti,ab,kw | 3539 |
| #29 | [mh Methylphenidate] | 1481 |
| #30 | Methylphenidate:ti,ab,kw | 2385 |
| #31 | Dexmethylphenidate:ti,ab,kw | 61 |
| #32 | [mh lisdexamfetamine] | 142 |
| #33 | lisdexamfetamine:ti,ab,kw | 277 |
| #34 | [mh guanfacine] | 153 |
| #35 | guanfacine:ti,ab,kw | 280 |
| #36 | #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 | 409830 |
| #37 | withdr*:ti,ab,kw | 35050 |
| #38 | discontin*:ti,ab,kw | 26722 |
| #39 | abstinence:ti,ab,kw | 6059 |
| #40 | avoid*:ti,ab,kw | 18614 |
| #41 | ceas*:ti,ab,kw | 1317 |
| #42 | cessation*:ti,ab,kw | 13290 |
| #43 | reduc*:ti,ab,kw | 317809 |
| #44 | remov*:ti,ab,kw | 24280 |
| #45 | stop*:ti,ab,kw | 16446 |
| #46 | Withhold*:ti,ab,kw | 876 |
| #47 | placebo:ti,ab,kw | 227716 |
| #48 | continu*:ti,ab,kw | 94124 |
| #49 | maintenance*:ti,ab,kw | 32274 |
| #50 | #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 | 577590 |
| #51 | #36 and #50 | 248242 |
| #52 | #10 or #51 | 249121 |
| #53 | #7 and #52 | 3537 |
| #54 | Review | 484 |
| #55 | Trials | 3040 |

Supplementary Table 3: Search syntax for Embase databases

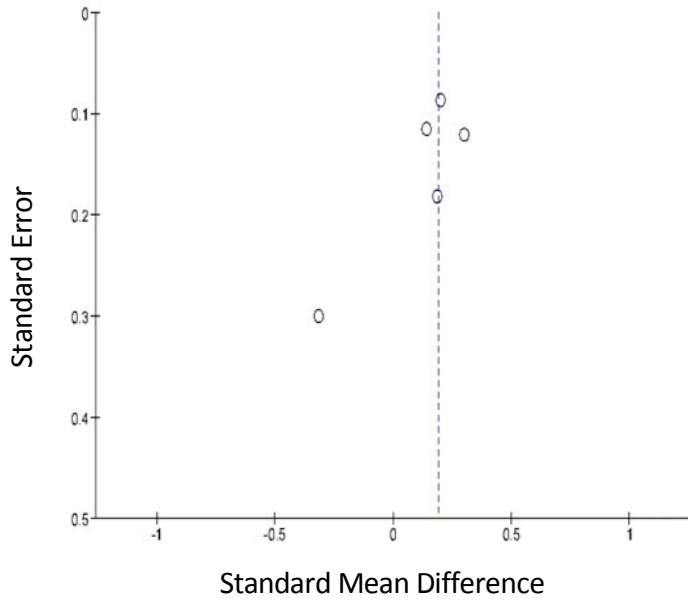
| # | Search terms | Number of references |
|-----|--|----------------------|
| #1 | attention deficit disorder'/exp/dm_dt | 11,077 |
| #2 | adhd:ti,ab,kw | 30,930 |
| #3 | ad hd':ti,ab,kw | 470 |
| #4 | addh:ti,ab,kw | 145 |
| #5 | attention* def*:ti,ab,kw | 35,311 |
| #6 | brain dysfunction*:ti,ab,kw | 4,509 |
| #7 | #1 or #2 or #3 or #4 or #5 or #6 | 51,651 |
| #8 | drug withdrawal'/de | 164,504 |
| #9 | placebo effect'/de | 5,088 |
| #10 | #8 or #9 | 169,506 |
| #11 | drug therapy'/de | 574,939 |
| #12 | drug*:ti,ab,kw | 2,057,126 |
| #13 | pharmacotherap*:ti,ab,kw | 50,027 |
| #14 | medication*:ti,ab,kw | 444,369 |
| #15 | amphetamine'/de | 33,926 |
| #16 | amphetamine*:ti,ab,kw | 29,994 |
| #17 | atomoxetine'/de | 4,849 |
| #18 | atomoxetin*:ti,ab,kw | 2,254 |
| #19 | clonidine'/de | 40,405 |
| #20 | clonidine':ti,ab,kw | 17,880 |
| #21 | methylphenidate'/de | 20,545 |
| #22 | methylphenidate':ti,ab,kw | 9,160 |
| #23 | dexmethylphenidate'/de | 667 |
| #24 | dexmethylphenidate':ti,ab,kw | 126 |
| #25 | lisdexamfetamine'/de | 1,111 |
| #26 | lisdexamfetamine':ti,ab,kw | 543 |
| #27 | guanfacine'/de | 3,034 |
| #28 | guanfacine':ti,ab,kw | 1,173 |
| #29 | #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 | 2,810,937 |
| #30 | withdr*:ti,ab,kw | 168,127 |
| #31 | discontinu*:ti,ab,kw | 176,476 |
| #32 | abstinence':ti,ab,kw | 26,846 |
| #33 | avoid*:ti,ab,kw | 459,593 |
| #34 | ceas*:ti,ab,kw | 28,175 |
| #35 | cessation*:ti,ab,kw | 88,143 |
| #36 | reduc*:ti,ab,kw | 3,810,259 |
| #37 | remov*:ti,ab,kw | 721,561 |
| #38 | stop*:ti,ab,kw | 174,091 |
| #39 | withhold*:ti,ab,kw | 9,203 |
| #40 | placebo':ti,ab,kw | 275,346 |
| #41 | continu*:ti,ab,kw | 1,221,297 |
| #42 | maintenance*:ti,ab,kw | 328,184 |
| #43 | #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 | 6,369,130 |
| #44 | #29 and #43 | 927,809 |
| #45 | #10 or #44 | 1,050,842 |
| #46 | #7 and #45 | 7,594 |
| #47 | 'crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR random*:de,ab,ti OR factorial*:de,ab,ti OR crossover*:de,ab,ti OR ((cross NEXT/1 over*):de,ab,ti) OR placebo*:de,ab,ti OR ((doubl* NEAR/1 blind*):de,ab,ti) OR ((singl* NEAR/1 blind*):de,ab,ti) OR assign*:de,ab,ti OR allocat*:de,ab,ti OR volunteer*:de,ab,ti | 2,286,136 |
| #48 | #46 and #47 | 3,085 |
| #49 | cohort analysis'/de OR 'longitudinal study'/de OR 'prospective study'/de OR 'follow up'/de OR cohort*:ti,ab,kw | 2,343,573 |
| #50 | #46 and #49 | 1,061 |
| #51 | #46 AND #47 AND [embase]/lim | 2,831 |
| #52 | #46 AND #49 AND [embase]/lim | 1,012 |
| #53 | #51 AND [embase]/lim NOT ([embase]/lim AND [medline]/lim) | 984 |
| #54 | #52 AND [embase]/lim NOT ([embase]/lim AND [medline]/lim) | 526 |

Supplementary Figure 1: Risk of bias summary

| | Random sequence generation (selection bias) | Allocation concealment (selection bias) | Blinding of participants and personnel (performance bias) | Blinding of outcome assessment (detection bias) | Incomplete outcome data (attrition bias) | Selective reporting (reporting bias) | Other bias |
|-----------------|---|---|---|---|--|--------------------------------------|------------|
| Arnold 2004 | - | - | + | - | - | - | - |
| Biederman 2010 | - | - | - | - | ? | + | - |
| Brams 2012 | - | - | - | - | + | + | - |
| Buitelaar 2007 | - | + | - | - | + | ? | - |
| Buitelaar 2012 | - | - | - | - | + | ? | - |
| Coghill 2014 | + | + | + | ? | - | + | - |
| Michelson 2004 | ? | - | + | ? | + | ? | - |
| Newcorn 2016 | + | + | - | - | ? | + | - |
| Upadhyahya 2013 | - | - | - | - | + | ? | - |

Supplementary Figure 2: Funnel plot of publication bias for the comparison between discontinuing and continuing ADHD medications on the quality of life after symptomatic remission

A. Studies measured quality of life



B. Studies reported relapse

