

Appendix A: List of medications included in the combination and switching analyses

Categories	Drugs
Stimulants	
Amphetamine short acting (AMPH SA)	Dextroamphetamine (Dexedrine)
Amphetamine long acting (AMPH LA)	Amphetamine (Adderall XR), Dextroamphetamine (Dexedrine Spansules), Lisdexamphetamine (Vyvanse)
Methylphenidate short acting (MPH SA)	Methylphenidate (Ritalin)
Methylphenidate long acting (MPH LA)	Methylphenidate (Biphentin, Concerta, Ritalin SR)
Atomoxetine HCl (non-stimulant)	Atomoxetine HCl
Clonidine IR (non-stimulant)	Clonidine IR
Atypical antipsychotics (AAP)	Aripiprazole (Abilify), Clozapine (Clozaril), Olanzapine (Zyprexa), Paliperidone (Invega), Quetiapine (Seroquel), Risperidone (Risperidal), Ziprasidone (Zeldox)
Typical antipsychotics (TAP)	Chlorpromazine, Droperidol, Flupentixol (Fluanxol), Fluphenazine, Haloperidol, Loxapine (Xylac), Methotrimeprazine (Nozinan), Perphenazine, Pipotiazine (Piportil), Prochlorperazine, Thioproperazine (Majeptil), Thiothixene (Navane), Trifluoperazine, Zuclopenthixol (Clopixol)
Bupropion	Bupropion
Serotonin–norepinephrine reuptake inhibitor (SNRI)	Duloxetine (Cymbalta), Venlafaxine (Effexor)
Selective serotonin reuptake inhibitors (SSRI)	Citalopram (Celexa), Fluoxetine (Prozac), Fluxovamine (Luvox), Paroxetine (Paxil), Sertraline (Zoloft)
Tricyclic antidepressants (TCA)	Amitriptyline (Elavil, Levate), Clomipramine (Anafranil), Desipramine, Doxepin (Sinequan, Imipramine), Nortriptyline (Aventyl), Trimipramine

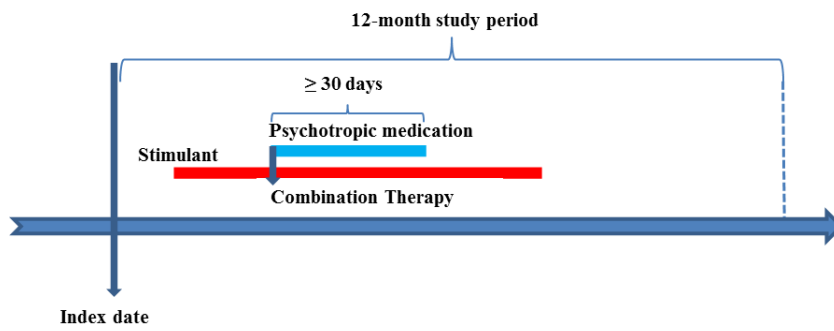
Appendix B: ICD-9 diagnosis codes for comorbidities

Comorbidity	ICD-9 Codes
Bipolar disorder	296.4x, 296.5x, 296.6x, 296.7x, 296.8x
Mania	296.0x, 296.1x
Depression	296.2x, 296.3x, 311.xx, 300.4x
Dementia	290.xx, 294.1x
Schizophrenia	295.xx
Tics (including Tourette's disorder)	307.2x
Adjustment reaction	309.xx
Anxiety disorder	293.84, 300.0x, 300.2x, 313.0x
Conduct disorder	312.xx
Insomnia ^[1]	307.4, 327.0x, 780.5
Learning disability	315.xx
Obsessive-compulsive disorder	300.3x
Oppositional defiant disorder ^[1]	313.8
Pervasive developmental disorder (including Asperger's and autistic disorder)	299.xx
Substance abuse	291.xx, 292.xx, 303.xx, 304.xx, 305.xx
Other psychotic disorders	293.81, 293.82, 297.1x, 297.3x, 298.8x, 298.9x
Epilepsy	345.xx
Other neurological disorders	320.xx-337.xx, 340.xx-349.xx excludes 345.xx
Accidents and injuries	800.xx-999.xx
Asthma	493.xx

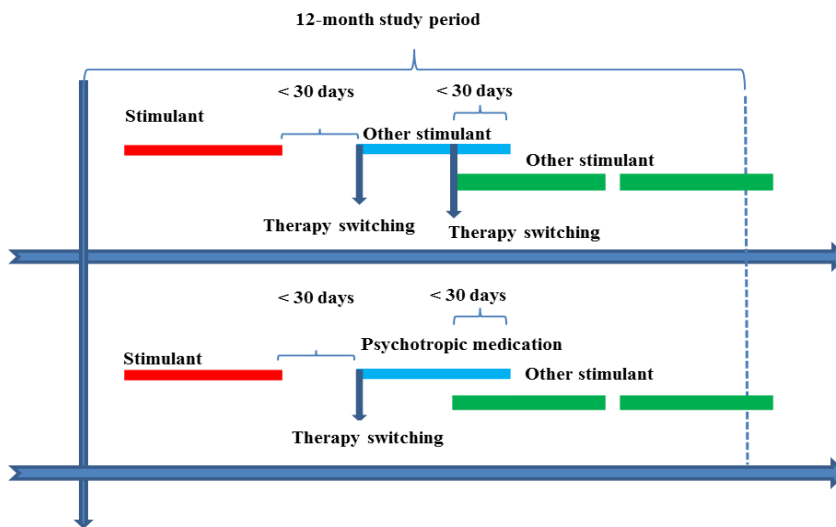
[1] Only the first four digits are reported in the RAMQ data. Therefore, diagnoses 307.41, and 307.42 for insomnia will be approximated by diagnosis 307.4 (sleep disturbance), diagnoses 780.51 and 780.52 for insomnia will be approximated by diagnosis 780.5 (specific disorders of sleep of nonorganic origin), and diagnosis 313.81 for oppositional defiant disorder will be approximated by diagnosis 313.8 (other or mixed emotional disturbances of childhood or adolescence).

Appendix C. Study measures

A. Combination therapy (an example for illustration)



B. Therapy switching (an example for illustration)



Appendix D: Baseline characteristics of patients with ADHD

Baseline characteristics	Overall (N=9,431)	Combination therapy		Therapy switch	
		With a combination (N=1,864)	Without a combination (N=7,567)	With a switch (N=1,767)	Without a switch (N=7,664)
<i>Demographic characteristics</i>					
Average age (years) ^[1] , mean ± SD [median]	11.30 ± 2.72 [11.0]	11.81 ± 2.70 [11.5]	11.18 ± 2.71 [11.0]	11.21 ± 2.72 [11.0]	11.33 ± 2.72 [11.0]
Children (6–12 years) ^[2] , N (%)	6,049 (64.1)	1,106 (59.3)	4,943 (65.3)	1,177 (66.6)	4,872 (63.6)
Adolescents (12–17 years) ^[2] , N (%)	3,382 (35.9)	758 (40.7)	2,624 (34.7)	590 (33.4)	2,792 (36.4)
Female, N (%)	2,608 (27.7)	428 (23.0)	2,180 (28.8)	458 (25.9)	2,150 (28.1)
<i>Enrolment type^[3], N (%)</i>					
Employment assistance recipient	2,457 (26.1)	560 (30.0)	1,897 (25.1)	491 (27.8)	1,966 (25.7)
Subscriber	6,974 (73.9)	1,304 (70.0)	5,670 (74.9)	1,276 (72.2)	5,698 (74.3)
<i>Number of distinct stimulants^[4], mean ± SD [median]</i>	1.15 ± 0.50 [1.0]	1.11 ± 0.55 [1.0]	1.01 ± 0.53 [1.0]		
<i>Class of baseline stimulants^[5], N (%)</i>					
AMPH SA	165 (1.7)	64 (3.4)	101 (1.3)	70 (4.0)	95 (1.2)
AMPH LA	1,849 (19.6)	565 (30.3)	1,284 (17.0)	520 (29.4)	1,329 (17.3)
MPH SA	2,604 (27.6)	404 (21.7)	2,200 (29.1)	427 (24.2)	2,177 (28.4)
MPH LA	5,072 (53.8)	1,107 (59.4)	3,965 (52.4)	947 (53.6)	4,125 (53.8)

Comorbidity profile, N (%)

Mental comorbidities					
<i>Adjustment reaction</i>	243 (2.6)	82 (4.4)	161 (2.1)	70 (4.0)	173 (2.3)
<i>Anxiety disorder</i>	192 (2.0)	85 (4.6)	107 (1.4)	68 (3.8)	124 (1.6)
<i>Learning disability</i>	252 (2.7)	71 (3.8)	181 (2.4)	64 (3.6)	188 (2.5)
Physical comorbidities					
<i>Accidents and injuries</i>	835 (8.9)	180 (9.7)	655 (8.7)	164 (9.3)	671 (8.8)
Number of comorbidities					
<i>Patients with 1 comorbidity</i>	1,657 (17.6)	426 (22.9)	1,231 (16.3)	395 (22.4)	1,262 (16.5)
<i>Patients with 2 comorbidities</i>	230 (2.4)	107 (5.7)	123 (1.6)	79 (4.5)	151 (2.0)
<i>Patients with ≥ 3 comorbidities</i>	45 (0.5)	23 (1.2)	22 (0.3)	17 (1.0)	28 (0.4)
<i>Patients with ≥ 1 psychiatric visit, N (%)</i>	1,873 (19.9)	877 (47.0)	996 (13.2)	591 (33.4)	1,282 (16.7)
<i>Mean number of psychiatric visits^[6], mean \pm SD</i>	4.37 \pm 7.11 [2.0]	3.71 \pm 4.74 [2.0]	3.94 \pm 8.77 [2.0]		
<i>[median]</i>					
<i>Physician specialty^[7]</i>					
<i>Paediatrics</i>	4,472 (47.4)	873 (46.8)	3,599 (47.6)	870 (49.2)	3,602 (47.0)
<i>Psychiatry</i>	1,083 (11.5)	615 (33.0)	468 (6.2)	360 (20.4)	723 (9.4)
<i>Neurology</i>	213 (2.3)	61 (3.3)	152 (2.0)	57 (3.2)	156 (2.0)
<i>Missing</i>	2,992 (31.7)	439 (23.6)	2,553 (33.7)	484 (27.4)	2,508 (32.7)

Notes:

- [1] Age group is calculated as of January 1st of the year of the index date. The average age is calculated as the midpoint for the age group the patient belongs to.
- [2] Age groups were calculated as of January 1st of the year of the index date; 75% and 50% of the patients in the 10–13 and the 11–14 age groups, respectively, were randomly allocated to the children category, the remaining patients in these age groups were allocated to the adolescent category.
- [3] As patients may switch health plan over time, for each enrolment type, the number of days for which patients were enrolled during the 6-month baseline period were added for all patients, and divided by 180 days to obtain the number of patients eligible full time.
- [4] Total number of distinct stimulant classes during baseline period (AMPH SA, AMPH LA, MPH SA, MPH LA).
- [5] Class of stimulant used during the baseline period. Classes were not mutually exclusive as some patients used more than one class during the baseline period.
- [6] Mean number of psychiatric visits for patients who had ≥ 1 psychiatric visit.
- [7] Physician having provided at least one medical service or having prescribed at least one psychotropic medication.