

# Functional Impairment of Patients with Attention-Deficit/Hyperactivity Disorder (ADHD): An Alternative Cost-Effectiveness Analysis of Clinically Proven Treatment Strategies based upon the NIMH MTA Study

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## Overview

- Beyond disease-defining core symptoms of inattention, hyperactivity, and impulsivity, ADHD is characterized by functional impairment of patients. The Columbia Impairment Scale (CIS) is a parent rating scale with relatively strong psychometric properties, tapping **four major dimensions: interpersonal relations, psychopathology, schoolwork, and use of leisure time.**
  - Severity of ADHD symptoms shows only low to moderate relationships (correlations) with specific measures of "functional impairment", i.e., the degree of impairment in major life activities.
  - Symptoms and impairment are distinct dimensions that should be considered as such in the diagnostic process as well as in treatment planning (cf. Barkley, 2006).
  - Therefore cost-effectiveness of treatments in terms of symptomatic normalization does not necessarily imply cost-effectiveness in terms of functional improvement.

### Objectives:

CIS ratings from the NIMH MTA Study (n=579 children with ADHD according to DSM-IV-criteria) were used as an alternative outcome measure to evaluate the cost-effectiveness of medication management (MedMgt, MM), intense behavioral treatment (Beh), both combined (Comb), or community care (CC) in the study population and in three subgroups: hyperkinetic disorder (according to ICD-10-criteria traditionally preferred in Europe); pure HKD or HKD/HKCD, and in pure ADHD, over 14 months.

### Methods:

For costing (societal and third-party payer's perspectives), patient-level resource utilization data were combined with country-specific unit costs for Germany, Netherlands, Sweden, United Kingdom, and United States (converted in Euro / year 2005). Incremental cost-effectiveness ratios (ICERs) were determined using functional improvement (CIS effect size [ES], Cohen's d) as clinical outcome criterion. Four treatment strategies and a hypothetical "Do Nothing" alternative were compared with each other.

### Results:

The four MTA treatment strategies were all clinically effective. Across jurisdictions, both CC versus "Do Nothing" (ICERs ranging from 1,200€/ES to 2,600€/ES) and MedMgt (ICERs versus "Do Nothing" from 1,000€/ES to 2,700€/ES, ICERs versus CC from dominance to 3,000€/ES) appeared attractive on grounds of cost-effectiveness. MedMgt dominated Beh, and ICERs for Comb versus MedMgt ranged from 500,000€/ES to 1,000,000€/ES. Results for subgroups with pure ADHD, HKD/HKCD, and pure HKD were broadly similar. Sensitivity analyses including probabilistic evaluations using non-parametric bootstrapping supported these findings.

### Conclusions:

Despite notable international differences in terms of diagnostic criteria, standards of care, and unit costs, the cost-effectiveness of MTA-based clinical treatment strategies for patients with pure ADHD seemed remarkably similar across jurisdictions. The impact of comorbidity remains to be explored.

## Methods Notes

- Modeling a hypothetical "Do Nothing" alternative (to account for context-specific "Community Care" arm of the MTA Study)
- Resource utilization data from the MTA Study, excluding its research component, substituting its initial double-blind titration protocol with a clinically proven algorithm (Klein et al., 2004)
- Unit costs (direct medical expenditures) determined from a societal perspective (D, NL, S, UK, USA) and from a payers perspective (D, NL)
- Incremental Cost-Effectiveness Ratios (ICERs; cost per effect size improvement on CIS over study period)
- Probabilistic Sensitivity Analyses (non-parametric bootstrapping using patient-level study data): Ellipsoid ICER Confidence Regions (Scatter Plots); Cost-Effectiveness Acceptability Curves (CEACs)

## Costs and Effects

ADHD (DSM-IV, "all")		CIS (Cohen's D)	Average Cost per Patient				
n	Germany		Sweden	Netherlands	UK	US	
Community Care	112	-0.74	912 €	1,908 €	986 €	1,607 €	1,155 €
Behavioural Treatment	111	-1.02	12,614 €	11,376 €	10,038 €	8,679 €	6,974 €
Medication Management	104	-1.12	1,602 €	3,051 €	1,141 €	2,723 €	1,276 €
Combined	115	-1.13	14,163 €	14,123 €	11,108 €	11,151 €	8,024 €

HKD/HKCD (ICD10)		CIS (Cohen's D)	Average Cost per Patient				
n	Germany		Sweden	Netherlands	UK	US	
Community Care	25	-1.27	1,007 €	2,168 €	1,109 €	1,823 €	1,319 €
Behavioural Treatment	29	-0.84	12,251 €	11,132 €	9,747 €	8,480 €	6,864 €
Medication Management	26	-1.41	1,655 €	3,132 €	1,154 €	2,784 €	1,280 €
Combined	25	-1.39	14,313 €	14,256 €	11,220 €	11,239 €	8,200 €

ADHD ("pure")		CIS (Cohen's D)	Average Cost per Patient				
n	Germany		Sweden	Netherlands	UK	US	
Community Care	32	-0.64	950 €	2,048 €	1,036 €	1,719 €	1,216 €
Behavioural Treatment	35	-0.69	12,623 €	11,425 €	10,047 €	8,710 €	6,975 €
Medication Management	36	-0.97	1,535 €	2,966 €	1,074 €	2,635 €	1,168 €
Combined	38	-0.81	14,270 €	14,287 €	11,199 €	11,263 €	8,088 €

HKD ("pure")		CIS (Cohen's D)	Average Cost per Patient				
n	Germany		Sweden	Netherlands	UK	US	
Community Care	10	-0.95	1,436 €	3,339 €	1,760 €	2,768 €	2,058 €
Behavioural Treatment	17	-0.92	12,103 €	11,090 €	9,646 €	8,455 €	6,822 €
Medication Management	16	-1.33	1,676 €	3,175 €	1,186 €	2,831 €	1,330 €
Combined	15	-1.08	14,584 €	14,566 €	11,430 €	11,533 €	8,356 €

## Cost-Effectiveness Ratios

Germany	ADHD all	ADHD only	HKD/HKCD	HKD only
MedMgt vs CC	€ 1,854.52	€ 1,771.31	€ 4,535.73	€ 622.39
Comb vs MedMgt	€ 1,050,909.58	inferior	inferior	inferior
Beh vs CC	€ 42,528.66	€ 210,739.26	inferior	inferior
Comb vs CC	€ 34,526.17	€ 78,291.13	€ 110,018.26	€ 98,145.31
Comb vs Beh	€ 14,253.07	€ 14,356.15	€ 3,736.45	€ 14,993.88
Beh vs MedMgt	inferior	inferior	inferior	inferior
CC vs DoNothing	€ 1,227.32	€ 1,486.02	€ 792.17	€ 1,514.12
Beh vs DoNothing	€ 12,386.39	€ 18,163.97	€ 14,584.25	€ 13,200.33
MeMgt vs DoNothing	€ 1,436.46	€ 1,583.09	€ 1,170.56	€ 1,255.97
Comb vs DoNothing	€ 12,566.29	€ 17,624.35	€ 10,283.79	€ 13,474.59

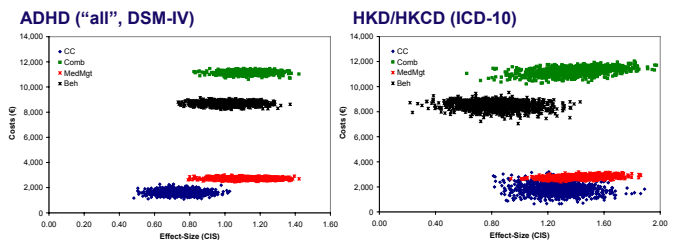
Netherlands	ADHD all	ADHD only	HKD/HKCD	HKD only
MedMgt vs CC	€ 416.44	€ 113.48	€ 318.17	dominant
Comb vs MedMgt	€ 833,912.11	inferior	inferior	inferior
Beh vs CC	€ 32,898.45	€ 162,684.90	inferior	inferior
Comb vs CC	€ 26,374.73	€ 59,737.35	€ 83,604.23	€ 72,179.74
Comb vs Beh	€ 9,847.88	€ 10,042.81	€ 2,669.52	€ 10,777.92
Beh vs MedMgt	inferior	inferior	inferior	inferior
CC vs DoNothing	€ 1,326.47	€ 1,620.49	€ 872.34	€ 1,856.26
Beh vs DoNothing	€ 9,856.80	€ 14,457.68	€ 11,603.33	€ 10,521.25
MeMgt vs DoNothing	€ 1,023.02	€ 1,107.71	€ 816.33	€ 888.79
Comb vs DoNothing	€ 9,855.94	€ 13,832.04	€ 8,061.65	€ 10,560.50

Sweden	ADHD all	ADHD only	HKD/HKCD	HKD only
MedMgt vs CC	€ 3,073.84	€ 2,784.36	€ 6,751.26	dominant
Comb vs MedMgt	€ 926,350.48	inferior	inferior	inferior
Beh vs CC	€ 34,409.44	€ 169,305.16	inferior	inferior
Comb vs CC	€ 31,828.26	€ 71,942.48	€ 99,944.95	€ 83,803.76
Comb vs Beh	€ 25,289.23	€ 24,943.86	€ 5,660.43	€ 20,999.27
Beh vs MedMgt	inferior	inferior	inferior	inferior
CC vs DoNothing	€ 2,566.64	€ 3,201.98	€ 1,705.60	€ 3,520.87
Beh vs DoNothing	€ 11,170.14	€ 16,440.78	€ 13,252.08	€ 12,096.48
MeMgt vs DoNothing	€ 2,735.77	€ 3,059.88	€ 2,215.60	€ 2,378.53
Comb vs DoNothing	€ 12,530.85	€ 17,645.77	€ 10,242.48	€ 13,457.83

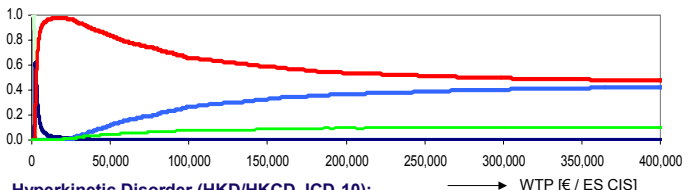
UK	ADHD all	ADHD only	HKD/HKCD	HKD only
MedMgt vs CC	€ 3,001.30	€ 2,776.15	€ 6,729.03	€ 162.04
Comb vs MedMgt	€ 705,115.64	inferior	inferior	inferior
Beh vs CC	€ 25,700.95	€ 126,230.93	inferior	inferior
Comb vs CC	€ 24,867.87	€ 56,215.57	€ 77,857.63	€ 65,420.96
Comb vs Beh	€ 22,757.38	€ 22,417.95	€ 5,001.90	€ 18,596.17
Beh vs MedMgt	inferior	inferior	inferior	inferior
CC vs DoNothing	€ 2,162.47	€ 2,687.66	€ 1,434.29	€ 2,919.06
Beh vs DoNothing	€ 8,522.25	€ 12,534.33	€ 10,094.13	€ 9,221.72
MeMgt vs DoNothing	€ 2,442.18	€ 2,717.77	€ 1,969.46	€ 1,220.91
Comb vs DoNothing	€ 9,894.14	€ 13,934.97	€ 8,075.39	€ 10,655.20

US	ADHD all	ADHD only	HKD/HKCD	HKD only
MedMgt vs CC	€ 325.76	dominant	dominant	dominant
Comb vs MedMgt	€ 564,545.94	inferior	inferior	inferior
Beh vs CC	€ 21,148.59	€ 103,970.92	inferior	inferior
Comb vs CC	€ 17,897.77	€ 40,391.45	€ 56,887.89	€ 47,012.43
Comb vs Beh	€ 9,662.31	€ 9,700.56	€ 2,421.10	€ 9,269.84
Beh vs MedMgt	inferior	inferior	inferior	inferior
CC vs DoNothing	€ 1,554.18	€ 1,901.67	€ 1,038.06	€ 2,170.47
Beh vs DoNothing	€ 6,848.32	€ 10,036.82	€ 8,170.69	€ 7,441.12
MeMgt vs DoNothing	€ 1,144.56	€ 1,204.88	€ 905.33	€ 996.32
Comb vs DoNothing	€ 7,119.52	€ 9,989.17	€ 5,891.35	€ 7,720.75

## Sensitivity Analyses



Attention-Deficit Hyperactivity Disorder (ADHD, "all", DSM-IV):



Hyperkinetic Disorder (HKD/HKCD, ICD-10):

