Incremental Cost-Effectiveness Ratios of Clinically Proven Treatments for Attention-Deficit/Hyperactivity Disorder (ADHD): Impact of Diagnostic Criteria and Comorbidity

Michael Schlander[1,2], E. Michael Foster[3], Peter S. Jensen[4], Oliver Schwarz[2,5], Joe Albert Garcia[4], Sherry Glied[4], Maura Crowe[4], Eric Taylor[6], MTA Cooperative Group

[1]University for Applied Economic Sciences Ludwigshafen (Germany); [2]Institute for Innovation & Valuation in Health Care (INNOVALHC), Eschborn (Germany);
[3]Pennsylvania State University, University Park, PA; [4]Columbia University, New York, NY; [5]University of Cooperative Education Mannheim (Germany); [6]King's College, London (England)

Rationale

ADHD is a common disorder in children and adolescents associated with a significant economic burden. Yet, little is known about the cost-effectiveness of therapeutic interventions.

The Multimodal Treatment Study (MTA), cosponsored by the National Institute of Mental Health (NIMH) and the Department of Education, represents the most important randomized trial to date[1], comparing the effectiveness of clinically proven treatment strategies for ADHD over a period of 14 months (including initial assessment and titration).

Diagnostic criteria (ICD-10 Hyperkinetic Disorder [HKD] and Hyperkinetic Conduct Disorder [HKCD] vs. DSM-IV: ADHD) and comorbidity – frequently present in patients with ADHD – are known moderators of clinical treatment response[2].

[1]MTA Cooperative Group, Arch. Gen Psych., 1999, 56: 1073-1086 and 1088-1096.
[2]P.S. Jensen et al., J. Am. Acad. Child Adolesc. Psychiatry, 2001, 40: 147-158.

Objectives

To evaluate, based upon the MTA data,

- the cost-effectiveness of the major proven forms of ADHD treatments;
- the impact of diagnostic criteria and comorbidity on treatment cost-effectiveness;
- the uncertainty around these estimates by means of probabilistic sensitivity analysis;
- the dimension of expected cost / QALY associated with the treatment strategies under study.

Methods

In the MTA study, 579 children with ADHD, combined type, aged 7 to 9.9 years, were assigned to 14 months of

- Community care (treatments by community providers; "CC", n=146): psychotherapeutic treatments and medication (in 67.4%; principally methylphenidate [MPH], mean total daily dose at study completion 22.6mg, averaging 2.3 doses per day),
- Medication management[3] (titration followed by monthly visits; "MedMgt", n=144): principally MPH, mean total daily dose 37.7mg (3 doses per day),
- Behavioral treatment[4] (intensive parent, school, and child components, with therapist involvement gradually reduced over time; "Beh", n= 144),
- Or the two (MedMgt and Beh) combined ("Comb", n=145); the medication component again principally MPH, mean total daily dose 31.2mg (3 doses / day).

Patient subgroups were defined by comorbidity (none: "pure" ADHD, or internalizing, externalizing, or both comorbidities, according to DSM-IV) and by recoding according to ICD-10 criteria (HKD, F90.0, or HKCD, F90.1) – see Results: Tab. 1.

Treatment success was evaluated according to ADHD symptom normalization rates (SNAP-IV scale[5] – see Results: Tab. 2).

Direct medical costs, excluding the research component of the study, were calculated based on resource utilization data from the MTA study documentation; unit costs were calculated from the U.S. societal perspective and adjusted to year 2000 dollars using the consumer price index (CPI)[6].

Utility gains were estimated using data from two studies of health-related quality of life in children with ADHD[7].

[3]L.L. Greenhill et al., J. Am. Acad. Child Adolesc. Psychiatry, 1996, 34: 1304-1313; L.L. Greenhill et al., J. Am. Acad. Child Adolesc. Psychiatry, 2001, 40: 180-187.
[4]K. Wells et al., J. Abnormal Child Psychology, 2000, 28: 483-505; cf. also K. Wells J. Clin. Child Psychology, 2001, 30: 131-135.
[5]J.M. Swanson et al., J. Am. Acad. Child Adolesc. Psychiatry, 2001, 40: 168-179.
[6]P.S. Jensen et al., Am. J. Psychiatry (2005, in press)
[7]Base Case: parent estimates: D. Coghill et al., 16th IACAPAP Congress, Berlin 2005; Best Case: expert estimates: J. Lord, S. Paisley, NICE; London: August 2000.

Results

Tab. 1: MTA Patient Population by Comorbidity and Diagnostic Criteria

	ADHD DSM IV					HKD/HKCD ICD10				
Pure ADHD	Total 184					Total 68				
	CC 42	MedMgt 46	Beh 43	Comb 53		CC 17	MedMgt 17	Beh 18	Comb 21	
ADHD & Internalizing	Total 81					Total 3				
	CC 19	MedMgt 20	Beh 23	Comb 19		CC 1	MedMgt 1	Beh 3	Comb 0	
ADHD & Externalizing	Total 136					Total 69				
	CC 54	MedMgt 40	Beh 42	36		CC 18	MedMgt 17	Beh 19	Comb 14	
ADHD & Both Comorbidities	Total 142					Total 5				
	CC 31	MedMgt 38	Beh 36	Comb 37		CC 1	MedMgt 1	Beh 1	Comb 0	
Total	Total 579					Total 145				
	CC 145	MedMgt 144	Beh 144	Comb 146		CC 33	MedMgt 36	Beh 41	Comb 35	

Tab. 2: MTA Effectiveness Data: "Patient Normalization Rates" (SNAP-IV-Scale)

	ADHD DSM IV					HKD/HKCD ICD10				
Pure ADHD	Total 51%					Total 51%				
	CC 31%	MedMgt 57%	Beh 42%	Comb 70%		CC 23%	MedMgt 50%	Beh 44%	Comb 76%	
ADHD & Internalizing	Total 53%					Total 33%				
	CC 21%	MedMgt 80%	Beh 39%	Comb 74%		CC -	MedMgt -	Beh 33%	Comb -	
ADHD & Externalizing	Total 41%					Total 38%				
	CC 28%	MedMgt 58%	Beh 19%	Comb 67%		CC 26%	MedMgt 53%	Beh 18%	Comb 64%	
ADHD & Both Comorbidities	Total 40%					Total 20%				
	CC 16%	MedMgt 39%	Beh 39%	Comb 62%		CC 0%	MedMgt 33%	Beh 0%	Comb -	
Total	Total 46%					Total 43%				
	CC 25%	MedMgt 56%	Beh 34%	Comb 68%		CC 24%	MedMgt 50%	Beh 29%	Comb 71%	

Tab. 3: Cost per Patient by Parallel Study Group

		CC	MedMgt	Beh	Comb
Components of Costs	Costs of Medication	$222	$624	$104	$538
	Medication Visit Costs	$91	$393	$34	$408
	Psychosocial Costs	$757	$163	$6,840	$6,881
	Total Costs	$1,071	$1,180	$6,988	$7,827

Fig. 1: Cost-Effectiveness Plane for MTA Treatment Strategies

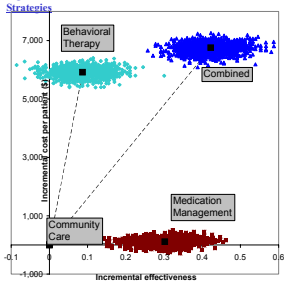
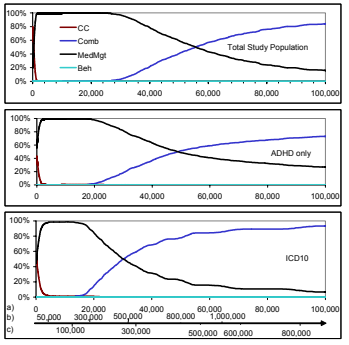


Fig.2: Cost-Effectiveness Acceptability Curves (CEACs)



Willingness To Pay [US-$]:
(a) per patient "normalized"; (b) per QALY (Base Case); (c) per QALY (Best Case)

Tab. 4: Cost-Effectiveness Results

Tab. 4a: Cost-Effectiveness [US-$ / patient "normalized"]

Diagnosis		DSM-IV				ICD-10
Comorbidity	MTA overall	ADHD only	ADHD+intern.	ADHD+extern.	ADHD+both	HKD/HKCD
Comparison						
MedMgt vs. CC	**352**	**dominant**	**869**	**137**	**1,000**	**124**
COMB vs. MedMgt	**55,392**	**48,915**	**inferior**	**75,978**	**29,439**	**31,445**
BEH vs. CC	65,744	47,749	27,245	inferior	22,737	113,462
COMB vs. CC	15,712	14,071	12,062	15,319	13,020	14,350
COMB vs. BEH	2,468	936	4,831	2,090	4,235	2,535
BEH vs. MedMgt	inferior	inferior	inferior	inferior	inferior	inferior

Tab. 4b: Cost-Utility Erstimates [US-$ / QALY]

(a) Best Case:			**n.a.**	**n.a.**	**n.a.**	
MedMgt vs. CC	**3,009**	**dominant**	**n.a.**	**n.a.**	**n.a.**	**1,060**
COMB vs. MedMgt	**473,436**	**418,077**	**n.a.**	**n.a.**	**n.a.**	**268,761**
BEH vs. CC	561,915	408,111	n.a.	n.a.	n.a.	969,761
COMB vs. BEH	21,094	8,000	n.a.	n.a.	n.a.	21,667
(b) Base Case:						
MedMgt vs. CC	**5,500**	**dominant**	**n.a.**	**n.a.**	**n.a.**	**1,938**
COMB vs. MedMgt	**865,500**	**764,297**	**n.a.**	**n.a.**	**n.a.**	**491,328**
BEH vs. CC	1,027,250	746,078	n.a.	n.a.	n.a.	1,772,844
COMB vs. BEH	38,563	14,625	n.a.	n.a.	n.a.	39,609

Discussion

Based on the MTA study, the MedMgt strategy appears to be clearly cost-effective compared to standard CC for treatment of children with ADHD, dominating the Beh strategy (i.e., it is both cheaper and more effective). This observation holds for all subgroups analyzed.

The cost-utility estimates provided should be interpreted as indicators of dimensions, not as accurate tabulations, since they refer to health-related quality of life research done elsewhere. Therefore, likely ranges are reported instead of "precise" calculations. A key assumption is that ADHD symptom relief translates into improved quality of life. While this is reasonable for pure ADHD, in patients with co-existing morbidity, broader clinical endpoints – than ADHD symptomatology captured with the SNAP-IV scale – would seem more appropriate.

Hence, such analyses have been initiated using the Columbia Impairment Scale (CIS)[8], which covers broader psychopathology and functional domains compared to the SNAP-IV scale. Preliminary results from these analyses suggest a tendency towards somewhat better cost-effectiveness of the Beh and Comb strategies, while the MedMgt strategy continues to dominate Beh.

Therefore, this data again confirm the cost-effectiveness results for the MedMgt strategy (compared to routine CC, which itself doubtlessly represents an effective treatment strategy), with associated cost per QALY estimates falling well within the boundaries of what is commonly accepted.

Though not supported by currently available health economic evidence, a Beh strategy may be preferred in real life by patients, parents and physicians. Therefore cost-effectiveness results are also presented for Beh versus CC and for adding MedMgt to Beh (i.e., Comb vs. Beh), see Tab. 4.

The robustness of the results presented has been confirmed by deterministic (one and two way) and probabilistic sensitivity analyses (cf. Figs. 1 and 2).

Limitations

Limitations of the analyses presented include the time horizon of the study as well as the fact that, as common in studies of this type, process-related utility has not been taken into account, as a result of the consequentialist nature of cost-effectiveness analysis in general.

[8]H. Bird et al., Journal of Methods in Psychiatric Research, 1996, 6:295-308.

Disclaimer:

The opinions and assertions contained in this report are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of Health and Human Services, the National Institutes of Health, or the National Institute of Mental Health.

Correspondence:

Prof. Dr. Michael Schlander, c/o Institute for Innovation & Valuation in Health Care e.V., Rathausplatz 12-14, D-65760 Eschborn/Germany.