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**Attention-Deficit/Hyperactivity Disorder**

**Cost-Effectiveness of ADHD Treatments by Diagnostic Subgroups and Comorbidity**

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**INTRODUCTION**


**ADHD**

**Treatment Options!**

- ↪ **Evidence-Based Treatment** (supported by Clinical Guidelines)
  - ↪ "Multimodal" Treatment Strategy, usually including:
    - ↪ Pharmacologic Treatment
    - ↪ Psychosocial Treatment (Behavioral Therapy)
  - ↪ **Other Interventions** (e.g., interventions within the school setting)
- ↪ **Less-Proven, Complementary and Alternative Medicine**
  - ↪ Physical exercises
  - ↪ Neurofeedback
  - ↪ Chelation therapy
  - ↪ Systemic antifungal treatment
  - ↪ Various diets (elimination diets, dietary supplements, vitamins)
  - ↪ Homeopathy, acupuncture, herbal regimens

©e.g., M.D. Rapley, 2005; R. Bussing et al., 2002

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**INTRODUCTION**

**ADHD**

**How Should These Evidence-Based Treatments be Sequenced?!**

- ↪ **Begin medication first?**
  - ↪ Predominant non-psychiatric physician practice in USA ...
- ↪ **Begin behavior therapy first?**
  - ↪ Very often parents' preference ...
- ↪ **Begin simultaneously?**
  - ↪ Physician preference in some European countries ...
- ↪ **What would you prefer to do with your own child?**
- ↪ **What can we afford as a society?**
- ↪ **What is the cost-effectiveness of these options?**

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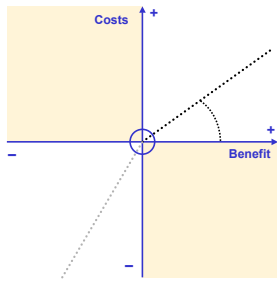
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## INTRODUCTION

Economic evaluation of medical interventions

### The Cost-Effectiveness Plane<sup>1</sup>



<sup>1</sup>W.C. Black (1996)

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by diagnostic subgroup and comorbidity



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Cost-Effectiveness of Clinically Proven ADHD Treatments

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## METHODS

Economic evaluation of ADHD treatment strategies

### The NIMH MTA Study<sup>1</sup>

- ↪ **Randomized Clinical Trial of Treatment Strategies**
  - ↪ Psychosocial Treatment Alone [BEH]
  - ↪ Pharmacological Treatment Alone [MM]
  - ↪ Combined Psychosocial and Pharmacological Treatment [COMB]
  - ↪ Community Comparison Group [CC]
- ↪ **579 subjects**
  - ↪ entered between January and May of three consecutive years
  - ↪ six sites (in the United States and Canada)
- ↪ **Treatment for 14 months**, follow-up for +22 months
- ↪ **Extensive standardization**
  - ↪ Treatment manuals
  - ↪ Coordinated staff training
  - ↪ Extensive measures of treatment fidelity for all components

<sup>1</sup>MTA Cooperative Group 1999a, 1999b

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Cost-Effectiveness of Clinically Proven ADHD Treatments

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## METHODS

Economic evaluation of ADHD treatment strategies

### Cost Data

- ↪ **Excluding the research component of the study**
- ↪ **Real treatment costs of the MTA Study**
- ↪ **Measured from a payer perspective**
  - ↪ Adjusted for inflation to year 2000 US-\$ (using the CPI)
  - ↪ Costs of medication were calculated using NDDF Plus data
  - ↪ Costs for psychiatrists, psychologists, and pediatricians were calculated on an hourly basis using yearly estimates<sup>1</sup>, e.g.:
    - ↪ Psychiatrists: US-\$ 143,000
    - ↪ Psychologists: US-\$ 80,500
  - ↪ Costs of the STP were calculated per attending day using the hourly wages of the staff needed for the program.
- ↪ **Sensitivity analyses ...**
  - ↪ ... were conducted as described in Jensen et al. (2005)

<sup>1</sup>Sources: AMA Socioeconomic Monitoring System Survey 1999; Scheffler et al. 1998; Bureau of Labor Statistics. All costs were included regardless of whether they were paid for by a patient, an insurer, or any third party.

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**METHODS**

Economic evaluation of ADHD treatment strategies

**Effectiveness Data**

- ↳ **Response Rates (SNAP-IV Normalization)**
  - ↳ Narrow band symptom scale, integrating parent and teacher scores
  - ↳ Capturing DSM-IV defined core symptoms of ADHD (inattention, hyperactivity/impulsivity; also opposition/defiance)<sup>1</sup>
- ↳ **Quality-Adjusted Life Year (QALY) Estimates**
  - ↳ Response rates defined by symptomatic normalization (SNAP-IV)
  - ↳ Health-related quality of life ("utility") weights derived from
    - ↳ Expert estimates ("best case" analysis):  $\Delta = 0.117^2$
    - ↳ Parent proxy ratings ("base case" analysis):  $\Delta = 0.064^3$
  - ↳ Note underlying normative assumption ("extrawelfarism") of QALY maximization; "a QALY is a QALY"...
- ↳ **Columbia Impairment Scale (CIS) Scores**
  - ↳ Global measure of impairment, tapping four domains: interpersonal relations, psychopathology, (job or) schoolwork, use of leisure time



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**METHODS**

Economic evaluation of ADHD treatment strategies

**Cost-Effectiveness and Sensitivity Analyses**

- ↳ **Incremental Cost-Effectiveness Ratios (ICERs)**  
$$ICER = \frac{C_B - C_A}{U_B - U_A}$$
- ↳ **One- and Two-Way Deterministic Sensitivity Analyses ...**
  - ↳ ... for various cost assumptions did not change overall results
  - ↳ Details available on request (contact Peter Jensen at Columbia U)
- ↳ **Probabilistic Sensitivity Analyses**
  - ↳ Non-parametric bootstrapping using patient-level data
  - ↳ **Ellipsoid ICER Confidence Regions / Scatter Plots**
    - ↳ Reflecting the covariance in cost and effect differences
  - ↳ **Cost-Effectiveness Acceptability Curves (CEACs)**
    - ↳ Representing the probability that a strategy is most cost-effective given the MTA data (as a function of "willingness-to-pay", WTP), taking parameter uncertainty fully into account



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**METHODS**

Subgroup analyses by comorbidity and diagnostic criteria (DSM-IV vs. ICD-10)

**Diagnostic Criteria**



"ADHD" (DSM-IV)	"HK[C]D" (ICD-10)
↳ <b>Inattention</b> <ul style="list-style-type: none"><li>↳ <math>\geq 6/9</math> symptoms</li></ul> <i>and / or</i>	↳ <b>Inattention</b> ( $\geq 6/9$ symptoms)
↳ <b>Hyperactivity and impulsivity</b> <ul style="list-style-type: none"><li>↳ <math>\geq 6/9</math> symptoms</li></ul>	↳ <b>Hyperactivity</b> ( $\geq 3/5$ symptoms)
↳ <b>Symptoms causing impairment</b> <ul style="list-style-type: none"><li>↳ Have persisted for <math>\geq 6</math> months</li><li>↳ Are present before 7 years of age</li><li>↳ Are "pervasive", i.e., present in <math>\geq 2</math> settings (e.g., home, school, work)</li><li>↳ Are not better accounted for by another mental disorder</li></ul>	↳ <b>Impulsivity</b> ( $\geq 1/4$ symptoms)
	↳ <b>Symptoms</b> criteria like DSM-IV (left)
	↳ <b>Hyperkinetic Disorder:</b> <ul style="list-style-type: none"><li>↳ If criteria above are met (-&gt; F90.0)</li></ul>
	↳ <b>Hyperkinetic Conduct Disorder:</b> <ul style="list-style-type: none"><li>↳ If additional symptoms of conduct disorder are present (-&gt; F90.1)</li></ul>

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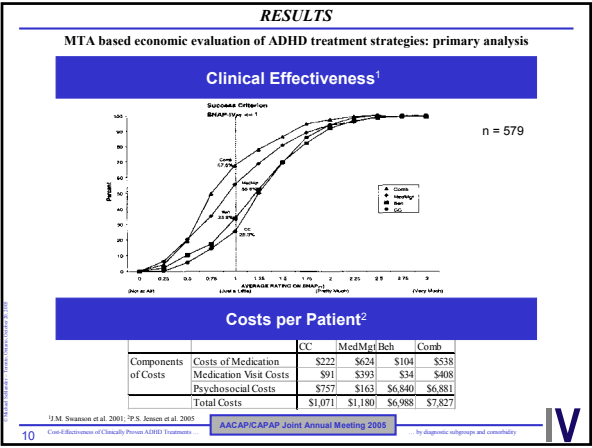
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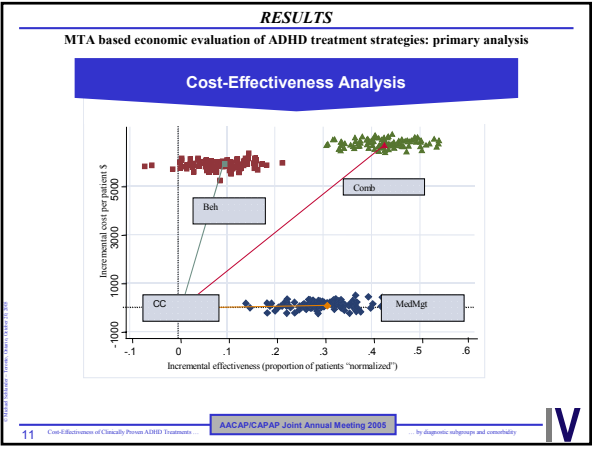
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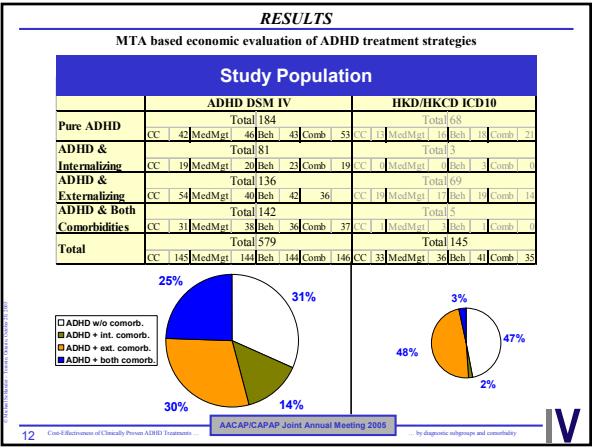
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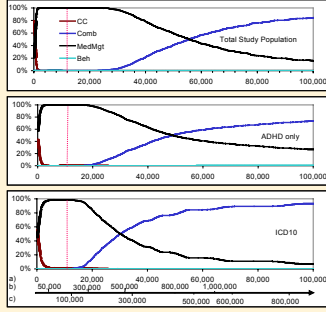
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RESULTS

Interpreting the primary cost-effectiveness analysis of the MTA

MTA: Cost-Effectiveness Acceptability Analysis



Likelihood  
"Best Option"

Decision Makers' Willingness To Pay [US-\$]  
a) per patient "normalized"  
b) per QALY gained (base case)  
c) per QALY gained (best case)

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RESULTS

MTA based economic evaluation of ADHD treatment strategies

Extended Analyses: Data Overview

	CC	Medication Management	Behavioral	Combined	Total
Pure ADHD	CIS (Cohen's d)	-0.77	-1.07	-0.73	-1.04
	% normalization	0.31	0.61	0.46	0.79
	Costs	1,265	1,132	7,256	8,330
	Sample Size	32	36	36	38
ADHD & Internalizing only	CIS (Cohen's d)	-0.25	-0.93	-1.11	-0.73
	% normalization	0.19	0.80	0.44	0.73
	Costs	784	1,386	6,536	8,421
	Sample Size	16	15	18	16
ADHD & Externalizing only	CIS (Cohen's d)	-1.07	-1.34	-1.01	-1.53
	% normalization	0.30	0.58	0.26	0.64
	Costs	1,316	1,271	7,451	8,374
	Sample Size	40	31	31	28
ADHD & Both Comorbidities	CIS (Cohen's d)	-0.88	-1.33	-1.48	-1.49
	% normalization	0.21	0.50	0.41	0.65
	Costs	1,205	1,296	7,507	8,029
	Sample Size	24	22	27	34
Total	CIS (Cohen's d)	-0.74	-1.10	-1.01	-1.15
	% normalization	0.27	0.61	0.39	0.70
	Costs	1,202	1,245	7,254	8,263
	Sample Size	112	104	111	116
ICD-10	CIS (Cohen's d)	-1.22	-1.36	-0.87	-1.44
	% normalization	0.28	0.62	0.38	0.76
	Costs	1,373	1,249	7,138	8,445
	Sample Size	25	26	29	29

Cohen's d computed using the two standard deviations:  $d = (M_1 - M_2) / \sqrt{(\sigma_1^2 + \sigma_2^2) / 2}$

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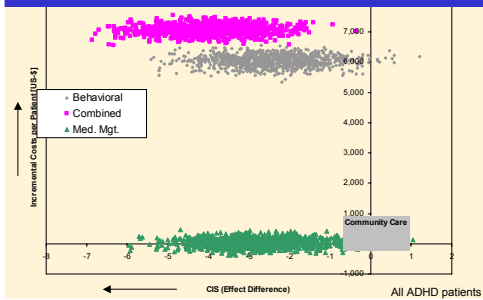
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RESULTS

MTA based economic evaluation of ADHD treatment strategies

Secondary Cost-Effectiveness Analysis (CIS)

Ellipsoid ICER Confidence Regions




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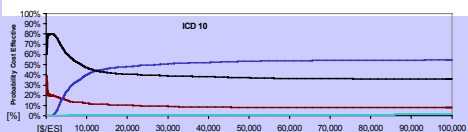
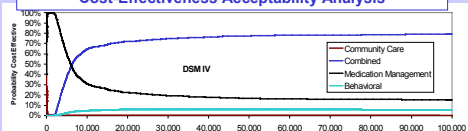
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## RESULTS

### MTA based economic evaluation of ADHD treatment strategies

#### Secondary Cost-Effectiveness Analysis (CIS)

##### Cost-Effectiveness Acceptability Analysis



##### Analysis by Diagnostic Criteria



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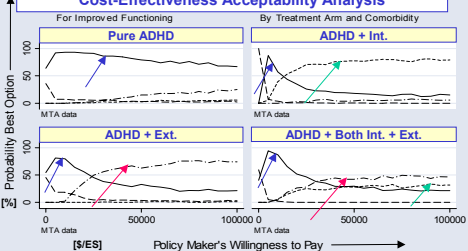
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## RESULTS

### MTA based economic evaluation of ADHD treatment strategies

#### Secondary Cost-Effectiveness Analysis (CIS)

##### Cost-Effectiveness Acceptability Analysis



##### Analysis by Comorbidity



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## RESULTS

### MTA based economic evaluation of ADHD treatment strategies

#### Some Conclusions

- A carefully monitored, intense medication management strategy as defined by the MTA protocol is clearly cost-effective<sup>1</sup>.
- This observation holds across all subgroups analyzed (by comorbidity and diagnostic criteria) as well as by all measures of effectiveness studied.
- Our cost/QALY estimates<sup>2</sup> are US-\$ 3,000 – 5,500 for all patients (n=579) and US-\$ 1,000 – <2,000 for patients with hyperkinetic disorder (HKD/HKCD; n=145).
- Compared to "all" patients and those with "pure" ADHD, behavioral interventions are relatively more cost-effective in terms of achieving improved functioning in patients with more complex comorbidities (both internalizing and externalizing).

#### Some Limitations

- Cost-effectiveness of less intense and/or better targeted behavioral interventions?
- Longer time horizons than employed in our present analyses may modify conclusions, particularly re. the cost-effectiveness of behavioral interventions.
- Normative premises of cost-effectiveness and cost-utility analyses should be kept in mind when interpreting these findings.

<sup>1</sup>Compared to all other interventions tested. <sup>2</sup>Compared to community treatment, the least attractive cost per QALY estimate may be derived from the subgroup with both comorbidities, at an estimated US-\$ QALY ranging from 8,550 to 15,600 which by current standards would reflect acceptability. However, cost/QALY estimates in the presence of comorbidity are difficult to interpret and bias, therefore, we have presented them here.



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