Cost-Effectiveness of Disease-Modifying Therapy for Multiple Sclerosis:

A Population-based Evaluation

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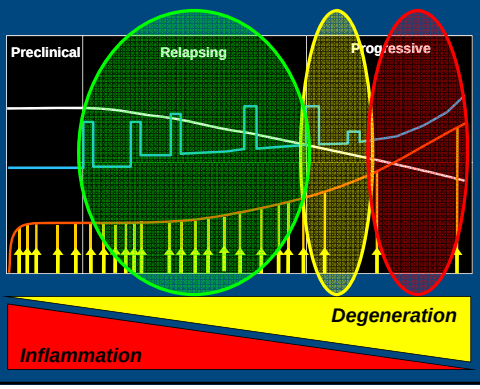
Multiple Sclerosis (MS) is associated with disability and high expenses

- MS is a autoimmune neurodegenerative condition
- MS is the second most frequent cause of disability in early- to middle-aged adults, after trauma
- Annual direct and indirect costs of MS care can total over $50,000 (2008 U.S.) per patient, mostly related to:
  - Medications
  - Earnings loss
  - Informal care

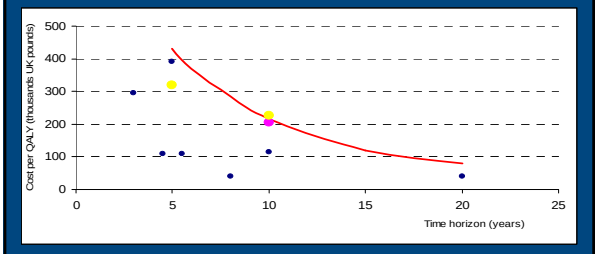
The Course of MS



Disease modifying therapies (DMTs)

- In the US, current treatments for relapsing-remitting (RR) and secondary progressive MS include Avonex, Betaseron, Rebif, and Copaxone
- The cost of DMTs approaches $40,000/year
- Knowledge of the cost-effectiveness of DMTs has been controversial

Effect of Study Sponsor on the ICER of DMT



NICE (Chilcott et al. 2003)
Pharmaceuticals
NMSS (Prosser 2003)
Parkin et al. 1998

Limitations of the Current CE Evaluation of MS DMT

- Cost and utilization estimates obtained from various sources
- Outdated data sources
- Use of small convenience sample
- Variation in study assumptions and methodologies
- Limited info about DMT effectiveness
  - No long-term randomized data
  - Lack of information on drug switching
  - No integration of the NAb effect
  - Limited information about adherence and side effects

Objectives

- *Short-term:* To evaluate the cost-effectiveness of Avonex, Betaseron, Rebif, and Copaxone compared to basic supportive therapy in the US for patients with RR and SP MS
- *Long-term:* To build a modifiable decision making model to be used for development of MS-specific clinical guidelines and health policies, and to be updated based on the availability of new data

Data

- 2000-2005 Sonya Slifka Longitudinal MS Survey
  - Followed over 2000 people with all courses and durations of MS
  - Representative of MS population, from all regions of the U.S.
  - Information on:
    - MS severity
    - HRQOL
    - types and extend of disability
    - demographics
    - healthcare utilization
    - employment
    - DMT use (non-randomized)

Study Population

- Final sample, ~ 900 people
- Only individuals with relapsing remitting and secondary progressive MS
- Excluded participants:
  - Who completed only one interview
  - Those with missing information on key information (e.g., disease duration, disease state or demographics)

Model Structure

- Disability-based disease states (DS)

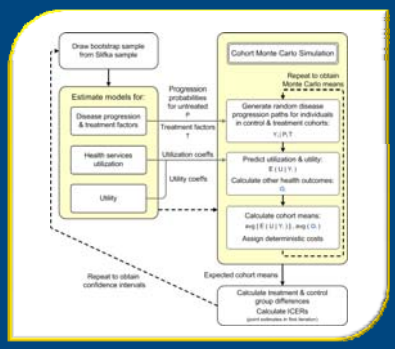
Cross-walk from EDSS to Disease States

EDSS CATEGORY	DISABILITY STATUS SCALE
EDSS 0-1.5	1: NO MS SYMPTOMS
EDSS 2-2.5	2: MILD SYMP, NON-LIMITING
EDSS 3-4	3: MILD SYMP, NOT AFFECTING WALKING
EDSS 4.5-5.5	4: PROBLEM W/WALKING, DON'T USE AID 4: 25 FT W/O CANE OR AID
EDSS 6	5: 1-SIDE CANE OR AID FOR 25 FT
EDSS 6.5-7	6: 2-SIDE CANE OR AID FOR 25 FT
EDSS 7.5-8.5	7: ONLY WHEELCHAIR/SCOOTER
EDSS 9-9.5	8: COMPLETELY BED RIDDEN

Model Structure

- Disability-based disease states (DS)
- First-order Markov model with annual cycles for transitions between DS
- Transition probabilities and relapses estimated with multinomial logit regressions
- Published DMT effects used to modify progressions for individuals on DMT to model “natural history” of MS
- 10-year disease progression paths

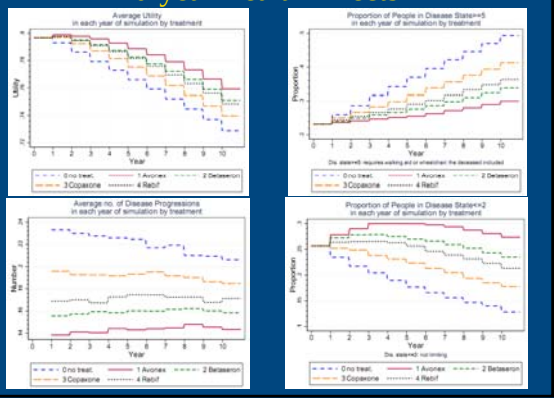
Simulation Diagram



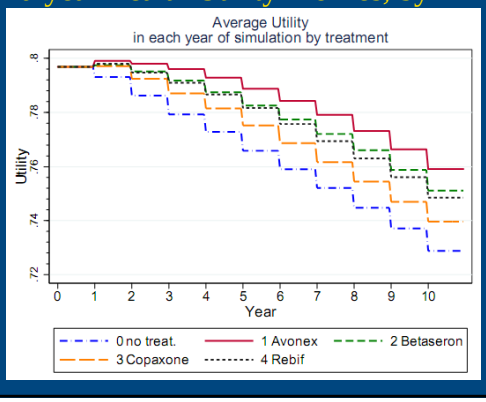
Methods: Estimation

- Utility and health care utilization assigned to DS using estimation models for count data
- Outcomes measured as:
  - Gains in quality-adjusted life years (QALY)
  - Relapse-free years
  - Number of avoided disease progressions
  - Gains in years spent in lower DSs
- Medicare reimbursement rates used to cost utilization

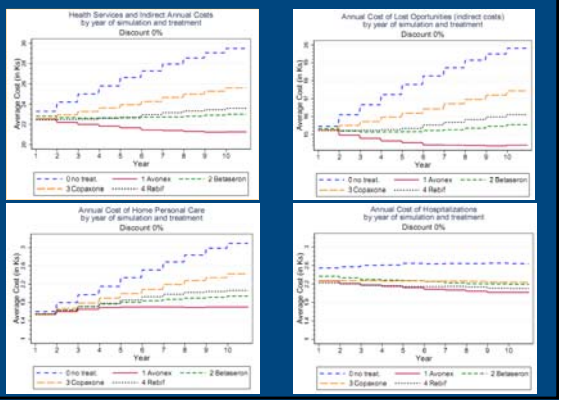
10-year Health Effects



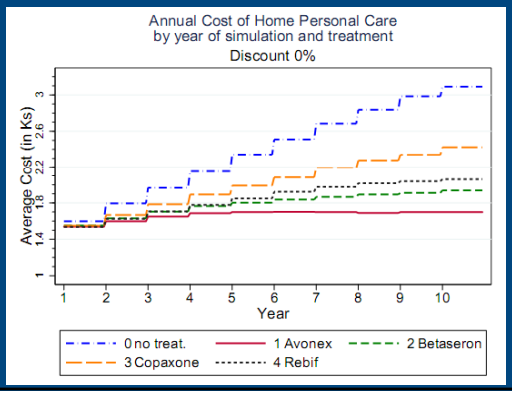
10-year Health Utility Profiles, by DMT



10-year Expenses Profiles



10-year Profile of Personal Home Care Costs



Methods: Uncertainty Evaluation

- Total expected costs and effects over 10 years estimated through Monte Carlo simulations
- Confidence intervals obtained via bootstrap resampling
- CE acceptability curves: full and discounted pricing
- Sensitivity analyses conducted to evaluate robustness of results to study assumptions

ICER: Basecase

Differences in 10-year totals between DMTs & basic supportive care (3% discounting)				
MEASURE	**AVONEX**	**BETASERON**	**COPAXONE**	**REBIF**
OUTCOMES				
QALYS	0.18	0.133	0.072	0.121
COSTS				
All costs	175,817	205,899	184,500	193,003
Excluding DMA	-41,234	-32,477	-21,521	-31,273
Exc. DMA & Inpatient	-37,009	-29,490	-18,477	-27,345
ICERS				
QALYS	975,861 (743,693; 1M)	1,547,368 (1.1M; 1.7M)	2,569,813 (1.6 M; 2.8M)	1,594,481 (1.1 M; 1.8M)

ICER: Sensitivity Analyses

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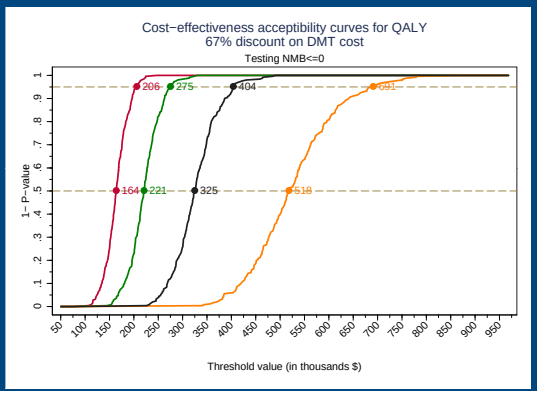
ICERS (QALYS)				
Base case	975,861 (743,693; 1M)	1,547,368 (1.1M; 1.7M)	2,569,813 (1.6 M; 2.8M)	1,594,481 (1.1 M; 1.8M)
Staring @ DS 2	690,199 (568,861; 768,301)	1,052,394 (850,211; 1.2M)	1,875,703 (1.3M; 2.2M)	1,102,434 (871,465; 1.3M)
Staring @ DS 3	715,300 (649,265; 923,883)	1,130,780 (997,873; 1.4M)	1,547,572 (1.4M; 2.5M)	1,198,268 (989,972;1.5M)
Including DS 8	417,398 (330,540; 467,523)	638,890 (510,494; 694,378)	1,109,003 (809,951; 1.2M)	687,114 (539,496; 732,229)

ICER: Sensitivity Analyses



Study Limitations

- "All models are wrong, but some are useful…"
  George E. P. Box
- Our study sample only contained a small number of MS patients with late disease
- HRQOL synthetic profile (data are cross-sectional, not longitudinal)
- Heterogeneity in definition of control ("supportive") therapy and treatment recommendation

Conclusions

- The incremental cost-effectiveness ratios of each of the DMTs are far above currently accepted standards
- DMT's would be cost-effective if their prices were reduced substantially (~68%)
- Incorporating health outcomes and expenses associated with greater disability states (DS 8/EDSS 9+: being bed ridden) may improve ICER
- Offering DMT to patients with early MS improves overall cost-effectiveness compared to treating all

Practice and Policy Implications

- The current practice of recommending DMTs for patient with any stage of relapsing or secondary progressive MS may need to be reconsidered
- While most MS therapies address relapses, it is the long-term disability that has the greatest impact on DMT cost-effectiveness
- Better understanding of individual preferences for treatment and associated complications is needed
- Data on long-term care use and outcomes for MS patients are lacking

THANK YOU!

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http://www.urmc.rochester.edu/cpm/divisions/hsr/index.html