A Comprehensive Cost-Effectiveness Analysis of Treatments for Multiple Sclerosis

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The purpose of this study was to examine the cost-effectiveness of four disease-modifying drugs (DMDs) used to treat multiple sclerosis (MS): glatiramer acetate (GA; Copaxone), interferon beta-1a (IFN β -1a) intramuscular (IM) injection (Avonex), IFN β -1a subcutaneous (SC) injection (Rebif), and interferon beta-1b (IFN β -1b) SC injection (Betaseron). Cost-effectiveness analyses are useful in countering the financial uncertainties and treatment efficacy concerns faced by people with MS. We conducted simulation analyses of the principal findings of a 2009 study by Goldberg et al. (Goldberg LD, Edwards NC, Fincher C, et al: Comparing the cost-effectiveness of disease-modifying drugs for the first-line treatment of relapsing remitting multiple sclerosis. J Manag Care Pharm. 2009;15:543–555) to frame the researchers' findings from the perspectives of cost-conscious and cost-neutral MS patients. We found that for the cost-conscious consumer, the ranking of most (1) to least (4) preferred DMDs was 1) IFN β -1a IM (Avonex), 2) GA (Copaxone), 3) IFN β -1a SC (Rebif), and 4) IFN β -1b SC (Betaseron). For the cost-neutral consumer who places priority on effectiveness over costs, the ranking was 1) IFN β -1a SC (Rebif), 2) IFN β -1b SC (Betaseron), 3) GA (Copaxone), and 4) IFN β -1a IM (Avonex). Future studies could examine cost-effectiveness over extended periods of time (eg, 15–20 years) and more closely examine the cost-effectiveness of natalizumab (Tysabri) relative to the four primary DMDs. Int J MS Care. 2011;13:128–135.

The cost of health care in the United States is escalating rapidly, placing continual strain on the US economy and causing the number of people without health insurance to increase. Thus, it is essential to examine every aspect of the current health-care system to identify solutions and reduce costs. Although technological improvements tend to enhance health-care outcomes, they have also led to higher expenses.

Cost-effectiveness analyses are used to assess the monetary cost of disease-modifying drugs (DMDs) relative to their effectiveness in achieving a predefined purpose. According to the Centers for Disease Control and Prevention (CDC), a cost-effectiveness analysis represents “a type of economic evaluation that examines both the

costs and health outcomes of alternative intervention strategies . . . [by comparing] the cost of an intervention to its effectiveness as measured in natural health outcomes.”¹ For people with multiple sclerosis (MS), examples of relevant costs are the cost of medication, office visits, and hospital stays; examples of relevant health outcomes are the avoidance of complications such as relapses, physical disability, fatigue, and depression. To counter the financial uncertainty and concerns of MS patients, medical professionals should be knowledgeable about the cost-effectiveness of those disease-management therapies for which costs and health outcomes are readily quantifiable.

Comparative Effectiveness Research

Comparative effectiveness research aims to identify the most cost-effective medical treatments and, as a result, curb spending on expensive pharmaceutical therapies such as those often used by MS patients. On February 17, 2009, President Barack Obama signed into law the economic stimulus package stipulated by

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the American Recovery and Reinvestment Act of 2009, \$1 billion of which was allocated to comparative effectiveness research for the subsequent 2 years. The objective of the research was to facilitate wiser spending of health-care dollars through the selection of drugs that have been proven effective while costing less than other options.² More recently, the enactment of the Patient Protection and Affordable Care Act marked the creation of the Patient-Centered Outcomes Research Institute, a nonprofit agency designed to conduct comparative effectiveness research. Given the pressure on clinicians by pharmaceutical companies to prescribe their newest and “best” drugs, a physician’s recommendations to patients may not be based on objective, high-quality research. Better patient outcomes and higher levels of patient satisfaction might result from a systematic approach whereby the health-care provider can identify the most cost-effective treatment available for an individual patient.

Supporters of comparative effectiveness research maintain that the federally funded research will result in a reliable method of identifying the most appropriate treatments while reducing the amount of money spent on pharmaceuticals in the United States.¹ Opponents of the research include pharmaceutical companies and some clinicians who might stand to lose income if spending on pharmaceuticals decreased. Other opponents believe that cost should not be a factor in decisions about patients’ health; they may fear that comparative analysis would lead to a system of health-care rationing.³ Moreover, they suggest that this process will limit the growth of health-care innovations, which would ultimately be detrimental to the health-care system and the economy as a whole.¹

Supporters of the research have pointed out that the concept of identifying cost-effective treatments is not new; it has long been integral to many private health insurance plans, as well as Medicaid and the Veterans Affairs (VA) program. These programs attempt to determine which treatments work best for the cost and promote those treatments among their covered populations. Many states’ Medicaid programs have saved millions of dollars by using this cost-effectiveness approach. The proposed program would simply identify the best and most cost-effective drugs for a patient to start treatment with; if those drugs turned out to be unsuccessful for the patient, other, more expensive options could be tried until an effective treatment was found. Thus, patients would still be entitled to receive pharmaceutical thera-

pies proven to have positive results. Clearly, comparative effectiveness research offers an opportunity to greatly reduce health-care costs.¹

Comparative Cost-Effectiveness of Standard DMDs versus Natalizumab

Current treatment options for patients with MS include recombinant interferons (interferon beta-1b [IFN β -1b] subcutaneously [SC], Betaseron; interferon beta-1a [IFN β -1a] SC, Rebif; and IFN β -1a intramuscularly [IM], Avonex), glatiramer acetate (GA; Copaxone), and natalizumab (Tysabri). In a 2008 United Kingdom study, Gani et al.⁴ performed a simulation on data from the 2005 UK Multiple Sclerosis Survey and data from the AFFIRM study and found natalizumab to be more cost-effective than both GA and the interferons. AFFIRM was a 2-year double-blind, randomized, placebo-controlled trial involving 942 patients. Kobelt et al.⁵ used data from the AFFIRM study in combination with patient-level data from the Swedish MS Registry to compare the cost-effectiveness of natalizumab with that of standard DMDs. They found natalizumab to be a slightly less costly and more effective treatment than IFN β -1a SC (Rebif), IFN β -1a IM (Avonex), GA (Copaxone), intravenous immunoglobulin (IVIG), and mitoxantrone.

Article Review: A Comprehensive Comparison of First-Line Therapies

Overview

In a 2009 publication entitled “Comparing the cost-effectiveness of disease-modifying drugs for the first-line treatment of relapsing-remitting multiple sclerosis,” Goldberg et al.⁶ constructed an elaborate economic model to analyze the cost-effectiveness of four first-line therapies for MS. They used data from pivotal randomized placebo-controlled clinical trials (RCTs) to determine the most cost-effective therapy, defined as the therapy with the most favorable cost per relapse avoided over a 2-year period. The DMDs studied were GA (Copaxone), IFN β -1a IM injection (Avonex), IFN β -1a SC injection (Rebif), and IFN β -1b SC injection (Betaseron).

Model Design

The researchers used Microsoft Excel (Microsoft Corp, Redmond, WA) to compare the effectiveness and costs of the DMDs studied with regard to therapies, relapses, and disease progression. A 2-year time horizon was used for consistency with the 2-year dura-

tion uniformly used across all RCTs studied. The cost-effectiveness of DMDs was measured in terms of the cost per relapse avoided because “(a) the original pivotal studies of DMDs were all 2 years in duration; (b) disease progression in MS is a slow process; and (c) U.S. payers typically prefer shorter time periods (e.g., 1 to 3 years) when conducting economic analyses.”⁶

Clinical Inputs

At the 2-year end point, all DMDs were found to be effective in terms of relapses avoided. Results and effectiveness measures across the four RCTs are summarized in Table 1.

To reflect reality, this study derived a persistence rate to reflect the “real-world” discontinuation of therapy that was not taken into account in the four RCTs.⁷⁻¹² A persistence rate of 89.4% was computed based on data from two observational studies.^{13,14} This indicates that on average, 10.6% of individuals will stop participating in their respective clinical trials.

Treatment Response

Treatment response was measured in terms of the number of relapses and disability progression steps avoided over the 2-year period. The study adopted the Schumacher definition of relapse: “the appearance of a new symptom or worsening of an old symptom persisting over at least 24 hours. The abnormality is preceded by stability of improvement for at least 30 days and is confirmed by a neurologist to be attributed to MS activity within 7 days.”¹⁵ Based on trends observed in two RCTs,^{9,12} an average untreated patient can expect to experience 2.58 relapses over a 2-year period (undiscounted). Disability progression steps observed are in

Table 2. Clinical input parameters (undiscounted)

Clinical input	Value
DMD persistence rate (applies to all four DMDs)	89.4% ^{13,14}
No. of relapses in an untreated patient over 2 years	2.58 ^{9,12}
No. of EDSS steps in an untreated patient over 2 years	0.45 ⁷⁻⁹

Abbreviations: DMD, disease-modifying drug; EDSS, Expanded Disability Status Scale.

Source: Data from Goldberg et al.⁶

accordance with the Kurtzke Expanded Disability Status Scale (EDSS), which ranges from 0 to 10, with 0 indicating no disability and 10 indicating death from MS. Based on trends observed in three RCTs,⁷⁻⁹ an average untreated patient can expect to experience 0.45 disability progression steps over a 2-year period (undiscounted). Clinical input parameters are outlined in Table 2.

Cost Inputs

Total monetary costs incurred by a patient consist of the following components: 1) the cost of DMD therapy, 2) the cost of relapses, and 3) the cost of disability steps. Cost input parameters are outlined in Table 3.

The cost of DMD therapy was computed on a monthly basis using the drug’s wholesale acquisition cost (WAC) as identified in the April 2009 *Drug Topics Red Book*.¹⁶ A WAC is the price at which wholesalers purchase a product from its manufacturer. A \$25 member copayment and 0% discount (rebate) were deducted from the WAC, and any costs of monitoring disease activity (eg, laboratory and diagnostic testing) were added to the WAC in order to arrive at a net cost of DMD therapy per month. The estimated frequency of monitoring disease

Table 1. Clinical trials and effectiveness measures used in the Goldberg et al. model

Source	Treatment	Mean baseline number of relapses	Mean baseline EDSS score	2-year number of relapses (placebo, treatment)	2-year disability progression rates (placebo, treatment)
Johnson et al., 1995 ⁷	Glatiramer acetate, 20 mg SC daily	2.9	2.8	1.68, 1.19	24.6%, 21.6%
Jacobs et al., 1996 ⁸	IFNβ-1a, 30 µg IM weekly	1.2	2.4	1.64, 1.34	34.9%, 21.9%
PRISMS Study Group, 1998, 2001 ^{9,10}	IFNβ-1a, 44 µg SC 3 times weekly	3.0	2.5	2.56, 1.73	38.3%, 26.8%
IFNB Multiple Sclerosis Study Group, 1993, 1995 ^{11,12}	IFNβ-1b, 250 µg SC every other day	3.4	3.4, 3.0	2.62, 1.81	28.0%, 20.0%

Abbreviations: EDSS, Expanded Disability Status Scale; IFNβ-1a, interferon beta-1a; IFNβ-1b, interferon beta-1b; IM, intramuscularly; SC, subcutaneously.

Source: Data from Goldberg et al.⁶ Refer to the source studies for details about clinical participant criteria, relapse definitions, and sample sizes.

Table 3. Cost input parameters (undiscounted)

Cost input	Value
Average cost of relapse	\$4682
Average cost of EDSS step	\$1788
Monthly costs of therapy ^a (WAC)	
GA SC (20 mg daily)	\$2322 (\$2283) ¹⁶
IFNβ-1a IM (30 µg weekly)	\$2294 (\$2243) ¹⁶
IFNβ-1a SC (44 µg 2 times weekly)	\$2384 (\$2334) ¹⁶
IFNβ-1b SC (250 µg every other day)	\$2461 (\$2411) ¹⁶
Monthly costs of monitoring therapy/adverse events	
GA SC (20 mg daily)	\$64 ¹⁶
IFNβ-1a IM (30 µg weekly)	\$75 ¹⁶
IFNβ-1a SC (44 µg 2 times weekly)	\$75 ¹⁶
IFNβ-1b SC (250 µg every other day)	\$75 ¹⁶

Abbreviations: EDSS, Expanded Disability Status Scale; GA, glatiramer acetate; IFNβ-1a, interferon beta-1a; IFNβ-1b, interferon beta-1b; IM, intramuscularly; SC, subcutaneously; WAC, wholesale acquisition cost.

Source: Data from Goldberg et al.⁶

^aMonthly cost of therapy = annual cost of disease-modifying drug ÷ 12, offset with a \$25 member copayment, net discounts, and monitoring.

activity and adverse events was based on the opinions of five neurologists who were colleagues of the Goldberg et al.⁶ study's primary author.* The 2008 Centers for Medicare and Medicaid Services (CMS) fee schedule was used to determine the costs of these services.¹⁷

An average cost of relapse (\$4682) was derived by computing a weighted average of the cost of relapse by severity,¹⁸ weighted using relative incidence rates of severity types,^{19,20} and adjusted for inflation using 2008 figures from the US Department of Labor.²¹ An average cost of a one-step increase in disability (\$1788) was derived from a study of mean annual costs for MS patients in relation to their functional capacity.²²

Model Outputs

Four key metrics were used to highlight the study's results: 1) medical costs, defined as “the cost associated with the stated event rates of relapses and progression in steps of disability”; 2) cost of DMD therapy, defined as “the cost of DMD therapy reflecting the stated treatment persistence rate of 89.4%”; 3) medical sav-

ings, defined as “the direct medical costs (related to relapses and progression in steps of disability) not incurred as compared with no DMD treatment”; and 4) cost per relapse avoided, defined as “the primary model outcome” (Figure 1).⁶ To reiterate, the final measure of cost-effectiveness was defined as the cost per relapse avoided. Results for each metric and DMD are shown in Tables 4 and 5.

Model Assumptions

Some key assumptions were made in the study. First, the costs of treating or further investigating adverse effects related to DMDs (eg, injection-site reactions, flu-like symptoms) were not taken into account, largely because such effects are minor and easily treatable. Furthermore, if such effects seriously bother the patient, he or she is likely to discontinue therapy, and this discontinuation is already taken into account through the persistence rate. Second, all DMD effects on disability progression were taken into account regardless of their degree of statistical significance. Third, mortality and health plan membership rates were not accounted for, as the researchers assumed these to have similar consequences across all treatment groups. Finally, the presence and impact of neutralizing antibodies (NABs) were disregarded, as these are assumed to be inherent to the efficacy measures documented in each RCT.⁶

Conclusion

From their principal findings, the researchers concluded that the cost-effectiveness ranking of the DMDs analyzed (from most to least cost-effective according to each therapy's cost per relapse avoided) was as follows: 1) IFNβ-1a SC (\$80,589), 2) IFNβ-1b SC (\$87,061), 3) GA (\$88,310), and 4) IFNβ-1a IM (\$141,721). Assuming the accuracy of both 1) the relative risk reduc-

Generally:

$$= \frac{(\text{Medical costs} + \text{Cost of DMD therapy})}{(\text{No. of relapses without DMD therapy} - \text{No. of relapses with DMD therapy})}$$

For glatiramer acetate, discounted:

$$= \frac{(\$9,517.36 + \$49,095.28)}{(2.55 - 1.88)}$$

$$= \underline{\$87,481.55} \text{ discounted}$$

Figure 1. Cost per relapse avoided

DMD, disease-modifying drug.

*The five neurologists were not paid for their opinions. See Goldberg et al.'s Table 2, footnote (b), for more details.

Table 4. Results: discounted per patient clinical outcomes over 2 years

	GA	IFNβ-1a IM	IFNβ-1a SC	IFNβ-1b SC	No DMD treatment
Relapses	1.88	2.13	1.84	1.81	2.55
Relapses avoided ^a	0.66	0.42	0.74	0.70	—
EDSS steps	0.40	0.30	0.33	0.33	0.44
EDSS steps avoided ^b	0.05	0.15	0.12	0.11	—

Abbreviations: DMD, disease-modifying drug; EDSS, Expanded Disability Status Scale; GA, glatiramer acetate; IFNβ-1a, interferon beta-1a; IFNβ-1b, interferon beta-1b; IM, intramuscularly; SC, subcutaneously.

Source: Data from Goldberg et al.⁶

^aRelapses avoided = (number of relapses for no DMD treatment) – (number of relapses for placebo in DMD trial – number of relapses for DMD), reduced by 10.6% to account for an assumed persistence rate of 89.4%.⁶

^bEDSS steps avoided = (number of EDSS steps for no DMD treatment) – (% placebo patients progressing in DMD trial – % of DMD patients progressing), reduced by 10.6% to account for an assumed persistence rate of 89.4%.⁶

Table 5. Results: discounted per patient costs and savings over 2 years

	GA	IFNβ-1a IM	IFNβ-1a SC	IFNβ-1b SC	No DMD treatment
Medical cost for relapses and disease progression ^a	\$9537	\$10,513	\$9060	\$9231	\$12,733
Medical savings ^b	\$3196	\$2221	\$3673	\$3502	—
Cost of DMD therapy ^c	\$49,068	\$48,473	\$50,389	\$52,010	\$0
Total MS-related cost ^d	\$58,605	\$58,986	\$59,449	\$61,241	—
Cost per relapse avoided ^e	\$88,310	\$141,721	\$80,589	\$87,061	—

Abbreviations: DMD, disease-modifying drug; GA, glatiramer acetate; IFNβ-1a, interferon beta-1a; IFNβ-1b, interferon beta-1b; IM, intramuscularly; MS, multiple sclerosis; SC, subcutaneously.

Source: Data from Goldberg et al.⁶

^aMedical cost for relapses and disease progression = (number of relapses × average cost per relapse) + (number of EDSS steps × average cost per EDSS step).⁶

^bMedical savings = cost of disease with no DMD therapy (\$13,301) – medical cost of individual DMD.⁶

^cCost of DMD therapy = cost of DMD treatment ÷ cost of monitoring of adverse events for DMD (monthly monitoring cost of \$64.06 for glatiramer acetate and \$75.37 for the interferons).⁶

^dTotal MS-related cost = cost of DMD therapy + medical cost for relapses and disease progression.⁶

^eCost per relapse avoided = (medical cost + cost of DMD therapy) / (number of relapses avoided).⁶

tion in relapses and disease progressions over the 2-year period studied, and 2) the treatment costs and economic consequences in terms of their projections of actual outcomes, costs, and consequences, we can reasonably conclude that IFNβ-1a SC (Rebif) is the most cost-effective DMD of those studied.

Strengths and Weaknesses

The Goldberg et al. study has many notable strengths. First, the researchers carefully and precisely defined all inputs into their model. Furthermore, these inputs appear reasonable given the resources used and assumptions made. The study also focused on costs and clinical outcomes (ie, relapses and disability progression steps) rather than preference-based measures, such as quality-adjusted life-years (QALYs).

A notable weakness of the Goldberg et al. study is the researchers' treatment of the EDSS scale as continuous,

when in fact it is an ordinal rating scale ranging from 0 to 10, with half-point increments within the range of 1 to 10; larger values indicate worse disability. The continuity of the EDSS values used in the Goldberg et al. study is clearly evident in Table 4, in which EDSS steps realized and avoided are given as values lying on a continuous scale (eg, 0.40, 0.30, and 0.33—none belonging to the set of ordinal values).

Simulation Analysis of the Cost-Effectiveness of the Four First-Line Therapies

Overview

The Goldberg et al. study is worthy of further economic analysis. We aimed to derive a cost-effectiveness acceptability curve (CEAC) to serve as a graphical representation of the researchers' findings.

Data and Methods

We gathered all formulas, cost inputs, and average clinical outcome measures from the Goldberg et al. study and used them to build a series of linked Excel workbooks. In doing so, we created our own Excel-based model to simulate the cost-effectiveness of the four first-line DMDs over a relevant range of relapses avoided. Our purpose in performing this simulation was to derive a CEAC.

We first defined the relevant range of relapses avoided as a 95% confidence interval about the mean number of relapses avoided among the four therapies, with the range computed to be 0.34 to 0.92 relapses avoided about a mean number of relapses avoided of 0.63. From our simulated results, we then identified the relevant range of cost per relapse avoided ([medical costs + cost of DMD therapy]/relapses avoided, per Figure 1) as the maximum and minimum cost per relapse avoided corresponding to the lower and upper bounds, respectively, of the relevant range of relapses avoided. The resulting

CEAC, plotting the number of relapses avoided against the cost per relapse avoided, is displayed in Figure 2.

Discussion of Results

The mean numbers of relapses avoided as identified in the Goldberg et al. study are plotted on their respective curves. This CEAC enhances the researchers' work by offering a graphical interpretation of key findings. A few key inferences can be made from this graph. First, the slope of each DMD's curve is indicative of a mixed cost structure. Specifically, the slope is a direct function of the change in relapses and disability progression steps avoided; that is, as more relapses and disability progression steps are avoided, the cost per relapse avoided (and cost per disability progression step avoided) declines, since total MS-related costs (DMD therapy plus medical costs) are assumed to be fixed at all rates of relapse. We also assumed that the number of relapses avoided exists in fixed proportion to the number of disability progression steps avoided, and these proportions were easily derived from the study's principal findings (Tables 2 and 3).

Figure 2. Cost-effectiveness acceptability curve (CEAC)

Costs per MS relapse avoided over a 2-year period (costs and clinical outcomes discounted). IFNβ-1a, interferon beta-1a; IFNβ-1b, interferon beta-1b; IM, intramuscularly; SC, subcutaneously.

A second key finding depends on the assumption that the four first-line DMD therapies are equally effective in terms of preventing relapses. In this case, we consider the cost-conscious consumer—that consumer who rationally and wisely wishes to minimize the cost of therapy since all treatments are presumed equally effective. For this cost-conscious consumer, the optimal therapy is IFN β -1a IM (Avonex), the therapy plotted as the innermost curve (closest to the point at which the x and y axes intersect). In this instance, IFN β -1a IM would be equally effective as competing therapies in terms of avoiding relapses but would carry a lower cost to the patient for all numbers of relapses avoided over the identified relevant range. For this cost-conscious consumer, the ranking of most (1) to least (4) preferred DMD therapies is 1) IFN β -1a IM (Avonex), 2) GA (Copaxone), 3) IFN β -1a SC (Rebif), and 4) IFN β -1b SC (Betaseron).

A third key finding depends on the assumption that the four first-line DMD therapies are *not* equally effective in preventing relapses. In this case, we consider the cost-neutral consumer—that consumer who wishes to be treated with the most effective therapy (ie, the DMD offering the largest mean number of relapses avoided), regardless of how much the therapy costs. For the cost-neutral consumer, the optimal therapy is IFN β -1a SC (Rebif), and the ranking of most (1) to least (4) preferred DMD therapies is consistent with the principal conclusions of Goldberg et al.'s study: 1) IFN β -1a SC (Rebif), 2) IFN β -1b SC (Betaseron), 3) GA (Copaxone), and 4) IFN β -1a IM (Avonex).

PracticePoints

- Cost-effectiveness analyses are useful in countering the financial uncertainties and treatment efficacy concerns faced by people with MS and in selecting the most appropriate therapy for a given patient.
- People with MS may fall into one of two categories: 1) cost-conscious (priority given to cost minimization over treatment efficacy) or 2) cost-neutral (priority given to treatment efficacy over cost minimization).
- The ranking of the four primary disease-modifying drugs used in MS from most preferred to least preferred varies depending on the patient's perspective on cost.

Weaknesses

Because we used the Goldberg et al. summary data to construct our simulation, any assumptions and weaknesses inherent to their study carry over to ours. A previously mentioned weakness of the Goldberg et al. study is their treatment of the EDSS scale as continuous, whereas EDSS scores are in fact ordinal (rank-based) in nature. We also concede that not every consumer will fall into a strict “cost-conscious” (favoring low-cost treatments regardless of their relative effectiveness) or “cost-neutral” (favoring the most effective treatments regardless of their associated costs) category; in fact, some consumers will be somewhere in between. We expect clinical practitioners to readily recognize this reality and adjust their recommendations to patients accordingly.

Conclusion

Major Conclusions

We can draw a few major conclusions from our literature review and economic analysis. First, natalizumab has been found to be a more cost-effective therapy than the conventional first-line therapies such as interferons and GA. However, since natalizumab is a newer treatment option, safety concerns and side effects of the therapy are still under investigation. Second, we can conclude that IFN β -1a SC (Rebif) is the most cost-effective therapy of the first-line DMDs (IFN β -1a SC, Rebif; IFN β -1b SC, Betaseron; GA, Copaxone; and IFN β -1a IM, Avonex) based on the cost per relapse avoided, where cost inputs include the costs of the DMD, disease monitoring, relapse occurrence, and disability progression. Furthermore, if all DMDs were equally effective in terms of their ability to prevent relapses, a cost-conscious consumer would elect to use IFN β -1a IM (Avonex) while the cost-neutral consumer would opt for IFN β -1a SC (Rebif). These conclusions differ in the sense that a range of therapies were compared within each study; for example, we conducted an in-depth economic analysis of a study that exclusively examines the cost-effectiveness of first-line therapies and gives no consideration to newer treatment options such as natalizumab.

Future Research

Preliminary findings show natalizumab to be potentially the most cost-effective therapy for MS patients. However, insufficient consideration has been given to the safety of natalizumab; rather, efficacy and cost measures have been given priority. Once safety con-

cerns have been thoroughly identified and confirmed through clinical trials, the cost-effectiveness of natalizumab should then be compared with that of first-line therapies. In this case, a meaningful definition of cost-effectiveness must take into account the side effects and negative health consequences inherent to each therapy. Another area for future research is cost-effectiveness over an extended period of time (eg, 15–20 years). Most cost-effectiveness analyses available to date deal with a shorter period of time (eg, 2–3 years). Because many MS therapies have been introduced only within the last decade, measurement of cost-effectiveness over the long term has not been feasible.

Relevance of the Literature

Cost-effectiveness research derives its relevance from a growing awareness of rising health-care costs among patients, providers, and government authorities. President Obama has financed comparative effectiveness research initiatives designed to combat these rapidly escalating costs, particularly within the pharmaceutical industry. The effectiveness of MS therapies is continually being examined. Furthermore, cost-effectiveness can be defined in a variety of ways using different research models. As new treatment variations are introduced and stakeholders become increasingly aware of rising health-care costs, the number of cost-effectiveness analyses will increase. Ideally, comparative effectiveness research will serve its purpose in combating rising health-care costs, resulting in significant savings and positive health outcomes for patients. □

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