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Multiple sclerosis and disease-modifying therapies

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Over the past 18 years, treatments for multiple sclerosis (MS) called disease-modifying therapies (DMTs) have been developed. These therapies are designed to decrease the number of MS attacks, and to slow the progression of the disease. They have become a standard part of the current treatment for MS. There are different classes of the currently available DMTs: interferons, glatiramer acetate, natalizumab, and mitoxantrone. Although they are effective, these medications have significant side effects, and many are very expensive.

WHAT DID THE RESEARCHERS DO? The study by Noyes et al.¹ was designed to create a new model to examine the cost-effectiveness of DMTs for relapsing-remitting MS in the United States. Researchers used data from an ongoing survey that was sent to over 2,000 people in the United States with MS. Twice a year, participants were asked questions about health care utilization. In other words, they were asked about things like how often they saw a doctor, went to the hospital, or visited the emergency department. Once a year, the same group was asked questions about income, insurance, and their work situation.

The researchers examined over 800 of the surveys. Based on this, they estimated the cost of the person's health care. This included the number of hospital stays, outpatient treatments, emergency room visits, office visits, mental health visits, home health provider and home health aide visits, and laboratory and MRI studies. Since each hospital might have different charges for each procedure or tests, the authors used average Medicare reimbursements and published rates for home care to make an estimate of the overall cost of health care for MS.

Lost productivity costs were also measured. The authors estimated how much MS might cost the patient, including lost wages from unemployment, part-time labor, time off from school, and short-term absences from work or school because of MS. The lost wage and time off from school estimates were based on age- and gender-specific wages from the Bureau of Labor Statistics.

The study also measured the group's overall quality of life, and the number of attack-free years. They defined an attack as 24 or more hours in which new symp-

toms occur, or a worsening of the patient's existing symptoms. Dr. Noyes and colleagues used all of this information to review the cost-effectiveness of DMTs. They also estimated the cost-effectiveness if the DMTs were given early as compared to later in the disease (in other words, starting a treatment after the MS had already progressed to cause mild to moderate disability).

WHAT WERE THE RESULTS? The authors found that taking an MS DMT for 10 years yielded small gains. For example, untreated patients were estimated to go about 5 years without an attack. If a person were taking one DMT, the treated person went about 6 years without an attack. Essentially, patients gained about 1 year without MS symptoms.

The treatment for MS is expensive. The cost of treatment over a 10-year period was estimated to be about \$467,712 for people who were taking one DMT. This compares to about \$220,340 for a person who was on no DMT for their MS. When summarized, many factors went into the overall cost of treatment of MS. However, the cost of the medication, loss of productivity, inpatient admissions, and in-home nonmedical care accounted for over 90% of the costs. When they looked at the total costs (such as doctor's fees and hospital charges), the authors found that the cost of the medication was a big part of the overall cost. Comparing treatments, they found that all interferons had similar cost effectiveness. However, the cost of glatiramer acetate was significantly higher.

WHY IS THIS STUDY IMPORTANT? Based on their estimates, Dr. Noyes and colleagues said that the cost of DMTs for MS is much more expensive when compared to the costs of accepted treatments for other chronic illness. Since the cost of the drug was a large factor in the overall cost of medical treatment, Noyes proposed that if the cost of the drugs were lower, such as those in the United Kingdom, use of DMTs would be cost-effective. However, this would require a cost reduction of 67%.

REFERENCE

1. Noyes K, Bajorska A, Chappel A, et al. Cost-effectiveness of disease-modifying therapy for multiple sclerosis: a population-based study. *Neurology* 2011;77:355–363.

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About multiple sclerosis

WHAT IS MULTIPLE SCLEROSIS? Multiple sclerosis (MS) is an inflammatory disease that affects the CNS (the brain and spinal cord). It affects women about twice as often as men. It usually starts at age 30.

The cause of MS is unknown. However, there are several clues about how MS begins. For instance, MS occurs more often in people who live in northern latitudes. Some have proposed that northerners are exposed to an infection in childhood. The infection is probably mild, and the immune system forms antibodies to the cause of the infection (no one is certain, but it could be a bacteria or virus).

This is where things become very unclear. Sometime between childhood, when the infection occurs, and adulthood, when MS begins, the immune system becomes confused. The antibodies that it made to the infection that occurred in childhood begin attaching to a protein in our bodies. This protein is part of the coating of the nerve cells, and the body begins destroying the myelin coating. In other words, the body makes a mistake—it thinks that the protein is part of an infection, and tries to destroy it.

The myelin coating is important because it allows the nerve cells to send electrical signals very quickly from one place to another. When the myelin is destroyed, nerve cell signals travel much more slowly. This causes weakness, numbness, and other neurologic symptoms.

Another clue about MS is that it is more likely to occur in first-degree relatives (mother, father, brother, or sister) than in distant relatives or unrelated individuals. A total of 25% of identical twins, who have identical genetic makeup, develop MS. In comparison, only 2% of fraternal twins, whose genetic makeup is like a brother or sister, develop MS. In short, a person's genes may be at least partly responsible for how MS occurs.

Much research has been focused on looking at our genes, and how genes tell our immune system what to do. The genetic research in MS focuses on how our bodies are able to recognize foreign substances. For instance, in organ transplantation, the immune system may see the transplanted organ as “foreign” and “reject” it. Research into the genetics of MS may show how some people's bodies become “confused.”

This would help us to identify who is more likely to develop illnesses like MS, where the body attacks its own myelin.

Most people think MS is an illness that mostly affects white matter. Studies show that MS affects gray matter as well. When MS affects gray matter, the nerve cells die. Nerve cell death causes a decrease in the volume of the gray matter. A reduction in volume is called atrophy.

Years ago, before MRI, an autopsy might show atrophy. Today, MRI can identify atrophy in the living brain. Newer MRIs are able to detect subtle changes even more easily.

If MS primarily affects the white matter, why do nerve cells die? Some scientists believe that an attack on myelin also affects the axon. Some nerve cells cannot live without their axons. When a nerve cell dies due to axonal injury, it is called Wallerian degeneration.

Others have proposed that MS affects the nerve cell body directly. In other words, the nerve cell body is destroyed first. Which is correct? Is it the axon first, or is an attack on the cell body the beginning of what we call MS? The answer to this question could lead to a cure of this illness.

To complicate things further, there are several types of MS. In one, the symptoms come and go. In between the symptoms, the person may feel fine. This type of MS is called relapsing-remitting MS.

The other main type is called progressive MS. This type slowly worsens, resulting in a gradual loss of neurologic function. Some have observed that white matter is more involved in the relapsing-remitting type, while gray matter may be more involved in the gradually progressive form.

Are they separate illnesses? Do they overlap? The answers to these questions remain unclear.

FOR MORE INFORMATION

AAN Patients and Caregivers site: American Academy of Neurology

<http://patients.aan.com>

Multiple Sclerosis Association of America

<http://www.msassociation.org>

Multiple Sclerosis Foundation

<http://www.msfocus.org>

National Multiple Sclerosis Society

<http://www.nationalmssociety.org>

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