

When neurologist and patient disagree on reasonable risk: new challenges in prescribing for patients with multiple sclerosis

Norman J Kachuck

University of Southern California,
Keck School of Medicine,
Los Angeles, CA, USA

Abstract: New more powerful therapies for the treatment of multiple sclerosis may also confer a potential for unprecedented life-endangering side effects. How does a physician respond to a patient's request for a treatment the benefit of which cannot be clearly established as worth its risk? The current challenge with prescription of natalizumab (Tysabri[®], Biogen Idec) is used to illustrate how this conflict creates an opportunity to re-examine our goals as physicians and the nature of the physician–patient relationship. Understanding the physician's role in that partnership, and the ethical and psychological issues impacting on how reasonable risk is determined, can improve the neurologist's capacity to explicate such quandaries. Redefining what is required to mediate disagreement between doctors and patients about reasonable risk is at the heart of why many of us became physicians. However, such nuanced interpersonal dynamics of patient care can be neglected due to the time and resource pressures of our practices. These demands have increased the seductiveness of the efficiencies promoted by the trend toward the pseudo-objectification of evidence-based care, which has arguably monopolized the healing conversation often to the detriment of the shared narrative. We examine and attempt to reframe the fiduciary and biopsychosocial contretemps of the doctor and patient disagreeing on risk, emphasizing its humanistic, relational dimensions.

Keywords: multiple sclerosis, natalizumab, medical ethics, medical decision-making, patient-physician relationship

Introduction

Neurologists treating patients with multiple sclerosis (MS) have emerging therapy choices that offer potential improved benefit over non-treatment, and perhaps may be superior to previous options. New research promises to expand the armamentarium to include medications with novel mechanisms of actions and more tolerable routes of administration than frequent, self-injected therapy. Oral therapies and IV therapies with infrequent dosing requirements – albeit with risks not previously relevant to the MS therapy decision process – are available now or will become so in the near future.

The years since FDA approval of the beta-interferons (IFN-Beta 1a IM (Avonex[®]), IFN-Beta 1b (Betaseron[®], Extavia[®]), IFN-Beta 1a SQ (Rebif[®]), and glatiramer acetate (Copaxone[®]) may have lulled the MS community into a false sense of security, given the relatively low toxicity and modest side effect profiles of these so-called platform drugs. We are lulled no longer. The more recently approved natalizumab (Tysabri[®], Biogen Idec) and fingolimod (Gilenya[®], Novartis) have demonstrated what may be increased effectiveness in control of the disease compared to the previous platform therapies, using relapse rates, progression of disability, and MRI T2, T1, and Gd+ enhancement

Correspondence: Norm Kachuck
USC MS Center, 1520 San Pablo St,
#3000, Los Angeles, CA 90033, USA
Tel +1 818 753 9639
Fax +1 818 761 2346
Email nkachuck@usc.edu

lesions as outcome measures in controlled trials.¹⁻⁵ Though generally well tolerated, progressive multifocal leukoencephalopathy (PML), a currently untreatable viral infection of the brain that may cause severe disability or death, and other opportunistic infections, are associated with Tysabri use. Gilenya, recently FDA-approved for relapsing forms of MS, is associated with significant increased risk of herpesvirus-related primary and re-activation infections, along with bradyarrhythmias and ophthalmologic, dermatologic, hepatic, and pulmonary complications. In spite of these issues, Tysabri's once-monthly infusion schedule, and Gilenya's ease of use as an oral daily therapy, are compelling reasons for their being considered for patients with relapsing forms of MS. Other emergent therapies such as rituximab, ocrilizumab, alutuzumab, cladribine, and daclizumab may be associated with PML, extra-CNS toxicities, autoimmune diseases other than MS, as well as possible increased risks for opportunistic infections and secondary malignancies. Other drugs that may enter the market in the near future as oral therapies trade off minimized health risk for more modest efficacy claims. Doctors and patients alike are reasonably concerned about the potential for undue harm with the more powerful drugs, and with compromising benefit to minimize risk with the others. Even given these issues, patients may find the potential quality of life aspects of the new therapies compelling.

The choice to start, stop, or change a drug has multi-dimensional societal implications, for government oversight organizations and committees, healthcare insurers, managed care organizations, as well as at the point of contact in the clinic. A therapy's cost to, and value for, policy-makers and the healthcare market have increasingly become a part of the neurology treatment delivery equation. The existential question, however, beyond resource utilization and the greater good, is mostly confronted in the process of decision-making in the exam room between the patient and physician, and centers on what value-basis it is worth putting this particular patient's life at risk. That judgment requires in no small part a shared assessment of both known and unknown medical risks and benefits of the medication. And, as is well recognized, the benefits of choosing or changing therapy, beyond potential long-term medical outcomes and treatment success, hinge on patient satisfaction and compliance.

It is the aim of this essay to argue that the decision-making process must also navigate through the ways that the patient and the physician may collaborate in the process of recognizing and sharing not just the facts, but also the feelings and motivations that each of them, doctor and patient, brings to

risk assessment, and the iterative process of revisiting the decision as that patient's disease, and medical choices evolve.

In their 2009 *Annals of Neurology* editorial, Hauser and Johnston elucidated the issues facing those who must weigh the risks and benefits of higher risk MS therapy like Tysabri.⁶ They appealed to the doctor's capacity to practice the art of medicine when the choices are not clear-cut, and noted that awareness of the personal biases in fulfilling one's role as educator and expert are essential in helping patients as they consider and reconcile to the potential risks of a therapy. What does this process entail from the standpoint of concatenating objective and scientific evidence-based valuation, with the subjectivity inherent in the psychologically rich, meaningful, empathic, and compassionate communication of the doctor-patient encounter?

The case below exemplifies what may happen after the facts are known and shared to a reasonable and acceptable extent, all tests are performed and interpreted, the uncertainties expressed as numerators and denominators, and the options laid out – but no consensus can be established on how to proceed. The solutions then suggested are, essentially, how to reformulate the question being asked. I have written this essay as a neurologist reaching out to fellow physicians, but there is no intent to exclude any and all interested or relevant parties from the conversation.

Case vignette

Ms S is a 35-year-old married attorney with two children. She runs marathons, sometimes pushing her running stroller for miles during practice. Her six-year history of MS started with a mixed optic neuritis and hemi-lateral sensory loss that resolved to near normal. Her screening MRIs showed three brain lesions and one in the cervical cord. At her request, therapy was initiated at the clinically isolated syndrome (CIS) stage – a decision with which her doctor agreed, given her probable high risk for subsequent conversion to definite MS.^{7,8} She has required high dose steroids twice for worsening of symptoms in the same distribution, despite treatment with high-dose interferon with good compliance. Her neurologic disability, as measured using the Kurtzke Extended Disability Status Scale (EDSS), remains minimally abnormal at 2.0, with optic pallor and some unilateral nonrefractile reduction in visual acuity,⁹ along with the sensory loss on her dominant side.

Ms S reports that she has had no new neurologic symptoms since her last visit. Her exam has not changed appreciably and her MRIs have been stable until the most recent study, done for this visit, which shows one new 2 cm T2 lesion in

the left posterior parietal white matter. Her neurologist has told her that it does not unequivocally warrant a change in her therapy.

She returns in two weeks for a requested counseling visit. Ms S is aware of new therapies available on the market and in development that would replace her self-administered injections. She believes she will have improved treatment success and long-term quality of life if she switches to Tysabri, and requests that it be prescribed for her. She is aware of, and comfortable with the risks as described in the scientific and lay literature, package insert and assent, which she has assembled in a portfolio and refers to during her visits.

The neurologist's opinion is that it is not clear that the benefits of Tysabri's use in this case outweigh the rare chance of a serious adverse event. He considers burdening the patient with off-prints of important literature, having a nurse come in to reason with her, even referring her for counseling with the group's social worker or psychologist. As her physician, he knows that she is comfortable trusting her intuition after having researched a problem, talked it through, processed it and come to a decision. She is outspoken and commanding, emphatic, and sure of herself; discussions with her can be more like sparring with a courtroom adversary than like an expert with the supplicant patient. These personal qualities, and a capacity for research and self-advocacy, which she can value over and above the physician's expertise and opinion, have created tensions in her medical care. The physician is also aware that she shares her decision-making process with her younger spouse, a motocross daredevil who enjoys bungee jumping with her from bridges.

The physician realizes that applying some insights into the psychology of the decision-making process – both Ms. S's and the physician's – would contribute to managing the differences of opinion. The degree to which Ms S's ostensible comfort with risk outweighs the cautionary issues brought up with her, and has interpersonal and ethical implications. Ms S's request is not uncommon for neurologists to have to consider, and is increasingly being encountered in MS clinical practice. The physician emphasized with Ms S that it was critical for them both to value her way of arriving at her decisions, imbedded in that unique doctor-patient relationship. The physician suggested that exploring the patient's narrative, properly elucidated and clarified, could possibly suggest a solution to their disagreement. She agreed to this strategy.

In their subsequent discussions, Ms S realized – with the doctor's help – that the disagreement on risk was not just about the drug, or even the disease per se. The shared

dilemma offered an opportunity for the discussion to move to a deeper level of motivation and intent. They discovered that underlying the ostensible issue of drug risk was the existential dilemma of Ms S's desire to control her life, and reconcile that need with other critical needs, feelings, and desires that were perhaps more difficult to identify and manage. She became aware that this decision involved how she shared her life and values with others, and that the relational dynamics arising from such crises affected not just specific decisions such as the choice of her MS therapy, but also her capacity to deepen self understanding and insight.

The discussion turned to issues of the patient's sense of the vulnerability of her well-being, along with fears of loss of independence and power, her desire to have more children, the state of her marriage, the roles she played in her social constellations, attitudes about her employment, and her approach to psychological insight. The physician was able to reflect back to her how their shared approach to articulating these issues affected how Ms S's personal and medical choices were formed, as well as how she interacted with physicians and others in the process of establishing value and meaning. This allowed a mutual re-framing of the issues at hand, as well as a better understanding of the ways the doctor-patient relationship could facilitate and value such communication. This took several sessions, and referral to a clinical psychologist for co-management, during which time the decision to change treatment was postponed. At this time, she is off all medications in anticipation of another pregnancy, and the decision to start Tysabri will be revisited after this next child is born.

The special case of Tysabri

There are over-arching general principles to which this essay will subscribe. However, instead of propounding this or that manifesto in an abstract, top-down manner, our way to wisdom is from the bottom up, starting with the particulars of a real-life situation that has the usual welter of complexifying factors that are the norm in clinical practice. Prioritizing the uniqueness of the patient narrative, and the physician's ways of responding to it, are critical to the principles that are advocated.

In situations in which patients are doing poorly on platform therapy, escalation to a treatment with increased risk may be a reasonable option. Indeed, ongoing discovery of the occult immunopathology of the disease suggests that patients may benefit from more aggressive early treatment to prevent later disability.^{10,11} However, in situations such as profiled in our vignette of Ms S, the patient may be realizing

reasonable success with a first-line therapy at least according to our current assessment strategies. She is not toxic on her present therapy, nor is she noncompliant. In the clinical trial literature relevant to this case, even though Tysabri decreased MS-related disease activity very effectively when it was tested against placebo, it has yet to be tested in head-to-head trials comparing it to other available or emerging therapies. (Recall that the AFFIRM trial was a two arm trial with a placebo control group, and SENTINEL used the combination of Tysabri and Avonex compared to Avonex alone; there was no Tysabri-only cohort.) Tysabri has not been indicated by the FDA, nor universally empirically accepted as, a therapy to be given to patients who have not exhausted a platform therapy.^{12–14} Whether the new MRI lesion qualifies as evidence of inadequate treatment response is controversial and not currently understood.

Thus, we have little data to support an alternative therapy on the benefit side, and we cannot identify any mitigation of risk specific to her case that would support a safety-associated justification for change in therapy. Unless a zero tolerance policy is established for *any* new clinical or radiological activity due to MS as our threshold for adequate versus inadequate therapy, the presence of the new MR lesion is not necessarily connoting a loss of efficacy. As well, using present methods we have few ways of assessing an improvement in her treatment response on a riskier therapy. Measuring a potential benefit in such situations is problematic given the lack of sensitivity of our surrogate markers of the disease in clinical practice, and paucity of adequate long-term follow-up of patients on any MS therapy. There also may be unforeseen future risks that these immunosuppressive therapies portend, especially in young patients with long post-exposure life expectancies.

What risks would be deemed acceptable in this situation? If a medication offers a 1/10,000, or even a 1/1000 chance of possibly fatal complications, but an enhanced quality of life, would that be a tolerable risk? If patients are young and in good health, like Ms. S., do we expect them to take more risk, or less, than those who are older, or more disabled? One of the unspoken expectations many have allowed to creep into the risk-benefit process for MS is that the older or more disabled the patients, the less they putatively have to lose, and the more risk they can tolerate. The logic behind this is inadequate to support the thesis, given any real-life experience with patients who have complex and idiosyncratic ways of establishing reasonable risk. Heesen et al found that patients, regardless of their disability status, were significantly more likely than physicians to accept higher risks of PML, an opinion that could not be explained by risk calculation abilities or lack of

understanding.¹⁵ It is not surprising, given these findings, that the field of evidence-based metrics of healthcare outcomes has had to supply hypothetical values for estimating benefits for patients with multiple sclerosis to establish data based on quality of life years.¹⁶

Doctors are often risk-averse, and may look for reasons to affirm a psychologically (and medico-legally) safe position.^{15,17} However, if Tysabri resulted in a persistent and superior reduction of MS clinical and radiological activity over years, the incremental benefit might be worthwhile even for patients with few lesions and relatively benign disease. For Ms S, with her commitment to running, and personal and physical independence as major themes in her life, the relative benefit might allow her to preserve her activities for a longer duration, conferring significant improvement in quality of life.

Given the number of ways one might define the priorities in this process, it may be quite difficult for a physician to assess the potential benefits for an individual patient on *any* MS therapy. In the case of Tysabri, the situation is even more complex: the toxicity issue is a moving target. Surveillance and vigilance protocols for diagnosis and treatment of PML are still being developed. Up-to-date incidence numbers, and the consequences of the diagnosis, which may fall on a broad spectrum of resultant disease severity and outcomes after treatment, are not part of TOUCH™, the US registry associated with Tysabri's FDA-mandated Risk Evaluation and Mitigation Strategy (REMS),¹⁸ and as such are not considered to fall under research protocol reporting requirements. Thus, the timely dissemination and full explication and follow-up of serious adverse events, such as that required by participant protections in research, are not mandated duties for the sponsor or the physician. Arguments for the incorporation of research aims and oversight for such REMS programs have been made.¹⁹

Medical decision-making

When healthcare decisions incorporate some uncertainty (as most do), physicians and their patients engage in a shared risk-benefit analysis to determine the relative benefit of a course of action.²⁰ The physician may know (or needs to make an informed guess) about the relative risk associated with possible complications, eg, organotoxicity, the risk of PML, malignancy, or infection associated with a given medication. The physician may be biased by personal experience, as Hauser and Johnson point out,⁶ but ideally an attempt is made to imbed an opinion in the available research, reflecting the expert community's consensus. Hurst et al found that in facing ethically difficult decisions, the internists they surveyed sought to avoid conflict, obtain assistance, and protect the integrity of

their conscience and reputation as well as the integrity of the patient, but that these goals could be in conflict.²¹

It has yet to be established whether a comparable group of neurologists would accede to reaching out to external sources to help resolve ethical issues. Many consider themselves the reasonable arbiters of such conflicts. As well, many neurologists would disagree with this essay's contention that we need to work continuously on our biopsychosocial skill set, as we do in fulfilling CME requirements, or using the AAN's *Continuum* series, to help maintain our knowledge base about neurologic disease and therapy. Those holding this contrarian position are likely to look askance at any discussion of physician as "healer", and will argue that one should be more concerned about a grasp of the facts and demonstrated competence at the craft than these more intuitional issues.

Suffice it to say that physicians are not the first to come up against the tensions in the relation of fact to meaning, truth to value, logic to feeling, expertise to understanding, knowledge to wisdom, science to the humanities. In this process of practicing medicine, physicians are working with the inheritance of wisdom with which they have been gifted, as their guild has made its contributions to human health through the centuries.²² We as physicians can be justifiably proud of how medicine can imbed science's hypothesis-tested, generalizable knowledge in the ongoing process of making a society better able to satisfy its needs for "eudaemonia" (Plato's ideal for human flourishing). We also are accustomed to being accorded respect for how we apply our expertise to our encounters with life and death, as doctors with patients. But recently that hegemony is being questioned and even doubted. We come up against ethics panels and congressional oversight committees concerned about our capacity for decision-making and resolving conflicts of interest and commitment. We regularly encounter patients confident that they have a better idea about their health than their doctor, with data gleaned and opinions formed from the Internet, social networking, books, and alternative and nontraditional healthcare models. Many Americans are riding a sociopolitical wave of distrust for any institutional compromise of their individual rights. In this context, many physicians are taking a step back to try and understand how to help restore people's trust in their physicians to make the hard decisions on what is good healthcare.

How a physician responds to a patient request for a particular medication in this setting derives from how one understands both the goals of medicine and the nature of the physician-patient relationship. There is a psychological and sociological context in which such conversations take place,

which requires the physician's response to be conditioned by the issues arising from this nexus. Verbalizing one's understanding of a patient-initiated desire to switch therapies upholds and empowers patients in their capacity as autonomous agents, and defines and strengthens their alliance with their doctor as well as with the family, friends, and advisors who make up their social support network. If we then weigh in with the facts and our expertise, and if the competent, nondelusional patient can agree that a reasonable process has been pursued how can there be a problem?

Applying models of the patient-physician relationship

The physician's role in the therapeutic alliance has been defined with the help of various models of interaction and transaction, and a given physician may vary the degree to which the models are utilized in different patients and situations.^{20,23} Table 1 itemizes Degner's continuum of five relational styles adopted in medical decision-making by patient preference.

Conventionally, physicians may see their role as that of: 1) a gatekeeper managing access to potentially beneficial therapies; 2) a dispenser of knowledge and treatments from the privileged perspective earned by training and experience; or 3) as a business person offering a service and commodity that includes access to reasonable medications for paying customers.²⁴⁻²⁶ Whether these roles exhaust the possible ways doctors relate to patients has been the subject of much conversation about humanistic, patient-centered medicine.²⁶⁻²⁹

The paternalism that may be invoked when engaging one's expertise and experience in such a decision-making process is our inheritance from the last few centuries of medical tradition. Several trends, sometimes running counter to one another, have allowed that hoary tradition of physician-hood to evolve. Notwithstanding the evolutionary effects of a resur-

Table 1 The control preferences statement set

Active roles

- A. I prefer to make the decision about which treatment I will receive. (Pure autonomy)
- B. I prefer to make the final decision about my treatment after seriously considering my doctor's opinion. (Informed choice)
- C. I prefer that my doctor and I share responsibility for deciding which treatment is best for me. (Shared decision making)

Passive roles

- D. I prefer that my doctor makes the final decision about which treatment will be used, but seriously considers my opinion. (Professional-as-agent)
- E. I prefer to leave all decisions regarding treatment to my doctor. (Paternalistic)

Note: Heeson et al⁴⁸ adapted from Degner et al 1997.

gent humanistic medicine and the biopsychosocial model of medicine, there is another rather subtler modifier, that is influencing how physicians think about their capacity to own the information. This blessing/curse has put a new face on the sharing of medical care, and that face is actually legion. It is now common practice to rely on “evidenced-based” standardized methods of diagnosing and treating medical problems, as published in guidelines and algorithms by respected and well-intentioned researchers, institutions, and organizations in and out of government. Managed care decision makers, and all of us who share the dream of scientific medicine for the public good, embrace these innovations.

But one can ask, at what cost is this process to the medical “moment” in which a doctor and a patient’s criteria for success must cohere? Recourse to evidence-based decision-making can depersonalize the care we deliver, and delegitimize the authority of physicians, from the most caring, compassionate, and nurturing to the most paternalistic. No one argues that in many ways the intent of these innovations is virtuous and is creating a more powerful, scientifically based medical practice. The cautionary point might be to realize and then cope with whatever impact this has on us as experts in this hybrid mechanic-as-shaman profession. When a patient such as that of our vignette has made it clear that she wishes the potential benefit of a therapy, and the algorithms guiding our work recommend against her doing so, can we be sure that the “scientific” process has this particular patient’s best interests in mind?

Sharing autonomy

The paternalistic approach is commonly contrasted with a partnership model that acknowledges autonomy and self-defensive needs for both partners. Theoretically, the physician-patient partnership allows the patient to feel comfortable expressing confidences and vulnerabilities, which can aid the physician in obtaining knowledge necessary for optimal medical care.¹⁷ Medical ethical codes have long recognized this inequality of control, and required that the physician-patient relationship aspire to the highest standards of virtuous conduct. Dating back to the Hippocratic Oath, by which physicians swore to act only for the “benefit of the sick, remaining free of all intentional injustice, of all mischief”, engaging with patients obliges physicians to act for the patient’s best interest, without intentional misconduct or causing harm to the patient.²⁵

As in our vignette, respect for autonomy may conflict with other principles generally upheld by the medical profession. When a proposed treatment poses an increased risk, a physician may feel that non-maleficence outweighs the duty

to respect patient autonomy. At what level of potential harm this concern is triggered is of course subject to interpretation. In situations involving modest/moderate risk, it might be worthwhile to facilitate patient self-determination. Looking to societal standards, many activities with associated risk are perceived as extreme, but within the bounds of appropriate behaviors. There are many otherwise sane citizens who regularly put themselves in harm’s way on double diamond downhill ski slopes, at the ends of bungee cords, and in sand-dune-leaping all terrain vehicles. Risk may be limited by rules or laws, eg, requiring helmets, or other safety measures – but citizens can and do choose to engage in risky activities without compromising their ability to contribute to the social good and the individual pursuit of happiness.

Following this tradition, the physician-patient relationship confers a duty on the physician to act as a guardian for the patient’s best interests, while assuming greater knowledge and experience in medical decisions, and an awareness of the autonomy accorded the physician as a person with expertise and authority in the professional role assumed in the relationship. This obligates the physician to prevent harm to the patient. For example, when patients ask for excessive narcotics, most physicians refuse, using the protection of the patient’s best interests as justification. In a partnership model, the physician and patient work together toward achieving a meaningful result, with the patient participating in decision-making and goal setting. Although not necessarily in conflict with a fiduciary relationship, a partnership model relies more on cooperation and less on the physician’s unilaterally determining the best course. The partnership model requires extremely high standards of interpersonal communication, as patient and physician work to establish mutually acceptable goals.³⁰

Conversely, it has been noted that, at the other end of the spectrum, when the final decision about medical care rests with the patient and the relevant evidence-based algorithm solely, it “can lead to a clinician-patient relationship based on contractual considerations rather than on trust”.²⁵ Given that the central tenet of modern medical practice asserts that physicians should respect the autonomy of the patient, it’s been opined that physicians can and should allow the patient to choose from among medically reasonable alternatives.²⁶ The ethical quandary arises when the physician and patient disagree on which options are “medically” reasonable.

Similarly, in their capacity as the provider end of the medical-industrial complex, a physician might readily agree to prescribe treatment that has a less-than-clear indication. For instance, an anti-depressant may be prescribed as a “quick fix” for the “blues” at a patient’s request. In such cases,

without the possibility of excessive harm, some discussion of risks and benefits might satisfy the physician's need for non-maleficence (and a means of reaching out to the patient) while still recognizing patient autonomy (although firm advice to pursue lifestyle changes and/or psychological counseling can be reinforced along the way).

In the case of medications with potential for more serious harm, this tactic may be inappropriate. By agreeing to prescribe, the physician implicitly takes on legal and moral responsibility for the choice of medication,³¹ even as the competent patient provides informed consent and willingly accepts the consequences of the decision. (Note: even a patient's diminished cognitive ability may not preclude the capacity to make reasonably informed medical decisions).⁴³

As in our case vignette, if the physician declines the patient's request, can that unduly compromise the patient's autonomy? If the physician acquiesces to a medically unnecessary request, can that unacceptably compromise the physician's autonomy and/or professional obligations? The physician may choose to refrain from prescribing Tysabri because of an unwillingness to accept the responsibility for potential harm to the patient. One should explain the reasoning behind that opinion and encourage dialog about the process. It is, of course, critical that there be clear documentation of this in the medical record. Nonetheless, no matter what the outcome, or whether anyone feels that the ethical obligations of justice, beneficence, or the respect for persons were or were not honored, there will be an effect of an ultimate disagreement on that physician's alliance with the patient, and that physician's subsequent capacity to act as that patient's caregiver.

Does a Tysabri prescription for a patient on alternative therapy constitute minimal, significantly increased, or excessive risk? This is not yet calculable for populations or for individuals. As we better understand MS, along with our ways of measuring its progress and the success of our interventions, this question's objective aspects should move closer to a consensus answer. Other uncertainties will undoubtedly take their place. Physicians will always need to be able to negotiate reasonable approaches with each of their patients in the face of great uncertainty, while trying to acknowledge and protect both the patient's autonomy and their own. How will the application of our "physician's art" likely resolve the case vignette's conundrum?

Working out the details of managing disagreement on risk

There is little in the available literature to guide physicians in helping their patients find a clear path on tailoring an MS

therapy to the individual case. Uncertainties abound concerning the long-term relevance of the primary and secondary endpoints in pivotal clinical trials. And though the age of personalized medicine is dawning, there are as yet no surrogate markers that will prospectively identify which drug is right for a given patient, or tests that predict success after treatments are started, or even short-term ways of knowing if that success will come at all. Little is known about the long-term safety and efficacy of the newer choices, or what restrictions on subsequent alternatives may be relevant if that therapy is in turn deemed suboptimal.

Not that the MS community does not recognize ethical and communication challenges in the therapy decision-making process. Christoph Heesen's group has studied how patients in their MS clinic make medical decisions.^{11,15,32,33} They document how the various educational and evaluative strategies used to establish benefit and risk by patients and doctors differ. They have also have established innovative tools to allow the two parties' processes to conform to one another's expectations, including studies on the risk/benefit analysis for the use of Tysabri.¹⁵ An impressive literature has accrued concerning the medical decision-making process utilizing qualitative as well as quantitative data.^{21,29,30,34}

Where the risk analysis performed by a doctor and an MS patient verge on our vignette's conundrum has been less discussed since Augustus Rose wrote of his task as an MS doctor in 1980.³⁵⁻³⁸ As a community of physicians and clinical researchers working with patients and families coping with this devastating disease, we have remained mostly mute on how one's practice might accommodate the process of such relational decision-making. Indeed, this subject was omitted entirely from a recent summation of ethical challenges for MS physicians.³⁹ Unless it is a one-page apologia or pithy observation that fits neatly in between the scientific papers in our favorite journals, such conversation is often consigned to a humanities journal where, in its obscurity, it will not prey on practicing physicians' consciences.

Even if one "girds loins" and pursues the beast into the forbidden garden of non-neuroscience literature, it rapidly becomes clear that the writers publishing in these genres have often failed to bridge the gap between their laudable academic pursuits and the way those ideas can be communicated effectively to those enmeshed in the day-to-day process of doctoring. Although there has been much opined, thought through, and published in the general subjects of physician-patient relations, medical decision-making, and the ethical aspects of these vital portions of our lives as physicians, we,

the MS physicians, are, judging from our literature, apparently not participating in the conversation.

The reasons, to be sure, will be many. Beyond the sequestration-of-published-conversation issue, we will need to admit that, however much the subject may prick our interest, clinical neurologists don't pursue it because they are busy, stressed, and barely can get through the primary professional journals, let alone go searching Entrez PubMed to satisfy ethical, psychological, and spiritual yearnings. Perhaps we believe that, as mature, well-trained professionals, our days of learning how to talk and listen to patients are over, and no further work need be done to help us hold up our end of the physician-patient relationship. The days when one passionately read through books on the art of medicine and the nature of suffering may seem to be far-off history (with apologies to Eric Cassell). And even if the foray is made, very few authors one discovers – let alone we readers – can articulate how to move the conversation from a study-finding's hyper-specificity, or over-generalized abstractions, to the life-wrenching, painful, complex, messy circumstances that surface in the exam room.

Most critically, beyond what appears in our literature, might we physicians confess that our conversations about practice, when focused on what we do as doctors, neglect how we cope with the subjective, the feeling-states that are part of our internal process as we work with patients, along with those in the patient that feed their ways of working with us? When the focus of the disagreement about risks seems to have moved beyond the data, beyond the facts and any quantitative, evaluable, literature-supported aspects of the decision-making, how do we elucidate and work out the psychological and interpersonal issues efficiently, empathically, and successfully? How can we imagine that this discussion is something we know how to do well instinctively, and, unlike our capacity to assess and analyze data, is a skill that doesn't require practice and improvement?

The problem not re-defined but its depth reconsidered – a short aside

This essay does not aim at redefining the patient-physician relationship anew; nor does it aspire to establish an algorithm for problem-solving the biopsychosocial dimensions of this or that MS healthcare conundrum. It speaks to “ethical behavior”, as if this idea's realization in medical care could be defined in the same way as “demyelination” or “axonopathy”. One might wish for a one-size-fits-all formalization of “right conduct” in our roles as physicians, researchers, and educators. Of course, ethics are nothing like facts about tissues

and cells, or at least they bound a territory less amenable to reductionist explanations. Ethical behavior is not committed in isolation; it describes conduct performed in relation to an Other, in a complex context bounded by culture and language; and the enactor in this case, the physician, is only a part of the experiencing relational whole in which this behavior will be judged. However, when we hear the catch-words “ethics” or “moral behavior” nowadays, it is mostly in the context of bioethics, conversations on the use of stem cells, or end of life, or even closer to home, on our control of the flow of information and resources between us and the pharmaceutical industry. In the main, we may have failed to pay attention to the larger historical, sociopolitical, and economic context of our profession's fight to maintain its guild control over its work,²² and the moral imperatives that govern our contribution to the healing encounter. Our articulation of “ethics” problems has been mostly reactive in response to the issues of managing financial conflicts of interest, and as such, has forced us away from the issues concealed below.

Those publicly contentious issues are of course worthy of attention. However, this essay's concern is elsewhere, and in some ways deeper. In conversation with colleagues in private and academic practices, physicians in all stages and phases of their careers, several issues come up repeatedly that are critically relevant to the issue at hand, and as well seem to go to the heart of what we do as doctors. Neurologists in practice are seemingly under the gun to divide their clinic schedules into quarter-hours or less to increase volume. They complain that there is little time or wherewithal left to engage in that most-holy work of person-to-person caring in clinical practice. This is often left to a “physician extender”, a euphemism for someone less well trained and cheaper than a doctor, whose task is to actually listen to and talk with the patient. Many neurologists have relinquished an essential piece of what has defined what physicians and patients do together.

Given similar constraints on our time and energy by the exigencies of day to day duties, it appears that neurologists rarely discuss with their colleagues the complexities accompanying many medical decisions – scientific issues, of course, but also interpersonal and psychological. They complain that access to new information about care issues is limited by the time we spend seeing more and more patients, doing procedures, performing the required paperwork, not to mention complying with the limitations placed by our practice or institution on contacts with key opinion leaders, let alone medical liaisons and salespersons of drug companies.

It is the author's impression that the American MS neurologist, in academia or community office, in an HMO

or private practice, is isolated in ways that may compromise the practice of good medicine – the capacity to have the time and energy to listen; to think; to express and consider; to share and reflect, and reframe issues that arise in the practice of working up close with the suffering and fearful; and to learn and process that learning intellectually, critically, and emotionally. That is what this essay is in essence conveying, and why this larger perspective is so necessary in order to bring our issues into correct focus.

The medical and ethical benefits of considering psychological aspects of why physician and patient disagree

As Heesen et al point out, although patients often perceive their disease as more dangerous than their doctor does, their knowledge of the objective data is often subordinated to what are labeled “other factors” – biopsychosocial nuances – in the decision process.³² What one might thus infer is that being alert to the psychological issues impacting on how patients arrive at certain notions and attitudes can profoundly improve a physician’s capacity to help resolve the ethical quandaries that healthcare can present. An evaluative instrument, developed to address personal attitude, normative belief, and control beliefs contributing to decisional attitude, has been presented at ECTRIMS 2010.⁴⁰ Further study of this process by the authors and their coworkers is planned (the AutoMS Project).

To the extent that physicians don’t consider themselves competent or possessed of the time or energy (or financial compensation) to incorporate such aspects of the healing encounter into their patient care, many opportunities to imbue medical decision-making in a shared defining of goals can be missed or under-utilized. A treatment is a failure if the patient’s life isn’t improved by it, no matter how effective it may be by some objective measure. And that improvement can very much be “in the eye of the beholder”. To miss the necessity of reconciling different opinions on what constitutes “quality of life” is to lose sight of the goals of medical therapy – namely, human flourishing.

In our vignette, Ms S’s age, her desire to have more children, her employment, her marriage, her roles in various social constellations, and her approach to understanding herself and others, will all affect how she interacts with physicians, and how her medical choices are formed. Making a foray into the psychodynamics of the patient’s decision-making illuminates how much Ms S’s approach to

life taps into traits and behaviors that may be incongruous as they persist from previous phases of her life, or are reflections of significant unresolved internal (intrapsychic) and external (social, interpersonal) conflicts that are finding expression in this disagreement. It allows us to ask, is she using a decision-making process that worked well for a single woman in her 20s, but is inappropriate now that she is a married mother? Does this strategy reflect her inability to grapple with the facts of her mortality and its consequences to those who depend on her? And how is her relationship with her husband, family, children, her own parents, being reflected in this process, and how much is the physician obliged to consider these issues with her as differences in opinion about risk become clear? Why does she, perhaps, want to oppose or conflict with her physician, and how does this figure into her psychology and capacity to make decisions that truly reflect her best interests? And, most importantly, how can such insights allow the physician to re-approach the patient with a reframing of the issues at hand, and allow the doctor–patient partnership to use the opportunity to better understand itself and the values it embodies? Who pursues these issues with her, and how important is it to work through such difficult material before establishing the decision point regarding this treatment option? The physician’s awareness of the patient’s goals and desires beyond her medication choices, and the capacity to help the patient understand herself better, can improve insight into the how’s and why’s of her choices, and lead to clearer and more productive communication and relational decision-making.

Thinking about the psychological forces that motivate both the patient and physician provides an additional role for the latter in the decision-making process. This sensibility is the capacity in which the physician serves as a healer interacting with a person, an interaction that can be perceived from a larger, more holistic, subtle, and complex view of the healthcare dyad of physician and patient.⁴¹ Francis Peabody’s 1927 “secret of good patient care is caring for the patient”⁴² is one of those pearls of wisdom that might be emblazoned on our white coats the way the motto “To protect and to serve” is on every police car in Los Angeles. Technological innovations and decision trees to the contrary, this essay’s position is that medical “caring” isn’t the algorithmic application of values to a fixed set of variables. Without making the judgment excessively harsh on the necessary accrual of scientific information in healthcare, every physician should be considering the forces that make the work seem like an evidence-based medical decision-making Turing machine.

We know implicitly, but occasionally need to be reminded explicitly, that the “right” choice for a given patient, in a particular setting at a particular time in that life, is not necessarily mandated by the literature, or a decision-tree, or even by the physician’s experience with other patients.

In this light, the ethical approach to understanding the process of establishing risk and benefit for a given patient may be illuminated by understanding what conflicts and commitments, beliefs and expectations, fears and hopes, are operative in the patient’s psyche, and which may be driving opinions in decision-making. That may be a tall enough order for most of us to consider our psychological dues paid. But, alas, relational work goes both ways. In order to accomplish the task of bringing such insights back to the relationship, and reframing the decision process for the patient as it may be informed by such dynamics, the physician will likely try to understand what is driving *him/her-self* in the relationship with this particular patient, and how such issues of projection, transference, counter-transference, trust, and emotional connectedness prioritize and value what is at stake in moving beyond the immediate disagreement.

Carl Schneider points out that the personal bond that once existed between doctors and patients, based on trust, faith in expertise, and a soul-to-soul connection of one with the other, has been shriven by the quest to allow patients autonomy and contractual rights. He even goes so far as to say that rights have replaced trust in the bioethicist’s imprint of necessary impersonality on the present medical service industry.²⁶ Trust misplaced is trust betrayed, and one must earn the respect and share the value of that trust with those who create the relationship defined by it. The whole literature on medical professionalism attests to our interest in keeping these issues alive and controversial.^{26,28,31}

On the other hand, there are those in our midst who cringe at the thought of imputing a moral aspect to professionalism in medicine, and question whether it plays a role in establishing competency.⁴⁴ To this skeptical audience, we can counsel that the work of diagnosing and treating diseases of the nervous system, the most complex and adaptive system of the body, embodying the organ of individuality, identity, awareness, psyche, and selfhood in addition to its manifesting of the disease process, should give us pause every time a decision based on population data is conferred on an individual case, and that individual balks at regressing to the mean of the grouping which supposedly defines him or her.

Making this reframing process more about the process of caring than casuistry contextualizes the issues in the relationship of the involved parties, and as such makes the

ethical issue less about the drug or its risks and benefits. It is about how the meanings of things, the feelings, the personal and interpersonal power dynamics of a relationship, and the sharing and articulation of these critical values, become embodied in the roles being played in the decision process, and enrich – or potentially additionally wound – the lives of those involved.

Conclusion

The commitment physicians make to the health of their patients is not solely directed at a particular complaint, test result, or diagnosed disease, nor to a given drug or any other intervention. Rather, as Steven Sergay so eloquently expressed in his 2009 American Academy of Neurology annual conference plenary address, there is a duty and obligation to imbue expertise, professional authority, opinion, and the physician’s personal needs in the act of realizing the full individuation and flourishing of the patient.⁴⁵ Without such consideration, physicians’ capacities to establish the correct recommendation and guidance for particular patients will be inadequate and may result in pain and injury to all concerned.

Good medical judgment requires not simply considering the obvious health risks attendant to a particular course of therapy, but also coming to understand one’s own, and the patient’s, values, goals, and unique personal and cultural circumstances brought to that therapy as its crucible. As it has been put in various contexts, it follows that doctors need to listen to patients, to acknowledge the power of the patient’s narrative, and doctors must realize the consequences of the biopsychosocial aspects of medical care.

But once the physician is doing these things, and even doing them well, there may still be a gaping discrepant chasm between doctor and patient, unless that information is processed in some way that brings into the equation your sense of who you are, your methods of using sensation, intuition, thinking, feeling, judging and perception, and those same characterologic, temperament and intelligence traits of the patient, together. This capacity to be confidently vulnerable as you engage with empathy allows the two of you to cross over the divide, and come up against the Other. How do you know how to manage such interactions, and learn to better do so? Are you aware of, and able to work on, the psychological impact of such interactions on *yourself*, as well as on the dataset of your specialty area? And if these competencies are not in your skill set, can you still practice good medicine? What does your character, temperament, and intelligence allow you to comfortably provide in these

situations? What have we allowed our profession to become, if such goals are not among our key priorities?

Risk-benefit analysis, cost, and professional associations' manifestos of ethical standards for neurologic practice all merit consideration.^{46,47} Our competence as physicians relies on our ability to master the mechanics and information flow of our specialty. But situations such as the one profiled in this essay seem to require that physicians be aware of how they respond to the uniqueness of each of their physician-patient relationships, and be willing to explore ways in which the psychological and interpersonal dynamics influence ethical choices within them. Considering the range of reasons for physician burn-out as weaknesses in the financial aspects of the American medical market system, and evidence-based and population-based medical practice principles, have intruded on our autonomy in the doctor-patient relationship, would it be unreasonable to ask if some of that frustration is due to not being able to create and invest in the kind of interpersonal relationships with patients that ultimately feed the physician's soul as much as allow us to deliver excellent care?

Redefining what we do to mediate in cases such as the exemplar vignette of this essay goes to the heart of what many would like to reclaim as the real work that physicians came to their medical career expecting to perform, but have been increasingly denied the time, valuation, and even the professional expectation, of the moral authority and psychological strengths that are required to aspire to, and practice good medicine. Some of us are more willing to go down these roads than others, and that may bespeak a set of personal needs that we bring to our work that reflect what type of persons we are. And neurologists are not clinical psychologists. Neither are we psychiatrists, although the specialties are traditionally associated one with the other in their training and qualifying procedures. Some physicians are simply not going to enjoy or value the approach that is advocated in this essay. And that is an interesting fact that is worth exploring, in terms of the expectations that the neurological specialty has for the competencies of those who choose it. It may be that physicians who do not value an overtly psychological, or for that matter, a morally defensible, approach to neurology practice do a fine job in their work with patients. In the same light that society may consider how it can be moral without a shared religious basis of that morality, practicing medicine without articulating a psychologically-aware position on the "right conduct" of that work, is a question that merits further investigation.

Intelligent and competent physicians may ultimately reach different conclusions in clinical situations such as the one

described here. It is our challenge to establish how making such decisions within a wider and admittedly psychological contextual consideration of physician-patient interaction, facilitates a broader understanding of how the decision will affect the patient's life and health. It is this essay's thesis that the approach described here makes for better and more competent, compassionate doctoring, and perhaps, more fulfilled physicians. Attending to such a process of iterative reflection and examination and mutual articulation of the usually unspoken and unacknowledged, might allow physicians serving those who suffer from neurologic complaints and diseases, to improve, and enjoy, the care that embodies our duty to that patient, the community, and ourselves, in the pursuit of human health and well-being.

Notes

Portions of this essay were previously published as the ethical perspectives in neurology article for the Multiple Sclerosis issue of *Continuum: Lifelong Learning in Neurology* Oct 2010.⁴⁹

Disclosure

No conflicts of interest were declared in relation to this paper.

References

1. Kachuck NJ. Challenges and opportunities: what we are learning from the natalizumab experience. *Expert Rev Neurotherapeutics*. 2005;5: 605–615.
2. Cohen JA, Barkhof F, Comi G, et al. Oral fingolimod or intramuscular interferon for relapsing multiple sclerosis. *N Engl J Med*. 2010;362: 402–415.
3. Kappos L, Radue E-W, O'Connor P, et al. A placebo-controlled trial of oral fingolimod in relapsing multiple sclerosis. *N Engl J Med*. 2010;362: 387–401.
4. Rudick RA, Stuart WH, Calabresi PA, et al. Natalizumab plus interferon beta-1a for relapsing multiple sclerosis. *N Engl J Med*. 2006;354: 911–923.
5. Polman CH, O'Connor PW, Havrdova E, et al. A randomized, placebo-controlled trial of natalizumab for relapsing multiple sclerosis. *N Engl J Med*. 2006;354:899–910.
6. Hauser SL, Johnston SC. Balancing risk and reward: the question of natalizumab. *Ann Neurology*. 2009;66:A7–A8.
7. Frohman EF, Goodin SS, Calabresi PA, et al. The utility of MRI in suspected MS. Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology*. 2003;61:602–611.
8. Montalban X, Tintore M, Swanton J, et al. MRI criteria for MS in patients with clinically isolated syndromes. *Neurology*. 2010;74: 427–434.
9. Heesen C, Bohm J, Reich C, Kasper J, Goebel M, Gold SM. Patient perception of bodily functions in multiple sclerosis: gait and visual function are the most valuable. *Mult Scler*. 2008;14:988–991.
10. Dutta R, Trapp BD. Mechanisms of neuronal dysfunction and degeneration in multiple sclerosis. *Prog Neurobiol*. 2011;93:1–12.
11. Heesen C, Solari A, Giordano A, Kasper J, Köpke S. Decisions on multiple sclerosis immunotherapy: new treatment complexities urge patient engagement. *J Neurol Sci*. 2010 Oct 2. [Epub ahead of print].

12. Rudick RA, Stuart WH, Calabresi PA, et al. Natalizumab plus interferon beta-1a for relapsing multiple sclerosis. *N Engl J Med*. 2006;354:911–923.
13. Polman CH, O'Connor PW, Havrdova E, et al. A randomized, placebo-controlled trial of natalizumab for relapsing multiple sclerosis. *N Engl J Med*. 2006;354:899–910.
14. Hutchinson M, Kappos L, Calabresi PA, Confavreux C, Giovannoni G, Investigators AFFIRM and SENTINEL. The efficacy of natalizumab in patients with relapsing multiple sclerosis: subgroup analyses of AFFIRM and SENTINEL. *J Neurol*. 2009;256:405–415.
15. Heesen C, Kleiter I, Nguyen F, et al. Risk perception in natalizumab-treated multiple sclerosis patients and their neurologists. *Mult Scler*. 2010;16:1507–1512.
16. Wundes A, Brown T, Biene EJ, Coleman CI. Contribution of intangible costs to the economic burden of multiple sclerosis. *J Med Econ*. 2010;13:626–632.
17. Weng H-C. Does the physician's emotional intelligence matter? Impacts of the physician's emotional intelligence on the trust, patient-physician relationship, and satisfaction. *Health Care Manag Rev*. 2008;33:280–288.
18. Public Health Service. Tysabri risk minimization action plan: summary of TOUCH. Available at: <http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM107197.pdf>. Accessed March 15, 2011.
19. Kachuck N. *REMS, research, and regrets: when is a passive post-marketing registry insufficient for patient safety?* Los Angeles, CA: USC Keck School of Medicine; 2011.
20. Emanuel L, Emanuel J. Four models of the physician-patient relationship. *JAMA*. 1992;267:2221–2226.
21. Hurst SA, Hull SC, DuVal G, Danis M. How physicians face ethical difficulties: a qualitative analysis. *J Med Ethics*. 2005;31:7–14.
22. Krause EA. *Death of the guilds: professions, states, and the advance of capitalism, 1930 to the present*. New Haven, CT: Yale University Press; 1996.
23. Charles C, Gafni A, Whelan T. Decision-making in the physician/patient encounter: revisiting the shared treatment decision-making model. *Soc Sci Med*. 1999;49:651–661.
24. Brennan T; Foundation Project of the ABIM, Foundation ACP-ASIM, Medicine European Federation of Internal. Medical professionalism in the new millennium: a physician charter. *Ann Intern Med*. 2002;136:243–246.
25. Spencer E. Professional ethics. In: Fletcher JC, Boyle R, editors. *Introduction to clinical ethics*. 2nd ed. Hagerstown, MD: University Publishing Group; 1997.
26. Schneider CE. *The practice of autonomy: patients, doctors, and medical decisions*. New York City: Oxford Univ Press; 1998.
27. Engel GL. The need for a new medical model: a challenge for biomedicine. *Science*. 1977;196:129–136.
28. Ludmerer KM. *Learning to heal: the development of American medical education*. Baltimore, MD: Johns Hopkins University Press; 1985.
29. Parascandola M, Hawkins J, Danis M. Patient autonomy and the challenge of clinical uncertainty. *Kennedy Inst Ethics J*. 2002;12:245–264.
30. Caldicott C, Danis M. Medical ethics contributes to clinical management: teaching medical student to engage patients as moral agents. *Med Educ*. 2009;43:283–289.
31. Pellegrino ED. The medical profession as a moral community. *Bull NY Acad Med*. 1990;66:221–232.
32. Heesen C, Kasper J, Köpke S, Richter T, Segal J, Mühlhauser I. Informed shared decision making in multiple sclerosis—inevitable or impossible? *J Neurol Sci*. 2007;259:109–117.
33. Kasper J, Köpke S, Mühlhauser I, Nübling M, Heesen C. Informed shared decision making about immunotherapy for patients with multiple sclerosis (ISDIMS): a randomized controlled trial. *Eur J Neurol*. 2008;15:1345–1352.
34. Redelmeier D, Shafir E. Medical decision making in situations that offer multiple alternatives. *JAMA*. 1995;278:302–305.
35. Rose A. Long-term care of patients with multiple sclerosis: a neurologist's perspective. *Neurology*. 1980;30:59–60.
36. Burnfield A. Doctor-patient dilemmas in multiple sclerosis. *J Med Ethics*. 1984;10:21–26.
37. Leino-Klipi H, Katajisto J. Elements of empowerment and MS patients. *J Neurosci Nurs*. 1998;30:116–123.
38. Nelson RF. Ethical issues in multiple sclerosis. *Semin Neurol*. 1997;17:227–234.
39. Hohlfeld R. Review: 'Gimme five': future challenges in multiple sclerosis. ECTRIMS Lecture 2009. *Mult Scler*. 2010;16:3–14.
40. Kasper J, Köpke S, Heesen C. Analysing immunotherapy choices using the theory of planned behavior. ECTRIMS 2010: Gothenburg, Sweden; 2010:S167.
41. Engel GL. The clinical application of the biopsychosocial model. *Am J Psychiatry* 1980;137:535–544.
42. Peabody RW. The care of the patient. *JAMA*. 1927;88:877–882.
43. Marewski J, Gassmaier W, Gigerenzer G. Good judgments do not require complex cognition. *Cogn Process*. 2010;11:103–121.
44. Stossel TP. Response to AMA's Council on ethical and judicial affairs draft report on "ethical guidance for physicians and the profession with respect to industry support for professional education in medicine". Available at: <http://www.medscape.com/viewarticle/575760>. Accessed March 14, 2011.
45. Sergay SM. Doctoring 2009: embracing the challenge. *Neurology*. 2009;73:1234–1239.
46. American Academy of Neurology. AAN Code of Conduct. Available at: <http://www.aan.com/go/about/ethics/conduct>. Accessed March 14, 2011.
47. American Medical Association. Principles of medical ethics. Available at: <http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/principles-medical-ethics.shtml>. Accessed March 14, 2011.
48. Heesen C, Kasper J, Segal J, Köpke S, Mühlhauser I. Decisional role preferences, risk knowledge and information interests in patients with multiple sclerosis. *Mult Scler*. 2004;10:643–650.
49. Conway J, Kachuck N. Ethical perspectives in neurology: ethical considerations of when doctors' and patients' attitudes differ on risk aversion. *Continuum: Lifelong Learning Neurol*. 2010;16:234–237.

Neuropsychiatric Disease and Treatment

Publish your work in this journal

Neuropsychiatric Disease and Treatment is an international, peer-reviewed journal of clinical therapeutics and pharmacology focusing on concise rapid reporting of clinical or pre-clinical studies on a range of neuropsychiatric and neurological disorders. This journal is indexed on PubMed Central, the 'PsycINFO' database and CAS, and is the official

Submit your manuscript here: <http://www.dovepress.com/neuropsychiatric-disease-and-treatment-journal>

Dovepress

journal of The International Neuropsychiatric Association (INA). The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.