Evaluating The Therapeutic Package for Diabetic Patients: The Whole Exceeds the Sum of Its Parts

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As health professionals treat patients under the Medicare Modernization Act, subtle but important changes in the experience of designing drug treatments for diabetes and related disorders are becoming apparent. The first change to affect providers is a clear rise in the frequency of requests for "prior authorization" of nonformulary prescription agents. This increase was a predicted effect of Medicare D, and its impact on physician work patterns and the costs of rendering care to diabetic patients is not at all welcome.[1] The increase in prior-authorization requests may also reflect a greater consumer awareness of insurance coverage for drugs and greater resistance to obtain drugs that are costly but not covered by insurance plans. As physicians are, in some way or another, profiled about the outcomes of the diabetes care they render ("pay-for-performance"), changes in physician prescribing behavior are predicted.[2,3] All of the recent and coming influences on providers and patients alike may lead to essential alterations in how both physicians and consumers view drugs that are prescribed for the treatment of individual patients.

The composite effects of these trends on prescribing behavior have not been fully assessed. However, there are many reasons to suggest that profound changes may be imminent in how physicians, patients, and pharmaceutical vendors interact over the selection of pharmacological agents and medical devices in the care of diabetic patients. Given the profound impact we are already seeing in the numbers of prior-authorization requests under Medicare D as an index of these coming changes, an assessment of these possible trends may be helpful to diabetes care providers.

Winds of Change

Experienced physicians know well what has not been clearly stated in the literature until recently: that the customary decision-making processes that are typically used to select treatments for diabetes and the influences used to encourage health providers to choose specific drugs can no longer be considered as they have in the past. Until now, providers have been encouraged to assess drugs individually, based on specific research studies, and to view data on the basis of how a drug, individually, is "in the best interests of the patient."[4] Now, this approach is being strongly challenged.

Changes in reimbursement for pharmacy benefits are exerting substantial influences on the dynamic between patients and providers as to whether a specific agent should or will be used. In addition, the studies used by drug companies to support their arguments for their products are often neither independent nor authoritative, as the companies suggest.[5] The data presented in these research studies may have little relevance to the effects of the drug on outcomes when used in a clinical setting. Issues such as cost and patient compliance are being shown to clearly outweigh possible differences in the efficacy of one drug versus another in the same treatment class.[2,6] These trends may alter the decision-making process regarding therapeutic design.

These trends may be especially important in diabetes. Patients with diabetes are often prescribed a polypharmacy.[7] This is not only because of the need to use a mixture of agents to treat diabetes, but also because so many have diabetes complications or associated problems, such as hypertension or hyperlipidemia. In addition, many patients have cardiac complications. All of these disorders raise the number, cost, and complexity of drug treatments for diabetic patients.[7,8]

Research studies in favor of specific treatments often fail to demonstrate the efficacy of the drug in clinical practice. For example, consider the literature in favor of the use of glitinides in the treatment of type 2 diabetes. Although there are studies that suggest these more expensive drugs may improve glycemic control in some clinical situations,[9,10] there are no studies available that directly compare the results, in large-scale clinical trials, of therapy with a glitinide versus an older and less expensive sulfonylurea. This does not necessarily mean that the newer therapies are not useful; however, it does mean that there is no proof that the outcomes of treatment with this class of diabetic agents will yield better clinical outcomes than older, less expensive sulfonylureas.

Clinical trials that demonstrate overall effectiveness on key outcomes when used in routine clinical settings may become the gold standard for judging specific agents for diabetes care. The Treat-to-Target Trial involving glargine insulin[11] and a smaller version of that study involving detemir insulin[12] may be examples. This is because, under

Medicare Modernization, there is a strong encouragement nationally to change physician reimbursement to a system in which payment for clinical services is based in part on whether measures of clinical status of patients with disorders such as diabetes meet specific goals.[13]

For diabetic patients, achieving the levels of hemoglobin A_{1c} (A1C) advocated by the American Diabetes Association[14] will be a probable outcome. However, many diabetic patients also have hypertension and hyperlipidemia. For patients with these comorbidities, specific outcomes will be required as well.[13] Thus, the relevance of these clinical goals to provider reimbursement will be much more intense in diabetic patients as a group than in most other patient populations. How individual drugs affect clinical outcomes for those disorders, when used in clinical settings, will become much more important.

Perhaps no recent article represents these trends better than a study in the April 2005 issue of the *American Journal of Managed Care*.[6] This study considered which factors influenced the likelihood that patients treated for hypercholesterolemia would achieve the clinical goals of the National Cholesterol Education Program (Adult Treatment Panel III).[15] It clearly demonstrated that the individual potency of specific cholesterol-lowering agents had no significant influence on the outcome of therapy. Instead, the cost of specific treatments to patients and the impression that treatment was relevant to the health status of patients (health beliefs model) were primary determinants of outcome. Cost has also been shown to be a primary determinant of outcome in elderly patients with diabetes in South Africa.[16]

Research Efficacy Versus Clinical Outcomes

Perhaps no single study better illustrates how these questions may function in assessing treatments for diabetes than the Diabetes Control and Complications Trial (DCCT).[17] When this study was initially reported, it was viewed as a substantial endorsement of the benefits of intensive insulin therapy.[18] Patients who were given multiple doses of insulin per day achieved significantly lower levels of A1C than patients who were given two shots of mixed insulin per day. However, the two groups were not completely matched in all respects other than the design of insulin therapy. The intensively treated group was also given the benefit of weekly (or more) contact with support personnel to encourage compliance to the treatment regimen. The control group met with health professionals every 3 months.

When the DCCT ended, some sites continued the protocol in an extension study, the DCCT Epidemiology of Diabetes Interventions and Complications (EDIC) trial.[19] However, in the EDIC trial, the weekly contact with the intensively treated patients ended. Without that support to compliance, A1C rose in the intensively treated group to levels statistically similar to those of the control group, despite the differences in insulin treatment. The difference was because of the lack of ongoing, intense communication to patients, which was provided weekly in the DCCT and was not in the EDIC.

In the EDIC trial, patients were served in the same manner as they would have been in any specialty clinical setting. Thus, strong reinforcement to comply may have counted much more in the success of therapy in these patients with type 1 diabetes than the design of insulin therapy itself. In this sense, the DCCT may have proved that vigorous reinforcements to patient compliance are much more important in the success of treatment of type 1 diabetes than the design of insulin therapy. Thus, in this watershed study, the research significance may not have adequately predicted clinical outcomes.

Treatment Design in the Era of Medicare D

Although the efficacy of individual agents remains an important consideration in therapeutic design, the literature suggests that in patients such as diabetic patients, other considerations are at least as important. Perhaps the first step in design is to consider the package of drugs that is prescribed for a specific patient. That package will function in a balance for both providers and patients in terms of the three other important influences on the success of treatment: cost, complexity, and fulfillment of patients' health beliefs.[20] The introduction of a costly or complex therapy may not only affect the success of treatment with that one drug, but may also influence how a patient uses the entire package of drugs.

Cost is a primary determinant of treatment success.[6,16] The simplicity of treatment may influence the success of therapy.[21,22] In general, dosing frequency and the simplicity of treatment for type 2 diabetes have been cited as primary determinants of outcome, more than the apparent efficacy of the drugs in research trials.[23]

There are no studies to describe the consequences of introducing a costly or more complex drug into an established treatment schedule; however, providers should keep in mind that there is no guarantee that patients will alter the prescribed treatment by omitting or changing the use of the newly prescribed drug. In our clinical experience, patients are likely to stop or alter other agents if they perceive that the new drug is very important to use. For example, many patients have limited budgets to spend on their monthly drug regimen. Just because an expensive new agent is added to that regimen does not mean that a given patient will increase expenditures on drugs to accommodate that therapeutic change. The patient might omit other drugs instead. This sort of dynamic in the success of drug treatment represents the sorts of considerations providers may face as time goes on in the era of Medicare D.

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