Insulin Therapy and Clinical Inertia:
The Costs for Patients and Health Systems

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Type 2 diabetes is a chronic, progressive metabolic disorder associated with obesity and physical inactivity.[1] Currently, 10.6 percent of people ages 20 and older in the United States have diabetes, but a recent report from the Centers for Disease Control and Prevention (CDC) predicted that by 2050, up to 1 in 3 Americans would have diabetes, most of them type 2.[2,3] As the authors of that study wrote, this is a "sobering picture of the future growth of diabetes." Even a best-case scenario showed 1 in 5 Americans with the disease, a prevalence "significantly worse" than the 1 in 10 Americans previously suggested. Given the staggeringly high costs of diabetes—more than $174 billion in 2007—and its high morbidity and mortality rates, these projections are, quite simply, frightening.[4]

Currently, the American Diabetes Association (ADA) and European Association for the Study of Diabetes (EASD) recommend that patients with Type 2 Diabetes Mellitus (T2DM) be treated with a combination of lifestyle changes and medications, including early initiation of insulin therapy, to attain and maintain an HbA_{1c} of <7 percent.[1] The American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE) recommend treating to an HbA_{1C} of ≤6.5 percent, using as many as three oral and/or injectable drugs before moving to insulin.[5] Unfortunately, there are no well-controlled randomized trials that rigorously establish which approach, if any, is preferable.

Although the professional societies have tried to develop guidelines and treatment algorithms that are as simple as possible, and while all are based on extensive clinical evidence, it is clear that patients in the United States and elsewhere with T2DM often do not receive guideline-recommended care.

Although glycemic levels in people with diabetes living in the United States have improved slightly since 1999, they are far from ideal. An analysis of data from the 2003-2004 National Health and Nutrition Examination Survey (NHANES) found that mean HbA_{1C} levels were 7.18 percent, which is significantly higher than recommended levels.[6] A more recent study using data from the 2005-2006 NHANES found that even as the prevalence of diabetes (Type 1 Diabetes Mellitus [T1DM] and T2DM) significantly increased, just 57.1 percent of patients achieved glycemic goals.[7]

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Thus, as the AACE noted in its 2007 guidelines for diabetes management, "Clearly, earlier and more aggressive application of available treatments and technologies is needed."[8]

Part of that aggressive approach to diabetes management involves initiating insulin therapy early. It is clear that early and maintained management of glucose levels can reduce the risk for microvascular and neuropathic complications in patients with T2DM. Additionally, when initiated early in the disease state, glucose control may have some benefit in preventing macrovascular complications.[1,9-12]

Patients who switched to insulin therapy from oral therapy, or for whom insulin is added to oral therapy, demonstrate significant improvements in quality of life and fewer physical complaints than prior to insulin initiation, primarily because of improvements in metabolic control.[13, 14]

There is also evidence that initiating insulin immediately upon diagnosis significantly improves glycemic control. In other words, the traditional step-based management algorithm increases the risk of complications in patients with T2DM.[15] When low doses of insulin are added to sulfonylurea therapy before such therapy fails completely, the combination can maintain lower HbA_{1C} levels than insulin alone and lead to more patients reaching target with no increased risk of weight gain or major hypoglycemia.[16]

Numerous studies also suggest that a short course of insulin therapy upon diagnosis may induce remission for up to two years in some patients while improving long-term glycemic control in others.[17-22]

There are also nonglycemic benefits to insulin therapy, including reduced inflammation and possible antiatherogenic effects that may potentially decrease morbidity and mortality following cardiovascular events.[23] This has not been definitively established, however.

Yet whether in the short term or long term, primary care physicians in this country wait too long to start their patients on insulin, contributing to an increased risk for complications as well as increased economic costs.[24] They tend to believe that insulin therapy should be delayed as long as possible.

The reason is clinical inertia.

Clinical Inertia Defined

Clinical inertia occurs when clinicians do not initiate or intensify therapy appropriately, even when the goals for managing a particular condition are well defined, effective therapies are widely available, and practice guidelines for each of these diseases has been disseminated extensively.[25] As Phillips et al noted in their 2005 seminal article on the topic, clinical inertia is "recognition of the problem, but failure to act."

Phillips et al suggest that clinical inertia is a problem of the healthcare professional and the healthcare system, and is unrelated to issues of patient access and adherence. It is not related to a lack of knowledge on the part of physicians, at least when it comes to diabetes. They suggest that clinical inertia results from overestimating the quality of care the physicians provide; the perception that the disease is controlled or that patient nonadherence is the reason for the lack of control; and a lack of education and training on implementing evidence-based medicine in daily practice. They also note that physicians have little education in treating to target. There may be a willingness to defer pharmacologic intervention based on the patient's stated intent to improve adherence to diet or exercise. Unfortunately this continues indefinitely as promised improvements never come to fruition.

There is significant evidence for clinical inertia in diabetes, particularly in the primary care setting, where most diabetes is managed. Among the evidence:

- When researchers evaluated clinical decision making over three years in a hospital-based diabetes clinic in Atlanta, they found that therapy was intensified just 36 percent of the time in patients for whom more intensive therapy was justified.[26]
- Ziemer et al compared glycemic control in patients attending a specialized diabetes clinic versus a primary care clinic, settings in which clinicians at both clinics had access to exactly the same medications: sulfonylureas, metformin, and insulin. Regardless of the type of therapy used, patients

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in the primary care clinic had higher glycemic levels. A major factor in the glycemic control difference was that fewer patients in the primary care clinic were receiving insulin.[27]

Physicians in the primary care clinic were significantly less likely to intensify therapy when random glucose levels were greater than 50 mg/dL above target (32 vs. 65 percent, P<0.0001), regardless of which therapy the patient was receiving. Of particular note is that patients already using insulin had their therapy intensified just 28 percent of the time, compared with 75 percent of the time for those seen in the specialty clinic.[28] Yet physicians who were more willing to intensify their patients' therapy had patients with lower HbA_{1C} levels (P<0.0001). A single episode of therapy intensification was associated with an average 0.7 percent reduction in HbA_{1C} levels.

"Overcoming clinical inertia is not likely to be easy, but it is essential if we are to substantially improve health outcomes for patients with diabetes." *—Berlowitz et al*

■ Berlowitz et al evaluated glycemic status and medications in 23,291 patients with diabetes in 13 Department of Veterans Affairs hospitals between 1997 and 1999. They found patient therapy was intensified just 9.8 percent of the time, despite the fact that 39 percent of patients had HbA_{1C} levels >8 percent. Even after an average of 11 visits per patient over 16 months of care, glycemic control among patients remained virtually unchanged. Yet, as expected, patients who received therapy intensification had the greatest improvement in control.[29]

The need to intensify therapy in patients with diabetes and uncontrolled HbA_{1C} levels is simple: If the HbA_{1C} level, a marker of glycemic control over several months, is not at goal, therapy should be changed. As Berlowitz et al noted: " ... Overcoming clinical inertia is not likely to be easy, but it is essential if we are to substantially improve health outcomes for patients with diabetes."

Barriers to Insulin Initiation

There are numerous barriers to insulin initiation on both the patient and physician sides. Patients may worry that they won't be able to manage insulin therapy on their own and fear the pain of injections and the potential for hypoglycemia. They may view their need for insulin as a personal failure; this is made worse when physicians "threaten" patients with having to use insulin if they don't eat right, exercise, lose weight, and take their oral medications. To some patients, moving to insulin suggests their disease has become much more serious, even if they don't feel any worse. Some patients worry that the insulin itself will make their disease worse, often because they saw the disease worsen in friends or relatives after beginning insulin. They don't understand the natural progression of T2DM, and attribute the adverse outcomes to the insulin treatment rather than the disease itself.[30, 31]

However, physicians have their own barriers to initiating insulin therapy. These include the time required to educate patients; a lack of confidence in clinician ability to properly dose insulin; concerns about unpleasant confrontations with patients; and beliefs that the patient is not competent to manage insulin properly. Providers also worry about hypoglycemia and weight gain and doubt that there are beneficial outcomes to insulin therapy in T2DM.[23] In fact, in one study only just over half of physicians and nurses agreed that insulin could have a positive impact on care.[24] There is also evidence that patient nonadherence contributes to clinical inertia; if physicians think that their patients won't use the medication as directed, they are less likely to prescribe it.[32]

In one survey of 505 primary care physicians, 80 percent thought their patients were afraid of insulin therapy, 72 percent said their patients would probably not accept a prescription for insulin therapy, and 66 percent said initiating insulin therapy was one of the most difficult areas of diabetes management.[33] Interestingly, the physicians said that the benefits of insulin therapy outweighed the risks and improved their patients' well-being.

In an interesting survey of 850 primary care physicians and diabetes specialists, the specialists reported no patient-related barriers to insulin initiation, whereas the primary care physicians said patient fears about insulin injections and their desire to give lifestyle changes and oral medications more time to work were major barriers.[32]

Overcoming Clinical Inertia

It is possible to overcome clinical inertia. First, highlighting the benefits of today's newer insulins, including simpler dosing algorithms, reduced risk of hypoglycemia and weight gain, and nearly painless delivery devices such as pens, is essential.[34-36] If primary care clinicians understand that these newer regimens can reduce the time required to educate patients and manage potential problems, they may be more willing to discuss the options with their patients. This is important, since the attitude of the physician directly impacts patient attitudes about therapy.[37,38]

It is also important to address physician misconceptions about insulin therapy. Among 550 primary care physicians in the United States surveyed about initiating insulin therapy in their patients, 40 percent said their patients wouldn't need insulin if they were more adherent to treatment recommendations, and a third thought that increased plasma insulin levels would increase cardiovascular risk.[33]

Practice-based interventions such as electronic or paper reminders to regularly check HbA_{1C} levels, flow charts, and face-to-face academic detailing have all demonstrated improved adherence to guideline-recommended care.[28, 39-42]

Ziemer et al found that internal medicine residents who received personalized feedback on their performance every two weeks with or without computerized reminders on patient-specific recommendations were more likely to intensify therapy in patients with diabetes than a control group ($P<0.001$). After three years, physicians who had received personalized feedback with or without computerized reminders demonstrated sustained improvement compared with control and the computerized reminder group only ($P<0.001$).[28]

Conclusion

As the obesity epidemic continues to grow in the United States, it is imperative from a public health and medical economics perspective that, if diabetes cannot be prevented, it be managed as well as possible to reduce the risk for complications.

Knowing when patients should begin insulin therapy is an important component of appropriate management, and one in which there is significant room for improvement in the primary care setting. Managed care organizations, by virtue of their focus on quality as well as cost, are in an optimal position to institute evidence-based interventions designed to improve glycemic control in their members with diabetes.

Current Guidelines for Glycemic Control in Patients with Type 2 Diabetes

- Perform the HbA_{1C} test at least two times a year in patients who meet treatment goals and have stable glycemic control and quarterly in patients who are not meeting glycemic goals.
- The goal to prevent microvascular complications is an HbA_{1C} <7 percent for most patients.
- Intervene at time of diagnosis with metformin and lifestyle changes.
- Continue augmenting therapy with additional agents, including early initiation of insulin therapy, to achieve and maintain recommended levels of glycemic control (HbA_{1C} <7 percent).

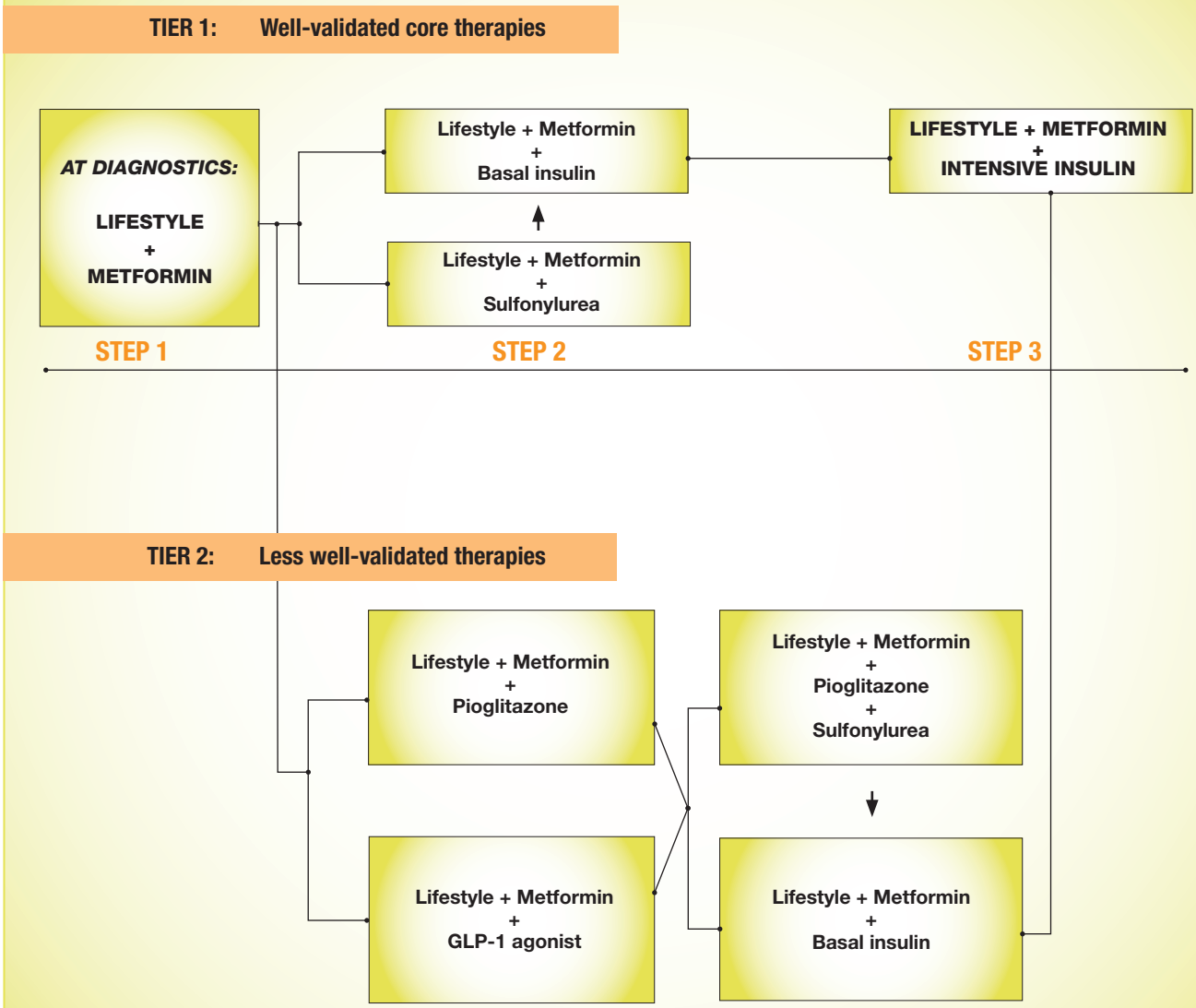
American Diabetes Association[1]

AACE/ACE Consensus Statement on the Treatment of Type 2 Diabetes Mellitus

- Achieve HbA_{1C} of 6.5 percent as primary goal, but customize according to individual patient considerations.
- Evaluate effectiveness of therapy every two to three months, including assessing HbA_{1C}.
- Rapid-acting insulin analogues are superior to regular human insulin and provide a better, safer alternative.
- Neutral protamine hagedorn (NPH) insulin is not recommended.
- Stratify therapy by HbA_{1C} level:
  - HbA_{1C} ≤7.5 percent, monotherapy may be sufficient.
  - HbA_{1C} 7.6 to 9 percent, dual therapy required.
  - HbA_{1C} >9 percent, triple therapy may be used inasymptomatic patients; initiate insulin therapy with or without oral agents in patients who are symptomatic or failed triple therapy.

American Association of Clinical Endocrinologists/ American College of Endocrinology[8]

Fig. 1 ADA AND EASD CONSENSUS ALGORITHM FOR INITIATION AND ADJUSTMENT OF THERAPY IN T2DM[43]



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