# Nonglycemic Targets in Diabetes

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**KEYWORDS**

• Diabetes guidelines • Diabetes treatment targets • Lipids • Hypertension
• Mental health • Nephropathy

**KEY POINTS**

- Blood pressure targets for all patients with diabetes are now less than 140/90 regardless of diabetic nephropathy. Geriatric guidelines concur with this target.
- All patients between 40 and 75 years of age should be considered for moderate- to high-intensity statin therapy. Patients older than 75 years should be preferentially treated with a statin if appropriate after lipid levels, risk, and longevity are considered and at doses that minimize side effects.
- Diabetes-related stress and depression has been identified as a major treatable factor that will improve outcomes.
- For medically obese patients with diabetes, there is increasing evidence that bariatric surgery decreases morbidity and mortality significantly and may be an appropriate treatment option.

## INTRODUCTION

Diabetes care and, subsequently, diabetes morbidity and mortality have changed dramatically in the last decades. In addition to new agents and methods for glycemic control, newer agents to control the progression of renal disease and knowledge about interventions to improve cardiovascular outcomes are now available. Importantly, we have learned much about the importance and primacy of diet, weight loss, exercise, and mental health as they affect the risk of and progression of diabetes, the last through the critical lens of compliance and self-care. We also have better

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information on outcomes demonstrating the importance of team care, with patients in the center of the team.

In the last 2 years, new guidelines for nonglycemic targets in diabetes include new hypertension guidelines, new lipid target and management guidelines, and new geriatric guidelines. Importantly, the advent of new guidelines and medications has decreased the recommendations for monitoring in some instances; for example, self-monitoring of blood glucose is now recommended only intermittently for patients on oral agents, and, in an era of cost-effective care, the new lipid guidelines recommend treating with fixed doses of medications rather than to a particular lipid target per se.

This article reviews the new guidelines, summarizes the evidence for nonglycemic targets, and provides practical clinical management recommendations, including some nontraditional areas, such as depression and team-management targets.

## HYPERTENSION AND RENAL DISEASE TARGETS

Diabetic renal disease commonly involves multiple primary and secondary pathologic processes that lead to a limited variety of clinical manifestations (**Box 1**). Genetic susceptibility to diabetic nephropathy, suggested by familial clustering of nephropathy,[1,2] is complex because of ill-defined pathophysiology and variable genetic expression.[3]

Classic diabetic nephropathy, with microalbuminuria progressing to macroalbuminuria and a decreased glomerular filtration rate (GFR), is common and easy to diagnose in type 1 diabetes but is responsible for less than 50% of cases of renal disease in type 2 diabetes. Renal biopsies from patients with type 2 diabetes (eg, hematuria, decreased GFR without significant albuminuria, absence of microvascular disease, and so forth) show changes consistent with diabetic nephropathy, other renal diseases, or a combination in roughly equal numbers.[4]

Indications for a renal biopsy in patients with diabetes and evidence of renal disease include the likelihood of other treatable renal disease and the patients' tolerance for any needed immunosuppressive therapy. Indications for renal biopsy include nephrotic range proteinuria in the absence of other microvascular disease or the combination of glomerular hematuria, significant proteinuria (>1 g/d), and renal impairment, particularly with clinical or serum biomarker evidence of diffuse immune-mediated diseases (antineutrophil cytoplasmic antibodies, double-stranded DNA).

The early diagnosis of diabetic nephropathy is even more problematic based as it is on the development of microalbuminuria, which is also associated with exercise, infections, and other renal diseases. These other causes of microalbuminuria probably explain transient microalbuminuria in 50% of the initial diagnoses of diabetic

**Box 1**
**Pathophysiology, anatomical pathology, and clinical manifestations of renal disease in patients with diabetes**

- Pathophysiology: activation of renin angiotensin aldosterone system; increased renal blood flow and intraglomerular pressure; deposition of glycosylated proteins into glomeruli, tubules, interstitium; secondary damage from hypertension, vascular disease and proteinuria
- Anatomical pathology: glomerular hypertrophy, nodular sclerosis, arteriolar hyalinosis, interstitial inflammation and fibrosis
- Clinical manifestations: albuminuria, deceased glomerular filtration rate, hematuria (less common)