



# Clinical decision making in diabetes: Use of glucagon-like peptide-1 (GLP-1) receptor agonists in clinical practice (where, when, and which?)—Introduction

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Diabetes management for outpatient accounts for millions of office encounters annually. Successful care for the patient with type 2 diabetes mellitus (T2DM) requires not only a focus on glucose management, but also comorbidities, including hypertension, dyslipidemia, and obesity.

Given the epidemic of T2DM, osteopathic physicians are seeing more patients with this condition and incurring more complex challenges. Primary care physicians are the front line in patient care. They are positioned to serve a pivotal role in managing obesity and diabetes. While coordinating appropriate medical treatment, osteopathic family physicians act as teachers and educated patients take a more proactive approach in their care.

Effective metabolic control has been shown to reduce the morbidity and mortality associated with T2DM.<sup>1-4</sup> However, a large proportion of patients are not achieving glycemic goals—less than 40% of patients are achieving the American Diabetes Association A1C goal of < 7%,<sup>5</sup> and only about 1 in 3 are achieving the American Association of Clinical Endocrinologists A1C goal of  $\leq 6.5\%$ .<sup>6</sup>

The key issues in the management of T2DM include early detection of problems, realistic goal setting, improved patient adherence, better knowledge and understanding of pharmacotherapeutic treatment options, and prompt intervention.<sup>16</sup> Successful treatment requires attention to the cardiometabolic effects of medications used to lower blood glucose and a comprehensive approach to the patient.<sup>15</sup>

Treatment for patients with T2DM should include lifestyle modification and should address other comorbidities for which the patient may be at risk.<sup>17</sup> Physicians must also be knowledgeable about the recommendations for glycemic goals and apply the treatment algorithms put forth by the American Diabetes Association/European Association for the Study of Diabetes<sup>18</sup> and the American Association of Clinical Endocrinologists/American College of Endocrinology in the management of patients afflicted with T2DM.<sup>14</sup>

Patients with T2DM have generally been treated similarly despite the fact that they may have underlying differences that could affect their therapeutic response.<sup>7</sup> For decades, the standard treatment paradigm has been “treat to fail” rather than “treat to succeed.” Typically, therapeutic strategies started with diet and exercise, with the slow and sequential addition of drugs.<sup>8</sup> Many patients and physicians have been frustrated with the limitations of currently available agents with regard to weight gain, hypoglycemia, and tolerability issues. Recent initiatives are calling for patient-specific and patient-oriented treatment approaches.<sup>7,9</sup> Primary care physicians must remain updated on the latest published diabetes literature and new treatment modalities to provide the greatest quality care for these increasingly complex patients.<sup>10</sup> Treatment recommendations for managing the hyperglycemia of T2DM continue to evolve.<sup>11-15</sup>

The availability of a new class of agents, the GLP-1 receptor agonists (GLP-1 RA), creates opportunities for family physicians to engage patients in discussion about their management.

This supplement reviews GLP-1 RAs, with not only their glycemic-lowering abilities, but also their pleiotropic effects on weight and cardiovascular risk factors. Additionally, a review of evidence from clinical trials supports their use as

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part of combination therapy. In closing, this supplement will help osteopathic family physicians and other healthcare providers develop strategies and discuss how to incorporate them successfully into patient care.

I am hopeful you find the read as enjoyable as it was to collaborate with experts in the preparation of this manuscript.

## References

1. EDIC. Sustained effect of intensive treatment of type 1 diabetes mellitus on development and progression of diabetic nephropathy: The Epidemiology of Diabetes Interventions and Complications (EDIC) study. *JAMA*. 2003;290:2159–2167
2. UKPDS. Intensive blood-glucose control with sulphonylurease or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. *Lancet*. 1998;352:837–853
3. Patel A, MacMahon S, Chalmers J, et al. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. *N Engl J Med*. 2008;358:2560–2572
4. Lachin JM, Genuth S, Nathan DM, Zinman B, Rutledge BN. Effect of glycemic exposure on the risk of microvascular complications in the diabetes control and complications trial—Revisited. *Diabetes*. 2008;57:995–1001
5. Hoerger TJ, Segel JE, Gregg EW, Saaddine JB. Is glycemic control improving in U.S. adults? *Diabetes Care*. 2008;31:81–86
6. AACE, State of diabetes in America: Striving for better control
7. Smith RJ, Nathan DM, Arslanian SA, Groop L, Rizza RA, Rotter JJ. Individualizing therapies in type 2 diabetes mellitus based on patient characteristics: What we know and what we need to know. *J Clin Endocrinol Metab*. 2010;95:1566–1574
8. Bolen SD, Bricker E, Samuels TA, et al. Factors associated with intensification of oral diabetes medications in primary care provider-patient dyads: A cohort study. *Diabetes Care*. 2009;32:25–31
9. Rodbard HW, Jellinger PS, Davidson JA, et al. Statement by an American Association of Clinical Endocrinologists/American College of Endocrinology consensus panel on type 2 diabetes mellitus: An algorithm for glycemic control. *Endocr Pract*. 2009;15:540–559
10. Sando KR, Barboza J, Willis C, Taylor J. Recent diabetes issues affecting the primary care clinician. *South Med J*. 2011;104:456–461
11. Nathan DM, Buse JB, Davidson MB, et al. Medical management of hyperglycemia in type 2 diabetes: A consensus algorithm for the initiation and adjustment of therapy: A consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care*. 2009;32:193–203
12. Rodbard HW, Jellinger PS. The American Association of Clinical Endocrinologists/American College of Endocrinology (AACE/ACE) algorithm for managing glycaemia in patients with type 2 diabetes mellitus: Comparison with the ADA/EASD algorithm. *Diabetologia*. 2010
13. Rodbard HW, Jellinger PS. Adding noninsulin antidiabetic drugs to metformin therapy for type 2 diabetes. *JAMA*. 2010;304:405–406. [author reply 406-407][author reply 406-407]
14. Rodbard HW, Jellinger PS, Davidson JA, et al. Statement by an American Association of Clinical Endocrinologists/American College of Endocrinology consensus panel on type 2 diabetes mellitus: An algorithm for glycemic control. *Endocr Pract*. 2009;15:540–559
15. Handelsman Y, Mechanick JI, Blonde L, et al. American Association of Clinical Endocrinologists Medical Guidelines for clinical practice for developing a diabetes mellitus comprehensive care plan: Executive summary. *Endocr Pract*. 2011;17:287–302
16. Zafar A, Davies M, Azhar A, Khunti K. Clinical inertia in management of T2DM. *Prim Care Diabetes*. 2010
17. Lavernia F. Improving glycemic control and cardiometabolic risk through integrated treatment plans. *J Am Osteopath Assoc*. 2010;110: eS13–eS19
18. Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of hyperglycemia in type 2 diabetes: A patient-centered approach: Position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care*. 2012;35:1364–1379