In Brief

Management of individuals with type 2 diabetes involves complex decision-making to attain good glycemic control. A personalized approach to the care of these individuals provides a unique management plan for each patient. This article reviews some of the important variables that require consideration for management of individuals with type 2 diabetes. We also provide a scoring scale to help clinicians make appropriate decisions regarding A1C targets while caring for these patients.

Personalized Diabetes Management: Moving from Algorithmic to Individualized Therapy

Savitha Subramanian, MD, and Irl B. Hirsch, MD

Individualization of therapy is a current trend in health care, particularly for chronic diseases, and is based on the hope that personalized approaches can ultimately result in improved outcomes. In type 2 diabetes, the availability of a variety of pharmacological therapies for blood glucose control has significantly increased the complexity involved in managing the condition. Algorithmic approaches have been utilized traditionally; however, such "one-size-fits-all" approaches are rigid, suboptimal, and seldom consider important variables involved in an individual's diabetes care.

A patient-centered and personalized approach to diabetes management was recently highlighted in a joint position statement of the American Diabetes Association and the European Association for the Study of Diabetes.[1] Similar guidelines have been developed by other organizations.[2,3] Although an individualized approach relaxes any therapeutic constraints on prescribing clinicians, it adds the burden of detecting nuances in treatment options without offering adequate guidance.[1] Nevertheless, a personalized approach could serve as a valuable tool in providing effective care and also helping to combat negative long-term outcomes. Herein, we attempt to address the various factors that should be considered when rendering individualized care to people with diabetes in the outpatient setting, using a scale to categorize individuals to help guide the intensity of glycemic goals, followed by illustrative cases.

What Does Personalized Care in Diabetes Mean?
The physical impact of type 2 diabetes is well known, and its management has substantial effects on individual and societal health, psychological well-being, and quality of life, as well as economic repercussions. Personalized care of type 2 diabetes presents as a "real-world" approach, providing care that is responsive to individuals' specific and unique needs, preferences, and values. Structured personalized care has been associated with reduced risks of myocardial infarction (MI) and diabetes-related end points in a 19-year registry.[4] In the care of patients with diabetes, an individualized approach is especially important because of the multitude of variables involved in decision-making, including therapeutic choices, disease duration, presence of complications and comorbid conditions, and economic factors.[5]

What Factors Do We Need to Consider in Personalized Diabetes Management?

Clinical characteristics

1. Patient age and life expectancy
Age is an important aspect of determining individual treatment goals. Type 2 diabetes now develops in younger individuals with increasing frequency. The younger a patient is, the longer the exposure to hyperglycemia, and the greater the risk of complications. Thus, younger patients may benefit from more strin-

gent A1C goals, especially given that they typically do not have comorbid conditions. Early intensive glycemic control significantly reduces the rates of complications over time, suggesting the presence of a "legacy effect."[6] This effect has also been termed "metabolic memory."[7] Benefit from early intensive control highlights the need for appropriate therapy as early as possible. On the other hand, patients who are older at diagnosis may have coexisting conditions and a shorter life expectancy and could warrant less stringent A1C goals.

2. Diabetes duration
Results of long-term follow-up from the U.K. Prospective Diabetes Study (UKPDS), which recruited patients with newly diagnosed type 2 diabetes, showed reduced micro- and macrovascular complications,[6] suggesting beneficial effects due to intensive early control. However, three large, multicenter studies involving patients with established type 2 diabetes (disease duration of 8–11 years), namely the Action to Control Cardiovascular Risk in Diabetes (ACCORD), Action in Diabetes and Vascular Disease: Pretrax and Diamicron Modified-release Control Evaluation (ADVANCE), and Veterans Affairs Diabetes Trial (VADT), did not show a protective effect of more intensive glycemic control against cardiovascular complications, suggesting that very intensive therapy may not be appropriate in this setting.[8–10]

3. Glycemic control history
Inadequate glucose control is usually the result of a combination of factors, including poor adherence, failure to understand the disease, and, as a consequence, delayed use of insulin for glycemic control. In these settings, it is important to address the cause of poor disease management. Aiming for an A1C as close to normal as possible with avoidance of hypoglycemia should be attempted. Additional diabetes education to enable patients to participate actively in their diabetes management is also helpful.

4. Comorbid conditions
The presence of other medical conditions can directly affect the nature and degree of glycemic control strategies implemented. Coexisting conditions may decrease life expectancy or result in debility and an increased risk of side effects from treatment modalities. In

such situations, a realistic approach would be to target the A1C to a less intensive range than in otherwise healthy individuals.

5. Vascular complications
Microvascular complications. Often, there is a considerable lag in diabetes detection, and microvascular complications can already be present at diagnosis. The presence of a microvascular complication in one organ suggests that other complications may also be present.[5] Chronic kidney disease may be present in its early stages in up to 40% of individuals with new or undiagnosed type 2 diabetes.[11] A low glomerular filtration rate (< 60 ml/min/1.73 m^2) is an independent risk factor for cardiovascular events and death in people with diabetes.[12]

Early, intensive glycemic control in patients with newly diagnosed type 2 diabetes resulted in a reduction in microvascular complications and a trend toward reduction of macrovascular complications.[6] Similarly, more intensive glycemic control in people with established type 2 diabetes and coexisting risk factors resulted in improvement of various microvascular outcomes. All four major trials (UKPDS, ACCORD, ADVANCE, and VADT) demonstrated improvement in microalbuminuria, and retinopathy outcomes improved in the ACCORD and UKPDS trials. These observations are particularly important because significant morbidity accompanies these complications.

Macrovascular complications. Cardiovascular complications contribute the major cause of morbidity and mortality in patients with diabetes. Diabetes is associated with a two- to fourfold increase in coronary disease risk.[13] The risk of cardiovascular disease also increases as the glomerular filtration rate declines in patients with diabetes.[11]

In the 10-year post-trial observational follow-up of the UKPDS, while the significant relative reduction in microvascular disease persisted, significant reductions in MI and all-cause mortality emerged in the intensively controlled group.[6] These benefits persisted many years after the initiation of the initial intervention (the so-called "legacy effect"). Although the underlying mechanism for this effect remains unclear, the presence of such a phenomenon emphasizes the importance of and need for early intensive therapy. However, as discussed earlier,

the ACCORD and ADVANCE trials evaluating near-normal glycemic control and its effects on cardiovascular events and mortality failed to show a reduction in cardiovascular events in the short term, with potential for harm in certain patients.[9,10] Nevertheless, these results should not be misinterpreted to diminish the importance of good glycemic control, and individualized A1C targets based on patient variables should be considered.

6. Risk of hypoglycemia
Severe hypoglycemia, requiring the assistance of another party, is a major impediment to good glycemic control and is a common accompaniment of intensive insulin therapy in diabetes, as observed in the large clinical trials. Two such trials in type 2 diabetes, ACCORD and ADVANCE, reported associations of higher mortality with hypoglycemia, but, thus far, no causality has been established.[9,10]

Hypoglycemia is more likely to be associated with cardiac ischemia.[14] Individuals who are susceptible to hypoglycemia are typically on intensive insulin therapy and have significant glycemic variability and possibly impaired renal function. In patients with autonomic neuropathy, there is increased risk of hypoglycemia unawareness and cardiac mortality. Increased rates of hypoglycemia have been reported in older individuals with cognitive impairment and dementia.[15] In these settings, less intensive A1C targets are considered acceptable.

Personal characteristics
Patients' preferences for treatment and health beliefs often play a large part in effective diabetes management. In the absence of symptoms, patients may not perceive their disease as serious enough to warrant taking medications. Treatment inertia can often arise from "psychological insulin resistance" or resistance to starting injectable therapies.[16] Complex medication regimens such as frequent dosing regimens that interfere with an individual's lifestyle are recognized barriers to adherence. Racial and ethnic factors have also been identified; the U.S. African-American and Hispanic populations with type 2 diabetes have higher A1C levels than Caucasians with diabetes.[17]

Psychosocioeconomic factors
Many of these issues are identifiable during a detailed clinic visit,

and the information obtained can be appropriately utilized to tailor therapy accordingly.

1. Support system

The importance of safety in the management of diabetes can never be overemphasized. Hypoglycemia is a major risk of therapy, particularly with intensive insulin regimens using basal-bolus therapy. Patients' living conditions and family support system should be adequately assessed when prescribing therapy. For example, intensive insulin therapy may not be appropriate for individuals who live alone with no routine contact with other individuals such as family, friends, or neighbors.

2. Psychological status

Depression is common in patients with diabetes.[18] Patients should be screened by their primary diabetes provider and appropriately referred. Patients may have difficulty coping with the stress of taking multiple daily injections and managing their activities of daily life. Negative stereotypes associated with type 2 diabetes can lead to psychological and behavioral issues in patients. Mitigating strategies such as education, counseling, and social support are essential.[19] Cognitive status assessment may uncover underlying mild cerebrovascular disease or Alzheimer's dementia.[5] Deterioration in glycemic control can be an important clue to a change in cognitive abilities.

3. Economic issues

The costs of treatment are prohibitive for many individuals. Newer agents for the treatment of diabetes, while effective, are expensive. Less expensive options can be utilized as effectively and should be considered when customizing therapy goals.

4. Quality of life

Quality of life (QOL) is a multidimensional factorial composed of an individual's subjective perception of physical, emotional, and social well-being. In the management of diabetes, QOL encompasses all the variables discussed above. It has been reported that improved A1C measures are associated with favorable mood.[20] Overall, QOL in patients with diabetes can be significantly improved by simple interventions such as education and counseling to improve coping skills.[21]

Elements of Diabetes Care Scoring Scale

Thus, establishing an individualized scoring system involves consideration of patients' clinical, personal, and psychosocioeconomic factors. We have loosely based the scale suggested here on the framework provided in a recent publication.[5] Clinical characteristics account for ~ 70% of the variables, and personal/psychosocioeconomic factors account for 30% in this scale, with the premise being that the presence of the latter is usually associated with significant clinical setbacks. In Table 1, we have used the variables to create the Elements of Diabetes Care Scale (EDCS), a scoring system that can be employed to individualize A1C targets for patients with type 2 diabetes. Although this scoring system is meant to be a general guide to help providers tailor therapy, clinical judgment should always be the first priority.

Setting Glycemic Targets

In Table 2, we show possible targets that can be utilized in patients based on clinical, personal, and psychosocioeconomic factors. In general, based on existing data, we suggest intensive control in younger individuals with a relatively recent onset of diabetes, with the goal of preventing microvascular complications in the long term. Older individuals with significant comorbidities, existing cardiovascular disease, and longstanding duration of diabetes should be subjected to a less intensive approach, where the main concern is hypoglycemia.

It is important to note that these set points are arbitrary and are an oversimplification of the complex decision-making process that is often involved in diabetes care. Patients may not fit typical profiles described in the scoring scale shown in Table 1. Furthermore, the A1C test itself has its own limitations and, in some patients, may not accurately reflect diabetes control.[22] Nevertheless, the EDCS method offers a crude guide to improving and individualizing care.

Conclusion

We have attempted here to incorporate the various elements involved in therapeutic decision-making in individuals with type 2 diabetes. A personalized approach to diabetes management can remove the constraints inherent in an algorithmic approach. Although the

EDCS is not meant to replace practitioners' clinical judgment, it can be helpful in providing physicians, other health care providers, and health care organizations with an efficient way to offer the best possible care on an individual basis for people with type 2 diabetes. Eventually, such a scale can be implemented for wider applicability, incorporated into electronic medical records, and further developed as a software application for smartphones, tablet computers, and other hand-held electronic devices.

Case Studies

Case 1: a younger individual with diabetes and no complications
Presentation. A 38-year-old male nurse with a 2-year history of type 2 diabetes presents for ongoing management of his condition. He is otherwise healthy and reports that he recently relocated to the area from the East Coast. His current therapeutic regimen includes metformin, 1 g twice daily. He is knowledgeable about his disease and has seen a diabetes educator recently.

He is on no other medications. There is no family history of premature coronary disease. His father, aged 64 years, has type 2 diabetes and hyperlipidemia, and his mother is healthy at age 60. He is a nonsmoker and lives with his wife and 3-year-old son. He reports that he is struggling to manage his diabetes with the pressures of his new job.

Examination reveals a well-built, well-nourished man with a blood pressure of 116/80 mmHg, weight of 201 lb, and BMI of 24 kg/m^2. The physical exam is otherwise unremarkable, and foot exam reveals preserved monofilament sensation. Laboratory test values reveal a creatinine of 0.8 mg/dl, urine microalbumin/creatinine < 1 mg/g, and A1C of 7.6%. How can this patient's care be tailored to suit him?

Discussion. Using the EDCS, this patient would score low on all variables; thus, the score would be < 5 on the scale. This is a younger individual with a short duration of diabetes and without comorbidities or existing vascular complications. He has some stressors, appears to have a good understanding of his disease, and has the support system required for managing this chronic condition. In this setting, an intensive glycemic control regimen aiming at an A1C

Table 1. Elements of Diabetes Care Scoring Scale

Factors	Score				
Clinical characteristics					
Life expectancy based on age in years	Long		Intermediate		Short
	Age < 40	40–55	56–65	65–79	> 80
	0	0.5	1	1.5	2
Duration of diabetes (years)	< 5		5–10	11–15	16–20
	0		1	2	3
Glycemic control history	Good		Fair		Poor/uncontrolled
	1		2		3
Comorbidities	None		Few or mild		Multiple or severe
	1		2		3
Vascular complications Microvascular	None		Early		Established
	0		1		2
Cardiovascular	0				3
Hypoglycemia risk	Low		Moderate		High
	1		2		3
Personal characteristics					
Attitudes and diabetes knowledge	Well versed/ up to date		Moderately knowledgeable		Lacking knowledge
	0		1		2
Psychosocioeconomic factors					
Resources/support system	Readily available		Limited		None
	0		1		2
QOL/psychological status	Good		Fair		Poor
	0		1		2
Economic issues	Minimal		Moderate		Severe
	0		1		2
TOTAL SCORE	**Maximum 27**				

Table 2. Suggested Glycemic Targets Based on EDCS Score

Suggested Target	EDCS Score			
	< 5	5–10	11–15	> 16
A1C (%)	≤ 6.5	6.6–7.5	7.6–8.0	~8–8.5

≤ 6.5% would be appropriate, based on current clinical trial data suggesting improved long-term micro- and macrovascular outcomes with early intensive therapy in type 2 diabetes. Achieving this goal could involve lifestyle modification with increased aerobic activity aimed at weight loss and, possibly, addition of another oral agent.

Case 2: an elderly patient with vascular complications
Presentation. An 83-year-old woman with type 2 diabetes for > 25 years presents for glycemic control management. In the past few years, her A1C levels have run in the range of 8.2%. She has severe osteoarthritis of her knees and is anticipating right knee replacement surgery in 2–3 months. She has known clinical coronary artery disease, having had a non-ST elevation MI 4 years ago requiring a stent placement. She also has hypertension and osteopenia. Her diabetes treatment regimen involves glargine, 30 units at bedtime, and aspart insulin based on a correction scale with meals. She also takes metoprolol, lisinopril, aspirin, and atorvastatin daily.

She lives by herself and has a son who visits her once or twice a week and also provides occasional monetary assistance. She is overall independent in her activities of daily life. The orthopedic surgeon referred her to the clinic for improved glycemic control because he believed her blood glucose levels should be < 120 mg/dl with an A1C of 6.5% before her impending surgery. What are your recommendations?

Discussion. This is an older patient with a longer duration of diabetes and known macrovascular disease. Although there is no mention of it, it is likely that she has concurrent microvascular disease given the longstanding nature of her diabetes. Her calculated EDCS score is 18. There is no evidence at present that intensive

glycemic control is beneficial in this age-group of patients with type 2 diabetes, particularly in the presence of cardiovascular disease, and there is the potential for possible harm, although this is unclear. A more relaxed glycemic target involving an A1C of ~ 8% may be quite acceptable for this patient. Close monitoring of blood glucose levels intra- and postoperatively will be important.

Case 3: psychosocioeconomic factors in diabetes management

Presentation. A 54-year-old African-American woman with a 6-year history of type 2 diabetes presents for ongoing management. She is on metformin, 1 g twice daily, and glargine, 35 units at bedtime. She is receiving treatment for hypertension and hypothyroidism. Her other medications include levothyroxine, hydrochlorothiazide, simvastatin, and aspirin.

She does not smoke or drink. She is employed part-time and works as the manager of a store. However, she reluctantly reports that she is currently homeless and lives alone in her car. She is compliant with her medications and eats two meals at work and dinner at a friend's home. She is estranged from her family.

Examination reveals a blood pressure of 130/74 mmHg, a BMI of 33 kg/m^2, and abdominal obesity but is otherwise unremarkable. Her A1C is 9%. How should this patient be treated?

Discussion. This patient has significant psychosocial stressors. Despite being employed, she is homeless and lacks family support. This is a major barrier to management not only of diabetes, but also of any chronic disease condition. Her EDCS score of 16 puts her in the range of > 8% for A1C. In such a situation, enlisting the help of social workers, arranging for psychological counseling, and allowing some laxity in her glycemic control until her social situation improves become necessary to improve and maintain her compliance.

References

[1]Inzucchi SE, Bergenstal RM, Buse JB, Diamant M, Ferrannini E, Nauck M, Peters AL, Tsapas A, Wender R, Matthews DR: 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* 35:1364–1379, 2012

[2]Bailey CJ, Aschner P, Del Prato S, LaSalle J, Ji L, Matthaei S: Individualized glycaemic targets and pharmacotherapy in type 2 diabetes. *Diab Vasc Dis Res* 10:397–409, 2013

[3]Pozzilli P, Leslie RD, Chan J, De Fronzo R, Monnier L, Raz I, Del Prato S: The A1C and ABCD of glycaemia management in type 2 diabetes: a physician's personalized approach. *Diabetes Metab Res Rev* 26:239–244, 2010

[4]Hansen LJ, Siersma V, Beck-Nielsen H, de Fine Olivarius N: Structured personal care of type 2 diabetes: a 19 year follow-up of the study Diabetes Care in General Practice (DCGP). *Diabetologia* 56:1243–1253, 2013

[5]Ismail-Beigi F, Moghissi E, Tiktin M, Hirsch IB, Inzucchi SE, Genuth S: Individualizing glycemic targets in type 2 diabetes mellitus: implications of recent clinical trials. *Ann Intern Med* 154:554–559, 2011

[6]Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA: 10-year follow-up of intensive glucose control in type 2 diabetes. *N Engl J Med* 359:1577–1589, 2008

[7]Nathan DM, Cleary PA, Backlund JY, Genuth SM, Lachin JM, Orchard TJ, Raskin P, Zinman B: Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. *N Engl J Med* 353:2643–2653, 2005

[8]Duckworth W, Abraira C, Moritz T, Reda D, Emanuele N, Reaven PD, Zieve FJ, Marks J, Davis SN, Hayward R, Warren SR, Goldman S, McCarren M, Vitek ME, Henderson WG, Huang GD: Glucose control and vascular complications in veterans with type 2 diabetes. *N Engl J Med* 360:129–139, 2009

[9]Gerstein HC, Miller ME, Byington RP, Goff DC Jr, Bigger JT, Buse JB, Cushman WC, Genuth S, Ismail-Beigi F, Grimm RH Jr, Probstfield JL, Simons-Morton DG, Friedewald WT: Effects of intensive glucose lowering in type 2 diabetes. *N Engl J Med* 358:2545–2559, 2008

[10]Patel AS, MacMahon J, Chalmers B, Neal L, Billot M, Woodward M, Marre M, Cooper P, Glasziou D, Grobbee P, Hamet S, Harrap S, Heller L, Liu G, Mancia CE, Mogensen C, Pan N, Poulter A, Rodgers B, Williams S, Bompoint BE, de Galan R, Joshi R, Travert F: Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. *N Engl J Med* 358:2560–2572, 2008

[11]Bakris GL: Recognition, pathogenesis, and treatment of different stages of nephropathy in patients with type 2 diabetes mellitus. *Mayo Clin Proc* 86:444–456, 2011

[12]So WY, Kong AP, Ma RC, Ozaki R, Szeto CC, Chan NN, Ng V, Ho CS, Lam CW, Chow CC, Cockram CS, Chan JC, Tong PC: Glomerular filtration rate, cardiorenal end points, and all-cause mortality in type 2 diabetic patients. *Diabetes Care* 29:2046–2052, 2006

[13]Fox CS, Coady S, Sorlie PD, D'Agostino RB Sr, Pencina MJ, Vasan RS, Meigs JB, Levy D, Savage PJ: Increasing cardiovascular disease burden due to diabetes mellitus: the Framingham Heart Study. *Circulation* 115:1544–1550, 2007

[14]Desouza C, Salazar H, Cheong B, Murgo J, Fonseca V: Association of hypoglycemia and cardiac ischemia: a study based on continuous monitoring. *Diabetes Care* 26:1485–1489, 2003

[15]Whitmer RA, Karter AJ, Yaffe K, Quesenberry CP Jr, Selby JV: Hypoglycemic episodes and risk of dementia in older patients with type 2 diabetes mellitus. *JAMA* 301:1565–1572, 2009

[16]Bailey CJ, Kodack M: Patient adherence to medication requirements for therapy of type 2 diabetes. *Int J Clin Pract* 65:314–322, 2011

[17]Harris MI, Eastman RC, Cowie CC, Flegal KM, Eberhardt MS: Racial and ethnic differences in glycemic control of adults with type 2 diabetes. *Diabetes Care* 22:403–408, 1999

[18]Nouwen A, Winkley K, Twisk J, Lloyd CE, Peyrot M, Ismail K, Pouwer F: Type 2 diabetes mellitus as a risk factor for the onset of depression: a systematic review and meta-analysis. *Diabetologia* 53:2480–2486, 2010

[19]Browne JL, Ventura A, Mosely K, Speight J: 'I call it the blame and shame disease': a qualitative study about perceptions of social stigma surrounding type 2 diabetes. *BMJ Open* 3:e003384, 2013

[20]van der Does F E, de Neeling JN, Snoek FJ, Grootenhuis PA, Kostense PJ, Bouter LM, Heine RJ: Randomized study of two different target levels of glycemic control within the acceptable range in type 2 diabetes: effects on well-being at 1 year. *Diabetes Care* 21:2085–2093, 1998

[21]Rubin RR, Peyrot M: Quality of life and diabetes. *Diabetes Metab Res Rev* 15:205–218, 1999

[22]Hirsch IB, Amiel SA, Blumer IR, Bode BW, Edelman SV, Seley JJ, Verderese CA, Kilpatrick ES: Using multiple measures of glycemia to support individualized diabetes management: recommendations for clinicians, patients, and payers. *Diabetes Technol Ther* 14:973–983; quiz 983, 2012

Savitha Subramanian, MD, is an assistant professor of medicine, and Irl B. Hirsch, MD, is professor of medicine in the Division of Metabolism, Endocrinology, and Nutrition at the University of Washington in Seattle.