Weighing the Potential Benefits and Risks of Antidiabetic Agents in Older Adults

Joshua J. Neumiller, PharmD, CDE, CGP, FASCP, Peggy Soule Odegard, BS, PharmD, CDE, FASCP, and Stuart T. Haines, PharmD, BCPS, BCACP, BC-ADM, FCCP

Case Study Part 1: The Initial Encounter

R.W. was referred by her case manager to the clinic pharmacist for a medication management consultation. She is an 81-year-old woman who recently presented to the emergency department (ED) after a fall in her kitchen and was subsequently hospitalized with a hip fracture. When asked about the circumstances surrounding her recent hypoglycemia event, she reports rushing to the kitchen to answer the phone and slipping on the tile floor. In the ED, her blood glucose was 58 mg/dl, which was considered contributory to her fall. She reports not experiencing any hypoglycemia symptoms before falling.

R.W.'s medical history includes type 2 diabetes diagnosed 12 years ago, hypertension, dyslipidemia, osteoporosis, and depression. In addition, she experienced a transient ischemic attack (TIA) 3 years ago and reports chronic back pain from several osteoporotic vertebral fractures. R.W.'s parents both had type 2 diabetes, and her father died at the age of 63 years after a myocardial infarction (MI).

R.W. lives alone in a single-bedroom apartment. Her husband died of bladder cancer 2 years ago, and her son lives 90 miles away. She reports that she eats sporadically throughout the day, and her diet primarily consists of processed foods, although she reports having a good appetite.

Her weight has increased by ~ 5 lb since the addition of glyburide to her medication regimen 1 year ago. She recently implemented a walking routine 3 days per week at the mall with a group of friends in hope of losing some weight. Her antidiabetic regimen consists of metformin, 500 mg twice daily, and glyburide, 5 mg twice daily. She reports never taking more than 500 mg twice daily of metformin, which was confirmed by a review of her medical history. She has experienced about six hypoglycemia events (blood glucose level < 70 mg/dl) confirmed by fingerstick glucose testing since initiating glyburide, with three of these episodes occurring in the week before her fall. Her blood glucose log, physical examination and laboratory data, and current diabetes regimen are shown in Table 1. She reports being adherent to her current medication regimen and uses a pill box, which she fills every 2 weeks, to manage her medications.

R.W.'s son, case manager, and primary care physician are seeking recommendations regarding her diabetes treatment plan in light of her recent hypoglycemia event and fall.

Treatment Plan Considerations

Hypoglycemia in the elderly

Older adults are at increased risk for hypoglycemia because of physiological changes that occur as a normal part of aging, as well as nonphysiological changes that may be associated with growing older. As the human body ages, there is a reduced sensitivity to the physiological signals and hormonal counterregulation of hypoglycemia, impairing an individual's ability to recognize or respond to low blood glucose. This reduced hypoglycemia awareness with aging is related to altered responses to epinephrine, glucagon, and cortisol and places

Table 1. R.W.'s Blood Glucose Log, Physical Examination and Laboratory Data, and Current Medications

Blood Glucose Log (mg/dl)

Waking	Pre-Lunch	Pre-Dinner
98	66	124
105	83	151
105	61	166
69	122	95

Physical Examination Data

Blood pressure (mmHg)	152/92
Pulse (bpm)	72, regular
Weight (lb)	215
Height (inches)	69
BMI (kg/m^2)	31.7

Laboratory Data From ED Visit

Test	Value	Normal/Goal Range
Sodium (mEq/l)	139	135–145
Potassium (mEq/l)	5.1	3.5–5.0
Chloride (mEq/l)	100	95–105
Blood urea nitrogen (mg/dl)	13	7–25
Serum creatinine (mg/dl)	1.3	0.5–1.0
Aspartate aminotransferase (units/l)	22	5–40
Alanine aminotransferase (units/l)	44	7–56
Glucose (mg/dl)	58	≥ 70
A1C (%)	6.7	< 7% or per individualized goal
Estimated creatinine clearance (ml/min)	52	80–125 (Cockroft-Gault)
Total cholesterol (mg/dl)	144	< 200
LDL cholesterol (mg/dl)	115	< 130
HDL cholesterol (mg/dl)	44	> 40
Triglycerides (mg/dl)	140	< 150

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older adults at greater risk of severe hypoglycemia.[1] Compounding this potential for reduced hypoglycemia awareness is another physiological change: a decline in renal function, potentially increasing the hypoglycemic effects of medications such as glyburide or insulin, which rely on the kidneys for elimination.

The nonphysiological changes that may increase the risk for hypoglycemia in older adults include environmental and socioeconomic factors, comorbid illness, and drug interactions. Table 2 provides a list of potential risk factors for hypoglycemia in the elderly.[2]

R.W. has reported several risk factors that may be contributing to her hypoglycemia. Namely, she reports inconsistent eating habits, has had a TIA, is receiving a sulfonylurea, and reports hypoglycemia unawareness with her recent hypoglycemia events.

Research regarding glycemic targets in the elderly

Guidelines from the American Diabetes Association suggest that the goal of treatment for healthy older adults with type 2 diabetes who are cognitively intact and have a long life expectancy should be the same as those for younger adults (A1C < 7%), but that the goal may be relaxed for older individuals with multiple comorbidities or a shorter life expectancy.[3]

The guidelines recommend using the amount of time reported in clinical trials to achieve the desired health benefit to determine whether intensive pharmacological treatment is warranted.[3] The long-term benefits of intensive glycemic control often require years of treatment to materialize. Very old or frail individuals are less likely to derive the same long-term benefits that young, otherwise healthy people with diabetes might be expected to gain.

On the other hand, hyperglycemia should not be ignored because poor glycemic control can lead to acute complications and affect quality of life. Significant hyperglycemia can compromise wound care, worsen urinary incontinence, affect vision, and lead to dehydration.

A panel convened by the California Healthcare Foundation/American Geriatrics Society suggested that an A1C < 8% may be a reasonable goal for patients with a life expectancy of < 5 years.[4] Additionally, the Veterans Affairs/Department of Defense clinical practice guidelines recommend a determination of A1C goal based on the presence of major comorbidities or advanced physiological age and microvascular disease.[5] It is recommended that individuals with major

Table 1. R.W.'s Blood Glucose Log, Physical Examination and Laboratory Data, and Current Medications, *continued from p. 173*

Current Medications	
Metformin	500 mg twice daily
Glyburide	5 mg twice daily
Hydrochlorothiazide	25 mg daily
Atorvastatin	10 mg daily
Carvedilol	25 mg twice daily
Fluoxetine	20 mg daily
Clopidogrel	75 mg daily

Table 2. Potential Risk Factors for Hypoglycemia in the Elderly[2]

- Reduced food intake
- Living in a nursing home
- Inadequate blood glucose monitoring
- Initial phase of oral antidiabetic agents
- Cardiovascular morbidity, previous stroke
- Altered physical activity
- Renal or hepatic dysfunction
- Alcohol
- Hypoglycemia unawareness
  - Medications
  - Physiological adaptations with aging

comorbidities or advanced microvascular disease achieve a more relaxed A1C goal of ≤ 9%.

Recent data regarding intensive management of type 2 diabetes shed some light on goal management in older adults. The U.K. Prospective Diabetes Study (UKPDS) enrolled patients who were newly diagnosed with type 2 diabetes.[6,7] Patients were randomized into several study groups. Two study groups were treated intensively with medications and lifestyle modification. Another group was treated less aggressively, primarily relying on lifestyle modifications and using medications only when blood glucose measurements exceeded 200 mg/dl. The initial study found that good glycemic control (mean A1C of 7% during the study) resulted in a reduction in clinically evident microvascular complications compared to patients with less well controlled diabetes (mean A1C of 7.9%).

Following the termination of the UKPDS, the investigators continued to follow-up with study participants. During the follow-up period, patients in the intensive and less aggressive treatment groups achieved similar blood glucose and blood pressure control. After 10 years of follow-up, the benefits observed during the initial study period were sustained, and the between-group difference actually widened over time, with a 24% (P = 0.001) relative risk reduction in microvascular complications for patients in the intensive treatment group who received sulfonylureas and insulin versus conventional therapy.[8] Furthermore, the risk of death and macrovascular complications such as MIs decreased by ~ 15% in patients who were initially randomized to the intensive treatment arm.[8]

Given that all UKPDS participants achieved similar glycemic control in the 10-year follow-up period, it was perhaps a surprising finding that the benefits of earlier glycemic control continued to accrue over time. This phenomenon, sometimes referred to as the "legacy effect," in which the body has "metabolic memory," suggests that early intensive glycemic control is important in preventing long-term diabetes complications in the setting of new-onset type 2 diabetes.

What about patients with longstanding type 2 diabetes and cardiovascular risk factors? Are older adults with multiple comorbidities, like R.W., likely to benefit from intensive glycemic control?

The benefits in this population are less clear-cut. The Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE) trial[9] compared intensive versus standard glycemic control in a group of older adults (mean age 66 years) who were at high risk for cardiovascular disease (CVD). After 5 years of treatment, the intensive-treatment group had achieved a mean A1C of 6.5%, compared to 7.3% in the standard-treatment group. Although the intensive-treatment group was able to achieve very good glycemic control, there were no significant differences in the risk of death or cardiovascular events in this study. However, microvascular complications were somewhat lower in the intensive-treatment group, and this result affirmed the benefits observed in the UKPDS.

The Action to Control Cardiovascular Risk in Diabetes (ACCORD) study[10] compared an intensive treatment strategy to standard treatment in older adults (mean age at baseline 62 years) with longstanding diabetes (mean duration 10 years) and multiple risk factors for CVD. The standard-treatment group was treated to achieve an A1C target between 7.0 and 7.9%, whereas the intensive-treatment group was attempting to achieve a target A1C of < 6.0%. The primary outcome of the ACCORD study was a composite of nonfatal MI, nonfatal stroke, or death from cardiovascular causes.

In 2007, the study was terminated early because of concerns regarding the safety of the intensive treatment

Table 3. Four Years Later: R.W.'s Blood Glucose Log, Physical Examination and Laboratory Data, and Current Medications

Blood Glucose Log (mg/dl)		
Waking	**Pre-Lunch**	**Pre-Dinner**
220	192	175
195	187	183
203	182	190
Physical Examination Data		
Blood pressure (mmHg)	135/82	
Pulse (bpm)	54, regular	
Weight (lb)	193	
Height (inches)	69	
BMI (kg/m^2)	28.5	
Laboratory Data From ED Visit		
Test	**Value**	**Normal/Goal Range**
Sodium (mEq/l)	145	135–145
Potassium (mEq/l)	4.0	3.5–5.0
Chloride (mEq/l)	103	95–105
Blood urea nitrogen (mg/dl)	15	7–25
Serum creatinine (mg/dl)	1.4	0.5–1.0
Aspartate aminotransferase (units/l)	24	5–40
Alanine aminotransferase (units/l)	41	7–56
Glucose (mg/dl)	172	> 70
A1C (%)	8.2	< 7% or per individualized goal
Estimated creatinine clearance (ml/min)	41	80–125 (Cockroft-Gault)
Total cholesterol (mg/dl)	182	< 200
LDL cholesterol (mg/dl)	133	< 130
HDL cholesterol (mg/dl)	37	> 40
Triglycerides (mg/dl)	162	< 150

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strategy. After a mean 3.5 years of follow-up, significantly more patients in the intensive-treatment arm had died (257 vs. 203 in the standard-treatment group, hazard ratio [HR] 1.22, 95% CI, 1.01–1.46, $P = 0.04$). The composite outcome of nonfatal MI, nonfatal stroke, and death from cardiovascular causes was similar in the two treatment groups at the time of study termination (HR 0.90, 95% CI 0.78–1.04, $P = 0.16$). Thus, the results of the ACCORD study suggest that very intensive glycemic control may be harmful to those with longstanding diabetes and multiple comorbidities.

Although the studies discussed above provide important information regarding tight glycemic control in individuals with CVD or risk factors, it should be noted that robust data in cohorts of individuals > 80 years of age are lacking; thus, extrapolation of these findings to the very old population should be done with caution.

Case Study Part 1: Recommendations

1. Discontinue glyburide. Because R.W. has experienced several blood glucose values < 70 mg/dl, lives alone, has some degree of hypoglycemia unawareness, has reduced renal function, and has experienced morbidity as a result of her hypoglycemia, this agent should be discontinued. Glyburide and its metabolites can accumulate in patients with reduced renal function (i.e., having a glomerular filtration rate [GFR] < 60 ml/min), increasing the risk of severe and prolonged hypoglycemia. This agent should generally be avoided in older adults in favor of pharmacological agents that convey a lower risk of hypoglycemia.

Given that R.W.'s most recent A1C was 6.7%, metformin monotherapy may be sufficient. Although increasing the dose of metformin for this patient would be considered controversial because of the perceived risk of metformin-associated lactic acidosis, some clinicians would continue to use metformin in this scenario,[11] and increasing the dose to 1,000 mg twice daily, if necessary to maintain good glycemic control, could be considered. Careful monitoring of renal function is required, however.

Given that R.W. has longstanding type 2 diabetes and multiple cardiovascular risk factors, an appropriate A1C goal in her case is 7.0–7.9%, if it can be achieved without causing hypoglycemia. An A1C target of < 9% may be appropriate when

Table 3. Four Years Later: R.W.'s Blood Glucose Log, Physical Examination and Laboratory Data, and Current Medications, *continued from p. 175*

Current Medications	
Metformin	500 mg daily
Pioglitizone	30 mg daily
Hydrochlorothiazide	25 mg daily
Lisinopril	5 mg daily
Atorvastatin	10 mg daily
Carvedilol	25 mg twice daily
Furosemide	20 mg daily as needed for edema
Fluoxetine	20 mg daily

considering the wishes and goals of R.W. and her family.[5]

2. Refer R.W. to a certified diabetes educator (CDE) or dietitian for education regarding diet and hypoglycemia management. Recent findings from ACCORD and other trials indicate that hypoglycemia should be avoided at all costs in patients with a history of cardiovascular events. Because R.W. has experienced several bouts of hypoglycemia, counseling regarding appropriate management of hypoglycemia is important for her safety.

R.W.'s eating habits are irregular, and her diet consists entirely of processed foods. A consultation with a dietitian may be beneficial to improve her nutrition and potentially help her avoid hypoglycemic events in the future.

3. Initiate lisinopril, 5 mg daily. Discussion with R.W. and her son, who monitors her blood pressure weekly in her home, reveals that the blood pressure readings have been increased during the past year. Because R.W.'s systolic blood pressure has been consistently elevated, the addition of an antihypertensive agent is warranted.

Lisinopril is a possible option that may also convey renal benefits. R.W. should be seen for a follow-up appointment with her primary care provider within 1–2 weeks after drug initiation to assess her renal function because of the possibility of a decline in renal function after the initiation of an ACE inhibitor.

4. Recommend an assessment of the home environment for fall hazards. In addition to the medication recommendations above, the case manager was advised to pursue an assessment of the home environment by an occupational therapist to minimize potential falling hazards within the home.

Case Study Part 2: Medication Management Follow-Up, 4 Years Later

Four years after her initial medication management consultation, R.W. was referred by her case manager for another consultation. R.W. is now 85 years old and was recently hospitalized after a stroke.

Her case manager and son are planning for her care after hospital discharge. Her son has decided to transition his mother into an assisted living facility because of concerns regarding her diminished ability to care for herself. Over the previous 4 years, R.W. has experienced several additional falls (one resulting in a forearm fracture), which were attributed to a decline in her mobility. R.W. reports being increasingly fatigued and has fluid retention in her ankles. The case manager would like her medications to be reviewed with the goal of simplifying the regimen, if possible, before her transition to assisted living.

R.W. continues to be adherent to her medication regimen, as outlined in Table 3, but she and her son question the number of medications she is currently taking. She does not report any recent hypoglycemia events and reports checking her blood glucose infrequently. In agreement with her primary care physician, R.W. checks her blood glucose three times daily for 3 days before meeting with any of her physicians or other health care providers.

Although R.W. and her son would like to decrease the number of medications she takes on a daily basis, they are concerned about the increase in her blood glucose values during the past several years. In response to this gradual increase in her blood glucose values, her primary care provider initiated pioglitazone therapy 2 years ago because of its low risk of causing hypoglycemia. R.W.'s son is additionally concerned about a recent report he read about a link between pioglitazone and bladder cancer. (His father died of bladder cancer.) Of note, R.W.'s case manager is concerned about potential drug interactions and her continued use of metformin in light of her advanced age and recent laboratory findings.

Treatment Plan Considerations

Metformin use in patients with renal impairment

Although metformin is considered the drug of choice for obese patients with type 2 diabetes[3] like R.W., the U.S. Food and Drug Administration (FDA) specifically warns against the continued use of metformin in patients with impaired kidney function. Because of concerns about an increased risk of lactic acidosis, according to the product labeling, metformin use is contraindicated in men with a serum creatinine (SCr) ≥ 1.5 mg/dl and in women with a SCr ≥ 1.4 mg/dl. However, there is controversy about the use of strict SCr cutoffs.

The risk of metformin-associated lactic acidosis is increased in individuals with renal impairment, heart failure, liver disease, and high alcohol intake and in those with a previous history of lactic acidosis.[12] Renal dysfunction is the most common risk factor implicated in

the development of lactic acidosis, and many clinical practice guidelines recommend that metformin be discontinued when the GFR is < 60 ml/min. Despite these recommendations, some clinicians continue to treat patients with metformin in the presence of mild to moderate renal impairment.[11] Proponents of this approach note its potential benefit compared to sulfonylureas and insulin, medications that can accumulate in patients with kidney dysfunction and contribute to hypoglycemia.

Although phenformin (metformin's predecessor) was removed from the U.S. market in 1977 because of the risk of lactic acidosis,[13] the incidence of lactic acidosis with metformin is considerably lower. Two recent, large meta-analyses reported no evidence of an increased risk of lactic acidosis with the use of metformin compared to non-metformin therapies.[14,15] One of these studies reported the upper limit for the true incidence of lactic acidosis per 100,000 patient-years to be 4.3 cases in metformin-treated patients and 5.4 cases in patients with diabetes who were not treated with metformin.[16] Similarly, a nested, case-controlled study including 50,048 patients with type 2 diabetes receiving antidiabetic medications found crude rates of lactic acidosis to be 3.3 cases per 100,000 metformin users and 4.8 cases per 100,000 sulfonylurea users.[15] A small, prospective, randomized study in patients who developed mild renal dysfunction (SCr 1.5–2.5 mg/dl) conducted in Europe had patients continue metformin (n = 198) or discontinue metformin (n = 195) and followed them for 2 years.[17] None of the patients in either group developed lactic acidosis, and plasma lactate concentrations were similar in both groups at study completion.

These data indicate that the risk of metformin-associated lactic acidosis is small, but it is still important to consider that lactic acidosis has a mortality rate of 50%. There are no clear data to define specifically at which level of renal impairment metformin should be contraindicated. However, the risk of lactic acidosis in those with mild to moderate renal impairment is believed to be less than in those with more severe renal impairment. Evidence is mounting to indicate that the risk of metformin-associated lactic acidosis is more likely to occur in patients who are acutely ill and experience acute changes in renal function.

Deciding to continue metformin therapy requires prescribers to carefully weigh the potential risks and benefits. We do not target specific metformin serum concentrations in dosing. However, the reduced renal clearance will likely result in a higher blood concentration in patients with renal dysfunction. Given this fact, and that alternative therapies are also associated with significant risks, the continuation of metformin therapy at a lower dose (≤ 1,000 mg daily) in the face of mild to moderate renal dysfunction is reasonable, especially if the desired effect is achieved at a lower dose.

If R.W. is deemed an appropriate candidate for continued low-dose metformin therapy, a frank discussion regarding the potential risks and benefits of metformin is needed, and the outcome of that conversation should be clearly documented in her medical record. Moreover, R.W.'s renal function should be monitored every 3–4 months, and metformin therapy should be immediately stopped if she becomes acutely ill or if her renal function declines further.

Thiazolidinediones, fractures, and bladder cancer

The link between thiazolidinediones (TZDs) and fractures has received significant attention after two large, observational studies reported an increased risk of fracture with TZDs compared to other oral antidiabetic drugs.[18,19] Individuals taking TZDs in these analyses were 1.8–2.4 times more likely to suffer a fracture. Both studies observed an increased risk in women, regardless of age, whereas only one study reported an increased fracture risk in men.

Fracture data were also reported in the Rosiglitazone Evaluated for Cardiovascular Outcomes and Regulation of Glycaemia in Diabetes (RECORD) trial.[20] The RECORD trial was a multicenter, open-label study involving 4,447 patients with type 2 diabetes on metformin or sulfonylurea monotherapy with a mean A1C of 7.9% at baseline. Patients were randomized to receive either the addition of rosiglitazone (n = 2,220) in the treatment group or combination therapy with metformin plus sulfonylurea (n = 2,227) in the active control group.

The primary endpoint of the study was cardiovascular-related hospitalization or cardiovascular death, with a follow-up period of 5–7 years. A secondary outcome included self-reported fracture. Upper and distal lower-limb fracture rates were increased in female subjects randomized to the rosiglitazone group. In light of such findings, many authorities recommend that TZDs should be avoided in elderly women with comorbid osteoporosis if alternative antidiabetic therapies can be used.[21]

The prescribing information for pioglitazone was recently revised to include information related to the potential risk of bladder cancer with use.[22] In an interim analysis conducted at year 5 of a 10-year study designed to assess the long-term risk of bladder cancer associated with pioglitazone risk, the risk of bladder cancer was shown to increase with increasing dose and duration of pioglitazone use.[22] Interestingly, the risk of bladder cancer overall was not found to be increased in people receiving pioglitazone compared to case control subjects not exposed to pioglitazone (HR 1.2, 95% CI 0.9–1.5).[22] The HR after 2 years of treatment with pioglitazone was calculated at 1.4 (95% CI 1.03–2.0), which corresponded to an estimation that duration of treatment > 12 months was associated with 27.5 excess cases of bladder cancer per 100,000 person-years of follow-up compared to non-pioglitazone users.[22]

Although the overall risk appears to be low, the FDA did require that the aforementioned warnings be added to the prescribing information for pioglitazone and that people with active bladder cancer avoid its use.[22] Given that R.W. has had a fracture and is experiencing lower-extremity edema and that her family is concerned about the bladder cancer

warnings, the continued use of pioglitazone in this case should be questioned.

Other pharmacotherapy considerations in the elderly

Aging is associated with changes in glucose tolerance related to insulin release. However, aging-associated changes involving the production and release of other glucose regulatory hormones (e.g., incretins or amylin) has not been documented. Insulin release diminishes with aging compared to physiological insulin release in younger adults. In a 2008 study,[23] investigators found that first- and second-phase insulin release declined by ~ 0.7% per year (in people 20–70 years of age) in subjects who did not have diabetes or impaired glucose tolerance. The rate of decline was greater in those with impaired glucose tolerance, with first-phase insulin secretion, which occurs immediately after eating, most significantly affected ($P = 0.025$). Interestingly, insulin resistance was not correlated with age in this study.

Based on these physiological findings, therapeutic approaches that augment or supplement insulin secretion and thereby achieve prandial glucose control may have the greatest effect in older adults with diabetes. Therapies to consider when addressing postprandial hyperglycemic excursions include rapid-acting insulin, sulfonylureas, meglitinides, α-glucosidase inhibitors, glucagon-like peptide-1 (GLP-1) receptor agonists, amylin analogs, and the dipeptidyl peptidase-4 (DPP-4) inhibitors.

When initiating insulin in individuals with type 2 diabetes, commonly cited algorithms begin with a supplement of low-dose basal insulin (e.g., 0.2 units/kg body weight), with titration of the basal insulin dose to achieve the desired level of fasting glycemic control.[24,25] This approach may meet basal insulin needs but does not address the physiological tendency toward prandial insulin deficiency observed in older adults. Therefore, occasional peak (e.g., 2-hour) postprandial glucose monitoring is also important. When counseling patients who have started basal insulin, it is important to provide education on these two types of insulin needs (i.e., basal versus prandial) and the importance of monitoring to ensure that both needs are met.

Prandial needs may be met by adding a rapid-acting insulin initiated with the largest meal(s) of the day or by using oral agents such as the meglitinides, which are intended to promote insulin release at meals. Alternatively, newer agents such as GLP-1 receptor agonists and DPP-4 inhibitors, which reduce prandial hyperglycemia through actions mediated by the GLP-1 system on insulin release and glucose absorption, are also an option. Newer therapies have not been validated in large outcomes studies but may offer some advantages in older adults.

Although R.W.'s self-monitoring of blood glucose (SMBG) readings indicate that her blood glucose values are consistently elevated and would benefit from the addition of basal insulin, it would be prudent to have her additionally check her 2-hour postprandial glucose readings several days per week. Given R.W.'s fasting blood glucose readings, it does not appear that she would be at significant risk of fasting hypoglycemia with the addition of a low dose of basal insulin, followed by monitoring and careful dose titration to achieve target blood glucose and A1C levels.

Case Study Part 2: Recommendations

1. Initiate insulin glargine, 5 units daily.

Given that R.W.'s most recent A1C is above the desired goal and her fasting blood glucose is elevated throughout the day, additional pharmacotherapy could be considered in line with her goals and wishes. Using a conservative starting dose of a long-acting basal insulin such as insulin glargine, insulin detemir, or NPH would minimize the risk of hypoglycemia while addressing her lack of adequate glucose control. A single daily dose of basal insulin is an effective and safe approach (if titrated in small increments every 1–2 weeks) to lowering her fasting blood glucose and A1C. Because R.W. will be transitioning to an assisted living facility and will have assistance with injections, she and her son are willing to try insulin glargine in hopes of lowering her blood glucose.

R.W. reports that she feels better when her blood glucose levels are < 150 mg/dl. The recommendation to initiate insulin glargine was implemented by her primary care provider, and a CDE will be following up with her at the assisted living facility to help with dose titration.

2. Discontinue pioglitazone, 30 mg daily.

Because R.W. has experienced several fractures and worsening peripheral edema and her family is concerned about recent reports of bladder cancer, the pioglitazone should be discontinued. Furthermore, given that she is being started on insulin therapy, it should be anticipated that her peripheral edema would worsen with concurrent insulin and TZD use. If discontinuation of pioglitazone results in a resolution of her peripheral edema, the necessity of furosemide should be reevaluated.

Discussion and Conclusions

When treating elderly patients with type 2 diabetes, it is important to remember that treatment guidelines are intended to guide, but not dictate, decisions. Because the data presented in this case study have, in part, influenced treatment guidelines and recommendations for older individuals with a high burden of comorbidity, patients must be treated as individuals based on their overall health, personal beliefs, and treatment goals.

Treatment goals and strategies for older adults with type 2 diabetes should be individualized by weighing the potential benefits and risks. Treatment strategies should consider patients' comorbid health conditions, concurrent medication use, level of cognition, physical disabilities, and living situation, as well as the wishes and goals of the patients and their family members. Glucose management should be conservative, and medications should be methodically titrated, with careful consideration of potential side effects, drug-disease

and drug-drug interactions, and the risk of hypoglycemia.

The needs of older adults are diverse, and treatment requires careful consideration of individual patients' physical status. Effective communication among patients, family members, caregivers, and health care providers is crucial to safely achieving patient-centered treatment goals.

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Joshua J. Neumiller, PharmD, CDE, CGP, FASCP, is an assistant professor in the Department of Pharmacotherapy at Washington State University College of Pharmacy and co-owner and consultant pharmacist for Pharmacy Advocates, LLC, in Spokane. He is also an associate editor of Diabetes Spectrum. *Peggy Soule Odegard, BS, PharmD, CDE, FASCP, is a professor and chair of the Department of Pharmacy in the University of Washington School of Pharmacy and a clinical pharmacist and diabetes educator in the Department of Medicine at the University of Washington School of Medicine in Seattle. She is also an associate editor of* Diabetes Spectrum. *Stuart T. Haines, PharmD, BCPS, BCACP, BC-ADM, FCCP, is a professor and vice-chair for clinical services in the Department of Pharmacy Practice and Science at the University of Maryland School of Pharmacy in College Park.*