Montana Geriatric Education Center

Instructions on Completing the Module
Screening for Diabetes in Older Adults

*The results of the assessments and evaluations are confidential, and the data is used to meet requirements of our federally funded grant.

Please make sure to turn in Pre-Test, Post-Test, and Module Evaluation.

1. **Before** reading the module, and without looking at it, complete the **Pre-Test**.
   
   Record your answers on the examination form marked **Pre-Test. (Found at the start of the module.)** Keep the completed answer form to turn in at the completion of the module.

2. Complete the module as outlined.

3. **After** reading the module, please complete the **Post-Test**.
   
   Record your answers on the examination form marked **Post-Test. (Found at the end of the module.)** Keep the completed answer form to turn in at the completion of the module.

   Complete the **Module Evaluation. (Found after the post-test.)** Keep the completed module evaluation form to return with the pre-test and post-test at the completion of the module.

4. **To obtain credit for the module you must:**
   
   
   b. Turn in the **Pre-Test, Post-Test, and Module Evaluation**
   
   c. Obtain a score of 70% or better on the **Post-Test**

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Email: IPHARM@umontana.edu

Phone (406) 243-2339 & Fax (406) 243-4353
Pre-test: Screening for Diabetes in Older Adults

Record responses on examination form.

1. The primary defect in diabetes is:
   a. Increased insulin resistance in peripheral tissues
   b. Decreased beta-cell mass and function
   c. Hormonal dysregulation of cortisol, growth hormone, and epinephrine
   d. Increased rates of glucose absorption in the stomach

2. All of the following conditions are types of microvascular complications that can result from diabetes EXCEPT:
   a. Nephropathy
   b. Myocardial infarction (heart attack)
   c. Retinopathy
   d. Erectile dysfunction

3. Which of the following diseases is the leading cause of death among patients with diabetes?
   a. Kidney failure
   b. Cancer
   c. Cardiovascular disease
   d. Pneumonia

4. Native Americans are how many times more likely to be diagnosed with diabetes compared to non-Hispanic Whites of similar age?
   a. Similar diagnosis rate
   b. Over twice as likely
   c. Four times as likely
   d. Five times as likely

5. Which of the following characteristics is NOT commonly associated with type 2 diabetes?
   a. Obesity
   b. Insulin resistance
   c. Onset before age 40
   d. Varying degrees of endogenous insulin production

6. The American Diabetes Association recommends daily low dose aspirin therapy for primary prevention of cardiovascular events in which subset of patients:
   a. Men and women over age 70 with diabetes plus one additional risk factor.
   b. All adults over 30 years of age with type 2 diabetes.
   c. Adults between 50 to 70 years of age who are deemed a high risk for cardiovascular events, and not at an increased risk for bleeding
   d. Aspirin is not recommended for primary prevention, and should only be used in adults with type 2 diabetes who have already had a heart attack or stroke
7. Which of the following statements is TRUE regarding screening recommendations for diabetes in the general population?
   a. All adults should be tested annually after the age of 35.
   b. All adults who are overweight (BMI >25 kg/m² or ≥ 23 kg/m² if Asian American) and have one or more risk factors should be screened.
   c. All adults should be screened annually starting at age 45.
   d. All children who are overweight and have a sedentary lifestyle should be screened annually.

8. Patients with glucose values higher than normal but less than the diagnostic cut-off for diabetes are said to have:
   a. Gestational diabetes
   b. Prediabetes
   c. Adult onset diabetes
   d. Insulin resistance

9. Which of the following interventions is the most cost-effective at preventing onset of Type 2 diabetes in those with high risk of developing diabetes?
   a. Acarbose
   b. Metformin
   c. Pioglitazone
   d. Lifestyle modifications (weight loss and exercise)

10. The HbA1c test for screening for diabetes may be preferred over other tests because:
    a. It has good reliability when National Glycohemoglobin Standardization Program (NGSP)-certified methods are used.
    b. It is available as a point-of-care test.
    c. It does not require participants to be in a fasting state.
    d. All of the above statements are true.

11. Which of the following should be considered when choosing treatments for geriatric patients with diabetes?
    a. Financial resources
    b. Functional limitations
    c. Support system
    d. All of the above should be considered

12. Which of the following statements is TRUE regarding diabetic retinopathy?
    a. Diabetes is the second leading cause of blindness among American adults.
    b. Diabetic retinopathy is categorized into dominant and non-dominant forms of the disease.
    c. The majority of people with diabetic retinopathy are diagnosed early so that therapy is effective.
    d. All type 2 diabetic patients should receive an ophthalmologic dilated eye examination at the time of diagnosis.
13. Which of the following complications would NOT be considered to be a neuropathy?
   a. Neurogenic bladder
   b. Peripheral artery disease
   c. Inability to detect cold or heat
   d. Gastroparesis

14. Diabetes is the leading cause of non-traumatic lower-limb amputations in the United States. Which of the following situations would NOT increase the likelihood of incurring an amputation?
   a. Peripheral neuropathy
   b. Peripheral vascular disease
   c. Severe nail deformity
   d. Well controlled blood sugars

15. A 67-year-old female, American Indian patient who is obese and taking antihypertensive medications is being screened for diabetes using the Afinion™ HbA1c test. Her HbA1c result is 5.7%. What action would you recommend?
   a. This patient clearly has diabetes and should be referred for follow-up care.
   b. This patient has a normal HbA1c and doesn't require referral for follow-up care.
   c. This patient has multiple risk factors for diabetes, and given the A1c result, should be referred to her primary care provider at the patient’s earliest convenience to discuss the results.
   d. Counsel the patient to watch how much sugar she is eating.

16. A 72-year-old male patient, who appears to be in good health, is screened for diabetes using the Afinion™ test. His HbA1c result is 7.5%. What action would you recommend?
   a. This patient can be diagnosed with diabetes based on this value and should be referred for follow-up care.
   b. This patient should be referred to his primary care provider for follow-up care, as the HbA1c result suggests chronic hyperglycemia and he needs further testing.
   c. Counsel this patient on the importance of risk factor reduction.
   d. Both b & c

17. According to the American Diabetes Association, which of the following non-pharmacologic therapies is NOT recommended for most patients with type 2 diabetes?
   a. Weight loss of 5-10% of body weight
   b. Strict dieting to achieve a total caloric intake of less than 800 kcal per day
   c. Moderate exercise for 30 minutes for 5 days per week
   d. Smoking cessation
18. The American Diabetes Association recommends strongly that adults age 18-64 with diabetes should receive all of the following vaccinations EXCEPT:
   a. Annual influenza vaccine
   b. Hepatitis B vaccine
   c. Pneumococcal polysaccharide vaccine 23 (PPSV23)
   d. Pneumococcal conjugate vaccine 13 (PCV13)

19. Which of the following is NOT considered to be a risk factor for developing type 2 diabetes?
   a. Body mass index ≥ 25 kg/m²
   b. Chronic physical inactivity
   c. Female sex
   d. Hypertension (≥140/90 mmHg)

20. Which of the following statements regarding diabetic kidney disease is FALSE?
   a. Most people with diabetic kidney disease are aware that they have it.
   b. Diabetes is a leading cause of end-stage renal disease in the U.S.
   c. The presence of albumin in the urine is a marker of nephropathy.
   d. Treatment of hyperglycemia and other risk factors such as hypertension may reduce the risk of progression of diabetic kidney disease.
**PRE-TEST: Examination Form**  
*Screening for Diabetes in Older Adults*

**PARTICIPANT INFORMATION:**

1. Name: ____________________________________

2. Mailing address: __________________________
   __________________________
   __________________________
   __________________________

3. Date exam completed_____________________

**QUESTIONS: (PLEASE CIRCLE ONE RESPONSE PER QUESTION):**

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For credit, please return: MTGEC/IPHARM, Skaggs Building, Room 217, University of Montana, 32 Campus Dr., Missoula, MT 59812.
Screening for Diabetes and Prediabetes in Older Adults

By
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A 2-hour Module from the

Montana Geriatric Workforce Enhancement Program

Montana Geriatric Education Center Website

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Montana Geriatric Education Center
Montana Geriatric Workforce Enhancement Program Goals/Purpose
Improve health outcomes for older adults in rural Montana via increased knowledge of older adult care and treatment of health problems by health care professionals.

Successful completion of this continuing education activity includes:
• Completion of the Pre-Test
• Reading of text
• Viewing two embedded videos in the module
• Completion of the Post-Test with at least 70% accuracy
• Completion of the module evaluation

Contact Hours: 2, including 2 Rx Hours for Nurses

Montana Nurses Association (MNA)
The Montana Geriatric Education Center is an approved provider of continuing nursing education by the Montana Nurses Association, an accredited approver by the American Nurses Credentialing Center’s Commission on Accreditation.
MNA Continuing Nursing Education Expiration Date: January 6, 2022

Conflicts of Interest
The planners and presenters of the CE activity have disclosed no relevant financial relationship with any commercial companies pertaining to this activity.

The Montana Geriatric Workforce Enhancement Program is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) under grant number U1QHP28733, Geriatric Workforce Enhancement Program (GWEP); the total award is $3,750,000 and supports the program 100%. This information or content and conclusions are those of the author and should not be construed as the official position or policy of, nor should any endorsements be inferred by HRSA, HHS or the U.S. Government.
Description of Module

Content

This module provides an overview of diabetes, including the impact of diabetes on the nation. Risk factors and complications of diabetes are discussed and characteristics of older adults who should be screened are identified. Both written and video instructions are used to teach the correct use of the Afinion™ Analyzer. A role play video models referral and counseling strategies that can be used with older adults who are at risk for developing diabetes. Pharmacologic therapies and important life style changes are briefly addressed.

In addition to providing continuing education for health care professionals, the ImProving Health Among Rural Montanans (IPHARM) program at the University of Montana uses this module to train health professions students to perform diabetes screening at geriatric health screening events throughout the state.

Module Purpose

The purpose of this module is to enable learners to apply knowledge gained about diabetes and issues surrounding screening for diabetes to improve diabetes related care for older adults in the learners’ professional settings.

Learning Objectives

Specifically, the learner will be able to:

1. Summarize the impact of diabetes on population health in the United States, particularly in older adults and Native Americans.
2. Discuss the causes, risk factors, and strategies for prevention of diabetes.
3. Identify major comorbidities that increase the risk of complications associated with diabetes.
4. Identify patients who are good candidates for diabetes screening.
5. Describe how to perform a glycated hemoglobin (HbA1c) test using the Afinion™ HbA1c test.
6. Explain the meaning of A1c test results at a screening event
8. Identify which screened patients should be referred for follow-up for further testing and/or to other community resources.
Screening for Diabetes

I. Introduction

“Diabetes” refers to a group of metabolic conditions characterized by chronic high blood sugars (hyperglycemia) resulting from inadequate insulin secretion by the pancreas, improper action of insulin on tissues, or a combination of both. It is a complex, chronic condition that can ultimately progress to cause serious complications in multiple organ systems throughout the body. Chronic exposure to hyperglycemia may result in vision loss from retinopathy, renal failure from kidney disease, and nerve damage from neuropathy. (1) Additionally, hyperglycemia plays havoc with the vascular system resulting in diabetic patients being 2 to 4 times more likely to have a heart attack or stroke compared to other patients of the same age and sex without diabetes. (2)

“Prediabetes” is defined as having blood glucose levels higher than normal but less than needed to diagnose diabetes. More than 1 out of 3 adults in the United States, or 84.1 million individuals, have prediabetes. (3) Unfortunately, as many as 9 out of 10 of these individuals are unaware of their condition. The prevalence of prediabetes increases with age, and it is estimated that nearly half of those over the age of 65 have prediabetes. Without early intervention through lifestyle changes and weight loss, approximately 25% of those with prediabetes will progress to type 2 diabetes within 3–5 years, and up 70% will develop overt diabetes within their lifetime.

Those with prediabetes or diabetes are often asymptomatic, and may go undiagnosed for many years before receiving a diagnosis when they present with complications. Early identification of those with prediabetes or diabetes allows for earlier intervention, including education on lifestyle changes and appropriate referrals for care, which may prevent more serious future complications. Given the large percentages of the population that are likely unaware of their diagnosis, the need for identification of high-risk patients and implementation of appropriate screening strategies is a crucial component in addressing this public health concern.

While screening for prediabetes and diabetes is often conducted in a healthcare facility, community-based screening (CBS), such as that of the UM IPHARM screening program, can be a tool to help increase access to testing for those in rural areas. Organizations such as the American Association of Diabetes Educators (4) and the Indian Health Services (5) stress the importance of using best practice when conducting CBS. One of the core components of best practice is appropriate education for those conducting the screening to allow them to identify high-risk patients, and to teach those receiving the screening tests about diabetes, risk factors, prevention strategies, and the implications of test results for their overall health. This module is designed to
prepare learners with the knowledge and skills to conduct screening and education through IPHARM events in a manner that reflects these best practices.

II. Impact of Diabetes on Health

A. Prevalence of Disease

Diabetes mellitus represents a major health concern as a major cause of morbidity and mortality in the United States and worldwide. In 2016, an estimated 1.6 million deaths around the world were directly caused by diabetes, putting it in the top 10 causes of death overall. This reflects increasing global prevalence of adults with diabetes, which has nearly doubled since 1980. The number of people with diabetes in the United States is estimated to be approximately 30.3 million people, or roughly 9.4% of the population, and diabetes is considered the 7th leading cause of death in the U.S. In 2015, 252,806 deaths were attributed to diabetes which is likely an underestimate since diabetes is often listed as a secondary cause of death.

Over the last decade, predictions from the U.S. Centers for Disease Control and Prevention (CDC) have been bleak, with estimates predicting that 30% of the entire population will have type 2 diabetes within the next 30 years. However, the most recent 2019 analysis of data from the period of 1980-2017 has shown that after a 20-year period of increasing prevalence and incidence of newly diagnosed diabetes, the overall number of people living with diagnosed diabetes in the United States has stabilized for the last 8 years, and there has been a 35% decrease in the incidence of new cases of diabetes from 2008-2017.

While this data is encouraging, Healthy People 2020 still considers diabetes a major public health concern. Diabetes shortens life expectancy by up to 15 years and is the 7th leading cause of death in the United States (U.S. Department of Health & Human Services, 2016). Given the burden of diabetes and the adverse health consequences for individuals and the healthcare system as a whole, continued efforts in screening, education, and prevention remain a priority for healthcare in the United States. Trends in the prevalence of diabetes and prediabetes in the U.S. can be found in Figure 1 below.
The economic impact of diabetes represents a significant burden to both individuals and society as a whole. More than 1 in 10 health care dollars in the U.S. are spent directly on diabetes and its complications, more than 1 in 5 health care dollars in the U.S. goes to the care of people with diagnosed diabetes, and trends in diabetes spending continue to increase. In parallel with increasing prevalence, economic costs of diabetes have increased by 26% from 2012 to 2017 (total $327 billion), with the majority of increasing costs associated with patients over the age of 65. On an individual level, those with diabetes have medical expenditures that are approximately 2.3 times higher on average than those without diabetes. In Montana, direct healthcare costs to Medicaid were over $56 million and the total economic cost of diabetes was nearly $1 billion per year in 2013, while the average annual cost per patient with diabetes was $15,000.

As shown in Table 1 below, the prevalence of diabetes increases in older populations. In those over the age of 65, it is estimated that approximately 25.2% have diabetes and 48.3% have prediabetes. Since 1990, the age group with the greatest growth rate in diabetes is the 45 to 64 year old group.
Trends in the prevalence of diabetes in Montana run parallel with national trends, steadily increasing over the last several decades. The prevalence of diabetes in Montana rose dramatically from 2.8% in 1990 to 8.0% in 2011, but has now plateaued over recent years. Compared with the rest of the United States, however, the rate of diabetes in Montana is one of the lowest in the nation. Approximately 7.4% of Montanans report being aware of having a diagnosis of prediabetes, but with a national average of approximately 1 in 3 with prediabetes, it is likely that there are many Montanans who have prediabetes but have not yet been diagnosed.\(^{(14)}\)

**B. Special Populations**

In some populations, the prevalence and burden of diabetes is much higher than in the general population, and distribution of these burdens is heavily influenced by social determinants of health. Specifically, older adults, minorities, and those with lower levels of education or socioeconomic status are identified as some of the key demographics that carry a greater burden of diabetes and its associated complications. Montana also has disparities in the prevalence of diabetes across the spectrum of age, race/ethnicity, level of education, and level of income that are consistent with national statistics, as shown in Table 2 below:

<table>
<thead>
<tr>
<th></th>
<th>Prediabetes, millions (% population)</th>
<th>Undiagnosed Diabetes, millions (% population)</th>
<th>Diagnosed Diabetes, millions (% population)</th>
<th>Total Diabetes, millions (% population)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 18-44</td>
<td>27.4 (23.7%)</td>
<td>1.6 (1.3%)</td>
<td>3.0 (2.6%)</td>
<td>4.6 (4.0%)</td>
</tr>
<tr>
<td>Age 45-64</td>
<td>34.3 (40.9%)</td>
<td>3.6 (4.3%)</td>
<td>10.7 (12.7%)</td>
<td>14.3 (17.0%)</td>
</tr>
<tr>
<td>Age &gt;65</td>
<td>23.1 (48.3%)</td>
<td>2.1 (4.4%)</td>
<td>9.9 (20.8%)</td>
<td>12.0 (25.2%)</td>
</tr>
<tr>
<td>Total, age &gt;18</td>
<td>84.1 (33.9%)</td>
<td>7.2 (2.9%)</td>
<td>23.0 (9.3%)</td>
<td>30.2 (12.2%)</td>
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</tbody>
</table>
Table 2: Prevalence of Diabetes in Montana versus U.S.\(^{(15)}\)

<table>
<thead>
<tr>
<th>Subpopulation</th>
<th>Prevalence of Diabetes (Montana)</th>
<th>Prevalence of Diabetes (United States)</th>
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<tbody>
<tr>
<td><strong>Age (years)</strong></td>
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<tr>
<td>18-44</td>
<td>1.9%</td>
<td>2.9%</td>
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<tr>
<td>45-64</td>
<td>10.4%</td>
<td>14.5%</td>
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<tr>
<td>65+</td>
<td>15.3%</td>
<td>22.6%</td>
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<tr>
<td><strong>Race/Ethnicity</strong></td>
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<tr>
<td>Native American</td>
<td>19.0%</td>
<td>17.3%</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>7.4%</td>
<td>10.1%</td>
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<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than high school</td>
<td>13.5%</td>
<td>19.1%</td>
</tr>
<tr>
<td>College graduate</td>
<td>5.3%</td>
<td>7.3%</td>
</tr>
<tr>
<td><strong>Annual Income</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than $25,000</td>
<td>14.2%</td>
<td>18.2%</td>
</tr>
<tr>
<td>More than $75,000</td>
<td>5.6%</td>
<td>7.1%</td>
</tr>
</tbody>
</table>

Older patients typically have multiple health problems which reinforces the need to properly identify patients at risk for diabetes to help prevent or slow diabetic complications. As discussed previously, there is a greater prevalence of diabetes in older adults, and as would be expected, older patients with diabetes have higher rates of premature death as well as greater functional disability. Older adults with diabetes have the highest rates of major lower extremity amputations, heart attacks, and end stage renal disease of any age group. They also have higher rates of complications from diabetes treatment including emergency room visits for hypoglycemia episodes. Common geriatric conditions that may be exacerbated by diabetes include polypharmacy, depression, cognitive impairments, urinary incontinence, injurious falls, and persistent pain. Older patients with diabetes will have special needs not found in younger patients; thus, specific treatment recommendations have been developed by the American Diabetes Association (ADA) and the American Geriatrics Society (AGS).\(^{(16, 17)}\)
Native Americans are an important minority population in Montana, making up 6% of the state population (versus 91% Caucasian).\(^{(18)}\) Most Native Americans on the seven reservations located throughout the state receive their healthcare from the Indian Health Service (IHS)\(^{(19)}\), which continues to be chronically and severely underfunded.\(^{(20,21)}\) Native Americans and Alaska Native adults are over twice as likely as white adults to be diagnosed with diabetes, and have a higher risk of diabetes than any other U.S. racial group. Nationally, the IHS has estimated the prevalence of diabetes within its adult population to be approximately 15%. The percent population with diabetes varies by region from 6% among Alaska Native adults to 22% among Native American adults in southern Arizona.\(^{(2)}\) In Montana, the prevalence of diabetes in the Native American population is approximately 2.5 times that of non-Hispanic white populations, with 18.9% of American Indian/Alaska Natives reporting having been diagnosed with diabetes compared to 7.4% of White non-Hispanics.

Awareness of the issues surrounding diabetes in Native Americans is important to provide supportive care and counseling to these individuals, because not only do Native Americans acquire diabetes at a higher rate, they are at greater risk for complications.

Furthermore, Native Americans are 1.6 times more likely than the general population to die from diabetes.\(^{(22)}\) With a higher incidence of diabetes, higher rates of complications, and higher mortality related to diabetes, this chronic condition is one of the greatest health concerns facing Native Americans today.

### III. Overview of Diabetes

#### A. Definition of Diabetes Mellitus

As mentioned previously, diabetes is a chronic disorder caused by insufficient insulin secretion, improper action of insulin on tissues, or a combination of both which leads to impaired metabolism of carbohydrates, proteins, and lipids.

#### B. Classifications of Diabetes

The ADA has four general classifications for diabetes mellitus\(^{(1)}\):

1. Type 1
2. Type 2
3. Other (caused by genetics, infections, endocrine disorders, etc.)
4. Gestational (occurs in 7% of all pregnant women; these women are at greater risk of developing type 2 diabetes)
Type 2 diabetes, which accounts for 90 to 95% of all diabetes diagnoses, was previously referred to as adult-onset diabetes, as most of the people who are diagnosed are well into their adult years.² Trends towards increasing obesity and lack of exercise in the American population over the last 20 years have led to an increasing prevalence of type 2 diabetes diagnoses among all age groups.²³,²⁴

Only type 2 diabetes will be discussed further in detail, as this type pertains to most of the diagnosed cases and is the most receptive to lifestyle and dietary changes. However, as a brief review, Table 3 will describe some of the distinguishing characteristics between type 1 and type 2 diabetes.

Prediabetes is a condition in which blood glucose is elevated above the normal range, but does not yet meet the cutoff to be diagnosed with diabetes. It is closely associated with metabolic syndrome and obesity, and those with prediabetes have a high risk of progression to overt diabetes. Prediabetes will be discussed throughout this module, as it relates to screening and opportunities to intervene and delay or prevent progression to diabetes.

**Table 3: Comparison between Type 1 and Type 2 Diabetes**¹,²⁵

<table>
<thead>
<tr>
<th></th>
<th>Type 1</th>
<th>Type 2</th>
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<tbody>
<tr>
<td><strong>Typical age of onset</strong></td>
<td>Generally in childhood or adolescence</td>
<td>Usually &gt; 40 years old</td>
</tr>
<tr>
<td><strong>Synonyms</strong></td>
<td>Juvenile-onset Insulin-dependent diabetes mellitus (IDDM)</td>
<td>Adult-onset Non-insulin dependent diabetes mellitus (NIDDM)</td>
</tr>
<tr>
<td><strong>Etiology</strong></td>
<td>Immune-mediated idiopathic (unknown)</td>
<td>Insulin resistance and secretory deficiencies</td>
</tr>
<tr>
<td><strong>Body weight</strong></td>
<td>Non-obese</td>
<td>Obese (80%)</td>
</tr>
<tr>
<td><strong>Endogenous insulin secretion</strong></td>
<td>Minimal secretion</td>
<td>Varying degrees of secretion</td>
</tr>
<tr>
<td><strong>Insulin resistance</strong></td>
<td>Not usually</td>
<td>Common</td>
</tr>
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</table>

Our knowledge of the pathophysiology of type 2 diabetes has evolved over several decades. We now understand it to be a heterogeneous chronic condition that progresses over time due to a combination of variables, including environmental factors, genetics, inflammation, and metabolic stress. Despite the existence of multiple phenotypes with slightly different underlying pathologies, the ultimate driver of hyperglycemia associated with type 2 diabetes is loss of pancreatic beta-cell function, typically coinciding with decreasing sensitivity to insulin in peripheral tissues or “insulin resistance.”
In those without diabetes, the endocrine system regulates blood glucose levels within a normal range. This process of glucose homeostasis is complex, but two primary hormones are involved in regulation of blood glucose. Insulin is a peptide hormone produced by the pancreatic beta cells, which lowers blood glucose, and glucagon is a hormone produced by pancreatic alpha-cells, which stimulates glucose production from the liver. Insulin acts on liver, muscle, and fat tissues to stimulate cells to increase glucose uptake, and has a number of other effects on metabolism. Insulin is secreted by pancreatic beta cells in differing amounts throughout the day in response to elevated blood glucose levels. Plasma glucose rises after ingestion of food, stimulating the release of insulin from the pancreas, which then facilitates glucose transport into the cells. As glucose levels fall in response to insulin action, insulin secretion is reduced, and, if glucose levels fall below the desired range, glucagon is produced to raise blood glucose levels.

Research has more recently discovered another set of important metabolic hormones, known as incretins, which are produced in the gastrointestinal tract and play a major role in glucose homeostasis. The incretins, glucagon-like peptide 1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP), are secreted by specialized cells in the GI tract in response to oral glucose intake and nutrient absorption, and act on beta-cells to stimulate insulin secretion. GLP-1 not only stimulates insulin secretion, but also inhibits glucagon production, delays gastric emptying, and increases feelings of satiety.

GIP, also released in response to nutrient intake, is responsible for stimulating insulin secretion in a glucose-dependent manner. Together, the effects of these incretin hormones are responsible for approximately 90% of insulin secreted in response to an oral glucose load. Discovery of these hormones has led to the development of a newer class of highly effective diabetes medication, the GLP-1 receptor agonists, mentioned in the “Pharmacologic Therapy” section later in this module. Patients with type 1 diabetes and patients with long-standing type 2 diabetes also develop a significant amylin deficiency. Amylin is a glucoregulatory hormone secreted with insulin that helps lower blood glucose by slowing gastric emptying, suppressing glucagon output, and increasing satiety, and has also been identified as a target for drug therapy in diabetes.
Table 4: Pathophysiology of Diabetes\(^{(28)}\)

<table>
<thead>
<tr>
<th>Organ System</th>
<th>Normal Metabolic Function</th>
<th>Defect in Type 2 Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Major Role</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancreatic beta cells</td>
<td>Secrete insulin</td>
<td>Decline in beta-cell mass and function, decreased insulin secretion</td>
</tr>
<tr>
<td>Pancreatic alpha cells</td>
<td>Secrete glucagon</td>
<td>Impaired response to insulin, increased glucagon secretion</td>
</tr>
<tr>
<td>Muscle</td>
<td>Metabolizes glucose for energy</td>
<td>Decreased peripheral glucose uptake</td>
</tr>
<tr>
<td>Liver</td>
<td>Secretes glucose during fasting periods to maintain brain function; main site of gluconeogenesis (glucose production in the body)</td>
<td>Decreased sensitivity to insulin, increased endogenous glucose secretion</td>
</tr>
<tr>
<td>Adipose tissue (fat)</td>
<td>Stores small amounts of glucose for its own use. When fat is broken down, glycerol is released, which is used by the liver to produce glucose</td>
<td>Decreased sensitivity to insulin, increased lipolysis and free fatty acid production</td>
</tr>
<tr>
<td>Stomach/small intestine</td>
<td>Digests and absorbs carbohydrates and secretes incretin hormones</td>
<td>Decreased incretin effect leads to post-meal hyperglycemia, increased absorption of glucose</td>
</tr>
<tr>
<td>Colon/microbiome</td>
<td>Normal microbiome contributes to metabolic homeostasis, incretin</td>
<td>Abnormal microbiome, possible decreased GLP-1 secretion</td>
</tr>
<tr>
<td>Kidney</td>
<td>Reabsorbs glucose from renal filtrate to maintain glucose at steady-state levels; also an important site for gluconeogenesis (glucose production)</td>
<td>Increased glucose reabsorption</td>
</tr>
<tr>
<td>Brain</td>
<td>Utilizes glucose for brain and nerve function Regulates appetite</td>
<td>Neurotransmitter dysfunction, increased appetite</td>
</tr>
<tr>
<td>Immune system</td>
<td>Protects against infection, regulates inflammation</td>
<td>Increased inflammation, dysfunctional immune response</td>
</tr>
</tbody>
</table>
C. **Pathophysiology of Diabetes**

In the earliest stages of insulin and glycemic abnormalities, pancreatic beta-cells begin to lose the ability to sense and properly respond to elevations in blood glucose. Despite these early abnormalities, insulin is still produced in sufficient quantities to overcome insulin resistance in the peripheral tissues, and individuals may continue to have normal blood glucose. As the disease progresses, however, gradual loss of beta-cell mass results in impaired insulin production and an inability to maintain glucose homeostasis. Metabolic abnormalities, such as obesity, hyperglycemia and hyperlipidemia, contribute to disease progression.\(^{(29)}\)

Progressive beta-cell decline may occur over decades, and is typically slow in the earliest phases, with a decline in beta-cell function of approximately 2% per year. In later phases, however, beta-cell decline can occur much more quickly (~18% per year), ultimately leading to chronic hyperglycemia and overt diabetes. In those with prediabetes, there may be an overall reduction in volume of pancreatic beta-cells of up to 60%; by the time a patient is diagnosed with diabetes they may have lost over 80% of their beta-cell function.\(^{(30,31,32)}\)

Newer understanding of the pathophysiology of diabetes highlights the complexity of the disease process that contributes to chronic hyperglycemia. Named the “Egregious Eleven,” a more recent model of the defects includes not just abnormalities in beta-cell function, insulin secretion, and insulin resistance, but adds an understanding of the role that multiple organ systems play in the development of diabetes. While beta-cell defects remain central to disease process, other hormones and organ systems have been highlighted, see Table 4.\(^{(28)}\)

Deficiencies in incretin production from the GI tract and diminished response to incretin effects contribute to impaired insulin production and hyperglycemia.\(^{(29)}\) Lower incretin levels and resistance to their effects also result in increased gastric emptying, which may contribute to overeating and decreased feelings of satiety in the brain. In turn, this may further drive overeating, obesity, and other metabolic abnormalities that accelerate the progression of diabetes. Lower insulin levels and increased glucagon levels result in increased glucose absorption from the GI tract, increased glucose production from the liver, and increased reabsorption of glucose in the kidney.\(^{(33)}\) Chronic inflammation leads to abnormal immune function, which further contributes to destruction of pancreatic beta-cells. Some data also suggest that certain abnormalities in the gut microbiome play a role.\(^{(34)}\) Diabetes is no longer confined to the pancreas, but is actually a complex positive feedback cycle involving nearly all organ systems.
D. Risk Factors

Certain factors have been identified with an increased risk of developing type 2 diabetes; see the list below. Properly identifying patients with these risk factors is an important step to appropriately screen patients and initiate early interventions to prevent or delay the onset of diabetes. The list of risk factors below is reflected in the diabetes screening recommendations covered later in this module.

Risk Factors for Type 2 Diabetes \(^{(1,17,35)}\)

- Age ≥ 45 years old
- Overweight (Body mass index ≥ 25 kg/m\(^2\) or ≥ 23 kg/m\(^2\) if Asian American; See Appendix D)
- Acanthosis nigricans or nonalcoholic fatty liver disease
- First degree relative with diabetes
- Physical inactivity
- Race/ethnicity (African-American, Native Americans, Latinos, Asian Americans, and Pacific Islanders)
- Previously identified prediabetes {e.g., impaired fasting glucose (IFG), impaired glucose tolerance (IGT), or HbA1c >5.7%}
- History of gestational diabetes
- Hypertension (≥ 140/90 mmHg in adults or on antihypertensive therapy)
- HDL cholesterol <35 mg/dL and/or a triglyceride level >250 mg/dL
- Polycystic ovary syndrome
- History of cardiovascular disease
- Anti-psychotic therapy for schizophrenia and/or severe bipolar disease
- Sleep disorders (obstructive sleep disorders, chronic sleep deprivation) in the presence of glucose intolerance
- Chronic glucocorticoid exposure

E. Complications

As a result of the insidious nature of type 2 diabetes, complications are often present by the time diabetes is diagnosed. Once complications are present, interventions may slow their progression, but they cannot be reversed. Often the effects of chronic uncontrolled hyperglycemia have widespread consequences for multiple organ systems. Complications in those with diabetes may include emergency visits and hospitalizations due to hyperglycemic or hypoglycemic crisis, but are also often accompanied by chronic, progressive complications that develop over decades. These chronic issues are typically categorized as either macrovascular (those affecting large blood vessels) or microvascular (those affecting smaller blood vessels), and will be discussed in more detail below. Strong evidence demonstrates that appropriate glycemic control and appropriate management of other risk factors is essential to prevent these complications. An overview of the detrimental effects diabetes has on the body is outlined in the upcoming sections. Knowledge of
the various complications associated with poorly controlled diabetes may be helpful when counseling patients regarding the importance of proper glycemic control.

1. **Macrovascular Complications**

Macrovascular complications are primarily a result of atherosclerosis, and include cardiovascular disease, peripheral vascular disease, and stroke. People with diabetes are 2 to 4 times more likely to have a heart attack or stroke compared to people of the same age and sex without diabetes. In 2014, there were 7.2 million hospital discharges for patients with diabetes, with 1.5 million of those due to cardiovascular disease and stroke. In addition, cardiovascular disease is the leading cause of death in diabetic patients. Diabetic patients are at increased risk of atherosclerosis for three primary reasons:

A. The incidence of other cardiac risk factors is higher in those with diabetes, such as hypertension, high cholesterol, and obesity.

B. Diabetes is itself a risk factor for cardiovascular disease (CVD). Both the American College of Cardiology (ACC) and the American Heart Association (AHA) consider diabetes to be equivalent to having coronary heart disease.

C. Diabetes may act synergistically with other risk factors by increasing atherogenecity (i.e., altering lipid particles, modifying the blood vessel wall, or by promoting a prothrombotic environment).

Therefore, patients with diabetes need intensive treatment for coexisting risk factors in conjunction with blood glucose control. These risk factors include obesity, hypertension, dyslipidemia, and tobacco use. Appropriate management of these modifiable risks will be outlined in later sections of this module.

2. **Microvascular complications**

Microvascular complications affect smaller blood vessels and result in widespread effects throughout the body. The true mechanism for the development of microvascular complications (i.e. nephropathy, neuropathy, and retinopathy) is unclear, but three distinct metabolic pathways appear to be involved:

A. Excess glucose in the blood can interact and bind (glycate) proteins causing irreversible changes in the protein structure and potentially the function of the protein. This newly formed glycated protein is referred to as an advanced glycation end (AGE) product. AGE products have been linked to detrimental effects in the extracellular matrix as well as within the cell (intracellular).

B. High levels of intracellular glucose can cause the premature activation of enzymatic processes (i.e., protein kinase C) which can lead to increased
neovascularization in the eye, increased pro-inflammatory responses, and potentially prothrombotic states.\(^{37}\)

C. Some tissues such as nerves, retina, kidney and blood vessels do not require insulin to transport glucose intracellularly. In hyperglycemic conditions, increased intracellular glucose can be converted by the enzyme, aldose reductase, to sorbitol. This enzymatic reaction requires the cofactor NADPH, which results in the depletion of this cofactor. NADPH is also used to form glutathione which is one of the body’s more potent antioxidants. Therefore, elevated glucose levels indirectly lower our defense mechanisms against oxidative stress and damage.\(^{25,37}\)

Irregularities found in the arterioles and capillaries result in microvascular complications. As a result of undetected chronic hyperglycemia that exists before a patient is diagnosed with overt type 2 diabetes, microvascular complications are often already present to some degree at the time of diagnosis. The primary forms of microvascular complications, including nephropathy, retinopathy, and neuropathy, are discussed below.

\[\text{a) Diabetic kidney disease (nephropathy)}\]

The term “diabetic kidney disease” or “diabetic nephropathy” refers to a subset of the larger population of those with chronic kidney disease (CKD). While age, and uncontrolled hypertension are also major contributors to the development of CKD, it is estimated that approximately 25% of CKD is specifically attributable to diabetes after adjusting for age and demographics, and diabetes is the presumed cause of end-stage renal disease (ESRD) in approximately 50% of cases.\(^{38,39,40}\) Diabetic kidney disease (DKD) is both a common and underdiagnosed complication in those with long-standing diabetes. Approximately one in four of those with diabetes have diabetic kidney disease, yet it is estimated that only 3-10% of those with mild to moderate DKD are aware of their disease. This lack of awareness creates a major barrier to appropriately addressing risk factors that drive the progression of DKD\(^{39,41}\) in addition to controlling blood glucose, treatment of hypertension and dyslipidemia, and choosing medications that are associated with renal benefits, can all help reduce the risk of progression of DKD.\(^{42,43,44}\)

Just as the prevalence of diabetes has increased at national and state levels, so, too, has the incidence of CKD which increased steadily until 2006 and has now leveled off, with higher incidences in older adults and those with diabetes. In 2012, the prevalence of chronic kidney disease (stages 1–4) in U.S. adults was 36.5%. In 2014, a total of 52,159 people developed end-stage renal disease with
diabetes as the primary cause. Figure 2 shows the prevalence of chronic kidney disease by age and risk factor in the United States.

**Figure 2: Prevalence of CKD by age and risk factor, 1999-2014.**

![Graph showing prevalence of chronic kidney disease](image)

Abbreviations: BMI, body mass index; CKD, chronic kidney disease; CVD, cardiovascular disease; DM, diabetes mellitus; HTN, hypertension; SR, self-reported.

The pathophysiology of diabetic kidney disease is incompletely understood, but usually starts with a dysfunction in the glomerulus. In normal physiology, the glomerulus is comprised of a vascular capillary bed which filters the blood, generating a filtrate which progresses further down the nephron, the filtering unit of the kidney. Early in diabetes, changes in the glomerulus, i.e., thickening of the capillary vessels, cause a decrease in the volume of filtrate produced, which specialized cells within the kidney sense as low blood flow or pressure. This triggers the renin-angiotensin system, and often subsequent hypertension, to increase blood pressure to maintain adequate blood flow through the kidney. This hypertensive state also leads to progressive damage within the glomerulus.

As the glomerular function deteriorates, so does its ability to discriminate which types of molecules are being filtered. Albumin, a serum protein, is generally not filtered through the kidney, but with decreased glomerular function, small amounts of albumin are found in the urine. The detection of small amounts of albuminuria is often the first sign of diabetic kidney disease, and as the nephropathy progresses, larger amounts of albumin are found in the urine. Having 30 mg/24 hours of albumin or more in the urine is considered abnormal.
and requires further testing to confirm the results. Historically, ratios between 30 and 299 mg/24 hours were called “microalbuminuria” and those >300 mg/24 hours were called “macroalbuminuria” (Figure 6). Along with a decline in eGFR (estimated glomerular filtration rate), these endpoints mark progression of CKD.\(^{(27,46,47)}\)

**Figure 3: Progression of Diabetic Kidney Disease with Corresponding Decreases in Renal Function\(^{(46)}\)**

![Diabetic Nephropathy Disease Progression](image)

**b) Retinopathy**

In the United States, diabetes is the leading cause of blindness among adults between the ages of 20 to 74 years old. Roughly 4.2 million Americans have diabetic retinopathy, and 655,000 Americans have vision-threatening retinopathy.\(^{(48,49)}\). Approximately 29% of adults with type 2 diabetes have some degree of diabetic retinopathy.\(^{(7)}\) Furthermore, patients with diabetes have a higher prevalence of other visual impairments including cataracts and glaucoma (Figure 4).\(^{(48,50)}\)
Diabetic retinopathy, which usually affects both eyes, is a progressive disease characterized by two stages: non-proliferative and proliferative diabetic retinopathy.

(1) Non-proliferative diabetic retinopathy\(^{(25,46)}\)

Non-proliferative diabetic retinopathy usually occurs early in the disease. Initially, microaneurysms occur in retinal capillaries which increase the permeability of the vessel walls to fats, leading to hard, yellow exudates in the retinal vessel wall. Exudates in the area of the macula (point of central vision) can lead to macular edema. The progression of this stage eventually leads to decreased vascular flow in the retina or retinal ischemia. Figure 5 compares a normal retina to one with advanced retinopathy.

(2) Proliferative diabetic retinopathy\(^{(25,46)}\)

Secondary to the ischemic changes in the retina, new blood vessels are formed (neovascularization) to restore blood flow. Unfortunately, these blood vessels, which often appear near the optic nerve or macular region, are weaker and more susceptible to rupture. Retinal detachment and blindness can be the final stages if not treated.
Prevention of diabetic retinopathy is the goal. Early detection and diagnosis of diabetic retinopathy and timely treatment reduce the risk of vision loss. Optimizing blood glucose, cholesterol, and blood pressure control helps reduce the risk of developing retinopathy and these interventions may slow progression if retinopathy is already present. As mentioned previously, microvascular damage has often already begun by the time type 2 diabetes is detected. Therefore, it is recommended that those with type 2 diabetes receive a dilated eye exam at the time of diagnosis, and should receive an eye exam annually thereafter. Unfortunately, up to 50% of patients are not getting their eyes examined or are diagnosed too late for treatment to be effective.\textsuperscript{48}

Once a patient develops diabetic retinopathy, they should be referred to an experienced ophthalmologist. Laser photocoagulation therapy can be used to treat proliferative diabetic retinopathy and severe non-proliferative disease. Antivascular endothelial growth factor (VEGF) injection therapy is indicated for treating diabetic macular edema.\textsuperscript{47}

\textbf{(3) Neuropathy}

Neuropathies, which are functional disturbances of the peripheral nervous system, affect approximately 60 to 70\% of all patients with diabetes.\textsuperscript{46,50} There are four broad categories of neuropathies: sensory, gastrointestinal autonomic, cardiovascular autonomic, and motor.
a) Sensory

Loss of sensory nerve input (i.e., hot and cold), due to demyelination of peripheral nerves, results in symmetric distal polyneuropathies. Early symptoms include numbness or tingling sensations in the extremities (usually the feet and sometimes the hands) typically followed by painful neuropathies, and eventually the permanent loss of sensation in the affected areas. This progression of neuropathy can not only be painful, but the eventual loss of sensation can put patients with diabetes at a greater risk of injury to their feet and an inability to feel wounds and ulcers. This increases their risk of developing diabetic foot ulcers and infections which may become severe enough to require hospitalization and amputation.

b) Gastrointestinal/Miscellaneous Autonomic Neuropathies

Autonomic nerves support the involuntary activities of the body, such as actions of the stomach, bladder and intestines. Dysfunction of the autonomic nerves may lead to debilitating complications summarized in Table 5.

**Table 5: Common Autonomic Dysfunctions Found in People with Diabetes**

<table>
<thead>
<tr>
<th>Neuropathy</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastroparesis</td>
<td>A paralysis of the stomach causing delayed gastric emptying and impaired absorption of food. Symptoms include a bloated feeling after eating, nausea and sometimes emesis.</td>
</tr>
<tr>
<td>Diabetic diarrhea</td>
<td>Erratic functioning of the intestine resulting in episodic, voluminous, and watery stools which may be passed without warning. Periods of constipation may also occur, which may increase the risk of an impacted bowel.</td>
</tr>
<tr>
<td>Neurogenic bladder</td>
<td>The bladder fails to respond to normal nerve stimulation resulting in incomplete emptying of the bladder leading to urinary retention. The holding of residual urine in the bladder puts patients at increased risk of urinary tract and kidney infections.</td>
</tr>
<tr>
<td>Erectile dysfunction (ED)</td>
<td>The ability to attain and maintain an erection may be impaired in diabetic men, and ED may often be a presenting problem leading to a type 2 diabetes diagnosis.</td>
</tr>
</tbody>
</table>
c) **Cardiovascular Autonomic Neuropathies (CAN)**\(^{(47)}\)

CAN is the most studied and clinically important form of diabetic autonomic neuropathy because of its independent association with cardiovascular death. In early stages, CAN often lacks symptoms. Advanced disease may be expressed by resting tachycardia (>100 bpm) and orthostatic hypotension without a compensatory heart rate response.

**d) Motor Neuropathies**\(^{(25,46)}\)

Motor neuropathies, the rarest of the diabetic neuropathies, affect the nerves which cause movement, primarily in the extremities, and may result in decreased motor function and gait disturbances. People with diabetes are more likely to have falls than adults without diabetes. When a fall does occur, approximately 46% of people with diabetes reported being injured compared to 33% of people without diabetes in Montana.\(^{(52)}\)

Because the types and presentations of diabetic neuropathies are so diverse, a general recommendation is an annual screening for the above neuropathies by a health care provider. People with diabetes should be educated about the types and typical presentation of the various neuropathies. If signs or symptoms appear, patients should notify their provider for prompt further evaluation.

3. Infections

When compared to those without diabetes, patients with diabetes are more susceptible to nearly all types of infection, including genitourinary infection, candidiasis, skin and soft tissue infection, bone and joint infection, endocarditis, pneumonia, and sepsis. Furthermore, these patients often have a worse prognosis. One population-based study showed that those with type 2 diabetes had a 50% higher rate of infection requiring antimicrobial treatment, and had nearly twice the rates of hospitalization death due to infection.\(^{(53)}\)

The increased risk of infection may be related to an impaired cell-mediated immunity and phagocytic function, a decrease in peripheral circulation, or the increased growth of organisms under hyperglycemic conditions. Furthermore, hyperglycemia prevents adequate wound healing; therefore, glycemic control is paramount to speed wound healing.\(^{(46)}\) Because diabetic patients are at greater risk of infection, ensuring appropriate immunization practices is an important component of diabetes care. The ADA recommends immunization with a one-time dose of PPSV23 pneumococcal vaccine (Pneumovax) for all adults between the age of 18-64, unless otherwise contraindicated.
In addition to this one-time dose of PPSV23 between the ages of 18-64, it is important that patients with diabetes also receive the routine pneumococcal vaccination series for all adults over the age of 65, with one dose of PCV13 (Prevnar) followed by one dose of PPSV23 (Pneumovax) at least one year later. PCV13 (Prevnar) is not recommended for use in patients with type 2 diabetes who are between the age of 19-64 if there are no other immunocompromising conditions present. Anyone administering these vaccines should ensure that appropriate dosing intervals with respect to administration of prior pneumococcal vaccines are used for this series, as recommended by the CDC.\(^{54}\) A summary of important routine immunizations for people with diabetes can be found in Table 6 below:

**Table 6: Immunizations for Individuals with Diabetes\(^{54}\)**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Recommended Immunization Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza</td>
<td>Annually</td>
</tr>
<tr>
<td>Tdap</td>
<td>One booster dose every 10 years</td>
</tr>
<tr>
<td>Zoster vaccine</td>
<td>Two-dose series of recombinant zoster vaccine (Shingrix) for adults age 50 and older</td>
</tr>
<tr>
<td>Pneumococcal vaccine</td>
<td>One dose of PPSV23 for all adults age 19-64, plus Two-dose series of PCV13 followed by PPSV23 for adults age 65 and older</td>
</tr>
<tr>
<td>Hepatitis B vaccine</td>
<td>Three-dose series recommended for adults age 19-59 May be given in those age 60 and older at clinician discretion</td>
</tr>
</tbody>
</table>

4. **Lower Extremity Complications**

Diabetes is the leading cause of non-traumatic lower-limb amputations in the United States and worldwide.\(^2\) After decades of decline in rates of amputations in the United States, new statistics show that rates of amputations related to poorly controlled diabetes have increased 50% between 2010-2015.\(^{55}\) These increases were most evident in those age 18-64, amputations were more common in men than in women, and the greatest increase was seen in amputations of the metatarsal. This trend reversal represents an important indicator for comprehensive diabetes care and our need to continue to improve early detection and treatment of diabetes and its associated complications.
Patients with diabetes are predisposed to lower extremity complications and impaired wound healing due to neuropathies, poor peripheral circulation, and immune dysfunction. People with diabetes often cannot feel painful warnings of blister formation or an ingrown toenail. Therefore, it is essential to educate patients to inspect their feet daily for signs of skin damage and infection.\textsuperscript{(56)} Risk factors which have been identified with increasing likelihood of an amputation are\textsuperscript{(47)}:

- Peripheral neuropathy with loss of protective sensation
- Evidence of increased pressure (erythema, hemorrhage under a callus)
- Bony or foot deformity
- Peripheral vascular disease (decreased or absent pedal pulses)
- A history of ulcers or amputations
- Severe nail pathology
- Poorly controlled blood glucose
- Advanced diabetic kidney disease
- Visual impairment (so can’t self-monitor feet)
- Smoking

The best defense is once again good screening and detection of early signs of foot and lower extremity problems. Patients with diabetes should have at least an annual comprehensive foot examination, which includes visual inspection, palpation of dorsal and tibial pulses, reflex checks, and sensation, vibration, and monofilament testing.\textsuperscript{(6,7)} Higher risk patients with multiple risk factors should receive more frequent screening, and in some cases, specialist care.

People with diabetes should inspect their feet daily for signs of inflammation or wounds. Wearing cotton socks, good-fitting shoes, trimming nails straight across to avoid ingrown toenails, and keeping the skin in good condition are advised. People with diabetes should avoid going barefoot or wearing flip-flop sandals, using abrasive treatments (corn removers), and should stop smoking to help prevent lower extremity complications.

IV. Screening and Diagnosis

A. Diabetes Screening

While there is considerable evidence that intensive treatment of cardiovascular risk factors can reduce mortality in patients with established diabetes, there have been limited clinical trials to address the effectiveness of diabetes screening on decreasing mortality or morbidity, or on the cost-effectiveness of early detection. The ADA currently recommends diabetes
screening only be performed in patients at higher risk of developing diabetes. Testing should be considered in adults who are overweight or obese (BMI ≥25 kg/m² or ≥23 kg/m² in Asian Americans) and have one or more of the following risk factors:\(^1\):

- First-degree relative with diabetes
- High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
- History of cardiovascular disease
- Hypertension (≥140/90 mmHg or taking medication for hypertension)
- HDL cholesterol level <35 mg/dL (0.90 mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L)
- Women with polycystic ovary syndrome
- Physical inactivity
- Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)

Additionally, screening for diabetes should be performed in women with a history of gestational diabetes and adults over the age of 45. If test results are normal, then repeat testing every 3 years is reasonable. If a person’s A1c is found to be above 5.7% and they are diagnosed with prediabetes, they should be screened for diabetes annually.\(^1\)

There are two approaches to prevention of disease: population-wide or mass testing and prevention strategies or screening of high-risk patients and treatment of the identified subset. The United States and the United Kingdom use the screen and treat approach to manage diabetes. Because current screening practices for diabetes have a low sensitivity for detecting prediabetes, screening practices alone are unlikely to have a major impact on diabetes outcomes. Low sensitivity of screening tests results in a high number of false negatives where people are incorrectly identified as not having prediabetes.\(^{57,58}\) Because of this, participants in screening events should be encouraged to have repeat screening conducted periodically and still institute healthy lifestyle changes. More work is needed to determine effective screening strategies for those with prediabetes.

**B. Diagnosis of diabetes**

According to current ADA guidelines, diagnosis of diabetes can be determined through four different methods of testing blood glucose control. Any of the lab tests outlined in Table 7 below can be used to identify patients who have diabetes or prediabetes, although some tests may be more effective than others in detecting diabetes in certain populations (e.g., pregnant women). Unless a patient presents with symptoms of hyperglycemia and a blood glucose >200 mg/dL, one abnormal test value is insufficient to make a diagnosis of diabetes. A
diagnosis of diabetes may be made after the finding of two abnormal values. This may be either a repeat of the same test after finding that the initial lab value is abnormal (e.g., two consecutive abnormal A1c values, drawn at different times), or it may be that two different labs drawn at the same time (e.g., A1c and fasting blood glucose) are above the diagnostic threshold. In either scenario, the diagnosis of diabetes can be confirmed.

For the purposes of this module, we will focus on the use of hemoglobin A1c (HbA1c), the screening test used by IPHARM. As can be seen below, prediabetes is defined as an A1c between 5.7%-6.4%, and overt diabetes is defined as an A1c of 6.5% or higher. While you may find that a patient screened at an IPHARM event falls into one of these categories, remember that a follow up confirmatory test MUST be performed to make a definitive diagnosis.$^{(1,27)}$

Patients with an A1c greater than 5.7% can also be referred to the Montana Diabetes Prevention Program as a resource to learn more about ways they can engage in lifestyle changes to reduce their risk of progression to diabetes. More information on this program can be found at: https://dphhs.mt.gov/publichealth/Diabetes.

**Table 7: Diagnostic Criteria for Diabetes** $^{(1,17,27,59)}$

<table>
<thead>
<tr>
<th>Test Method</th>
<th>Diabetes</th>
<th>Prediabetes</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>HbA1c performed in a laboratory using a method that is National Glycohemoglobin Standardization Program (NGSP) certified and standardized to the DCCT assay.</td>
<td>≥6.5%</td>
<td>5.7-6.4%</td>
</tr>
<tr>
<td>2</td>
<td>Casual* plasma glucose with diabetes symptoms (i.e., polyuria, polydipsia, and unexplained weight loss.</td>
<td>≥ 200 mg/dL</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Fasting plasma glucose (no caloric intake ≥ 8 hours).</td>
<td>≥ 126 mg/dL</td>
<td>≥ 100 mg/dL but &lt; 126 mg/dL (Referred to as impaired fasting glucose or IFG)</td>
</tr>
<tr>
<td>4</td>
<td>Two-hour postprandial plasma glucose during an oral glucose tolerance test (OGTT). Patient should be fasted for ≥ 8 hours and then given 75 gm anhydrous glucose orally dissolved in water.</td>
<td>≥ 200 mg/dL</td>
<td>≥ 140 mg/dL but &lt; 200 mg/dL (Referred to as impaired glucose tolerance or IGT)</td>
</tr>
</tbody>
</table>

* Casual is defined as any time of day without regard to time since last meal.
C. **Use of HbA1c for Screening**

Hemoglobin, a protein found in red blood cells, is responsible for delivering oxygen to cells. Like most proteins, it has the ability to be glycated or linked with sugars found in the blood, such as glucose. Therefore, the amount or percentage of glycated hemoglobin in the blood is a measurement of how much glucose the hemoglobin has been exposed to in the preceding weeks. Since hemoglobin is only found within red blood cells, which typically have a lifespan of 120 days, the percent of glycated hemoglobin is a measure of glycemic control over the past 8 to 12 weeks. A person without diabetes usually has about 5% of the hemoglobin glycated, but for patients with chronic hyperglycemia, the percentage of glycated hemoglobin is considerably higher.\(^6\)^\(^{61}\)

The HbA1c test, which is a measurement of glycated hemoglobin, is routinely recommended for use at least twice a year as a monitoring tool for patients diagnosed with diabetes to assess how well the patients are managing their diabetes.\(^61\) The HbA1c test is currently used as a screening device, as studies have evaluated the HbA1c test in this capacity and have found good reliability when National Glycohemoglobin Standardization Program (NGSP)-certified methods are used.\(^17\),\(^59\)

The ImProving Health Among Rural Montanans (IPHARM) screening program chose to utilize the HbA1c test as a screening device for three main reasons.

First, analyses suggest that the HbA1c test has the best combination of sensitivity and specificity at a cut point of 5.7%, which can be used to identify cases of impaired fasting glucose. Among the nondiabetic population, an HbA1c of 5.6% corresponds to a fasting blood glucose (FPG) of 110mg/dL and an HbA1c of 5.4% corresponds to an FPG of 100mg/dL. Table 8 demonstrates further correlations of HbA1c and average plasma glucose. Clinical judgment is necessary to evaluate patients whose values fall between 5.7 - 6.4%, with considerable emphasis placed on co-existing risk factors. The HbA1c test can help identify individuals with high risk for future diabetes.\(^17\)
Secondly, the HbA1c test is easy to administer and only takes about five minutes to perform, requiring minimal blood sample collection. And finally, the test does NOT have to be performed in a fasted state. This is important as it is not practical for patients to attend screening events in the afternoon without eating a meal since the previous night.

It should be emphasized that the use of the HbA1c test for screening purposes is not a diagnostic procedure. Multiple factors, including hemoglobinopathies (e.g., sickle cell anemia) can interfere with test results, and results have to be confirmed. Conditions associated with increased red cell turnover, such as pregnancy (second and third trimesters), recent blood loss or transfusion, erythropoietin therapy, or hemolysis can also affect HbA1c results. An updated list of interferences is available at Harmonizing Hemoglobin A1c Testing. Follow-up care by a health care professional will be necessary to confirm a diagnosis of diabetes.

### D. **Use of the Afinion™ HbA1c test**

#### 1. The Afinion™ HbA1c test

The Afinion™ HbA1c test is a Clinical Laboratory Improvement Amendments (CLIA) waived, single-use, point-of-care test read by the fully automated Afinion™ Analyzer. The device uses a boronate affinity method unlike the more commonly used DCA immunoassay method. The HbA1c test cartridge contains all reagents necessary for the measurement of glycated hemoglobin. It utilizes 1.5 µL of blood to provide HbA1c results (measuring range of HbA1c of 4-15%) in about three minutes.

### Table 8: Correlation of Hemoglobin A1c with average plasma glucose

<table>
<thead>
<tr>
<th>HbA1c %</th>
<th>mg/dL</th>
<th>mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>126</td>
<td>7.0</td>
</tr>
<tr>
<td>7</td>
<td>154</td>
<td>8.6</td>
</tr>
<tr>
<td>8</td>
<td>183</td>
<td>10.2</td>
</tr>
<tr>
<td>9</td>
<td>212</td>
<td>11.8</td>
</tr>
<tr>
<td>10</td>
<td>240</td>
<td>13.4</td>
</tr>
<tr>
<td>11</td>
<td>269</td>
<td>14.9</td>
</tr>
<tr>
<td>12</td>
<td>298</td>
<td>16.5</td>
</tr>
</tbody>
</table>
The Afinion™ HbA1c test has demonstrated 98% accuracy when compared to a central laboratory high-performance liquid chromatography (HPLC) method.\(^{[56]}\) In CLIA waived labs, it is recommended to analyze controls with each new lot of HbA1c kits, at least every 30 days, when training new users, and anytime an unexpected test result is obtained.

A quick guide for use of the Afinion™ HbA1c test is found in Appendix C and provides information on the Afinion™ Analyzer, how to set up the testing device, and how to run a sample and controls.

There are several similar devices on the market. We are focusing on the Afinion™ model because this is the device we use in the MT Geriatric Education Center’s geriatric health screening program, also known as IPHARM.

2. **Performing a finger stick for blood collection**

   Obtaining an adequate quantity of blood from a finger stick is sometimes the most challenging component of diabetic screening.

   Among the following steps are some suggestions to assist with minimizing collection difficulties.

   a. Patients with thick calluses or poor peripheral circulation may be the most difficult. Warming the hands under warm water or holding onto hand warmers can substantially help with getting adequate blood supply down to the fingertips. For patients with thick calluses, try to look for a finger with the least amount of callus.

   b. It is generally a better idea to obtain the blood sample from the non-dominant hand, as a bandage may be placed on the finger utilized for the blood sample, and the non-dominant hand may be less callused.

   c. Inspect the patient’s fingers and gently press on the tips of the fingers to assess which fingertip has good blood return. (The tip should become a rosy-red color compared to the other finger areas.) The middle (3rd) finger or the ring (4th) finger is generally a good choice to perform the finger stick.

   d. Cleaning of the finger area with an alcohol swab prepares the site for penetration with the lancet. The fingertip needs to be completely dry prior to performing the finger stick.

   e. The recommended placement of the lancet on the finger is on the outside edge of the fingertip. (About the 2 o’clock position when looking at the fingertip.) Place the lancet firmly on
the tip, push downward, AND hold in place for two seconds. Holding the lancet in place prevents the reflexive impulse to pull the lancet away from the skin before it has fully penetrated.

f. When trying to get the area which was pricked to bleed, keep in mind the lancet provides a slit-like cut which responds better to gently opening the cut as opposed to squeezing the cut (which pushes the cut edges together.) A drop of blood should appear with gentle massaging. Try to avoid “milking” the finger (which is squeezing along the finger towards the tip), as this may lead to blood cell lysis and an inaccurate result.

   NOTE: If a patient will not bleed after two different attempts, ask the patient to drink about 2 cups of water and return in an hour as the patient may be dehydrated. If the patient still cannot provide a sufficient sample, inform the patient that no further attempts will be made, and rescheduling for another day will be necessary.

g. Placing the collection capillary at a slight downward angle to the blood droplet and gently touching the side of the droplet with the capillary should result in the gentle sucking action of the blood. Blood will wick and completely fill the capillary (1.5 microliters), avoiding air bubbles. Once the blood fills the capillary, provide the patient with a tissue or gauze pad to press against the bleeding finger. Place a bandage on the finger if needed.

3. Interpretation of results

As mentioned previously, IPHARM utilizes the Afinion™ HbA1c test to screen patients who may be at higher risk of diabetes. Table 9 may be used as a general guideline for the interpretation of the results. Patients with an HbA1c ≥ 5.7% should be referred to a health care provider for follow-up, but it should be emphasized to the patient that this abnormal value does NOT diagnose them with diabetes.
Table 9: IPHARM Recommended Actions for Afinion™ Analyzer HbA1c Test Results

<table>
<thead>
<tr>
<th>HbA1c value</th>
<th>Action Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5.7%</td>
<td>No follow-up recommended, but general counseling on risk factor reduction is advised.</td>
</tr>
<tr>
<td>≥ 5.7%</td>
<td>Follow-up with a health care provider recommended; provide general counseling on risk factor reduction.</td>
</tr>
</tbody>
</table>

V. Videos of a Geriatric Health Screening Event

The MTGEC/IPHARM program provides wellness screening to people throughout Montana that might otherwise be unable to access this service. Additionally, the program provides patient care experience for students in their last professional year in the study of pharmacy, physical therapy, nursing and other health care fields.

The following videos illustrate a typical screening for HbA1c using the Afinion™ Analyzer. The first video shows how to set up the screening device. The second video is a sample of a typical patient consultation session. Watching the videos is a component of the contact hours for this module and should be completed at this time.

- Setting up the Afinion™ Analyzer
- Counseling the Patient

VI. Prevention and Treatment of Diabetes

A. Prevention of Diabetes

Diet and exercise are essential therapies for all patients with prediabetes or diabetes. It has been demonstrated that patients at risk for diabetes can prevent or delay diabetes onset with modifications in diet and weight control.\(^{(17,64)}\) As demonstrated in the Diabetes Prevention Program (DPP) study, intensive lifestyle changes (~7% weight loss and moderate physical activity of 30 minutes/day) can reduce the onset of diabetes by 58% in those patients at high risk for developing type 2 diabetes. This is the most cost-effective option for preventing diabetes when compared to the use of medications or other therapies. Follow up on this study showed a sustained effect of lifestyle changes in the rate of conversion of diabetes out to 15 years, with a 27% reduction in progression to diabetes with these lifestyle interventions. The ADA Consensus Development Panel recommends that all persons with prediabetes (IFG, IGT, or HbA1c 5.7-6.4%) should be referred to an intensive behavioral counseling program targeting loss of 7% of body
weight and increasing moderate-intensity physical activity (such as brisk walking) to at least 150 minutes/week. Periods of prolonged sitting should be interrupted every 30 minutes with short bursts of physical activity.

The following nutritional goals apply both to patients at risk for diabetes or those who have already been diagnosed with diabetes.\(^{(17)}\)

- Attain and maintain recommended metabolic outcomes, including glucose and HbA1c levels, cholesterol levels, blood pressure, and body weight.
- Prevent and treat the chronic complications and comorbidities of diabetes. Modify nutrient intake and lifestyle as appropriate for the prevention and treatment of obesity, dyslipidemia, cardiovascular disease, hypertension and kidney disease.
- Improve health through healthy food choices and physical activity.

Address individual nutritional needs, taking into consideration personal and cultural preferences and lifestyle, while respecting the individual’s wishes and willingness to change.

Any of the lifestyle interventions listed in Table 10 may be appropriate for patients at risk for diabetes. There are no ideal percentages of calories from carbohydrate, protein, and fat for all people with diabetes. Therefore, macronutrient portion amounts should be based on individual eating patterns, preferences, and metabolic goals. Increasing dietary fiber (14 g fiber/1,000 kcal), including eating whole grains, and limiting sugary drinks are also recommended. Before any patient initiates a physical activity program, it is advised that the patient be assessed by a healthcare provider.\(^{(17,64)}\)

**Table 10: Lifestyle Modifications for Patients with Diabetes\(^{(17,64)}\)**

<table>
<thead>
<tr>
<th>Topic</th>
<th>Comment/Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight loss in those with BMI (&gt;25\text{ }\text{kg/m}^2)</td>
<td>Mediterranean, Dietary Approach to Stop Hypertension (DASH), vegetarian, low-fat or low-carb diets may be effective for short-term weight loss. In those with a BMI (&gt;27\text{ }\text{kg/m}^2), pharmacotherapy for weight loss may also be considered if lifestyle factors alone are not enough. Those with BMI (&gt;35\text{ }\text{kg/m}^2) may qualify for metabolic surgery.</td>
</tr>
<tr>
<td>Smoking</td>
<td>Smoking cessation strongly advised.</td>
</tr>
<tr>
<td>Exercise</td>
<td>30 minutes of moderate exercise 5 days a week (150 min/week) plus strength training. Exercise should include adequate warm-up and cool-down periods (about 5-10 minutes each). Use proper footwear and inspect feet daily after exercise. Prolonged sitting should be broken up every 30 minutes.</td>
</tr>
<tr>
<td>Topic</td>
<td>Comment/Recommendation</td>
</tr>
<tr>
<td>----------------------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>minutes with bursts of activity. Older adults particularly benefit from balance &amp; flexibility exercises. Structured programs and wearable devices may help patients stick to exercise routine.</td>
<td></td>
</tr>
<tr>
<td>Dietary fat intake</td>
<td>Increase the intake of foods containing omega-3 fatty acids, polyunsaturated, and monounsaturated fatty acids. Limit the intake of saturated fat. Avoid <em>trans</em> fatty acids.</td>
</tr>
<tr>
<td>Sodium intake</td>
<td>Reduce sodium intake to &lt;2,300 mg/day (&lt;1 teaspoon of salt per day), even further if hypertensive.</td>
</tr>
<tr>
<td>Carbohydrate intake</td>
<td>Eat carbohydrates from vegetables, fruits, whole grains, legumes, and dairy products over intake from other sources. Limit foods that contain added fats, sugars, or sodium. Substitute low glycemic-load foods for higher glycemic-load foods.</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Abstain if possible. If using alcohol, daily intake should be limited to 1 drink/day in women or 2 drinks/day in men.</td>
</tr>
<tr>
<td>Sleep</td>
<td>Target at least 7 hours per night.</td>
</tr>
<tr>
<td>Behavioral support</td>
<td>Recommend community engagement and peer support, address any underlying mood disorders or mental health issues, and consider formal behavioral therapy support. Distress over diagnosis of diabetes may be present in nearly half of patients, and may impact ability to engage in effective self-management.</td>
</tr>
</tbody>
</table>

Research into the use of medications to prevent or delay the onset of diabetes has been of great interest over the last several decades. Several randomized, controlled trials have demonstrated the ability to prevent this devastating disease. Table 11 summarizes the most significant type 2 diabetes prevention trials with both lifestyle and medication interventions.\(^{65-69}\) Metformin, acarbose, orlistat, and pioglitazone have been shown to decrease the incidence of diabetes in those at risk of developing the disease. Metformin should be considered for patients with prediabetes, especially if they also have BMI \(>35\) kg/m\(^2\), are less than 60 years old, have a history of gestational diabetes, or have rising HbA1c levels despite lifestyle changes.\(^{16,17,70}\) More recently, use of the GLP-1 receptor agonist liraglutide has been shown to prevent or delay the progression to diabetes in high risk individuals, and is paired with benefits of weight loss and potential benefits in ASCVD risk reduction\(^{71}\). Despite these medication advances, however, lifestyle changes remain the most cost-effective intervention to prevent diabetes and associated complications.
**Table 11: Summary of Clinical Trials for Diabetes Prevention**\(^{(65-69)}\)

<table>
<thead>
<tr>
<th>Study Descriptor</th>
<th>Patient Population</th>
<th>Treatment Groups</th>
<th>Primary Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finnish Diabetes Prevention Study Group 2001(^{(43)})</td>
<td># of pts = 522 Sexes = male &amp; female Ave. age = 55 y.o. Ave. BMI = 31 kg/m(^2) Pre-diabetic pts (+ IGT) Years of follow-up = 3.2</td>
<td>1. Brief diet &amp; exercise counseling 2. Intense, individualized diet &amp; exercise counseling</td>
<td>Intensely counseled group had a 58% relative reduction in incidence of type 2 diabetes compared to brief counseling.</td>
</tr>
<tr>
<td>Diabetes Prevention Program 2002(^{(44)})</td>
<td># of pts = 3,234 Sexes = male &amp; female Ave. age = 51 y.o. Ave. BMI = 34 kg/m(^2) Pre-diabetic pts (+ IGT) Years of follow-up = 2.8</td>
<td>1. Lifestyle group: counseled on better nutrition &amp; exercise 2. Metformin 3. Placebo</td>
<td>Both the lifestyle and metformin groups had a 58% and 31% relative reduction, respectively, in the incidence of type 2 diabetes compared to placebo.</td>
</tr>
<tr>
<td>STOP-NIDDM 2002(^{(45)})</td>
<td># of pts = 1,429 Sexes = male &amp; female Ave. age = 55 y.o. Ave. BMI = 31 kg/m(^2) Pre-diabetic pts (+ IGT) Years of follow-up = 3.3</td>
<td>1. Acarbose (drug to slow carbohydrate absorption) 2. Placebo</td>
<td>The acarbose-treated group had a 36% relative reduction in the incidence of developing type 2 diabetes compared to placebo.</td>
</tr>
<tr>
<td>XENDOS 2004(^{(46)})</td>
<td># of pts = 3,277 Sexes = male &amp; female Ave. age = 43 y.o. BMI $\geq$ 30 kg/m(^2) Normal BG or IGT Duration = 4 years</td>
<td>1. Lifestyle changes + orlistat 120 mg TID 2. Lifestyle changes + placebo</td>
<td>The orlistat-treated group had a 37% risk reduction in incidence of type 2 diabetes compared to control. Orlistat group lost more weight.</td>
</tr>
</tbody>
</table>
### Study Descriptor, Patient Population, Treatment Groups, Primary Result

<table>
<thead>
<tr>
<th>Study Descriptor</th>
<th>Patient Population</th>
<th>Treatment Groups</th>
<th>Primary Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACT NOW 2011&lt;sup&gt;(47)&lt;/sup&gt;</td>
<td># of pts = 602 Sexes = male &amp; female Ave. age = 52 y.o. IGT Duration = 2.4 years</td>
<td>1. Pioglitazone 45 mg per day 2. Placebo</td>
<td>The pioglitazone-treated group had a 72% reduction in incidence of type 2 diabetes.</td>
</tr>
<tr>
<td>SCALE 2017&lt;sup&gt;(71)&lt;/sup&gt;</td>
<td># of pts = 2254 Sexes = male &amp; female Duration = 3 years</td>
<td>1. Liraglutide 3.0 mg daily + lifestyle intervention 2. Placebo + lifestyle intervention</td>
<td>The liraglutide-treated group had 2.7 times longer time to onset of diabetes vs those receiving placebo (hazard ratio = 0.21, 95% CI 0.13-0.34).</td>
</tr>
</tbody>
</table>

Key: BMI: body mass index, IGT: impaired glucose tolerance, BG: blood glucose

### B. Preventing Complications - Blood Glucose Control

Long-standing evidence supports the value of tight glycemic control in preventing complications. A landmark study, the United Kingdom Prospective Diabetes Study (UKPDS 33), was conducted over 10 years in newly diagnosed type 2 diabetic patients, and found that use of an intensive treatment regimen and tighter blood glucose control resulted in significant reductions in microvascular complications (e.g., diabetic kidney disease, retinopathy, and neuropathy) compared to conventional therapy. The goal set for fasting blood glucose for the intensive regimen was <108 mg/dL and the conventional group goal was set at <270 mg/dL, which resulted in median HbA1c values of 7% (intensive group) versus 7.9% (conventional group) – a relative reduction of 11%. A seemingly small difference in the HbA1c test, which is a measure of long-term glycemic control, resulted in significant reductions in all diabetes-related complications by 12%, microvascular endpoints by 25%, retinal photocoagulation (a treatment for retinopathy) by 29%, and a borderline reduction in myocardial infarction by 16%.<sup>(72)</sup>

In a similarly named study, the United Kingdom Prospective Diabetes Study 35 (UKPDS 35) compared the relationship of glycemic control (HbA1c test) to the incidence of micro- and macrovascular complications in 3,600 newly diagnosed type 2 diabetic patients. No therapeutic interventions were implemented, but rather patients were observed for approximately 10 years (7.5-12.5 years). Results strongly suggest a direct relationship between the risk of diabetic complications and glycemic control (Figures 6 & 7).<sup>(73)</sup> Every 1% reduction in HbA1c resulted in a 37% (median) decreased risk of microvascular complications and a 21% decrease in either a macro- or microvascular event or diabetes-related death.<sup>(74)</sup>
Although the UKPDS 35 study showed the above beneficial effects of reducing macrovascular complications (e.g., heart attack and stroke) with tight blood glucose control, other large trials since then have not yielded similar results. The Action in Diabetes and Vascular Disease: Preterax...
and Diamicron Modified Release Controlled Evaluation (ADVANCE) trial compared standard therapy (HbA1c goal of 7.3%) to intensive therapy (HbA1c goal of 6.5% or less) for over 11,000 patients with type 2 diabetes who were followed for complications over 5 years. Although tight blood glucose control did lower diabetic kidney disease risk, it did not reduce the risk of major cardiovascular events or deaths from cardiovascular disease. Rates of hypoglycemia were higher in the intensive treatment group.\(^{(73)}\)

In the Action to Control Cardiovascular Risk in Diabetes Study Group (ACCORD) trial, over 10,000 patients (with a mean age of 62 years) with a median HbA1c level of 8.1% were assigned to intensive therapy (goal HbA1c of 6.0%) or standard therapy (goal HbA1c of 7-7.9%). Of these patients, 35% already had cardiovascular disease. After 3.5 years, the intensive therapy arm was stopped because of an increased mortality rate without reducing risk of major cardiovascular events compared to the standard treatment group. Severe hypoglycemia and weight gain of more than 10 kg were more frequent in the intensive therapy group.\(^{(75)}\) Lowering blood glucose levels to the normal range in older patients, especially those with preexisting cardiovascular disease, appears harmful.

The ADA has adjusted HbA1c goals based on the results of these landmark trials. While controlling blood glucose will directly reduce the risk of microvascular complications, management of other modifiable risk factors can further reduce risks associated with conditions such as nephropathy or retinopathy. The prevention of macrovascular complications is more complex, and requires attention to other cardiovascular risk factors in parallel with blood glucose control. A brief review of strategies for management of the cardiovascular risk-enhancing comorbidities can be found in the sections below.

\section*{VII. Risk-Enhancing Comorbidities}

\subsection*{A. Obesity}

Considerable evidence exists which correlates increasing body weight with the increased risk of developing type 2 diabetes.\(^{(76)}\) Despite Montana having one of the lowest rates of obesity in the nation, 2017 data shows approximately 1 in 4 Montanans are considered obese, and thus at higher risk for diabetes and related complications.\(^{(77)}\)

Results from the 2013-2014 National Health and Nutrition Examination Survey (NHANES) show that 78% of the U.S. adult population weighs more than recommended. The survey estimated 32.7% of U.S. adults aged 20 and over are overweight (BMI 25.0–29.9), 37.9% are obese (BMI \(\geq\)30), and 7.7% are extremely obese (BMI \(\geq\)40 kg/m\(^2\)).\(^{(78)}\)

Obesity is unevenly distributed across the age spectrum, with the prevalence of obesity higher among middle-aged adults (42.8%) than among younger adults (35.7%).\(^{(79,80)}\) Additionally, Native American populations have 1.5 times higher rates of obesity versus non-Hispanic white
populations (43.7 vs 28.5%). Data suggest that for every kilogram increase in body weight, the risk for developing diabetes increases 4.5 to 9%\(^{(81)}\).

ADA and AACE guidelines highlight the need to evaluate patients with obesity and choose appropriate treatment modalities. Patients should receive an assessment of BMI and related cardiometabolic or biomechanical complications, and should have appropriate treatment strategies selected based upon their individual profiles. All treatment should include lifestyle modifications, but may also require pharmacotherapy or metabolic surgery, such as gastric banding or bypass, to achieve weight loss goals.

Diets should be individualized, with a target of achieving 500-750 kcal/day energy deficit, but no particular type of diet for weight loss has been shown to be superior to another. More extreme interventions, such as very-low calorie diets, should be supervised by a medical professional in carefully selected patients. Likewise, exercise routines should be designed to be both safe and sustainable for a patient. Starting with simple changes, like gradually increasing the distance or frequency of daily walks, can be an effective way to begin to increase physical activity and build healthy routines that fit patient lifestyle and preferences\(^{(65,87)}\).

B. Dyslipidemia

Insulin plays important roles in regulation of release, storage, and transport of fatty acids and lipoproteins in the liver and fat tissues, and thus lipid abnormalities are commonly seen in patients with diabetes. In 2009–2012, of adults with diagnosed diabetes, 65% had blood LDL cholesterol \(>100\) mg/dl or used cholesterol-lowering medications\(^{(2)}\). Insulin resistance seems to play a large role in the development of lipid abnormalities through changes in the uptake and metabolism of free fatty acids, and increases in hepatic lipase activity which creates smaller, denser LDL particles.

The typical abnormalities include\(^{(82)}\):

- Decreased high-density lipoproteins (HDL) cholesterol
- Elevated triglyceride levels
- Average to moderately elevated low-density lipoproteins (LDL) cholesterol, but these particles tend to be smaller, denser, and potentially more atherogenic than in patients without diabetes.

The cardiovascular risks associated with dyslipidemia in diabetes are largely modifiable, and lipid abnormalities should be evaluated and appropriately addressed in all patients with diabetes. Lifestyle changes are recommended for all patients with diabetes such as reducing saturated fat, trans fat, and cholesterol intake; increasing intake of omega-3 fatty acids, viscous fiber, and plant stanols/sterols; weight loss (if indicated); and increasing physical activity (30 minutes of moderate intensity physical activity five times weekly)\(^{(36,83)}\).
Current cholesterol management guidelines from ACC/AHA, published in 2018, highlight diabetes as a chronic condition that increases risk of atherosclerotic cardiovascular disease (ASCVD). Most adults with diabetes between the ages of 40 to 75 years are considered at intermediate to high risk of ASCVD. A patient’s 10-year risk of ASCVD is based upon factors such as age, sex, race, blood pressure, cholesterol levels, and history of diabetes or smoking. The ASCVD Risk Estimator online calculator tool can be used to estimate risk.

When making treatment decisions regarding the addition of statin therapy for primary prevention of cardiovascular events in patients with diabetes, patient age, ASCVD risk, and levels of LDL cholesterol are major considerations. Less evidence exists for use of statins in patients outside of the range of 40-75 years of age, but it is reasonable to start statins in some of these patients after consideration of risks and benefits. For those between the age of 40-75 years, moderate to high intensity therapy should be used for the majority of these patients. If a patient with diabetes has already had a cardiovascular event, high-intensity statin therapy is indicated for secondary prevention. A summary of detailed recommendations can be found below in Table 12.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Start a statin if:</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-39</td>
<td>If a patient has had T2DM for at least 10 years and also has 1 or more of the following risk factors: albuminuria, eGFR &lt;60 ml/min, retinopathy, neuropathy, ABI &lt;0.9: consider moderate intensity statin If patient has known ASCVD: start high intensity statin</td>
</tr>
<tr>
<td>40-75</td>
<td>If LDL 70-189 mg/dL: start moderate intensity statin regardless of ASCVD risk score If LDL &gt;190 or if high ASCVD risk/multiple risk factors present: start high intensity statin If patient has known ASCVD: start high intensity statin</td>
</tr>
<tr>
<td>&gt;75</td>
<td>In older patients, there is less evidence to support long term benefit. Shared decision-making after a discussion of risks and benefits is encouraged. If a patient is already on a statin, it is reasonable to continue statin therapy.</td>
</tr>
</tbody>
</table>

T2DM: Type 2 diabetes mellitus; eGFR: estimated glomerular filtration rate; ABI: Ankle- brachial index; ASCVD: Atherosclerotic cardiovascular disease; LDL: Low density lipoprotein
The American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE) published dyslipidemia guidelines in 2017 which are in line with the ACC/AHA guidelines but do specify LDL goals based on risk status. Those with diabetes are considered in the high-risk category with a LDL goal of less than 100 mg/dL. Persons with established cardiovascular disease, diabetes or chronic kidney disease (stage 3 or 4) with one other risk factor have a LDL goal of <70 mg/dl. Persons with extreme risk of cardiovascular events may benefit from a LDL goal of less than 55 mg/dL.\(^{(56)}\)

\textbf{C. Hypertension}

Hypertension affects the majority of patients with diabetes and contributes to both microvascular and macrovascular complications of diabetes. In 2009–2012, of adults with diagnosed diabetes, 71% had blood pressure \(>140/90\) mmHg or used prescription medications to lower high blood pressure.\(^{(2)}\) The prevalence of hypertension depends on a number of different factors, including the type of diabetes, age, race/ethnicity, BMI, glycemic control, and presence of kidney disease.\(^{(16)}\) Those with hypertension and diabetes are more likely to develop ASCVD, heart failure, and microvascular complications, as compared to patients with diabetes and normal blood pressure. Hypertension also plays a large role in the progression of diabetic kidney disease and retinopathy. Evidence\(^{(85)}\) from numerous studies has shown that hypertension is a modifiable risk factor, however, and that antihypertensive therapy can reduce the risk of microvascular and macrovascular complications\(^{(86)}\) when discovered and treated early. In patients with diabetes, blood pressure should be measured at every routine visit, ensuring proper measurement technique with appropriate cuff size, proper patient positioning, and an adequate period of rest prior to blood pressure measurement. Any elevated readings (>140/90 mmHg) should have appropriate follow-up to reassess blood pressure, with multiple readings on separate days to confirm the diagnosis of hypertension.

Current ADA guidelines recommend a blood pressure goal \(<140/90\) mmHg for most patients with diabetes, while acknowledging that lower targets may be appropriate for certain individuals. The guidelines specifically highlight using a lower target of \(<130/80\) mmHg for those with either existing ASCVD or a 10-year ASCVD risk greater than 15%.\(^{(86)}\) Alternative guidelines from the ACC/AHA and AACE recommend a goal of \(<130/80\) mmHg for all, and highlight the need for more aggressive titration of medication to reach this goal.\(^{(84,87)}\) Ultimately, the risks associated with hypotension and adverse drug events should be balanced against the benefits of tighter blood pressure control, with the knowledge that treatment of hypertension is one of the most important modifiable risk factors for both microvascular and macrovascular complications. Evidence from the UKPDS has shown that for every 10 mm Hg reduction in systolic blood pressure, there is an approximately 13% reduction in microvascular complications and a 12% decrease in risk of myocardial infarction.
As with other aspects of diabetes care, lifestyle management remains the foundation for treatment of hypertension. Interventions include weight loss, DASH diet, reducing sodium intake (<2300 mg/day), increased consumption of fruits and vegetables (8-10 servings/day), moderation of alcohol intake (no more than 2 drinks/day), and increased physical activity. In addition to lifestyle modifications, antihypertensive therapy should be initiated in a timely manner to achieve blood pressure goals.(86)

**D. Smoking**

Recent data, including the 2014 Surgeon General’s Report, has demonstrated that smoking significantly increases the risk of developing diabetes.(88) Smokers have a 30-40% higher risk of developing diabetes than nonsmokers, exposure to secondhand smoke is associated with a 22% higher risk of diabetes(89), and high consumption of smokeless tobacco has also been found to be a risk factor for developing diabetes.(90)

Furthermore, those with diabetes who are current smokers have more difficulty controlling their blood glucose and have higher risks for other complications. As in the general population, smoking is a well-known risk factor for the development of cardiovascular disease in patients with diabetes, with some evidence suggesting approximately 50% increase in risk of adverse cardiovascular events and a 10-20% increase in mortality compared with nonsmokers with diabetes.(91) Smoking has also been attributed to an increased risk of microvascular complications of diabetes, such as kidney disease, retinopathy, and peripheral neuropathy.

Smoking cessation is strongly advised for all patients with diabetes or who are at an increased risk for diabetes. Current data suggests that while the risk of developing diabetes remained elevated in people who recently quit smoking (<5 years), this excess risk returned to approximately that of never-smokers in those who had quit for 10 years or more. Smoking cessation is associated with a 30% reduction in risk of all-cause mortality in those with diabetes.(91)

**E. Antiplatelet therapy**

Low-dose aspirin is recommended in those with diabetes and a history of ASCVD for secondary prevention of ASCVD events in those who have had a prior stroke, myocardial infarction, or have other known atherosclerotic disease. The recommendation for use of aspirin for the primary prevention of ASCVD events, however, is less clear. While aspirin has been shown to reduce the risk of myocardial infarction and stroke through its effects on platelets, it also significantly increases the risk of bleeding events, including GI bleeding and intracranial hemorrhage.(92) As a result, it is recommended to carefully weigh the risks and benefits for an individual patient when using aspirin in primary prevention of cardiovascular events. Current ADA recommendations
highlight this balance, and recommend low-dose aspirin in those at increased cardiovascular risk, including men and women 50-70 years of age with at least one additional major CV risk factor, who are not at an increased risk of bleeding. Current evidence does not support a favorable risk to benefit profile for those younger than 50 or older than 70 years of age.\(^{(43,93)}\)

**VIII. Therapies for Diabetes**

A multidisciplinary approach to address the diverse needs of a diabetic patient may include expert involvement of physicians, physician assistants, nurse practitioners, nurses, pharmacists, diabetes educators, dieticians, physical therapists, mental health professionals and social workers. An individualized treatment plan with patient-specific goals, in conjunction with patient education, is essential to achieving successful therapeutic outcomes.

Table 13 describes the glycemic goals which have been established by the two main professional diabetes organizations: American Diabetes Association (ADA) and the American Association of Clinical Endocrinologists (AACE).\(^{(6,35)}\)

<table>
<thead>
<tr>
<th>Glycemic Parameter</th>
<th>Expert Group</th>
<th>Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c</td>
<td>ADA</td>
<td>&lt; 7%*</td>
</tr>
<tr>
<td></td>
<td>AACE</td>
<td>≤ 6.5%*</td>
</tr>
<tr>
<td>Pre-prandial plasma glucose</td>
<td>ADA</td>
<td>80-130 mg/dL</td>
</tr>
<tr>
<td></td>
<td>AACE</td>
<td>≤ 110 mg/dL</td>
</tr>
<tr>
<td>Post-prandial plasma glucose (generally 1-2 hours after the beginning of a meal)</td>
<td>ADA</td>
<td>&lt; 180 mg/dL</td>
</tr>
<tr>
<td></td>
<td>AACE</td>
<td>&lt; 140 mg/dL</td>
</tr>
</tbody>
</table>

*HbA1c targets should be individualized.

Lowering HbA1c to below 7% has been shown to reduce microvascular complications of diabetes, and, if implemented soon after the diagnosis of diabetes, is associated with long-term reduction in macrovascular disease. Therefore, a reasonable HbA1c goal for many non-pregnant adults is less than 7%. More stringent HbA1c goals (such as <6.5%) are reasonable for selected individual patients, if this can be achieved without significant hypoglycemia or other adverse effects. Appropriate patients might include those with short duration of diabetes, long life expectancy, and no significant cardiovascular disease. Less stringent HbA1c goals (such as less than 8%) should be considered for people with a history of severe hypoglycemia, limited life expectancy, advanced complications, extensive comorbid conditions, and those with long-standing diabetes. Many older patients with diabetes fall into this latter category. For these patients, the risks of
therapy (death or events associated with hypoglycemia) may not outweigh the benefits of tight blood glucose control that take years to fully appreciate. Goals should be individualized (Figure 8) and patients should know their glycemic goals.\textsuperscript{(17,35,87,94)}

\textit{Figure 8: Patient & Disease Factors that Affect Individual HbA1c Optimal Goal\textsuperscript{(95)}}

The ADA recommends a monitoring frequency of every 3 months for patients not meeting A1c goals, and every 6 months for those who are currently meeting A1c goals. Testing A1c more frequently than every 3 months may give results that do not accurately reflect the most recent changes in treatment or glycemic control. Patients may also self-monitor blood glucose at home with a meter. For those taking multiple daily insulin injections, self-monitoring of blood glucose is essential. However, there is debate about the utility and effectiveness of using this in some patient populations, such as those taking oral medications only, and results will only be useful if they are utilized to take definitive action in a patient’s treatment plan and lifestyle modifications.
Patients should be educated on how to interpret their blood glucose results, and how to use that data to adjust their diet, exercise, and/or medications accordingly.\textsuperscript{(87,94)}

Special Considerations in Older Adults:
As previously mentioned, diabetes is a common disease state in older adults, and is associated with a wide range of adverse outcomes in this population, from higher rates of all-cause dementia to premature death. A holistic approach to the older adult with consideration of medical, psychological, functional, and social geriatric domains is important to providing optimal care to these patients. In healthier older adults, a lower glycemic goal and more aggressive management of hyperglycemia and other risk factors may be appropriate, but consideration of comorbidities, risks of hypoglycemia and other adverse effects, and relative benefits of treatment must be carefully evaluated. For most older individuals, avoiding medications that may cause hypoglycemia is recommended. Medication cost, functional impairments, and the patient’s support system can also be important factors to consider. In many cases, simplification or reduction in the intensity of diabetes regimens may be appropriate as an individual ages, with the goals of reducing the risk of adverse effects and decreasing the medication burden.\textsuperscript{(96)}

A. Non-Drug Therapy
Lifestyle modifications, including diet and exercise, are an essential component of both prevention and management of diabetes. The lifestyle interventions outlined earlier in this module(Table 11) are appropriate for patients at risk for diabetes, as well as for those who have developed overt diabetes. Even modest changes in diet and exercise habits can have a noticeable impact on blood glucose control. While there are standard targets for diet and exercise, it is important to note that all lifestyle changes should be individualized.\textsuperscript{(97)}

When developing plans for diabetes management, a patient’s personal and cultural preferences, lifestyle, available support and resources, and overall willingness to change should all be considered in developing a plan. There are no ideal percentages of calories from carbohydrate, protein, and fat for the diet of all people with diabetes. Therefore, macronutrient portion amounts should be based on individual eating patterns, preferences, and metabolic goals. Patients should be assessed by their healthcare provider before attempting any extreme dieting efforts, such as a very low calorie diet (<800 kcal per day) or ketogenic diet.\textsuperscript{(97,98)} It is also advised that the patient be assessed by a healthcare provider prior to starting any exercise program, with the goal of preventing injury and developing a safe and sustainable exercise routine to achieve moderate weight loss and attain associated metabolic benefits.\textsuperscript{(17,64)}

B. Drug Therapy
While some patients can manage diabetes with lifestyle changes alone, most will need treatment with medication to reach their A1c goals. Medications for diabetes are not a substitute for meal
planning and exercise, and lifestyle changes should always be used in conjunction with drug therapy. While implementing drug therapy is beyond the scope of diabetes screening and will not be covered in depth in this module, patients may be concerned about what a diagnosis of diabetes means for them and what drugs they might be prescribed. Many are hesitant to start aggressive treatment to reach their A1c goal, but the most recent ADA guidelines stress the importance of early treatment to achieve A1c goal and prevent long-term complications associated with poorly controlled blood glucose levels. Assessment of a patient’s perceptions and beliefs about diabetes treatment, paired with thorough education by a diabetes educator or other health professional, can be instrumental in starting early treatment and achieving optimal diabetes control. Some of the newest medications available to patients have benefits beyond A1c reduction, such as weight loss, reduction of cardiovascular risk, and reduction of complications related to heart failure or kidney disease. A basic overview of the currently available options can be found in Table 14.\(^{(99)}\)

These medications may be used as monotherapy, in combination, or in some cases, may be combined with insulin. It is important to regularly monitor the person’s blood glucose levels and HgbA1C every 3-6 months as an indicator of efficacy of the drug therapy, and to make changes as needed to get the patient to their A1c goal. For newly diagnosed patients, metformin is usually the first medication prescribed. For those with an A1c greater than 1.5% of their goal, two medications may be started immediately in order to aggressively target achieving glycemic control. While insulin is the mainstay of therapy for those with type 1 diabetes, it is typically reserved as a second-line agent in those with type 2 diabetes who fail to achieve their goal A1c with at least 2 oral medications, or in those who have a particularly high A1c at diagnosis. A number of other factors should also be considered when choosing medications for people with diabetes, including\(^{(87,99)}:\)

- A1c goals and response to therapy
- Presence of heart failure or chronic kidney disease
- Presence of atherosclerotic cardiovascular disease
- Risks associated with hypoglycemia
- Medication effects on body weight
- Kidney and liver function
- Adverse effects
- Cost
- Patient preferences

In older adults, it is recommended to also assess other medical comorbidities and self-management abilities, as well as psychological and social domains to optimize diabetes care. Common geriatric issues, such as polypharmacy, cognitive impairment, and fall risk, may affect a patient’s self-management abilities and risk for medication-related adverse events. In healthy older patients with good functional status, treatment strategies and choice of medications may

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be similar to those used in younger patients. In those with multiple comorbidities, cognitive or functional impairments, or those at the end of life, medications that cause hypoglycemia, are difficult to administer, or contribute to significant polypharmacy may be avoided. A patient-centered approach should be taken to individualize treatment and ensure safe and effective diabetes care in all stages of life.\textsuperscript{(87,96)}
<table>
<thead>
<tr>
<th>Drug Class/Mechanism of Action/Benefits</th>
<th>Major Side Effects/Clinical Pearls</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Biguanides</strong></td>
<td>Commonly associated with diarrhea, nausea, vomiting, and GI discomfort, especially when starting or increasing dose. Patients should slowly increase their dose to minimize these effects. May cause B12 deficiency. Periodically check levels &amp; supplement if needed. <strong>Renal function</strong> must be monitored. Discontinue drug if eGFR is less than 30 ml/min.</td>
</tr>
<tr>
<td>Metformin (Glucophage®, Fortamet®, Riomet®)</td>
<td><strong>MOA:</strong> Decreases liver glucose production. Improves insulin sensitivity in peripheral tissues. Decreases intestinal absorption of glucose. Primarily affects fasting blood glucose. <strong>Benefits:</strong> First line therapy for type 2 diabetes unless contraindications present. <a href="#">56</a></td>
</tr>
<tr>
<td><strong>GLP-1 Incretin Mimetics</strong></td>
<td>Nausea, vomiting, diarrhea, headache, injection site reaction. GI side effects will usually improve. Dose is slowly titrated over time to minimize these effects and improve tolerance. Available in multiple different devices for injection, all using a very small pen needle. Education and demonstration of injection will overcome fears of injections for most who are apprehensive.</td>
</tr>
<tr>
<td>Exenatide (Byetta®, Bydureon®)</td>
<td><strong>MOA:</strong> Injectable therapy, enhances glucose-dependent insulin secretion. Suppresses inappropriate glucagon secretion. Slows gastric emptying &amp; promotes weight loss. <strong>Benefits:</strong> Decreases risk of ASCVD events, slows progression of kidney disease, promotes weight loss. Preferred add-on therapy for those with overt ASCVD or at high risk of CV events, or if weight loss is a primary goal. Also preferred as an add-on injectable prior to initiation of insulin in those who have failed other therapies.</td>
</tr>
<tr>
<td>Liraglutide (Victoza®)</td>
<td></td>
</tr>
<tr>
<td>Dulaglutide (Trulicity®)</td>
<td></td>
</tr>
<tr>
<td>Semaglutide (Ozempic®)</td>
<td></td>
</tr>
<tr>
<td>Lixisenatide (Adlyxin®)</td>
<td></td>
</tr>
<tr>
<td>Drug Class/Mechanism of Action/Benefits</td>
<td>Major Side Effects/Clinical Pearls</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td><strong>SGLT2 Inhibitors</strong></td>
<td></td>
</tr>
<tr>
<td>Canagliflozin (Invokana*)</td>
<td>Increased risk of lower extremity amputations, particularly in those with high risk of diabetic foot or prior amputations.</td>
</tr>
<tr>
<td>Dapagliflozin (Farxiga*)</td>
<td>Increased risk of diabetic ketoacidosis, even in the setting of normal blood glucose.</td>
</tr>
<tr>
<td>Empagliflozin (Jardiance*)</td>
<td>Increased risk of genitourinary infections.</td>
</tr>
<tr>
<td>Ertugliflozin (Stelagra*)</td>
<td></td>
</tr>
<tr>
<td><strong>MOA:</strong> Promotes glucose excretion by the kidneys into the urine by inhibiting glucose reabsorption via the SGLT2 transporter.</td>
<td></td>
</tr>
<tr>
<td><strong>Benefits:</strong> Preferred add on therapy for those with heart failure or chronic kidney disease; may decrease HF exacerbations and delay progression of renal disease. Associated with weight loss and modest decreases in blood pressure.</td>
<td></td>
</tr>
<tr>
<td><strong>DDP-IV Enzyme Inhibitors</strong></td>
<td>Headache, nausea, diarrhea, nasopharyngitis, severe joint pain.</td>
</tr>
<tr>
<td>Saxagliptin (Onglyza*)</td>
<td></td>
</tr>
<tr>
<td>Sitagliptin (Januvia*)</td>
<td></td>
</tr>
<tr>
<td>Linagliptin (Tradjenta*)</td>
<td></td>
</tr>
<tr>
<td>Alogliptin (Nesina*)</td>
<td></td>
</tr>
<tr>
<td><strong>MOA:</strong> Prolongs active incretin levels in gut, reducing fasting and postprandial glucose levels.</td>
<td></td>
</tr>
<tr>
<td><strong>Benefits:</strong> Weight neutral, not associated with hypoglycemia. Less expensive than other newer diabetes medications.</td>
<td></td>
</tr>
<tr>
<td><strong>Sulfonylureas</strong></td>
<td>Hypoglycemia, weight gain, nausea, &amp; headache.</td>
</tr>
<tr>
<td>Second generation</td>
<td>Will lose efficacy over time as beta-cell function declines.</td>
</tr>
<tr>
<td>Glyburide (DiaBeta*, Micronase*, Glynase*)</td>
<td></td>
</tr>
<tr>
<td>Glipizide (Glucotrol*)</td>
<td></td>
</tr>
<tr>
<td>Drug Class/Mechanism of Action/Benefits</td>
<td>Major Side Effects/Clinical Pearls</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td>Glimepiride (Amaryl®)</td>
<td></td>
</tr>
<tr>
<td><strong>MOA:</strong> Stimulates insulin release from the pancreas.</td>
<td></td>
</tr>
<tr>
<td><strong>Benefits:</strong> Inexpensive and widely available if patients have difficulty affording other options.</td>
<td></td>
</tr>
<tr>
<td>Thiazolidinediones (Glitazones)</td>
<td></td>
</tr>
<tr>
<td>Rosiglitazone (Avandia®)</td>
<td>Increases total cholesterol, LDL &amp; HDL; weight gain; edema; headache; fatigue; and nausea. Monitor liver function.</td>
</tr>
<tr>
<td>Pioglitazone (Actos®)</td>
<td>Avoid in patients with CHF, liver disease, alcohol abuse.</td>
</tr>
<tr>
<td><strong>MOA:</strong> Increases insulin sensitivity in peripheral tissues.</td>
<td></td>
</tr>
<tr>
<td><strong>Benefits:</strong> Relatively inexpensive if patients have difficulty affording other options, long-lasting efficacy.</td>
<td></td>
</tr>
<tr>
<td>Alpha-Glucosidase Inhibitors</td>
<td>Flatulence, diarrhea, and abdominal pain.</td>
</tr>
<tr>
<td>Acarbose (Precose®)</td>
<td></td>
</tr>
<tr>
<td>Miglitol (Glyset®)</td>
<td></td>
</tr>
<tr>
<td><strong>MOA:</strong> Delays intestinal absorption of carbohydrates resulting in decreased post-prandial glycemia.</td>
<td></td>
</tr>
<tr>
<td>Generally not recommended in current ADA guidelines, but included in AACE/ACE guidelines.</td>
<td></td>
</tr>
<tr>
<td>Meglitinides</td>
<td></td>
</tr>
<tr>
<td>Repaglinide (Prandin®)</td>
<td></td>
</tr>
<tr>
<td>Nateglinide (Starlix®)</td>
<td></td>
</tr>
<tr>
<td><strong>MOA:</strong> Increases insulin secretion from the pancreas.</td>
<td></td>
</tr>
<tr>
<td><strong>Benefits:</strong> Headache, weight gain, and hypoglycemia.</td>
<td></td>
</tr>
<tr>
<td>Due to similar MOA, should not be used in combination with sulfonylureas.</td>
<td></td>
</tr>
<tr>
<td>Drug Class/Mechanism of Action/Benefits</td>
<td>Major Side Effects/Clinical Pearls</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td>Generally not recommended in current ADA guidelines, but included in AACE/ACE guidelines.</td>
<td></td>
</tr>
<tr>
<td><strong>Amylin Analog</strong></td>
<td>Nausea, dizziness, headache, abdominal pain, anorexia, vomiting, weight loss &amp; hypoglycemia.</td>
</tr>
<tr>
<td>Pramlintide (SymlinPen ®)</td>
<td></td>
</tr>
<tr>
<td><strong>MOA:</strong> Modulates gastric emptying. Prevents post-prandial rise in plasma glucagon. Produces satiety leading to decreased caloric intake.</td>
<td></td>
</tr>
<tr>
<td>Generally not recommended in current ADA guidelines, but included in AACE/ACE guidelines.</td>
<td></td>
</tr>
<tr>
<td><strong>Dopamine Agonist</strong></td>
<td>Hypotension, drowsiness, hypoglycemia, stomach upset, nasal congestion, lazy eye</td>
</tr>
<tr>
<td>Bromocriptine (Cycloset*)</td>
<td></td>
</tr>
<tr>
<td><strong>MOA:</strong> Resets dopaminergic mediation of circadian rhythms that play a role in insulin resistance/obesity.</td>
<td></td>
</tr>
<tr>
<td>Generally not recommended in current ADA guidelines, but included in AACE/ACE guidelines.</td>
<td></td>
</tr>
<tr>
<td><strong>Bile Acid Sequestrant</strong></td>
<td>Constipation, dyspepsia, &amp; increased triglycerides</td>
</tr>
<tr>
<td>Colesevelam (WelChol*)</td>
<td></td>
</tr>
<tr>
<td><strong>MOA:</strong> Binds with bile acids to increase excretion in the feces.</td>
<td></td>
</tr>
<tr>
<td>Generally not recommended in current ADA guidelines, but included in AACE/ACE guidelines.</td>
<td></td>
</tr>
<tr>
<td>Drug Class/Mechanism of Action/Benefits</td>
<td>Major Side Effects/Clinical Pearls</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>-----------------------------------</td>
</tr>
<tr>
<td><strong>Insulin</strong></td>
<td></td>
</tr>
<tr>
<td><em>Rapid acting:</em></td>
<td></td>
</tr>
<tr>
<td>Lispro (Humalog®)</td>
<td>Hypoglycemia, weight gain. Patients should be counseled on appropriate management of hypoglycemia.</td>
</tr>
<tr>
<td>Aspart (Novolog®)</td>
<td></td>
</tr>
<tr>
<td>Glulisine (Apidra®)</td>
<td></td>
</tr>
<tr>
<td><em>Short acting:</em></td>
<td></td>
</tr>
<tr>
<td>Regular insulin (Novolin-R®, Humulin-R®)</td>
<td></td>
</tr>
<tr>
<td><em>Intermediate acting:</em></td>
<td></td>
</tr>
<tr>
<td>NPH insulin (Novolin-N®, Humulin-N®)</td>
<td>Keep refrigerated until opened for use. Note product-specific manufacturer recommendation for expiration date and storage information; most products must be used within 28-56 days after opening.</td>
</tr>
<tr>
<td><em>Long acting:</em></td>
<td></td>
</tr>
<tr>
<td>Glargine (Lantus®)</td>
<td>Absorption may be affected by location of injection site, volume of injection, and alterations in circulation at injection site due to heat, massage, or exercise.</td>
</tr>
<tr>
<td>Detemir (Levemir®)</td>
<td></td>
</tr>
<tr>
<td><em>Ultra-long acting:</em></td>
<td></td>
</tr>
<tr>
<td>Degludec (Tresiba®)</td>
<td></td>
</tr>
<tr>
<td>Glargine U-300 (Toujeo®)</td>
<td></td>
</tr>
<tr>
<td><strong>MOA:</strong> Mimics action of endogenous insulin. Stimulates glucose uptake and reduces serum glucose levels. Onset and duration of action vary among products.</td>
<td></td>
</tr>
<tr>
<td><strong>Benefits:</strong> Most effective antihyperglycemic medication. Required for treatment of type 1 diabetes. In type 2 diabetes, reserved for those with very high A1c at diagnosis or for those who do not reach goal A1c with 2 or more oral medications.</td>
<td></td>
</tr>
</tbody>
</table>


**C. Hypoglycemia**

When setting goals and managing patient treatment, it is important to consider a patient’s risk of hypoglycemia. Not all medications are associated with an increased risk of hypoglycemia, and
not all patients will experience hypoglycemia on a regular basis. If therapy is not managed properly, however, it can become a frequent problem and acute hypoglycemia can become a life-threatening medical emergency. Early symptoms of hypoglycemia (defined as blood glucose levels <70 mg/dL) include headache, fatigue, hunger, shakiness, irritability, and sweating. As blood glucose levels fall, symptoms can progress to confusion or abnormal behavior, vision changes, seizure, loss of consciousness, or death. While participating in IPHARM screening events, you may encounter patients with diabetes who are taking medications that increase their risk of low blood glucose. Knowing the symptoms and how to appropriately treat blood glucose is an important part of diabetes care.\(^{94}\)

Below are the classifications for hypoglycemia as defined by the ADA. Patients should be educated on the treatment of hypoglycemia if they are deemed at risk of any hypoglycemic event, due to medications or other factors.

\textbf{Table 15: Symptoms of Hypoglycemia}\(^{94}\)

<table>
<thead>
<tr>
<th>Signs &amp; Symptoms of Mild-Moderate Hypoglycemia (Blood glucose &lt;70mg/dL)</th>
<th>Signs &amp; Symptoms of Severe Hypoglycemia (Blood glucose &lt;54 mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hunger</td>
<td>Combativeness</td>
</tr>
<tr>
<td>Palpitations</td>
<td>Loss of consciousness</td>
</tr>
<tr>
<td>Sweating</td>
<td>Seizures</td>
</tr>
<tr>
<td>Tremors</td>
<td>Death</td>
</tr>
<tr>
<td>Confusion</td>
<td></td>
</tr>
<tr>
<td>Drowsiness</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td></td>
</tr>
<tr>
<td>Irritability/mood changes</td>
<td></td>
</tr>
</tbody>
</table>

Patients should be educated on how to manage hypoglycemia using 15 grams of fast-acting carbohydrates every 15 minutes until BG > 70 mg/dl. In the case of loss of consciousness due to hypoglycemia, the person should be treated urgently with a glucagon pen injected intramuscularly.\(^{94}\) Most recently, an intranasal formulation of glucagon has also been developed, which may make administration easier and results in rapid absorption and correction of hypoglycemia.\(^{100}\) Patients with frequent hypoglycemia should follow up with a healthcare provider to assess their diabetes management and reduce their risk of serious complications related to low blood sugars.
IX. Summary

Diabetes and prediabetes are highly prevalent and remain a major public health concern in the United States. The effects of chronic uncontrolled hyperglycemia are both costly and life limiting, and yet many are unaware of their issues with blood glucose control. As you have learned in this module, early identification of hyperglycemia and appropriate management are paramount to avoiding long-term complications of the disease. By achieving adequate control of blood glucose, and treating other modifiable risk factors such as hypertension, dyslipidemia, tobacco use, and obesity, we can reduce the impact of both microvascular and macrovascular complications. Screening high-risk patients to improve early detection, paired with providing interventions to prevent the onset or progression of diabetes, are vital steps in improving population health, particularly in populations with higher diabetes burden such as older adults and Native Americans. By having healthcare professionals trained in screening procedures and important patient education information, the IPHARM program provides one avenue to increase access to screening for Montanans and improve the overall health of Montana residents.
X. Useful Diabetes Websites

Listed below are some recommended websites to find further information on diabetes screening and management, as well as some useful mobile apps for patients to use to track blood glucose, diet, exercise, and other diabetes-related information.

Governmental

(a) National Diabetes Education Program (NDEP)
(b) National Institute of Diabetes & Digestive & Kidney Diseases
(c) Indian Health Service, Division of Diabetic Treatment & Prevention
(d) The Montana Diabetes Resource Center

Diabetes Organizations

(a) American Diabetes Association
(b) American Association of Diabetes Educators
(c) National Diabetes Education Initiative
(d) Defeat Diabetes Foundation, Inc.

Apps for Health Care Professionals

(a) ADA Standards of Care
(b) AACE Type 2 Diabetes Management Algorithm 2016
(c) CDE Coach
(d) Accurate Insulin Decisions AID

Apps for Patients

(a) OnTrack Diabetes
(b) Glooko
(c) Diabetes In Check
(d) Diabetic Connect
(e) UnderMYFORK
(f) Glucose Buddy
XI. References


35. American Association of Clinical Endocrinologists and American College of Endocrinology – clinical


60. A1c. Lab tests online. Accessed December 5, 2019 from https://labtestsonline.org/tests/hemoglobin-a1c


https://care.diabetesjournals.org/content/40/9/1273


Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2014.


APPENDIX A: (IPHARM) AUTHORIZATION TO TEST FORM

IMPROVING HEALTH AMONG RURAL MONTANAS (IPHARM) AUTHORIZATION TO TEST FORM

IPHARM will provide SCREENING test(s) to you today at your request and for the specific purpose of providing you with information that may relate to your health. An explanation of the results and how they may relate to your health will be provided by IPHARM personnel.

What will happen today?
IPHARM personnel will conduct the test(s) you have requested, obtain the results, and explain the results to you. You will receive the original and only copy of your complete test results. IPHARM personnel will record your results for statistical purposes on a data sheet that does NOT include your name. The results will be used in IPHARM reports compiled with all other test results and your results will never be individually identified or connected to you without your written permission. IPHARM will keep your agreement to be tested and the results sheets confidential, separated, and secure. IPHARM further agrees to use personnel trained to provide these tests and to follow general methods approved for these tests. IPHARM agrees to exercise due caution in those areas associated with the tests provided.

What do I agree to when I sign below?
By signing below, you indicate you have read and understand this form. You agree that IPHARM has no responsibility to contact your health care provider. You agree to receive testing from IPHARM for the test(s) you have requested. Finally, you agree to hold harmless IPHARM personnel for acts beyond their control or outside their responsibility in providing you these tests. *A copy of this form is available upon request.

Do I need to give these results to my health care provider?
IPHARM strongly encourages you to take your results to your provider when you next schedule an appointment. In some cases, IPHARM may suggest you schedule an appointment with your provider. IPHARM reminds you that a single screening test result whether abnormal or normal does not provide you or your provider enough information on which to make therapeutic decisions about your health. However, the tests may indicate that you should have further tests done or undertake changes in your life that could improve your health.

____________________________________________     _____________________
Client Signature                                      Date

____________________________________________     _____________________
Printed name of client                                Daytime phone number

______ Initial here if you will allow IPHARM to take a picture of you during testing to be used for publicity of the IPHARM program.

________________________ Client record number (record on results sheet also)
APPENDIX B: PROTECTION OF STAFF & PUBLIC FROM BLOOD-BORNE PATHOGENS

IPHARM will follow the procedures outlined below in order to protect individuals administering finger-stick tests and individuals exposed to finger-stick test waste that might cause injury. In all cases, IPHARM’s intent is to protect staff and the public from potential injury.

Procedure 1
All IPHARM workers will be instructed by an IPHARM Clinical Pharmacist Specialist (CPS), Principal Investigator (PI), or Project Coordinator (PC) before any tests are completed.

Procedure 2
All IPHARM workers administering finger-sticks must wear non-latex gloves on both hands prior to administering any finger-stick.

Procedure 3
All IPHARM workers will administer finger-stick tests only after training on the proper method for doing this procedure and only after observation of an instructor (PI, CPS, or PC) administering this test.

Procedure 4
The following items must be placed in a “Sharps” container after use:
   - Lancets (closed, open, or retractable), pipettes or other collection tubes, any other devices or potentially sharp objects that are used and come into contact with blood or body fluids. Items that may be discarded in a plastic garbage bag include the following: alcohol swabs, tissues including tissue with blood, used Band-Aids, and gloves that are properly removed and folded inside out into one another (gloves with blood may be handled in this manner also).

Procedure 5
After a person has a finger-stick test, they should be told to compress the site for at least 3-5 minutes with gentle but firm pressure. The IPHARM staff member working the station should inspect the site after this in order to determine if the person’s lancet wound has stopped bleeding. If not, a Band-aid shall be applied.

Procedure 6
In the event any worker believes they have come into contact with blood or body fluid and such contact has consisted of contact with an open sore or mucous membrane, the worker should immediately contact the IPHARM Clinical Pharmacist Specialist at the event.
Appendix C: Afinion™ HbA1c Quick Guide

Afinion™ HbA1c • Quick Guide

CLIA statement
This is a CLIA-waived test. A CLIA Certificate of Waiver is needed to perform testing in waived labs. If the laboratory modifies the test instructions, including quality control, the test will no longer meet the requirements for waived categorization. A modified test is regarded as highly complex and is subject to all applicable CLIA requirements.

Important!
- Read the entire Afinion™ HbA1c Quick Guide before testing patient samples or controls.
- See the Afinion™ AS100 Analyzer User Manual for more information about the operation of the Analyzer and Test Cartridge.
- See the Afinion™ HbA1c Package Insert for more information about the HbA1c assay.
- Use quality control materials to confirm that the Analyzer and test kit are working properly.

1 GETTING STARTED
Take time to familiarize yourself with the Analyzer and the test kit.

Afinion™ AS100 Analyzer

1 ON/OFF button
2 Light emitting diodes
3 Touch screen
4 The lid
5 Connectors

Cleaning the Analyzer
Clean the Analyzer every 30 days. Follow the procedure in the User Manual. See section "Cleaning and Maintenance".

Important touch buttons
- Patient sample mode
- Control mode
- Patient ID
- Control ID
- Enter
- Accept

Important information codes

<table>
<thead>
<tr>
<th>Code</th>
<th>Cause</th>
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<tbody>
<tr>
<td>103</td>
<td>Hemoglobin below 6.0 g/dL</td>
</tr>
<tr>
<td>104</td>
<td>Hemoglobin above 20.0 g/dL</td>
</tr>
<tr>
<td>105</td>
<td>HbA1c below 4.0%</td>
</tr>
<tr>
<td>106</td>
<td>HbA1c above 15.0%</td>
</tr>
<tr>
<td>202</td>
<td>Excess sample on the sampling device exterior</td>
</tr>
</tbody>
</table>
| 204  | - Hemolyzed or coagulated sample         
     | - Analyzer failure                       |

Afinion™ HbA1c Test Cartridge

Sampling device
Barcode
Capillary
ID area
2 PREPARE FOR TESTING

• Switch the Analyzer on.
• Allow 15 minutes for the Test Cartridge to reach operating temperature (64-86°F) before use.
• Open the pouch just before use. Hold the Test Cartridge by the handle.
• Label the Test Cartridge with sample ID. Use the ID area.
• Analyze Afinion™ HbA1c Control before analyzing patient samples.

3 PROCEDURE FOR COLLECTING THE SAMPLE

Sampling from a control vial
Follow the procedure described below.
See page 4 for control testing recommendations.

Sampling from finger
• Always use gloves.
• Cleanse the finger using alcohol. Allow the area to air dry.
• Use a lancet and firmly prick the finger (a). Properly dispose the lancet.
• Allow a good drop of blood to form before sampling (b).
• Apply digital pressure to the wound site with a clean gauze pad.

Specimen collection using the Afinion™ HbA1c Test Cartridge

1 Pull up the sampling device.
2 Touch the surface of the blood drop (a) or control (b).
3 Fill the capillary to the end. It is not possible to overfill.
4 Avoid air bubbles and incomplete filling (a). Avoid sample on the outside of the capillary (b).
   Do not wipe off.
5 Insert the sampling device immediately.
6 Within 1 minute place the Test Cartridge in the Analyzer.
4 RUNNING SAMPLES ON THE ANALYZER

1. **Patient sample:**
   - Touch \( \Box \) for patient samples.

2. **Control:**
   - Touch \( \Box \) for controls.
   - The lid opens automatically.
   - Insert the Test Cartridge.
   - The barcode should face left.

3. Close the lid manually.

4. **Patient sample:**
   - Touch \( \Box \) for patient samples.

5. **Control:**
   - Touch \( \Box \) for controls.
   - Enter ID during processing.
   - Touch \( \leftarrow \) to confirm.
   - Record the result when it appears on the screen.
   - Touch \( \checkmark \) to accept.

6. The lid opens automatically.
   - Remove and discard the cartridge.
   - Close the lid manually.

Information codes
Important information codes are listed on page 1. Consult the Analyzer User Manual for information codes not listed on page 1. Follow the actions listed in the User Manual to correct the error.

Verification of test results
Consult the HbA1c Package Insert. See section “Test result reporting”.

Verification of Control results
Compare the results with the values listed on the front of the Afinion™ HbA1c Control Package Insert.

Technical Support?
Call 1-877-4-Afinion or 1-877-423-4646. This is a toll free number. Available for use only in the United States of America.
US Technical Support can also be reached by E-mail. Send your request to: techsupport@us.axis-shield.com
CONTROL TESTING

Read the entire Afinion™ HbA1c Control Package Insert before use.

How often do I have to run controls?

In CLIA waived labs, it is recommended analyzing controls:

- With each new shipment of HbA1c kits.
- With each new lot of HbA1c kits.
- At least every 30 days.
- When training new users.
- Anytime an unexpected test result is obtained.

How should I use the Afinion™ HbA1c controls?

- Allow the control to reach room temperature before use. This takes about 30 minutes.
- Mix the control well by thoroughly shaking the vial for 30 seconds.
- Inspect the vial to ensure that the control solution is homogenous.
- Analyze the control using the procedures described on page 2 (Specimen collection) and page 3 (Running samples on the Analyzer).
- Compare the test results with the values listed on the front page of the Afinion™ HbA1c Control Package Insert.

What do I do if Afinion™ HbA1c Control results are not within the acceptable range?

- Do not analyze any patient samples.
- Check the control vial label to make sure it is not expired.
- Ensure that the control has not been used for more than 60 days.
- Verify that the controls and test cartridges have been stored correctly.
- Verify that there is no visual sign of bacterial or fungal growth in the control vial.

Correct any procedural error. Re-test the control.

If the control values are still not within acceptable range, repeat the test using a new vial of control. If the control results are still not acceptable, call Afinion™ Technical Support.

Technical Support?

Call 1-877-4-Afinion or 1-877-423-4646. This is a toll free number. Available for use only in the United States of America.

US Technical Support can also be reached by E-mail. Send your request to: techsupport@us.axis-shield.com
Appendix D: IPHARM Patient Brochure: Understanding Your Blood Sugars

Talk to Your Provider

⇒ If you have a family history of diabetes or feel you may be at risk for prediabetes, ask your health care provider about being tested.
⇒ If you experience any of the following symptoms, you may have prediabetes or diabetes, and should call your provider for further information.

• Frequent urination
• Excessive thirst
• Extreme hunger
• Unusual weight loss
• Increased fatigue (tiredness)
• Irritability

References:

Understanding your blood sugars

What you should know about the prevention and control of diabetes

I don't have diabetes; why should I worry about my blood sugar?

When we eat, our food is broken down into glucose (a sugar), which then enters the bloodstream. Insulin, a hormone released by the pancreas, helps the glucose get from the bloodstream into our cells to provide energy for our bodies. Lack of physical activity and excess weight can cause our bodies to stop using insulin properly, which can lead to blood sugar complications.

One complication is prediabetes. Prediabetes is when blood glucose levels are higher than normal, but not high enough to have diabetes.

How do I know if I have prediabetes?

There are three tests which can be used to determine if a person has prediabetes.

1. Fasting Plasma Glucose (FPG) – This test is a blood test taken after fasting for at least 8 hours.
2. Oral Glucose Tolerance Test (OGTT) – This test is also done after fasting for at least 8 hours and 2 hours after drinking a sugary liquid.
3. Hemoglobin A1c (HbA1c) – This test gives the average of your blood sugar control over the past 3 months.

Facts & Figures

• Approximately 30 million Americans have diabetes.
• Another 84 million Americans have prediabetes.
• The approximate cost of diabetes is $258 billion per year.
• Approximately 65% of people with prediabetes will develop diabetes within 6 years if they do not make changes.
• Complications of diabetes, such as eye problems (retinopathy), have been seen in up to 16% of people with prediabetes.

Risk Factors for Prediabetes

• Excess weight or obesity
• Age 45 or older
• A parent or sibling with diabetes
• Non-white ancestry
• History of gestational diabetes
• High blood pressure
• Abnormal cholesterol levels
• Lack of physical activity
• Polycystic ovarian syndrome
• Cardiovascular disease
• Previous high blood glucose levels
• A waist measurement of 40 inches or more for men and 35 inches or more for women
• Long-term use of certain medications, such as antipsychotics or steroids.

Symptoms

• Prediabetes usually does not have symptoms, but high blood glucose levels can still cause damage to the body if they are ignored.
Prevention and Treatment

✦ Good news! Lifestyle changes are very effective at reversing prediabetes and preventing its progression to diabetes.
  • Reduce weight by 5-10%.
  • Exercise 30-60 minutes per day at least 5 days per week.
  • Eat a healthy diet (See list on last page).
  • Stop smoking and avoid excess alcohol.

✦ Control blood pressure and cholesterol levels. The American Diabetes Association recommends the same guidelines for prediabetes that apply to diabetes.
  • Blood Pressure: A goal of less than 140/90 mmHg is recommended by the American Diabetes Association. Some health care providers may advise a lower goal for certain individuals.
  • Cholesterol: Check fasting cholesterol levels at least once a year.

✦ If lifestyle changes alone are unsuccessful, patients can talk to their provider about medications that can help control prediabetes.

What if I have pre-diabetes?

✦ Several tests should be performed at least once per year.
  • Fasting blood glucose should be checked with the FPG or OGTT test.
  • A hemoglobin A1c (HbA1c) test (measure of blood glucose control over 2-3 months).
  • Cholesterol levels.
  • Urinalysis to test for presence of protein in urine.
  • Blood pressure should be monitored regularly.

How to choose fruit...

One serving of fruit should contain 15 grams of carbohydrates.

The following fruit servings contain about 15 grams of carbohydrates:

• ½ medium banana
• 1 small apple
• 1 ¼ cup cubed watermelon
• 3/4 cup cubed pineapple
• 1 ¼ cup whole strawberries
• 1 small orange
• ½ large grapefruit

What are carbohydrates?

• Carbohydrates are a source of energy for your body.
• Foods with carbohydrates raise your blood sugar (glucose).
• Keeping track of carbohydrates can help keep your blood sugar in range.
• The three main types of carbohydrates include the following:
  • Starches - e.g., oats, rice, peas & potatoes
  • Sugars - naturally occurring (e.g., milk and fruit) and added sugar (e.g., soda)
  • Fiber - the indigestible parts of plants including fruits, vegetables, whole grains, nuts, and legumes.

✦ All carbohydrates have a glycemic index (GI), which is a number that helps classify carbohydrates based on how quickly and how high they boost blood sugar compared to pure glucose (sugar).
• In general, you want to choose foods with a low GI (score of <55).
• Also, the more a food is processed the higher its GI.
• Foods with a low GI are foods such as whole grains, beans, fruits, and vegetables.

Diabetes Super Foods!

These foods have a low GI and provide important nutrients.

<table>
<thead>
<tr>
<th>Food</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beans</td>
<td>Kidney, pinto, navy or black beans</td>
</tr>
<tr>
<td>Dark green leafy vegetables</td>
<td>Spinach, kale, collards</td>
</tr>
<tr>
<td>Citrus fruit</td>
<td>Oranges, grapefruits</td>
</tr>
<tr>
<td>Sweet potatoes</td>
<td>Full of fiber!</td>
</tr>
<tr>
<td>Berries</td>
<td>Strawberries, blueberries, raspberries</td>
</tr>
<tr>
<td>Tomatoes</td>
<td>Low-carb and full of fiber, vitamin A and C</td>
</tr>
<tr>
<td>Fish high in omega-3 fatty acids</td>
<td>Salmon</td>
</tr>
<tr>
<td>Whole grains</td>
<td>Pearl barley, oatmeal</td>
</tr>
<tr>
<td>Nuts</td>
<td>Almonds, walnuts, flax seeds</td>
</tr>
<tr>
<td>Dairy</td>
<td>Fat-free milk and yogurt</td>
</tr>
</tbody>
</table>
Post-test: Screening for Diabetes in Older Adults
Record responses on examination form.

1. The primary defect in diabetes is:
   a. Increased insulin resistance in peripheral tissues
   b. Decreased beta-cell mass and function
   c. Hormonal dysregulation of cortisol, growth hormone, and epinephrine
   d. Increased rates of glucose absorption in the stomach

2. All of the following conditions are types of microvascular complications that can result from diabetes EXCEPT:
   a. Nephropathy
   b. Myocardial infarction (heart attack)
   c. Retinopathy
   d. Erectile dysfunction

3. Which of the following diseases is the leading cause of death among patients with diabetes?
   a. Kidney failure
   b. Cancer
   c. Cardiovascular disease
   d. Pneumonia

4. Native Americans are how many times more likely to be diagnosed with diabetes compared to non-Hispanic Whites of similar age?
   a. Similar diagnosis rate
   b. Over twice as likely
   c. Four times as likely
   d. Five times as likely

5. Which of the following characteristics is NOT commonly associated with type 2 diabetes?
   a. Obesity
   b. Insulin resistance
   c. Onset before age 40
   d. Varying degrees of endogenous insulin production

6. The American Diabetes Association recommends daily low dose aspirin therapy for primary prevention of cardiovascular events in which subset of patients:
   a. Men and women over age 70 with diabetes plus one additional risk factor.
   b. All adults over 30 years of age with type 2 diabetes.
   c. Adults between 50 to 70 years of age who are deemed a high risk for cardiovascular events, and not at an increased risk for bleeding
   d. Aspirin is not recommended for primary prevention, and should only be used in adults with type 2 diabetes who have already had a heart attack or stroke
7. Which of the following statements is TRUE regarding screening recommendations for diabetes in the general population?
   a. All adults should be tested annually after the age of 35.
   b. All adults who are overweight (BMI >25 kg/m2 or ≥ 23 kg/m2 if Asian American) and have one or more risk factors should be screened
   c. All adults should be screened annually starting at age 45.
   d. All children who are overweight and have a sedentary lifestyle should be screened annually.

8. Patients with glucose values higher than normal but less than the diagnostic cut-off for diabetes are said to have:
   a. Gestational diabetes
   b. Prediabetes
   c. Adult onset diabetes
   d. Insulin resistance

9. Which of the following interventions is the most cost-effective at preventing onset of Type 2 diabetes in those with high risk of developing diabetes?
   a. Acarbose
   b. Metformin
   c. Pioglitazone
   d. Lifestyle modifications (weight loss and exercise)

10. The HbA1c test for screening for diabetes may be preferred over other tests because:
    a. It has good reliability when National Glycohemoglobin Standardization Program (NGSP)-certified methods are used.
    b. It is available as a point-of-care test.
    c. It does not require participants to be in a fasting state.
    d. All of the above statements are true.

11. Which of the following should be considered when choosing treatments for geriatric patients with diabetes?
    a. Financial resources
    b. Functional limitations
    c. Support system
    d. All of the above should be considered
12. Which of the following statements is TRUE regarding diabetic retinopathy?
   a. Diabetes is the second leading cause of blindness among American adults.
   b. Diabetic retinopathy is broken down into dominant and non-dominant forms of the disease.
   c. The majority of people with diabetic retinopathy are diagnosed early so that therapy is effective.
   d. All type 2 diabetic patients should receive an ophthalmologic dilated eye examination at the time of diagnosis.

13. Which of the following complications would NOT be considered to be a neuropathy?
   a. Neurogenic bladder
   b. Peripheral artery disease
   c. Inability to detect cold or heat
   d. Gastroparesis

14. Diabetes is the leading cause of non-traumatic lower-limb amputations in the United States. Which of the following risk factors would NOT increase the likelihood of incurring an amputation?
   a. Peripheral neuropathy
   b. Peripheral vascular disease
   c. Severe nail deformity
   d. Well controlled blood sugars

15. A 67 year old female, American Indian patient who is obese and taking antihypertensive medications is being screened for diabetes using the Afinion™ HbA1c test. Her HbA1c result is 5.7%. What action would you recommend?
   a. This patient clearly has diabetes and should be referred for follow-up care.
   b. This patient has a normal HbA1c and doesn’t require referral for follow-up care.
   c. This patient has multiple risk factors for diabetes, and given the A1c result, should be referred to her primary care provider at the patient’s earliest convenience to discuss the results.
   d. Counsel the patient to watch how much sugar she is eating.

16. A 72 year old male patient, who appears to be in good health, is screened for diabetes using the Afinion™ test. His HbA1c result is 7.5%. What action would you recommend?
   a. This patient can be diagnosed with diabetes based on this value and should be referred for follow-up care.
   b. This patient should be referred to his primary care provider for follow-up care, as the HbA1c result suggests chronic hyperglycemia and he needs further testing.
   c. Counsel this patient on the importance of risk factor reduction.
   d. Both b & c
17. According to the American Diabetes Association, which of the following non-pharmacologic therapies is NOT recommended for most patients with type 2 diabetes?
   a. Weight loss of 5-10% of body weight
   b. Strict dieting to eliminate all sugar and achieve a total caloric intake of less than 800 kcal per day
   c. Moderate exercise for 30 minutes for 5 days per week
   d. Smoking cessation

18. The American Diabetes Association recommends strongly that adults age 18-64 with diabetes should receive all of the following vaccinations EXCEPT:
   a. Annual influenza vaccine
   b. Hepatitis B vaccine
   c. Pneumococcal polysaccharide vaccine 23 (PPSV23)
   d. Pneumococcal conjugate vaccine 13 (PCV13)

19. Which of the following is NOT considered to be a risk factor for developing type 2 diabetes?
   a. Body mass index ≥ 25 kg/m2
   b. Chronic physical inactivity
   c. Female sex
   d. Hypertension (≥140/90 mmHg)

20. Which of the following statements regarding diabetic kidney disease is FALSE?
   a. Most people with diabetic kidney disease are aware that they have it
   b. Diabetes is a leading cause of end-stage renal disease in the U.S.
   c. The presence of albumin in the urine is a marker of nephropathy
   d. Treatment of hyperglycemia and other risk factors such as hypertension may reduce the risk of progression of diabetic kidney disease
**POST-TEST: Examination Form**

*Screening for Diabetes in Older Adults*

**Participant Information:**

1. Name: ______________________________________
2. Mailing address: ______________________________
   ____________________________________________
   ____________________________________________
   ____________________________________________
3. Date exam completed __________________________

**Questions: (Please circle one response per question)**

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For credit, please return: MTGEC/IPHARM, Skaggs Building, Room 217, University of Montana, 32 Campus Dr., Missoula, MT 59812.
**Evaluation: Screening for Diabetes in Older Adults**

Please indicate your major:

1. Based on the module description and stated objectives, this module met my expectations of the content it would deliver.

<table>
<thead>
<tr>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Neutral</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
<th>Don't Know</th>
</tr>
</thead>
<tbody>
<tr>
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<td>0</td>
<td>0</td>
<td>0</td>
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</tr>
</tbody>
</table>

2. How effective were the following in helping you understand the material?

<table>
<thead>
<tr>
<th></th>
<th>Very Effective</th>
<th>Effective</th>
<th>Neutral</th>
<th>Somewhat Effective</th>
<th>Not Effective</th>
<th>Not Applicable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-test</td>
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</tr>
<tr>
<td>Written Text</td>
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<td>Videos/Photos</td>
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<td>0</td>
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<td>0</td>
</tr>
<tr>
<td>Websites/Web Links</td>
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<td>References</td>
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<tr>
<td>Case Studies</td>
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</tr>
</tbody>
</table>

3. I learned something I can use in my practice/employment or personal setting.

<table>
<thead>
<tr>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Neutral</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
<th>Don't Know</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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</tr>
</tbody>
</table>
4. How do you plan to implement the information from this module to strengthen your practice, employment or personal goals? (check any that apply)

<table>
<thead>
<tr>
<th>Provide new information to patients/clients</th>
<th>Adjust practices with geriatric patients/clients</th>
<th>New program development or program enhancement</th>
<th>Provide new information to family/friends/co-workers</th>
<th>Train staff or provider</th>
<th>Other implementation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
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<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

* Describe 'other' implementation plan here:

5. How long did it take you to complete the module? (including pre-test, module review, post-test and evaluation)

<table>
<thead>
<tr>
<th>&lt;1 hour</th>
<th>1-2 hours</th>
<th>2-3 hours</th>
<th>3-4 hours</th>
<th>4-5 hours</th>
<th>&gt;5 hours</th>
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</thead>
<tbody>
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<td>0</td>
</tr>
</tbody>
</table>

6. The test questions were relevant to the module content.

<table>
<thead>
<tr>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Neither Agree nor Disagree</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
<th>Don't Know</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

7. Please provide suggestions to improve the online learning experience to meet your needs.

8. Please offer ideas or suggestions for new modules.

For credit, please return: MTGEC/IPHARM, Skaggs Building, Room 217, University of Montana, 32 Campus Dr., Missoula, MT 59812.