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Whole Patient Care & Diabetes: Recent Updates and Practice Changes

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Pharmacotherapy for diabetes is a rapidly evolving field. With new agents coming to market and emerging results of cardiovascular trials, medication selection has become increasingly complex. Accordingly, providers rely on pharmacists as medication experts to guide patient-centered decision making.

Learning Objectives

Pharmacist

1. Recognize the importance of selecting patient-specific glycemic and blood pressure goals.
2. Recognize the risks and benefits of daily aspirin therapy in patients with type II diabetes.
3. Identify appropriate elements of an evidence-based approach to managing hypertension in type II diabetics.
4. Recognize appropriate updates in managing hyperlipidemia in type II diabetics
5. Identify recommended vaccines, including vaccine sequencing, for type II diabetics

Pharmacy Technician

1. Recall common comorbid conditions associated with type II diabetes
2. Identify the risks of sub-optimal management of type II diabetes and comorbid conditions
3. Recognize common first line agents for managing comorbid conditions in type II diabetics
4. Identify routine vaccinations recommended for type II diabetics

Nurse

1. Recognize the importance of selecting patient-specific glycemic and blood pressure goals.
2. Recognize the risks and benefits of daily aspirin therapy in patients with type II diabetes.
3. Identify appropriate elements of an evidence-based approach to managing hypertension in type II diabetics.
4. Recognize appropriate updates in managing hyperlipidemia in type II diabetics
5. Identify recommended vaccines, including vaccine sequencing, for type II diabetics

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Introduction

Pathogenesis and Diagnosis

Type II diabetes is a chronic disease that disrupts the manner in which the body processes glucose resulting in progressive insulin resistance. In normal physiology, increasing blood glucose (for example, after a meal), prompts the cells to uptake the glucose from the blood for energy and the pancreas to release insulin to aid in the storage of glucose. As the body's ability to properly uptake and process glucose declines, the glucose remains in the blood and "blood sugar" levels rise. Despite the persistent rise in blood glucose, patients are often asymptomatic and diagnoses relies on routine laboratory screenings. Only when patients become highly insulin resistant do they begin to experience symptoms, which most commonly include polydipsia (increased thirst), polyuria (frequent urination), blurred vision.

As displayed in Table 1, type II diabetes may be diagnosed using various factors, all which include the measurement of blood glucose levels. In non-symptomatic cases, diagnosis is most commonly made using fasting blood glucose or hemoglobin A1C. Fasting blood glucose is defined as the level of the glucose in blood when a patient has not eaten for at least 8 hours. Hemoglobin A1C, often abbreviated as A1C, is a measure of the average blood glucose over the previous two to three months. In the absence of symptoms, diagnosis is typically confirmed using a second test. Best practice is to repeat the same test on a different day, however a fasting blood glucose greater than or equal to 126 mg/dl along with an A1C greater than or equal to 6.5% is also sufficient for diagnosis. (1)

Table 1: Diagnosis of Type II Diabetes (1)

- Fasting blood glucose greater than or equal to 126 mg/dL.

OR

- Blood glucose greater than or equal to 200 mg/dL after a 75 g oral glucose tolerance test

OR

- A1C greater than or equal to 6.5%.

OR

- Symptomatic hyperglycemia (polyuria, polydipsia, blurred vision) or hyperglycemic crisis AND a random blood glucose greater than or equal to 200 mg/dl.

Epidemiology and Disease Burden

As of 2015, the Center for Disease Control and Prevention estimated over 30 million people living in the United States of America have type II diabetes. (2) Among adults 18 years and older, this amounts to 12.2% of the U.S. population. Suboptimal disease state management is a serious risk factor for developing diabetes related complications which may lead to significant morbidity and mortality. Diabetes related complications can be divided into macrovascular and microvascular disorders. Macrovascular complications include coronary artery disease, peripheral arterial disease, and stroke. (3) Microvascular complications include nephropathy (disorders of the kidney), neuropathy (disorders of the nerves), and retinopathy (disorders of the eyes).

Table 2: Diabetes Related Complications

Macrovascular Complications	Microvascular Complications
• Coronary artery disease • Peripheral artery disease • Stroke	• Nephropathy • Neuropathy • Retinopathy

Blood glucose control is essential for slowing disease progression and subsequent development of macrovascular and microvascular complications. Likewise, proper management of hypertension (high blood pressure), hyperlipidemia (high cholesterol), and other cardiovascular risk factors is critical to preventing diabetes related morbidity and mortality. However, prevention and management of diabetes related complications is not a "one size fits all" approach; evidence is increasingly supporting a patient-centered or whole patient approach to diabetes care. In their most recent consensus statement, the American Diabetes Association and the European Association for the Study of Diabetes note the importance of shared decision making in the management of diabetes and diabetes related complications. (4) Shared decision making involves engaging patients and patient family or care givers as active participants in the treatment plan. A critical element of shared decision making includes incorporating patient preferences into the treatment plan and identifying patient-specific barriers which may hinder treatment success (i.e. medication costs, side effects, or belief systems). This manuscript will serve as an evidence-based guide to developing a patient centered approach to managing diabetes related complications and comorbidities.

Setting Patient Specific Glycemic Goals

There is some slight controversy among society recommendations regarding appropriate targets for glycemia goals. The American Diabetes Association considers an A1C less than 7% to be a reasonable goal for non-pregnant adults with type II diabetes whereas the American Association of Clinical Endocrinology endorses a more conservative target of less than or equal to 6.5%.(4, 5) The American Diseases Association does state that more stringent goals, such as an A1C less than or equal to 6.5%, may be considered for younger patients who can achieve lower targets without significant burden. The 2018 statement from the American College of Physicians now recommends a target A1C of 7- 8%. (6) Both organizations agree that less stringent goals (loosely defined as an A1C less than 8%) may be considered for frail patients, such as those with limited life expectancy or those at high risk of harm from hypoglycemia. This recommendation is also supported by the American Geriatrics Society. (7)

Table 3: Glycemic Goals for Type II Diabetics

Patient Population	Goal A1C
General adult patient with type II diabetes	≤6.5 – 7%
Young and/or healthy adults with type II diabetes	≤6.5%
Frail or elderly adults or those at high risk for hypoglycemia	<8%

Notably, evidence does not support routine self-monitoring of blood glucose in patients who are not prescribed insulin or an oral medication such as a sulfonylurea which places the patient at risk for hypoglycemia. (8) The costs of blood glucose testing supplies may be burdensome and recent literature has shown self-monitoring blood glucose alone does not significantly reduce A1C.

Benefits of Stringent Glycemic Targets

A multitude of literature has evaluated the effects of intensive glycemic control. While there is clear consensus that tighter control reduces the risk of microvascular complications, the evidence supporting benefits on macrovascular complications is limited. The largest trial to show long term benefits on macrovascular complications is the United Kingdom Prospective Diabetes Study (UKPDS). (9) UKPDS was a large

multicenter randomized controlled trial evaluating the impact of intensive versus non-intensive glycemic control among nearly 4000 patients newly diagnosed with type II diabetes. (9) Target goals for the intensive group was a fasting blood glucose less than or equal to 108 mg/dl; target goals in the conventional group were the "best achievable fasting blood glucose with diet management alone", with medications added if fasting blood glucose rose above 270 mg/dl or the patient developed symptoms of hyperglycemia. After 10 years, the average A1C was 7.0% (range 6.2% - 8.2%) and 7.9% (range 6.9% - 8.8%) in the conventional group. Patients treated using intensive targets had a 10% lower risk of death due to diabetes and a 6% lower risk of all-cause mortality, though neither of these findings reached statistical significance. The significance of the primary composite outcome was largely driven by the 25% reduction in risk of microvascular complications among the intensive treatment group. Select results are displayed in Table 4.

Table 4: Select Results from UKPDS (9)

Endpoint	Relative Risk with Intensive Management (95% Confidence Interval)	*p*
Any diabetes related endpoint	0.88 (0.79 – 0.99)	<0.05
Diabetes related death	0.90 (0.73 – 1.11)	NS
All cause mortality	0.94 (0.8 – 1.10)	NS
Myocardial Infarction	0.84 (0.71 – 1.0)	0.05
Stroke	1.11 (0.81 – 1.51)	NS
Amputation or death from peripheral vascular disease	0.65 (0.36 – 1.18)	NS
Microvascular complications	0.75 (0.60 – 0.99)	<0.05

NS = Did not reach statistical significance

After the completion of the study, patients were observed for an additional 10 years. (10) While glycemic control in the intensive group diminished within one year, cardiovascular benefits persisted. Patients who had been randomized to the intensive therapy group continued to show a reduced risk of myocardial infarction, diabetes related death and microvascular complications.

Risks of Stringent Glycemic Targets

UKPDS

Patients in UKPDS treated to intensive targets had a significantly higher risk of hypoglycemic events, with the event rate being 0.3 – 1.1% higher among patients treated intensively. (9) Additionally, weight gain is a common side effect of the medications used in the study and weight gain was significantly higher in the intensive target group. On average, patients receiving intensive therapy gained 4 – 8 pounds more than those treated with conventional targets.

The Action to Control Cardiovascular Risk in Diabetes Trial (ACCORD)

The ACCORD trial was a landmark study which evaluated the impact of intensive versus conventional glycemic control among over 10,000 adults with long-standing type II diabetes who were at high risk for cardiovascular events. (11) Patients randomized to the intensive group were treated to a target A1C of less than 6% and patients randomized to the conventional group were treated to a target of 7.0 – 7.9%. The study was stopped early due to an increased number of cardiovascular deaths within the intensive population (hazard ratio 1.22; 95% confidence interval 1.01 – 1.46). Additionally, patients in the intensive population experienced more severe hypoglycemic events as well as more weight gain.

Glycemic Control in Elderly Patients

Evidence evaluating glycemic targets in frail or elderly patients is limited. Adults aged 80 years and older comprised only a small proportion of diabetic landmark trials and frail patients, such as those with significant renal impairment or comorbidities are often excluded from clinical trials. Over the past several years, practice has evolved from extrapolating results observed among relatively young and healthy patients to accepting a more conservative approach in setting glycemic goals for frail patients and those with limited life expectancy. Evidence has shown microvascular benefits of stringent disease state control takes at least 8 years to emerge and macrovascular benefits may take even longer. (12) Data also suggests that intensive glycemic control is associated with a 1.5 - 3 fold increased risk of hypoglycemia. Hypoglycemic events present an additional risk of elderly or frail adults with underlying gate disturbances as falls can result in fractures, hospitalizations, and disability. Moreover, the presence of cognitive impairment may

further the risk of hypoglycemia if the patient struggles to maintain a regular diet or accurately manage their medications – this issue may be exacerbated among older adults with polypharmacy. For these reasons, expert guidelines now recommend less stringent glycemic goals, such as an A1C less than or equal to 8%, in frail patients or older adults in whom the risks of achieving stringent goals outweigh potential benefits. (4, 5, 8, 13)

Setting Patient Specific Blood Pressure Goals

Relative to the general population, patients with type II diabetes are at a higher risk of developing hypertension (high blood pressure). Without adequate blood glucose control, disease state progression may result in nephropathy, fluid retention, and arterial stiffness which can lead to blood pressure elevations. Additionally, diabetics frequently have additional risk factors such as obesity, sedentary lifestyle, and dietary habits which are independent risk factors for hypertension.

Independently, uncontrolled or sub-optimally controlled hypertension can lead to multiple complications including but not limited to heart attack, stroke, heart failure, and renal impairment. Therefore, type II diabetics with hypertension are at an increased risk for both microvascular and macrovascular complications including retinopathy, nephropathy, and cardiovascular events.

There is a large body of strong evidence which shows maintaining a blood pressure of less than 140/90 mmHg. (14, 15) However, in recent years, emerging evidence and expert guidelines have encouraged clinicians to set patient specific goals when determining goal blood pressure targets for type II diabetes. (5, 16, 17)

Table 5: Society Recommendations for Blood Pressure Goals in Type II Diabetics

Society	Goal Blood Pressure
American Diabetes Association(16)	At least <140/90 mmHg, lower if patient is at high risk for cardiovascular events and can achieve a lower goal without burden
American College of Cardiology/ American Heart Association (17)	< 130/80 mmHg
American Association of Clinical Endocrinologist/ American College of Endocrinology (5)	<130/80 mmHg for most patients, less stringent for frail or elderly patients and more stringent (<120/80 mmHg) for patients who can achieve an intensive goal without burden

As with glycemic control, the current body of literature strongly supports the selection of patient specific blood pressure targets. Intensive targets, such as a blood pressure of less than or equal to 120/80 mmHg may be considered for patients at high risk for cardiovascular disease who can achieve lower targets without undo burden of polypharmacy or adverse effects and younger relatively healthy individuals. Likewise, less stringent targets, such as a blood pressure of less than or equal to 150/90 mmHg may be appropriate for frail or elderly patients, particularly those who are at risk for falls.

One of the largest trials to evaluate blood pressure targets in type II diabetes was ACCORD BP. (18) ACCORD BP was a subset of the ACCORD trial which evaluated the risks and benefits of intensive versus standard glycemic control. (11) ACCORD BP was one of the first landmark trials to evaluate the risks and benefits of intensive blood pressure control relative to standard of care. (18) The trial included over 4,700 patients with type II diabetes and two or more risk factors for cardiovascular disease to treatment who were randomized to intensive blood pressure control (defined as a systolic blood pressure goal less than 120 mmHg) or standard of car (defined as a systolic blood pressure goal less than 140 mmHg). After almost 5 years, there was no significant differences in the primary composite outcome of nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular causes and no difference in cardiovascular or non-cardiovascular death between patients who randomized to intensive versus standard blood pressure targets. However, when evaluated alongside the results of the ACCORD trial, patients who randomized to receive intensive therapy in one or both trials did have a reduced risk of cardiovascular events. (19) Relative to patients randomized to receive standard targets, patients in the ACCORD BP intensive target group were found to have a 41% reduced risk of stroke. However, serious adverse effects such as hypotensive, fainting, electrolyte abnormalities, and renal failure occurred more frequently among patients randomized to the intensive treatment group. (18) Detailed results are displayed in Table 6.

Aside from ACCORD BP, much of the evidence used to select blood pressure targets in type II diabetes is extrapolated from trials which did not exclusively enroll diabetic patients. For example, the Systolic Blood Pressure Intervention Trial (SPRINT) is a large landmark trial that showed non-diabetic patients with hypertension who were treated to a target systolic blood pressure of less than 120 mmHg had a significantly lower risk of cardiovascular events and mortality relative to those treated to a target systolic blood pressure of less than 140 mmHg. (20) Consistent with other trials, rates of adverse effects were higher among the intensive treatment group relative to the standard treatment group. Though diabetics were excluded from SPRINT, the compelling findings

remain a consideration when setting treatment targets for type II diabetics, particularly those who are otherwise similar to the study population.

Table 6: Summary of Select Trials Evaluating Intensive versus Standard Blood Pressure Targets

Trial	Study Population & Criteria	Outcomes
ACCORD BP (18, 19)	• Enrolled 4,733 type II diabetics who had two or more risk factors for cardiovascular disease • Intensive blood pressure target defined as systolic blood pressure less than 120 mmHg • Standard blood pressure target defined as systolic blood pressure less than 140 mmHg	• No difference in primary composite outcome of nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular cause (hazard ratio 0.88; 95% confidence interval 0.73 – 1.06) • No differences in all cause mortality (hazard ratio 1.07; 95% confidence interval 0.85 – 1.35) • Patients in the intensive treatment goal had a significantly lower risk of stroke (hazard ratio 0.59; 95% confidence interval 0.39 – 0.89) • Relative to patients receiving both standard glycemic and blood pressure control, those who received intensive blood pressure with standard glycemic control had a reduced risk of cardiovascular events (hazard ratio 0.74; 95% confidence interval 0.55 – 1.00). • Relative to patients receiving both standard glycemic and blood pressure control, those who received intensive blood pressure and glycemic control had a reduced risk of cardiovascular events (hazard ratio 0.71; 95% confidence interval 0.52 – 0.96).

SPRINT (20)	• Enrolled 9,631 non-diabetic adults aged 50 years and older with hypertension and high cardiovascular risk (at least one of the following: age 75 years or older, cardiovascular disease [except prior stroke], renal impairment, or a 10-year Framingham Risk score greater than or equal to 15%) • Intensive therapy was defined as a systemic blood pressure less than 120 mmHg • Standard therapy was defined as a systolic blood pressure less than 140 mmHg	• After 3.26 years, the trial was halted early due to a significantly reduced risk of primary composite outcome of nonfatal myocardial infarction or other acute coronary syndrome, stroke, heart failure, or death from cardiovascular cause among patients receiving intensive treatment (hazard ratio 0.75; 95% confidence interval 0.64 – 0.89) • Risks of cardiovascular death (hazard ratio 0.57; 95% confidence interval 0.38 – 0.85) and all cause mortality (hazard ratio 0.73; 95% confidence interval 0.60 – 0.90) were significantly lower among patients receiving intensive therapy

Medication Management of Hypertension in Diabetes

When selecting a medication to treat hypertension in type II diabetes, the following should be considered: evidence that a given class of agents prevents cardiovascular events such as myocardial infarction or stroke, evidence that a given class of agents reduces mortality, and evidence that a given class prevents progression of diabetic kidney disease. To date, there is not strong evidence to suggest one class of antihypertensive agents is superior for prevention of other microvascular outcomes such as retinopathy or neuropathy. Ultimately, it is important to remember that blood pressure reduction by any means is the main factor in reducing the risk of macrovascular and microvascular complications. (21)

Evidence suggests use of an angiotensin converting enzyme inhibitor (ACEs) or an angiotensin receptor blocker (ARBs)can slow the progression of kidney disease among type II diabetics with nephropathy. (15, 22, 23) Given that current evidence does not support preferential use of an ACEs or an ARB in type II diabetics with diabetic nephropathy (specifically those with albuminuria), diabetics without existing renal

disease may be treated with any first line agent. First line agents are those which have proven cardiovascular benefits and include thiazide and thiazide-like diuretics, dihydropyridine calcium channel blockers, ACEs and ARBs. (24, 25) Despite the lack of evidence showing superiority of ACEs or ARBs among type II diabetics without albuminuria, these medication classes are still commonly selected as first line agents for treating high blood pressure in this population.

Table 7: Pharmacologic Agents for the Treatment of Hypertension

Medication Class ***Drug Names***	**Considerations**
First Line	
Angiotensin Converting Enzyme Inhibitors *Lisinopril (Prinivil/Zestril)* *Enalapril (Vasotec)* *Captopril (Capoten)* *Benazepril (Lotensin)* *Quinapril (Accupril)* *Ramipril (Altace)*	• Dry cough may occur in 5 – 20% of patients. Angiotensin converting enzyme inhibitor cough typically develops within the first 6 months of therapy and resolve within four days if drug is held and reoccur if same of other angiotensin converting enzyme inhibitors is initiated • Hyperkalemia (elevated potassium) and reduced renal function are common. A 30% increase in creatinine is generally acceptable to continue therapy. Monitor labs within 1 – 2 weeks of initiation, after dose changes, and periodically throughout therapy. • Angioedema: can develop at any time however 50% of cases occur within the first weeks of therapy. Though still rare, incidence is higher among African Americans. • Should not be used with angiotensin receptor blockers.
Angiotensin Receptor Blockers *Losartan (Cozaar)* *Valsartan (Diovan)* *Candesartan (Atacand)* *Irbesartan (Avapro)* *Olmesartan (Benicar)* *Telmisartan (Micardis)*	• Hyperkalemia (elevated potassium) and reduced renal function are common. A 30% increase in creatinine is generally acceptable to continue therapy. Monitor labs within 1 – 2 weeks of initiation, after dose changes, and periodically throughout therapy. • Dry cough is less common with angiotensin receptor blockers than with angiotensin converting enzyme inhibitors but may still occur. • Angioedema is less common than with angiotensin converting enzyme inhibitors but may still occur. Patients with a history of angiotensin converting enzyme inhibitor angioedema can trial an angiotensin receptor blocker at least 6 weeks after the angiotensin converting enzyme inhibitor is discontinued. • Should not be used with angiotensin converting enzyme inhibitors.
Thiazide and Thiazide-Like Diuretics *Hydrochlorothiazide (HCTZ)* *Chlorthalidone* *Indapamide*	• Minimally effective in patients with poor renal function (GFR <30 ml/min). • Higher doses (HCTZ ≥50 mg or equivalent) produce more fluid loss but have minimal added benefit on blood pressure reduction. • Electrolyte abnormalities including hyponatremia (low sodium) hypokalemia (low potassium), and hypomagnesemia (low magnesium) are common. Monitor labs within 1 – 2 weeks of initiation, after dose changes, and periodically throughout therapy.

	• May increase blood glucose by 5 – 10 mg/dl, particularly if used with a beta blocker. • Use with caution in patients with gout who are not receiving uric acid lowering therapies. • Chlorthalidone and indapamide may be preferable as they are dosed once daily and have established benefits on cardiovascular outcomes.
Dihydropyridine Calcium Channel Blockers *Amlodipine (Norvasc)* *Felodipine (Plendil)* *Nifedipine (Adalat,Procardia)* *Nicardipine (Cardene)*	• Edema: can be mitigated by reducing dose and/or adding angiotensin converting enzyme inhibitor or an angiotensin receptor blocker. Calcium channel induced edema is due to fluid shifts as opposed to fluid retention and therefore typically does not improve with diuretics. Use with caution in patients with heart failure with reduced ejection fraction. • Rarely, calcium channel blockers may cause gingival overgrowth or gingival hyperplasia. Most reported cases are with nifedipine but may occur with other calcium channel blockers as well.
Second Line	
Mineralocorticoid Receptor Antagonist *Spironolactone (Aldactone)* *Eplerenone (Inspra)*	• Side effects are dose related. Gynecomastia and impotence are less common with eplerenone. • Hyperkalemia (high potassium) is common. Risk is highest in patients with impaired renal function or using other drugs known to increase potassium such as angiotensin converting enzymes inhibitors or angiotensin receptor blockers.
Beta Blockers *Selective beta blockers: metoprolol (Lopresser,Toprol), bisoprolol (Zebeta) atenolol (Tenormin)* *Non-selective beta blockers: propranolol (Inderal)* *Beta and alpha1 active beta blockers: carvedilol (Coreg), labetalol (Trandate)*	• In the absence of other compelling indications such as prior myocardial infarction or atrial fibrillation, beta blockers are no longer considered first line for blood pressure control. • Carvedilol and labetalol also act on alpha1 receptors and therefore have a stronger effect on blood pressure reduction than other agents in the class • Atenolol requires dose adjustments if renal function declines below 35 ml/min. • Beta blockers should not be abruptly discontinued. To taper: reduce daily dose by 50% for 1 week then every other day for 1 week and then stop. If used with clonidine, the beta blocker should be discontinued before discontinuing clonidine.
Non-Dihydropyridine Calcium Channel Blockers *Verapamil (Calan,Veralan)* *Diltiazem (Cardizem, Cartia)*	• Less effective at reducing blood pressure than dihydropyridine calcium channel blockers. • Potential for clinically significant drug interactions is relatively higher with non-dihydropyridine calcium channel blockers than other antihypertensive classes of medications. • Avoid in patients with heart failure with reduced ejection fraction. • Use with beta blockers is generally avoided as there is a risk of bradycardia and heart block with concurrent use.
Third Line	
Alpha-1 Blockers *Doxazosin (Cardura)* *Terazosin (Hytrin)*	• May be considered third line therapy in patients with benign prostatic hyperplasia • Risk of orthostatic hypotensive, especially when medication is started or dose is increased. Use with caution in patients at risks for falls. • Avoid in patients with heart failure.

Central Alpha Agonists *Clonidine (Catapress)*	• Often poorly tolerated. Common side effects include hypotension, dry mouth, sedation, and topical reactions to the patch. • Cannot be abruptly discontinued. To taper, reduce dose by 50% every 3days and resume previous dose if withdrawal symptoms develop. Risk of withdrawal is greatest with immediate release tablets. If discontinuing clonidine and a beta blocker, withdraw beta block several days prior to tapering clonidine.
Vasodilators *Hydralazine (Apresoline)*	• Multiple daily doses may be a barrier for medication adherence. • Tachycardia (increased heart rate) is common and often resolves if hydralazine is used with a beta blocker. • Edema is a dose related side effect. • High doses (more than 200 – 400 mg/day) have been associated with drug induced lupus.

In their 2017 position statement, the American Diabetes Association recommends initiating a single antihypertensive agent in type II diabetics who have an initial blood pressure between 140/90 mmHg and 160/100 mg Hg and initiating two antihypertensive agents in type II diabetics who have an initial blood pressure greater than or equal to 160/100 mmHg. (24) Both groups of patients should also be encouraged to make lifestyle changes engaging in regular physical exercise and making dietary modifications such as increasing fruit and vegetable consumption and reducing sodium intake. Regimens for patients with albuminuria, defined as a urine to albumin creatinine ratio greater than or equal to 30 mg/g creatinine, should include an angiotensin converting enzyme inhibitor or an angiotensin receptor blocker. Hypertensive type II diabetics without albuminuria may be started on an ACE, ARB, dihydropyridine calcium channel blocker, or a thiazide or thiazide-like diuretic (chlorthalidone or indapamide preferred). Hypertensive diabetics who will be initiated on two antihypertensive agents should be started on an ACE or an ARB and a dihydropyridine calcium channel blocker, or a thiazide or thiazide-like diuretic (chlorthalidone or indapamide preferred). If blood pressure goals are not achieved, adherence should be confirmed prior to initiating an additional medication. Adherence may be verified through non-judgmental conversations with patients and/or contacting the patient's pharmacy to verify the dates medications were refilled and picked up. It is critical that barriers to adherence are identified and addressed prior to starting any additional medications. If adherence is confirmed and blood pressure control remains above target, doses may be increased and/or a third agent from the first line category can be added to the regimen. If blood pressure control remains suboptimal, a mineralocorticoid receptor antagonist may be initiated and/or referral to a cardiovascular specialist may be considered.

Many patients require multiple agents to achieve blood pressure targets. Unless there is a compelling indication to use a second- or third-line medication class, such as prior myocardial infarction, multi-drug regimens should use either an ACE or an ARB along with a dihydropyridine calcium channel blocker and/or a thiazide or thiazide-like diuretic. Though ACEs and ARBs have individual benefits, patients should not be treated with both an ACE and an ARB at the same time. Studies have shown that combination therapy with an ACE and an ARB produces no additional cardiovascular or mortality benefits than monotherapy and carries an increased risk of serious adverse effects such as hyperkalemia (high potassium) and acute renal failure. (26, 27) When multi-agent antihypertensive regimens are used, at least one medication should be taken at bedtime. Recent literature has shown adjusting dose schedules to allow at least one antihypertensive agent to be taken at bedtime reduces the risk of cardiovascular events, however these results are controversial as they were not consistently replicated in other studies. (28-30) Though the body of evidence around bedtime dosing is mixed, the risks of adjusting administration times are minimal (so long as adherence is maintained) and a number of expert guidelines now recommend at least one antihypertensive agent is dosed at bedtime. (24, 25)

Managing Hyperlipidemia in Type II Diabetics

Statins

As with hypertension, hyperlipidemia (high cholesterol) is common among patients with type II diabetes. Along with hyperglycemia and hypertension, hyperlipidemia increases the risk of atherosclerotic cardiovascular disease thus placing patients at risk for cardiovascular events such as myocardial infarction and stroke. Additionally, statins have been firmly designated as first line pharmacotherapy, with dosing recommendations based on the agent's ability to reduce LDL cholesterol. Low intensity regimens can be expected to reduce LDL levels by less than 30%, moderate intensity regimens can be expected to reduce LDL levels by 30% - 49%, and high intensity regimens can be expected to reduce LCL levels by greater than or equal to 50%. (31) Low, moderate, and high intensity statin regimens are displayed in Table 8.

Table 8: Statin Intensity

Low Intensity Regimens	Moderate Intensity Regimens	High Intensity Regimens
Simvastatin 10 mg daily Pravastatin 10 mg – 20 mg daily Lovastatin 20 mg daily Fluvastatin 20 – 40 mg daily	Atorvastatin 10 – 20 mg daily Rosuvastatin 5 – 10 mg daily Simvastatin 20 – 40 mg daily Pravastatin 40 – 80 mg daily Lovastatin 40 – 80 mg daily Fluvastatin 40 – 80 mg daily Pitavastatin 1 – 4 mg daily	Atorvastatin 40 – 80 mg daily Rosuvastatin 20 – 40 mg daily Simvastatin 80 mg

Generic (Trade Name) Key: - Atorvastatin (Lipitor) - Fluvastatin (Lescol) - Rosuvastatin (Crestor) - Lovastatin (Mevacor) - Pitavastatin (Livalo) - Pravastatin (Pravachol) - Simvastatin (Zocor)

Clinically, atorvastatin or rosuvastatin tend to be commonly initiated regimens. Both agents are highly potent thus allowing room for dose increases without switching agents. Unlike simvastatin, which is also potent, atorvastatin, and to a greater degree, rosuvastatin, are less prone to drug interactions. In 2011, the Food and Drug Administration (FDA) released a Drug Safety Communication regarding the potential for statin-related toxicities with simvastatin resulting from drug interactions. (32) This update recommends limiting the doses of a number of medications, including many commonly used by patients also receiving statin therapy. In many cases, the potential for drug interactions limits the use of simvastatin to less than or equal to 20 mg per day, thus reducing or eliminating its potential use in moderate or high intensity regimens. The Drug Safety Communication also recommends against initiating new patients on simvastatin 80 mg as this dose is associated with a higher risk of statin-related side effects and toxicities including myopathy and rhabdomyolysis. The FDA recommends patients who are established on simvastatin 80 mg (i.e. on therapy for at least 12 months) remain on the agent as long as tolerance is not an issue; those receiving short durations of therapy or who wish to reduce the risk of drug interactions or adverse effects may switch to an alternative statin at an equipotent dose. Additionally, atorvastatin does not require renal dose adjustments and therefore is a preferred option for patients with kidney disease. Moreover, both atorvastatin and rosuvastatin are now available generically, thus reducing potential cost barriers to adherence. In all cases, statin therapy should be used in additional to lifestyle changes.

Second Line Agents

Though there are several classes of agents used to treat hyperlipidemia, expert guidelines now strongly advocate for the use of statin therapy as the primary means of cholesterol management. Many non-statin therapies such as niacin and the fibrates, fenofibrate and gemfibrozil, are no longer recommended, or recommended in very select scenarios. This practice change is due to the fact that these agents have failed to show significant benefits on cardiovascular morbidity and mortality and in some cases increase risks of harm. A recent meta-analysis found fibrates were associated with increased risk of non-cardiovascular mortality and a trend towards increase risk of all-cause mortality and cardiovascular mortality. (33) A second meta-analysis concluded use of fibrates had no impact on all-cause mortality or cardiovascular mortality and a trend towards increased risk of non-cardiovascular mortality. (34) The benefits of fibrates appear to be largely isolated to patients with hypertriglyceridemia (high triglycerides). (35) Updated guidelines now recommend considering fibrates as second line therapy for patient with severe hypertriglyceridemia who have not fully responded to statin therapy.

In addition to minimal benefit, benefit isolated to a small subset of patients, or potential harm, use of non-statin therapies can create additional burdens such as drug interactions and polypharmacy. Fibrates, particularly gemfibrozil, can reduce the metabolism of other drugs and cause supratherapeutic levels and potentially toxic adverse effects. Fibrates are known to reduce the metabolism of many statins which can lead to myopathy, myalgia, and in rare cases, rhabdomyolysis. Moreover, studies have shown that patients who take multiple medications (also called polypharmacy) often struggle to maintain adherence. (36) Poor adherence and polypharmacy may be attributed to a number of specific factors including high pill burden and the financial costs of acquiring numerous medications.

For type II diabetics on statin therapy, the American College of Cardiology recommends evaluating treatment success based on the percent of LDL cholesterol reduction from baseline. (37) Treatment success for type II diabetics is considered a reduction in LDL cholesterol 50% or more from baseline or an LDL cholesterol less than 70 mg/dl. For patients who fail to meet these metrics, adherence to statin therapy should be assessed. If adherence is confirmed, the regimen can be increased to high intensity (if the patient is not already taking this) and lifestyle changes should be encouraged. If lipid goals continue to not be met, the American College of Cardiology encourages shared decision making to determine if additional agents should be started. The clinician should educate the patient on what additional reduction in risk of cardiovascular events they can be expected to derive if a non-statin agent is added to their regimen. The clinician should also review the potential for adverse effects, drug interactions, and the costs of the

medications. If the patient wishes to proceed with adding additional therapies, the American College of Cardiology recommends adding ezetimibe (Zetia) to the regimen. Ezetimibe is a generically available oral agent that is generally well tolerated with relatively few drug interactions. In the past, practice has moved away from ezetimibe after it failed to show reduced risk of cardiovascular events despite its ability to reduce LCL cholesterol. (38) However, the results of the recently released IMPROVE-IT trial have brought the drug back into favor. (39) IMPROVE-IT was a large randomized controlled trial that evaluated the impact of a statin plus ezetimibe versus a statin alone among patients who were recently hospitalized for acute coronary syndrome. The study found that over 6 years, combination therapy slightly but significantly reduced the risk of the primary composite endpoint, cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, unstable angina requiring hospitalization, or coronary revascularization relative to statin monotherapy (hazard ration 0.94; 95% confidence interval 0.89 – 0.99). There was no difference in all cause mortality or cardiovascular mortality between groups. Incidence of adverse effects were similar among patients who received ezetimibe plus a statin or a statin alone. For patients who fail to achieve lipid goals when an ezetimibe is added to maximally tolerated statin therapy, the American College of Cardiology recommends initiating a proprotein convertase subtilisin/kexin 9 (PCSK9) inhibitor, in addition or in replacement of statin therapy. The PCSK9 inhibitors, alirocumab (Praluent) and evolocumab (Repatha), are newly approved monoclonal antibodies that profoundly reduce LDL cholesterol by an average of 60 – 70%. (40, 41) Furthermore, they have shown to reduce risk of cardiovascular events by up to 50%. (42, 43) Unlike the other agents for hyperlipidemia which are all orally administered, both PCSK9 inhibitors are administered as subcutaneous injections. Nevertheless, both alirocumab and evolocumab are generally well tolerated, with the most common side effects being injection site reactions. While serious adverse effects or toxicities appear uncommon with PCSK9 inhibitors, the drugs are relatively new to market and therefore the long term effects of these agents remains unknown. Additionally, the high cost of these drugs may present a significant barrier to patients, particularly those who are uninsured or underinsured.

Therapy Based on 10-Year Risk

In recent years, new expert guidelines have prompted major practice changes in the treatment of hyperlipidemia. For decades, treatment for hyperlipidemia was initiated based on blood cholesterol levels and used low density lipoprotein (LDL) cholesterol as a therapeutic target. However, in 2013, the release of new clinical guidelines prompted practice to evolve from treat-to-target cholesterol management to basing treatment

decisions on the patient's 10-year risk of events. (44) Since patients with type II diabetes are at a high risk for cardiovascular events, the American Heart Association/ American College of Cardiology recommends type II diabetics age 40 – 75 years with an LDL cholesterol greater than or equal to 70 mg/dl start a moderate intensity statin regimen. (31, 44) The organizations recommend considering a high intensity statin regimen for type II diabetics who have multiple risk factors for atherosclerotic cardiovascular disease such as hypertension or renal impairment. They also note it is reasonable to assess a patient's 10-year risk for patient specific guidance in selecting a moderate or high intensity statin regimen. The American Heart Association/ American College of Cardiology also notes it may be reasonable to add ezetimibe to the maximally tolerated statin regimen in type II diabetics with a 10-year risk greater than or equal to 20%. Likewise, the American Diabetes Association recommends all patients with type II diabetes and atherosclerotic cardiovascular disease receive high intensity statin therapy regardless of age. (16) For type II diabetics age 40 – 75 without additional risk factors for atherosclerotic cardiovascular disease, the organization recommends starting moderate intensity statin therapy. For type II diabetics who are less than 40 years of age and do not have additional risk factors for atherosclerotic cardiovascular disease, they recommend considering the use of moderate intensity statin therapy.

The decision to initiate or continue statin therapy in older adults is controversial and the American Heart Association/ American College of Cardiology encourages shared decision, with the clinician explaining the potential benefits and risks. (31) Given that therapeutic decisions are made based on the ability of statins to reduce the likelihood of a cardiovascular event over a 10-year period, patients and clinicians must consider the likelihood the patient has an additional 10 years of life and balance the benefits with the risks of statin-related adverse effects, drug interactions, and pill burden. Likewise, limited evidence is available for younger patients with type II diabetes. The American Heart Association/ American College of Cardiology states it may be reasonable to initiate statin therapy in type II diabetics aged 20 – 39 years who have long-standing diabetes (greater than or equal to 10 years duration) or diabetic related complications such as albuminuria, renal failure, or neuropathy.

Table 9: Society Recommendations for Statin Therapy in Type II Diabetics

Society	Recommendations for Statin Therapy
American Heart Association/ American College of Cardiology(31)	• Initiate moderate intensity statin therapy in patients with type II diabetes, age 40 – 75 years. • High intensity statin therapy may be considered for type II diabetics age 40 – 75 years who have multiple risk factors for atherosclerotic cardiovascular disease. • It is reasonable to add ezetimibe to statin therapy for type II diabetics with a 10-year risk for atherosclerotic cardiovascular events greater than or equal to 20%. • It is reasonable to continue therapy in type II diabetics greater than 75 years of age who are established on statin therapy. • Shared decision making should be used when considering the benefits and risks of starting statin therapy in type II diabetics age 75 and older. • It may be reasonable to start statin therapy in younger type II diabetics (age 20 – 39 years) who have had the disease greater than or equal to 20 years, have renal impairment, retinopathy, or neuropathy
American Diabetes Association(16)	• Type II diabetics with atherosclerotic cardiovascular disease should be stated on high intensity statin therapy. • Type II diabetics age 40 – 75 without atherosclerotic cardiovascular disease should be started on moderate intensity statin therapy. • Type II diabetics over 75 years of age should be started on moderate intensity statin therapy. • Shared decision making may be used to consider the use of moderate intensity statin therapy in type II diabetics less than 40 years of age who have additional risk factors for atherosclerotic cardiovascular disease. • Type II diabetics with atherosclerotic cardiovascular disease and an LDL cholesterol greater than or equal to 70 mg/dl on maximally tolerated statin therapy may be started on ezetimibe or a PCSK9 inhibitor. Ezetimibe may be preferred due to cost.

Daily Aspirin Therapy in Type II Diabetes

Many patients have long considered low dose daily aspirin therapy to be a mainstay of preventative healthcare. However evolving evidence suggests the risks of low dose daily aspirin therapy many outweigh the benefits in certain subsets of lower risk patients. While the benefits of low dose daily aspirin therapy for secondary prevention of cardiovascular events including myocardial infarction and stroke are well established, evidence supporting the use of low dose daily aspirin therapy for primary prevention is a

bit controversial. (45-48) In patients who are at lower risk for cardiovascular events, particularly those who have not had a prior event, the risk of aspirin induced bleeding may outweigh the cardiovascular benefits. For this reason, the decision to start aspirin in type II diabetes should be individualized by patient using a model of shared decision making.

Aspirin for Secondary Prevention in Type II Diabetes

It is understood that patients with type II diabetes are at an increased risk for cardiovascular disease and the risk of cardiovascular events is especially high in patients who had a previous myocardial infarction or stroke. The benefits of antiplatelet therapy for secondary prevention are well established among patients with and without type II diabetes. (49) One of the largest studies showing this benefit was a meta-analysis which included 287 studies and over 200,000 patients. The combined results of these trials found that high risk patients who were treated with antiplatelet therapy had a 25% reduced risk of any vascular event, approximately a 33% reduced risk of non-fatal myocardial infarction, and approximately a 25% reduced risk of non-fatal stroke. Among diabetics specifically, this trial showed those treated with antiplatelet therapy had a 7% decrease in risk of cardiovascular events, though this failed to achieve statistical significance.

Aspirin for Primary Prevention in Type II Diabetes

Prior position statements had recommended the use of low dose daily aspirin therapy for primary prevention in patients with type II diabetes. (50) However, recommendations have evolved to favor a patient specific approach as emerging evidence supporting use of low dose daily aspirin for primary prevention is conflicting. One of the largest meta-analysis to evaluate the role of low dose daily aspirin included six trials that enrolled over 95,000 non-high-risk patients, approximately 4,000 of whom were diabetic. (51) This study found that among non-high- risk patients, low dose daily aspirin reduced the risk of vascular events by 12%. This finding was largely driven by an 18% reduction in risk of non-fatal myocardial infarction. No significant differences were observed with regard to coronary heart disease or non-fatal stroke.

A second trial evaluated the impact of low dose daily aspirin therapy for primary prevention among 15,000 type II diabetics who were at least 40 years of age and were not known to have cardiovascular disease. (47) After 7.4 years, patients randomized to receive daily aspirin therapy had a lower incidence of serious vascular events, defined as myocardial infarction, stroke, transient ischemic attack, or death from any cause except intracranial hemorrhage (rate ratio 0.88, 95% confidence interval 0.79 – 0.97). However,

relative to placebo, major bleeding events were more frequent among patients receiving daily aspirin therapy (4.1% versus 3.2%, respectively, p = 0.003). The majority of bleed events involved the gastrointestinal tract or other extracranial sources of bleeding.

Previous position statements have offered sex specific recommendations for primary prevention with low dose daily aspirin therapy. (50) However recent evidence has shown the risk of heart disease and stroke is equivalent, if not higher, among women. (16) Therefore, sex specific recommendations for low dose daily aspirin therapy are no longer used.

Aspirin for Patients with Type II Diabetes Who are Less Than 50 Years of Age

Presently, the American Diabetes Association does not recommend daily aspirin therapy in patients with type II diabetes who are less than 50 years of age and do not have other major risk factors for atherosclerotic cardiovascular disease. (16) Current evidence suggests the risks of aspirin induced bleeding may outweigh the potential cardiovascular benefits in this subset of lower risk patients. However, as with all aspects of diabetes management, patient preference, values, and individualized risk factors should be taken into account when making therapeutic decisions, particularly in cases when there is a paucity of literature. (52)

Table 10: Recommendations for Low Dose Daily Aspirin Therapy in Type II Diabetes(16)

Patient Population	Recommendations for Aspirin Therapy
Type II diabetics with a history of atherosclerotic cardiovascular disease (secondary prevention)	• Low dose daily aspirin therapy recommended
Type II diabetics who have not had a prior cardiovascular event but have additional risk factors for atherosclerotic cardiovascular disease (primary prevention) *Risk Factors for Atherosclerotic Cardiovascular Disease* • *Age 50 years and older AND* • *Family history of early atherosclerotic cardiovascular disease* • *Hypertension* • *Hyperlipidemia* • *Smoker* • *Albuminuria*	• Low dose aspirin therapy may be considered. Individualized shared decision making should be employed to evaluate if the benefits of therapy outweigh the potential risk of aspirin induced bleeds. • Recommendations do not differ based on patient gender.

Type II diabetics who have not had a prior cardiovascular event and do not have additional risk factors for atherosclerotic cardiovascular disease (primary prevention)	• Low dose daily aspirin therapy generally not recommended as risk of aspirin induced bleeding may outweigh cardiovascular benefits.

Immunizations in Type II Diabetes

Relative to the general population, diabetics are at an increased risk of complications from infectious diseases. (53) This risk may be even higher among poorly controlled type II diabetics and those with other chronic disease states. Immunizations are the best way to prevent infections and complications from vaccine preventable diseases. For this reason, the Centers for Disease Control and Prevention Advisory Committee on Immunization Practices has provided specific recommendations for patients with type II diabetics.

Influenza

Patients with even well-controlled type II diabetics are at risk for flu complications, which may become serious or deadly. Complications such as pneumonia and bronchitis can lead to hospitalizations and even death, particularly if patients are older. Influenza vaccinations have been associated with a 79% reduced risk of hospitalizations among patients with diabetes. (54) Moreover, influenza can prompt erratic blood glucose which may cause serious hyperglycemic or hypoglycemic events. Accordingly, the Centers for Disease Control and Prevention Advisory Committee on Immunization Practices (CDC/ACIP) recommend type II diabetics receive an annual influenza vaccine to reduce the risk of influenza infection and influenza related complications.

Patients with type II diabetes should receive one of the injectable influenza vaccines each year before the end of October. The injectable influenza vaccines contain inactivated strains of the influenza virus and the safety is well established among patients with and without type II diabetes. Injectable products are available as quadrivalent or trivalent formulations. Trivalent products contain three inactivate strains of influenza virus whereas quadrivalent products contain four inactive strains of influenza virus. The live attenuated influenza vaccine nasal spray is not recommended for patients with type II diabetes. Type II diabetics can receive any of the inactivated injectable vaccine formulations; other patient specific factors such as age may be used to guide formulation choice. Notably, the most updated guidelines state that patients with an egg allergy may receive any age-appropriate influenza vaccination. (55) Patients who have a history of a serious reaction to eggs such as angioedema, respiratory distress, lightheadedness, recurrent vomiting, and those who have required epinephrine

or another emergency medical intervention should be vaccinated in a medical setting equipped to manage emergency medical needs. To date, the CDC/ACIP has not expressed a preference for one inactivated injectable vaccine formulation.

Table 11: Inactivated Influenza Vaccinations Available in the United States(55)

Product Name	Age Indication	Egg-Grown Virus
Quadrivalent Standard Dose Products		
Afluria Quadrivalent	0.5 ml prefilled syringe: ≥5 years 5.0 ml multidose vial: ≥5 years Jet injector: 18 – 64 years	Yes
Fluarix Quadrivalent	≥6 months	Yes
Flulaval Quadrivalent	≥6 months	Yes
Fluzone Quadrivalent	0.25 ml prefilled syringe: 6 – 35 months 5.0 ml multidose vial: ≥6 months 0.5 ml prefilled syringe: ≥3 years 0.5 ml single dose vial: ≥3 years	Yes
Flucelvax Quadrivalent	≥4 years	No
Flublock Quadrivalent	≥18 years	No
Trivalent Standard Dose Products		
Afluria Quadrivalent	0.5 ml prefilled syringe: ≥5 years 5.0 ml multidose vial: ≥5 years Jet injector: 18 – 64 years	Yes
Fluad	≥65 years	Yes
Trivalent High Dose Products		
Fluzone High Dose	≥65 years	Yes

Pneumococcus

As with influenza, type II diabetics who become infected with a pneumococcal disease are at risk for serious complications. Pneumococcus can produce a variety of infections including meningitis, pneumonia, and infections of the blood stream. In the United States, there are two approved pneumococcal vaccines: Prevnar 13 and Pneumovax 23. Pneumovax 23 is a polysaccharide product that protects against 23 of the most commonly infecting pneumococcal serotypes. Prevnar 13 is a conjugate product that protects against 13 common pneumococcal serotypes. Indications for and sequencing of Pneumovax 23 and Prevnar 13 is determined by patient specific factors including age, comorbidities, and prior vaccination status. For adults aged 64 and younger with type II diabetes, the CDC/ACIP recommends a single dose of Pneumovax 23. (56)

Pneumococcal vaccines are also recommended for all adults age 65 and older. Patients aged 65 and older who have previously received a dose of Pneumovax 23 (such as

diabetics) should receive a second dose of Prevnar 13 when they are 65 years or older, at least one year after the dose of Pneumovax 23 and then a second dose of Pneumovax 23 after at least one year and after at least 5 year from the first Pneumovax 23 dose. (57)

This multidose, patient-specific schedule can lead to vaccine administration errors. If either vaccine is administered earlier than the specified dosing interval, do not repeat the dose.

Table 12: Pneumococcal Vaccine Scheduling for Type II Diabetes and Patients Ages 65 and Older (57)

Patient Scenario	Pneumococcal Vaccine Recommendations
Type II diabetics ages 19 - 64	• One dose of Pneumovax 23
Type II diabetics and non-diabetics ages 65 and older who previously received Pneumovax 23	• One dose of Prevnar 13 at least 1 year after first Pneumovax 23 dose • Second dose of Pneumovax 23 at least 1 year after Prevnar 13 and at least 5 years after the first Pneumovax 23 dose

Hepatitis B

Hepatitis B is a viral infection that causes inflammation of the liver which can lead to serious scarring of the liver and liver failure. Relative to the general population, adults with type II diabetes have a 60% higher prevalence of current or prior hepatitis B infection and twice the odds of acquiring the disease. (58) Risk of mortality related to hepatitis B is also higher among patients with type II diabetes. The CDC/ACIP now recommends patients age 19 – 59 years with type II diabetes be vaccinated against hepatitis B. Decisions to vaccinate type II diabetics ages 60 and older may be made using shared decision making between the patient and clinician.

Table 13: Single Antigen Hepatitis B Vaccinations for Adults Available in the United States (58)

Product Name	Dosing Schedule
Recombivax HB	0, 1, and 6 months
Engerix-B	0, 1, and 6 months
Heplisav-B	0 and 1 months

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LESSON EVALUATION

Please fill out this section as a means of evaluating this lesson. The information will aid us in improving future efforts. Either circle the appropriate evaluation answer, or rate the item from 1 to 7 (1 is the lowest rating; 7 is the highest).

1a. PHARMACISTS AND NURSES ONLY: Does this lesson meet the learning objectives? (Circle choice).

Recognize the importance of selecting patient-specific glycemic and blood pressure goals.	YES	NO
List commonly used topical treatments. Counsel patients regarding administration, side effects, and precautions.	YES	NO
Discuss the epidemiology and contributing factors for the development of psoriasis.	YES	NO
Compare and contrast systemic treatments used for psoriasis, including effectiveness, side effects, and precautions.	YES	NO

2a. TECHNICIANS ONLY: Does this lesson meet the learning objectives? (Circle choice).

Recall common comorbid conditions associated with type II diabetes	YES	NO
Identify the risks of sub-optimal management of type II diabetes and comorbid conditions	YES	NO
Recognize common first line agents for managing comorbid conditions in type II diabetics	YES	NO

2. Was the program independent & non-commercial? YES NO

	Low Relevance						Very Relevant
3. Relevance of topic	1	2	3	4	5	6	7

4. What did you like MOST about this lesson? _____

_____

5. What did you like LEAST about this lesson? _____

_____

6. How would you improve this lesson? _____

_____

Activity Test

1. Which of the following is a potential complication of sub-optimally managed type II diabetes?

    A. Peripheral artery disease
    B. Neuropathy
    C. Retinopathy
    D. B and C only
    E. A, B, and C are potential complications of type II diabetes

2. Which of the following conditions is a common comorbidity associated with type II diabetes?

    A. Benign prostatic hyperplasia
    B. Hyperlipidemia
    C. Rheumatoid arthritis
    D. All of the above are common comorbidities associated with type II diabetes

3. Which of the following is considered a macrovascular complication of type II diabetes?

    A. Nephropathy
    B. Hyperlipidemia
    C. Hypertension
    D. Peripheral artery disease

4. Which of the following is considered a microvascular complication of type II diabetes?

    A. Nephropathy
    B. Hyperlipidemia
    C. Hypertension
    D. Peripheral artery disease

5. Based on available evidence, what would be the most appropriate goal A1C for the following patient: 50-year-old male newly diagnosed with type II diabetes and hypertension.

    A. <5.0%
    B. ≤6.0%
    C. ≤7.0%
    D. <8.0%

6. Based on available evidence, what would be the most appropriate goal A1C for the following patient: 84-year-old female with diagnosed with diabetes 20 years ago who also has dementia and frequent falls.

    A. <5.0%
    B. ≤6.0%
    C. ≤7.0%
    D. <8.0%

7. Based on available evidence, what would be the most appropriate blood pressure goal for the following patient: 78-year-old male with type II diabetes and hypertension who enjoys running 5Ks. At today's visit, his blood pressure was 138/88. His current medications include metformin and lisinopril.

    A. <150/90
    B. <140/80
    C. <130/80
    D. <120/80

8. Based on available evidence, what would be the most appropriate blood pressure goal for the following patient: 84-year-old female with diagnosed with diabetes 20 years ago who also has dementia and frequent falls.

    A. <150/90
    B. <140/80
    C. <130/80
    D. <120/80

9. Based on available evidence, which of the following medication classes would be most appropriate for the following patient: 61-year-old male with type II diabetes and hypertension. Blood pressure today is 158/90. Current medications include metformin and sertraline.

    A. Angiotensin receptor blocker
    B. Angiotensin converting agonist
    C. Beta blocker
    D. Loop diuretic

10. Based on available evidence, which of the following medication regimens would be most appropriate for the following patient: 48-year-old male with type II diabetes and hypertension. Blood pressure today is 180/100. Current medications include metformin and glipizide.

A. Lisinopril + valsartan
B. Valsartan + chlorthalidone
C. Lisinopril + hydrochlorothiazide
D. Valsartan + metoprolol

11. Based on available evidence, which of the following lipid regimens would be most appropriate for the following patient: 75-year-old male with type II diabetes, hypertension, hyperlipidemia, and a prior myocardial infarction with a 10-year risk of 15%?

A. Lovastatin
B. Fenofibrate
C. Rosuvastatin
D. Rosuvastatin + fenofibrate

12. Which of the following is considered a high intensity statin regimen?

A. Atorvastatin 20 mg
B. Rosuvastatin 20 mg
C. Simvastatin 40 mg
D. B and C
E. A, B, and C

13. Which of the following is true regarding management of hyperlipidemia?

A. Both a statin and a fibrate should be initiated in all patients with type II diabetes and a 10-year risk of >10%
B. All patients with type II diabetes should always be initiated on statin therapy
C. Gemfibrozil is an appropriate alternative for patients who cannot tolerate statin therapy
D. Statins are considered first line therapy for hyperlipidemia

14. True or False: Evidence suggests all type II diabetics should take low dose daily aspirin therapy.

A. True
B. False

15. Which of the following is true regarding the use of aspirin in type II diabetics?

A. All type II diabetics should use aspirin for secondary prevention
B. All type II diabetics should use aspirin for primary prevention
C. Low dose daily aspirin therapy is not recommended for diabetics over the age of 75
D. A and B are true
E. A, B, and C are true

16. Which of the following is not considered a risk factor for atherosclerotic cardiovascular disease?

    A. Smoking
    B. Hypertension
    C. Male gender
    D. Age greater than or equal to 50 years

17. Which of the following is true regarding influenza vaccines in type II diabetics?

    A. Type II diabetics can receive either the injectable or nasal form of the influenza vaccine
    B. Type II diabetics with a history of egg allergies should only receive the nasal vaccine
    C. Type II diabetics are at an increased risk of influenza related complications
    D. A and B are true
    E. A, B, and C are true

18. Mrs. Jones is a 68-year-old patient with type II diabetes and chronic kidney disease who presents to clinic for an influenza vaccine. She has not received a flu vaccine in the past because she was nervous about her egg allergy. She is prescribed an epinephrine auto injector pen for use if she inadvertently eats eggs. She last used the pen about 3 years ago when her lips and tongue began swelling after accidently injecting egg. Which of the following is the most evidence-based course of action?

    A. Vaccinate Mrs. Jones with the nasal vaccine which does not contain eggs
    B. Advise Mrs. Jones that the risks of vaccinating her against influenza outweigh the benefits and do not administer the vaccine
    C. Vaccinate Mrs. Jones at the clinic which has an emergency kit containing epinephrine and numerous providers trained in emergency medical care
    D. Provide Mrs. Jones with a prescription for oseltamivir to use if she is exposed to influenza

19. Which of the following is the most appropriate pneumococcal vaccination schedule for a 66-year-old woman with type II diabetes who received Pneumovax 23 when she was 58 years old?

    A. Prevnar 13 today, then Pneumovax 23 at least one year later, then Prevnar 13 at least one year later
    B. Pneumovax 23 today, then Prevnar 13 at least one year later, then Pneumovax 23 at least one year later
    C. Prevnar 13 today, then Pneumovax 23 at least one year later, then Prevnar 13 at least one year later followed by annual Pneumovax 23 vaccinations

D. Pneumovax 23 today, then Prevnar 13 at least one year later, then Pneumovax 23 at least one year later followed by annual Pneumovax 23 vaccinations

20. True or False: All patients with type II diabetes should be vaccinated against hepatitis B?

A. True
B. False