Review of Current Diabetes Guidelines in Older Adults

Objectives

- Identify three components of care addressed in the 2013 AGS update.
- Identify the AGS goals for Blood Pressure and Glycemic Control according to AGS Guidelines
- Identify one screening tool that can be used to evaluate a potential Geriatric Syndrome.

AGS Guidelines Purpose

- Purpose: To improve the care of the older person with DM by providing evidence based recommendations individualized to adults with DM who are age 65 and older
- Not meant to be an exhaustive review of DM care in older adults, but rather a focus on the important aspects of care for older adults that differ significantly or deserve special emphasis in comparison to DM care in the younger person.

Applying the Evidence

- Clinical and functional heterogeneity of older adults
- Life expectancy may be shorter than the time needed to benefit from an intervention.
  - 8 years of glycemic control to reduce microvascular complications
  - 2-3 years to see benefits from better control of BP and Lipids
- For older adults who are frail, have high burden of comorbid conditions, short life expectancy or significant difficulty adhering to treatment regimens:
  - May not use aggressive BP, lipid or glucose goals
  - Prioritize therapeutic goals to enhance quality of life

Classification

- **(Prediabetes** – risk factor for developing Type 2 DM (T2DM) in the future)
- Type 1 – Characterized by β-cell destruction→insulin deficiency
- **Type 2** – Characterized by progressive defects in insulin secretion with insulin resistance
- Gestational – diabetes diagnosed during pregnancy
- **Diabetes due to other causes**: genetic deficiencies, diseases of exocrine pancreas, drug/chemical-induced, monogenic

Diabetes Diagnosis

A1C: ≥6.5% or

FBG: ≥126 mg/dL or

OGTT: ≥200 mg/dL or

Random: ≥200 mg/dL*

Guidelines for Improving the Care of Older Adults with Diabetes Mellitus: 2013 Update

AGS

Guideline Focus

AGS

- DM Components of Care
  - Aspirin
  - Tobacco cessation
  - Hyperglycemia management
  - Hypertension management*
  - Dyslipidemia management*
  - Eye care
  - Foot care
  - Diabetes self-management education and support (DSME/S)

Guideline Focus

AGS

- Geriatric syndromes
  1. Polypharmacy
  2. Cognitive impairment
  3. Depression
  4. Urinary incontinence
  5. Injurious falls
  6. Persistent pain

Guideline Focus

AGS

- 2013 Update
  - Aspirin no longer recommended for primary CVD prevention*
  - Dyslipidemia treatment with statins but not to target levels
  - Glycemic control continues to be tailored to
    - Burden of comorbidity
    - Functional status
    - Life expectancy
  - Patient-centered recommendations regarding lifestyle modifications for healthy older adults

Evidence Grading

AGS

Quality Level	Description
Level I	Evidence from ≥1 properly RCT
Level II	Evidence from ≥1 well-designed clinical trial lacking randomization, cohort or case-controlled analytical studies, multiple time-series studies, or dramatic results in uncontrolled experiments
Level III	Evidence from respected authorities based on clinical experience, descriptive studies, or reports from expert opinion

RCT = randomized controlled trial

Evidence Grading

AGS

Strength Level	Description
A	Good evidence to support use of recommendation; "Should do this *all* the time"
B	Moderate evidence to support use of recommendation: "Should do this *most* of the time"
C	Poor evidence to support or reject use of recommendation; "May or may not follow recommendation"
D	Moderate evidence against use of recommendation; "Should *not* do this"
E	Good evidence against use of recommendation; "Should *not* do this"

Aspirin

- *If an older adult has DM and known cardiovascular disease, daily aspirin therapy 81 to 325 mg/day is recommended, unless contraindicated or the patient is taking other anticoagulant therapy. (IA)*
- Strong evidence for secondary prevention of MI and Stroke
- No evidence that a higher dose is more effective then 75mg daily
- No longer recommended for primary prevention.
- Risk of adverse side effects and bleeding may outweigh benefits
- Adults >80 y/o - Aspirin should be used with caution

Smoking

- *Older adults with DM who smoke should be assessed for readiness to quit and should be offered counseling and pharmacologic interventions to assist with smoking cessation. (IIA)*
- Within 2–3 years of smoking cessation, the former smoker's risk of coronary heart disease appears to decline to levels comparable to those of persons who never smoked.

Hypertension

AGS

- Goal <140/90 mmHg if tolerated (IA)
- Potential harm if goal SBP <120 mmHg (IB)
- Treat within 3 months if BP 140 – 160/90 – 100 mmHg (IIIB)
  - Within 1 month if BP >160/100 mmHg (IIIB)

SBP = systolic blood pressure; BP = blood pressure

Hypertension Treatment AGS

- Promote DASH diet adjunctively to pharmacologic treatment
- Diuretics = ACE inhibitors/ ARBs = β-blockers = Calcium channel blockers in ↓ CV morbidity/mortality
  - ARBs (like ACEIs) may have CV and renal benefits
- ACE inhibitor/ARB or diuretic use
  - Monitor renal function and potassium (IIIA):
    - >1 – 2 weeks after initiation
    - When ↑ dosage
    - At least annually

DASH = dietary approaches to stop hypertension; ACE = angiotensin-converting enzyme; CV = cardiovascular; ARB = angiotensin II receptor blocker

Hypertension

American Diabetes Association	AGS	AACE
Goal BP • <140/80 mmHg (B) BP >120/80 mmHg lifestyle therapy (B) BP>140/80 mmHg lifestyle AND pharmacologic therapy (B)	Goal BP* • <140/90 mmHg if tolerated (IA) Treat within 3 months if BP 140 – 160/90 – 100 mmHg (IIIB) • Within 1 month if BP >160/100 mmHg (IIIB)	Goal BP • <130/80 mmHg

BP = blood pressure; SBP = systolic blood pressure

Hypertension Pharmacologic Treatment

American Diabetes Association	AGS	AACE
ACE inhibitor or ARB (C) Also β-blockers, Diuretics, Calcium channel blockers Usually ≥2 antihypertensives required to achieve BP goal (B)	ACE inhibitors = Diuretics = β-blockers = Calcium channel blockers in ↓ CV morbidity/mortality ARBs (like ACEIs) may have CV and renal benefits	ACE inhibitors or ARB Thiazide = β-blockers = Calcium channel blockers

ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker; BP = blood pressure; CV = cardiovascular;

Glycemic Control

- *Target goal for HbA1c in older adults generally should be 7.5% - 8%.*
- *HbA1c 7% - 7.5% may be appropriate if it can be safely achieved in healthy older adults with few comorbidities and good functional status.*
- *HbA1c 8–9% are appropriate for older adults with multiple comorbidities, poor health, and limited life expectancy*
- *Potential harm in lowering HbA1c < 6.5% in older adults with type 2 DM. (11A) – hypoglycemia, increased mortality*

Treatment goals

American Diabetes Association.	AGS	AACE
A1C • <7% (B)† • <8% (B) • <8.5% (E) FBG: 70 – 130 mg/dL PPBG <180 mg/dL	HbA1c[¤] • 7 – 7.5% (IA) • 7.5 – 8% (IA) • 8 – 9% (IIA)	A1c‡ • ≤6.5% • >6.5% • <7% FBG <110 mg/dL for most with T2DM PPBG <140 mg/dL* (Grade B, BEL 2)

A1C, HbA1c, A1c = hemoglobin A1C; FBG = fasting blood glucose; PPBG = post-prandial blood glucose

BG Monitoring

AGS

- Unable to meet target HbA1c (IIIB)
  - Monitor at least every 6 months
- Stable HbA1c over several years (IIIB)
  - Monitor annually
- Evaluate whether self-monitoring BG schedule should be implemented (IIIB)
- Evaluate hypoglycemia management plan (IIIB)
  - Refer for education
  - Determine precipitants of hypoglycemia and attempt to reduce recurrence
  - Increase contact with healthcare team during therapy adjustment

HbA1c = hemoglobin A1C; BG = blood glucose

Monitoring

American Diabetes Association	AGS	AACE
Meeting treatment goals • A1C ≥2 times yearly (E) Change in therapy or not meeting goals • A1C quarterly (E)	Unable to meet target HbA1c (IIIB) • Monitor at least every 6 months Stable HbA1c over several years (IIIB) • Monitor annually	Monitor effectiveness of therapy e.g. at least every 3 months until stable* A1c ≥2 times yearly in all DM patients (Grade D; BEL 4)[¤] Not meeting goals • A1c quarterly (Grade D; BEL 4)[¤]

HbA1c and A1C = hemoglobin A1C

Pharmacologic Treatment AGS

- Lifestyle therapy with metformin unless contraindicated (IA)
  - Use eGFR (not SCr) <30 mL/min/1.73m^2 as limit to use (IIB)
  - If eGFR = 30 – 60, ↑ monitoring renal function and use <doses (IIB)
- Little/no efficacy or safety data exists for "newer agents" in the elderly (e.g. exenatide, saxagliptin, sitagliptin)
- Avoid: glyburide, chlorpropamide due to ↑ risk hypoglycemia
  - Sulfonylureas associated with 20-30% increased hazard of cardiovascular outcomes compared with metformin
- Insulin may be used safely in healthy, high functioning patients (Expert opinion)

eGFR = estimated glomerular filtration rate

Pharmacologic Treatment

American Diabetes Association	AGS	AACE
1st: Metformin (A) Consider insulin ± other agents in newly diagnosed T2DM with markedly ↑BG/HbA1c (E) 2nd: Add GLP-1 agonist, insulin (A)	1st Lifestyle therapy with metformin unless contraindicated* (IA) Little/no data exists for "newer agents" Avoid‡ glyburide, chlorpropamide Safe use of insulin in high functioning patients	1st: Metformin Alt: GLP-1 agonists, DPP-4 inhibitors, alpha-glucosidase inhibitors TZDs, SUs, glinides

T2DM = type 2 diabetes; GLP-1 = glucagon-like peptide; DPP-4 = dipeptidyl peptidase-4; TZDs = thaizolidinediones; SUs = sulfonylureas

Prediabetes

American Diabetes Association.	AGS	AACE
IFG: • 100 – 125 mg/dL IGT: • 140 – 199 mg/dL A1C: • 5.7 – 6.4%	Not addressed	IFG: • 100 – 125 mg/dL IGT: • 140 – 199 mg/dL Metabolic syndrome

IFG = impaired fasting glucose; IGT = impaired glucose tolerance; A1C = hemoglobin a1c

Dyslipidemia

AGS

- <75 years old treat with
  - Lifestyle therapy AND statin – no evidence for LDL goal (IB)
  - No support for combination statin with other non-statin cholesterol-lowering medication (e.g. niacin, fenofibrate)
  - No clinical trials in DM patients >80 y/o
- Medical Nutrition Therapy, enhanced physical activity and weight loss for everyone!
- Supports ADA (2013) goals:
  - HDL > 40 mg/dL (♂) and >50 (♀)
  - TG <150 mg/dL

LDL = low density lipoprotein; HDL = high density lipoprotein; TG = triglyceride

Dyslipidemia

AGS

- Monitoring
  - Patients started on statin should have alanine aminotransferase checked prior to initiation and as clinically indicated (IIIB)
  - Most DM patients require lipid panel ≤ annually
  - Low-risk lipid values (LDL<100 mg/dL; HDL >50; TG<150) at baseline should have lipid panel checked every 2 years

LDL = low density lipoprotein; HDL = high density lipoprotein; TG = triglyceride

Dyslipidemia Goals

American Diabetes Association	AGS	AACE
Statins to target LDL LDL <100 mg/dL without overt CVD [B] LDL <70 mg/dL with overt CVD [B] HDL >40 mg/dL (♂) and >50 mg/dL (♀) TG <150 mg/dL	<75 years old: Treat with statins AND lifestyle therapy but not to target LDL HDL >40 mg/dL (♂) and >50 mg/dL (♀) TG <150 mg/dL	Statins to target LDL LDL <100 mg/dL without overt CVD LDL <70 mg/dL with overt CVD TG <150 mg/dL Non-HDL-C: <130 mg/dL without overt CVD <100 with overt CVD

LDL = low density lipoprotein; HDL = high density lipoprotein; TG = triglyceride

Dyslipidemia Goals

American Diabetes Association.	AGS	AACE
Monitor annually in most [Q2yrs if low risk [LDL<100 mg/dL, HDL>50, TG<150]	Monitor annually in most Q2yrs if low risk [LDL<100 mg/dL, HDL>50, TG<150] New start statin monitor ALT before and PRN after (no evidence to monitor LFTs)	TC/HDL-C: <3.5 without overt CVD; <3 with overt CVD Apo B: <90 mg/dL without overt CVD; <80 mg/dL with overt CVD LDL-P: <1200 nmol/L without overt CVD; <1000 nmol/L with overt CVD

LDL = low density lipoprotein; HDL = high density lipoprotein; TG = triglyceride; Apo B = apolipoprotein B; CVD = cardiovascular disease

New Cholesterol Guidelines

Eye Care

AGS

- Newly diagnosed
  - Initial dilated eye-exam with funduscopy (IB)
- High-risk*
  - Eye disease present, retinopathy, glaucoma, cataracts, on initial exam or ≤2 yrs; A1C ≥8%, T1DM, BP ≥140/90 mmHg
  - Annual dilated eye-exam with funduscopy (IIB)
- Low-risk
  - Biennial dilated eye-exam with funduscopy (IIB)
- Incidence of Retinopathy: glycemic control over 6 years and BP
- Progression of Retinopathy: older age, male sex, hyperglycemia
- More common in Diabetics: glaucoma, cataract and macular degeneration
- Focus on BP, lipid and glycemic control

Retinopathy Monitoring

American Diabetes Association	AGS	AACE 2011
Optimize BG and BP control to reduce/slow progression (A) Initial dilated and comprehensive eye exam¤ <5 years of diagnosis (T1DM) and shortly after diagnosis (T2DM) (B) Annual to biennial thereafter (B)	Newly diagnosed • Initial dilated eye-exam with funduscopy (IB) High-risk* • Annual dilated eye-exam with funduscopy (IIB) Low-risk • Biennial dilated eye-exam with funduscopy (IIB)	Initial dilated and comprehensive eye exam¤ within 5 years of diagnosis (T1DM) (Grade D; BEL 2) and at time of diagnosis (T2DM) (Grade D; BEL 4) Annual exam thereafter (Grade D; BEL 4)

T1DM = type 1 diabetes mellitus; T2DM = type 2 diabetes mellitus

Neuropathy

American Diabetes Association	AGS	AACE 2011
Screen for initial distal symmetric polyneuropathy (DPN) 5 years after diagnosis (T1DM) (B) and at diagnosis (T2DM) (B) After initial screen, annually thereafter with simple clinical tests	Indirectly addressed in "Geriatric Syndromes"	Differentiate painful neuropathy from other pain conditions (Grade D; BEL 4) ↓ Oxidative stress, improve glycemic control, dyslipidemia, hypertension (Grade A; BEL 1) TCAs, anticonvulsants, SSRI/SNRI useful (Grade A; BEL 1)

T1DM = type 1 diabetes mellitus; T2DM = type 2 diabetes mellitus; TCAs = tricyclic antidepressants; SSRI = selective serotonin reuptake inhibitor; SNRI = serotonin norepinephrine reuptake inhibitor

Foot Care

AGS

- At least an annual comprehensive exam to assess:
  - Skin integrity
  - Loss of sensation or decreased perfusion
  - If either are found- more frequent examination is recommended *(IIIA)*
  - Components of the comprehensive foot examination are described by the ADA
- Foot examination should be done at all non-urgent outpatient visits

Foot Care

American Diabetes Association.	AGS	AACE 2011
Educate on foot self-care (B) with daily visual inspection Annual comprehensive foot exam for risk factors for (B) • Ulcers • Amputations Assess (B) • Foot pulses • Loss of protective sensation (LOPS)*	Education on risk factors for foot ulcers and amputation with evaluation of physical ability to provide proper foot care (IB) At least annual exam to assess: • Skin integrity • Loss of sensation or ↓ perfusion	Large-fiber neuropathies: • Orthotics to treat/prevent foot deformities • Tendon lengthening for pes equinis from Achilles tendon shortening (Grade A; BEL 1) Small-fiber neuropathies: • Foot protection (Grade A; BEL 1)

Nephropathy

AGS

- Albuminuria testing
  - At diagnosis of T2DM
  - Annual screening after first screen and in the absence of prior micro-/macroalbuminuria (IIIA)
  - If taking an ACE inhibitor or ARB, there is no need for nephropathy screening

T2DM = type 2 diabetes mellitus; ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker; SCr = serum creatinine

Nephropathy

American Diabetes Association.	AGS	AACE 2011
Optimize BG and BP control to reduce/slow progression (A) Annual screen of albuminuria in T1DM patients with DM ≥5 years and in ALL T2DM starting from diagnosis (B)	Albuminuria testing at diagnosis of T2DM (IIIA) Annual screening after first screen and absence of prior **micro-** or **macro**albuminuria (IIIA)[α]	Optimize BG (A1C <7%) and BP control (<130/80 mmHg) to reduce/slow progression Annual screen of albuminuria in T1DM at puberty or <5 years of diagnosis and in ALL T2DM starting from diagnosis

T1DM = type 1 diabetes mellitus; T2DM = type 2 diabetes mellitus

Nephropathy

American Diabetes Association.	AGS	AACE 2011
ACE inhibitor or ARB= primary prevention of diabetic kidney disease (B)* (ARBs do not prevent onset in normotensive patients but do slow progression) Monitor SCr/eGFR and potassium when ACE inhibitor, ARB, or diuretic used (E) Dietary protein restriction can be considered	If taking ACE inhibitor or ARB, no need for nephropathy screening Monitor SCr and potassium • after 1 – 2 weeks of ACEI or ARB use • with dosage change • at least annually (IIIA)	

ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker; SCr = serum creatinine; eGFR = estimated glomerular filtration rate
DM = diabetes mellitus

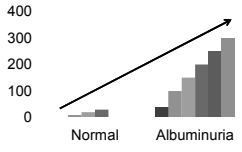
ACE Inhibitor Induced Renal Failure

- SCr increases by >0.5mg/dL if SCr was initially <2.0 mg/dL
- SCr increases by >1.0mg/dL if SCr was initially >2.0 mg/dL
- Risk factors:
  - Hypotension at levels that cannot sustain renal perfusion
  - Dehydration (volume depletion from diuretic therapy)
  - Bilateral renal artery stenosis, stenosis of a dominant or single kidney, arteriolar narrowing (from long term HTN or Chronic cyclosporine use)
  - Patients on vasoconstrictive agents (NSAIDS or cyclosporine)
- In the absence of risk factors, a decrease in GFR in patients with CKD is usually <20%, transient, and is followed by stabilization or decrease in SCr due to ACE I renoprotection.
- Prevention:
  - ID early (monitor SCr and eletrolytes before and 1 week after ACE I initiation).
  - Establish tolerable upper limit for SCr in advance.
- Management:
  - Stop ACE I - renal function generally improves within 2-3 days if caught early. ARBs are not an appropriate substitute under these conditions.
  - Volume repletion and discontinuation of diuretic if caused by dehydration.
  - Can rechallenge ACE I therapy if underlying cause has been rectified.

Albuminuria

American Diabetes Association.

- Nomenclature changes
  - "Microalbuminuria" or "Macroalbuminuria" no longer used
  - Emphasizes albuminuria as a continuous risk factor
  - Normal albumin
    - <30 mg/24 hr
  - "Persistent Albuminuria"
    - 30 to 299 mg/24 hr
    - >300 mg/24 hr



Other Components of Comprehensive DM Care:
X
Y
Z

Diabetes Self-Management Education and Support

- Provides ongoing skill-development and knowledge for patients to manage their prediabetes and diabetes
- All patients and caregivers should receive DSME/S with reinforcement and reassessment as needed (IA)
- Self-monitoring blood glucose techniques should be reviewed (IIIB)
- Patients with normal cognition and functional status
  - Exercise ≥150 min of moderate-intensity aerobics weekly (IA)
  - Aerobics and resistance exercises to the best of their ability (IA)
  - Physical Activity at least 3 days per week

Diabetes Self-Management Education and Support

- Medical nutrition support (MNT) counseling (e.g. high-cholesterol foods, carbohydrates) and benefits of weight reduction (IA)
  - Personalized meal planning
    - personal preferences
    - cultural and religious practices
    - other chronic and acute conditions
    - living situation
    - activities of daily living (ADL) or other impairments
- Counseled on new medication, purpose of the drug, how to take, common side effects and important adverse reactions, and compliance with reinforcement (IA)
  - Health Literacy: font size, reading level, language
- Education on risk factors for foot ulcers and amputation with evaluation of physical ability to provide proper foot care (IB)
  - Cognitive impairment, visual impairment, osteoarthritis, and other physical limitations in functioning that prevent movement

Diabetes Self-Management Education and Support

American Diabetes Association.	AGS	AACE 2011
Should receive DSME/S according to National Standards or DSME/S at diagnosis and as needed after (B) Self-management and quality of life are cornerstone to DSME/S and should be assessed (C)	All patients and family should receive DSME/S with reinforcement/ reassessment (IA) SMBG techniques reviewed (IIIB) Should receive medication use education (IA)*	Receive comprehensive DSME/S at diagnosis and as needed thereafter (Grade D; BEL 4)

DSME/S = diabetes self-management education and support; SMBG = self-monitoring blood glucose

Physical Activity

American Diabetes Association	AGS	AACE
Exercise ≥150 min of moderate-intensity (50-70% max HR) aerobics weekly (A) • ≥3 times weekly* ≥Biweekly resistance training (A)	In those with normal cognition and functional status should • Exercise ≥150 min of moderate-intensity aerobics weekly (IA) Aerobics and resistance exercises to the best of their ability (IA) Exercise 3 days per week	Physical activity 5 days/week for >30 min (>60% HR)

HR = heart rate

Medical Nutrition Therapy

American Diabetes Association	AGS	AACE
For CVD prevention: monotherapy if mild ↑BP (B) DASH-diet with ↓ sodium intake (<1.5gm/day) ↑ Fruits, vegetables (8 – 10 servings/day) ↑ Low-fat dairy (2 – 3 servings/day) Limit alcohol servings: ≤2/day for (♂) ≤1/day (♀)	Medical nutrition support (MNT) counseling (e.g. high-cholesterol foods, carbohydrates) and benefits of weight reduction (IA)	Dietary modifications to lower LDL-C* Limit saturated fat, cholesterol ↑ Viscous fiber, plant stanols/sterols Dietary modifications to lower TG* ↓ Calories ↑ Omega-3 ethyl esters Restrict alcohol

DASH = dietary approaches to stop hypertension; LDL-C = low density lipoprotein-C; TG - triglycerides

Geriatric Syndromes

AGS

Geriatric Syndromes* AGS

1. Depression
2. Polypharmacy
3. Cognitive impairment
4. Urinary incontinence
5. Injurious falls
6. Persistent pain

Depression AGS

- Often underdiagnosed and undertreated
- Screen within 1st 3 months of diagnosis of DM and with any ↓ in clinical status (IIB)
- Treat/refer within 2 weeks of onset/change in depression (IIIB)
  - For patients who show evidence of substance abuse or dependence, wait until the patient is drug- or alcohol-free
- Use standardized screeners such as
  - Patient Health Questionnaire (PHQ 9)
  - Geriatric Depression Scale

Depression

- Effectiveness of therapy for depression should be assessed within 6 weeks of initiation (IIIB)
  - important to reevaluate the patient if medication for depression is not effective
  - Elderly patients with dementia may appear depressed.

American Diabetes Association.	AGS	AACE 2011
Depression Routinely screen (B)	**Depression** Discussed under "Geriatric Syndromes"	**Depression** Routinely screen

Patient Health Questionnaire 9 (PHQ-9)				
Over the last 2 weeks, how often have you been bothered by any of the following problems?	**Not at all**	**Several days**	**>Half the days**	**Nearly daily**
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself – or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself in some way	0	1	2	3
Total score: 1 – 4 Minimal depression; 5 – 9 Mild depression; 10 – 14 Moderate depression; 15 – 19 Moderately severe depression; 20 – 27 Severe depression				

AGS

Psychosocial Management

- Psychosocial problems other than depression can also be associated with self-management and health-related outcomes
  - Attitudes about DM
  - Quality of life
  - Diabetes-related distress
  - Lack of financial resources

Polypharmacy

AGS

- Patients should keep an updated list of current medications (IIA)
- The medication list of an older adult with DM who presents with depression, falls, cognitive impairment, or urinary incontinence should be reviewed. (IIA)
- Geriatric patients are more vulnerable to drug side effects (SEs), drug-drug interactions (DDIs), drug-disease interactions
- Explain risk of drug SEs, DDIs, drug-disease interactions
- Discuss expected benefits/risks/side effects of each
- AGS Beers Criteria

Cognitive Impairment AGS

- Interferes with lifestyle therapy, taking medications, insulin use
- Assess with standardized screens within the initial evaluation period and change in clinical status (e.g. ↑ Difficulty with self-care) (IIA)
  - Mini-Mental State Exam (MMSE)- not public domain
  - Montreal Cognitive Assessment tool
- If cognitive impairment is present and delirium excluded as cause, identify conditions that can cause/exacerbate condition within 1st 3 months after diagnosis and/or change in clinical status (IIIA)
  - Depression
  - B^{12} deficiency
  - Hypothyroidism
  - Structural neuroimaging to identify lesions for those recently diagnosed
  - Medications

Cognitive Impairment AGS

- DM (especially Type 2) has been associated with accelerated decline in cognitive function
- Dementia more likely in persons with DM
- Hypoglycemia is associated with dementia
- Hyperglycemia induced cognitive dysfunction:
  - Improvement in memory and learning, particularly verbal learning , seen after 2 weeks of treatment
  - ACCORD study of adults 55–80 years old,: no benefits with intensive glycemic control or SBP < 120 mmHg.

Urinary Incontinence AGS

- Older adults with DM should be evaluated for symptoms of urinary incontinence during annual screening. (IIIA)
- Older women at increased risk
- Risk increased with length of DM diagnosis
- Estimated that 17% of incontinence and up to 50% of severe incontinence attributable to DM
- Focus on conditions associated with older age/DM:
  - Polyuria (glycosuria)
  - Overflow secondary to neurogenic bladder and autonomic insufficiency
  - Fecal impaction due to autonomic insufficiency
  - Atrophic vaginitis
  - Prolapse
  - UTI (can cause/exacerbate urinary incontinence)
  - *Candida* vaginitis
  - Restricted mobility
- Treatment:
  - Weight loss
  - Caution with medications- anticholinergic

Injurious Falls

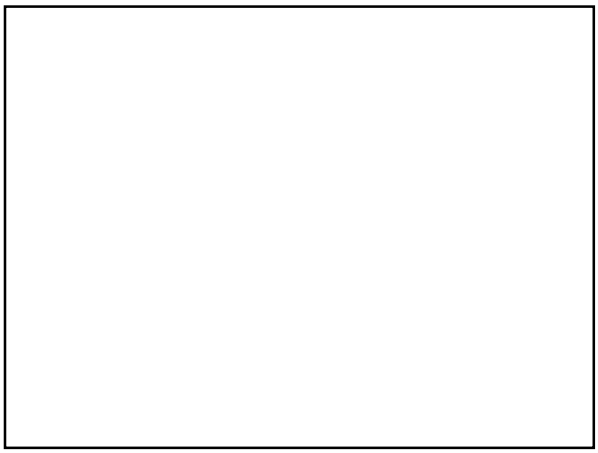
AGS

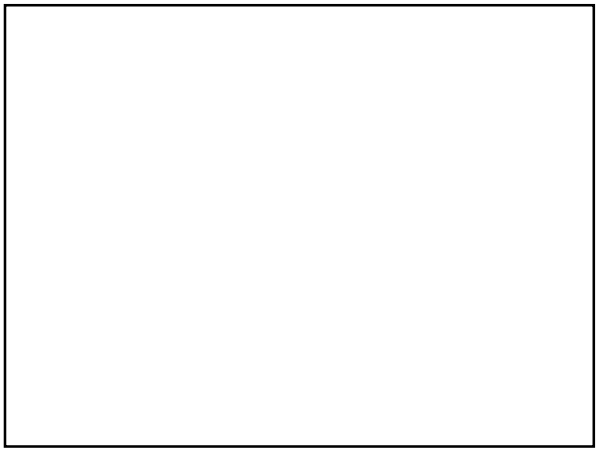
- *Older adults with DM should be asked about falls every 12 months or more frequently if needed. (IIIB)*
- *If there is evidence of falls, the clinician should document a basic falls evaluation, including an assessment of injuries and examination of potentially reversible causes of the falls (e.g., medications, environmental factors). (IIIB)*
- Associated with severe morbidity/mortality/rapid functional decline
- Risk factors: frailty and functional disability, gait disturbances, visual impairment, peripheral neuropathy, hypoglycemia, orthostatic hypotension, polypharmacy
- Prevention techniques:
  - Exercise programs
  - home visits to assess safety and modify environmental hazards
  - Withdrawal of psychotropic medications
  - Correction of underlying medical contributors: orthostatic blood pressure measurement, vision assessment, gait and balance evaluation, cognitive evaluation.
  - AGS Guideline for the Prevention of Falls in Older Persons (2010) also provides detailed recommendations on effective interventions to reduce falls.

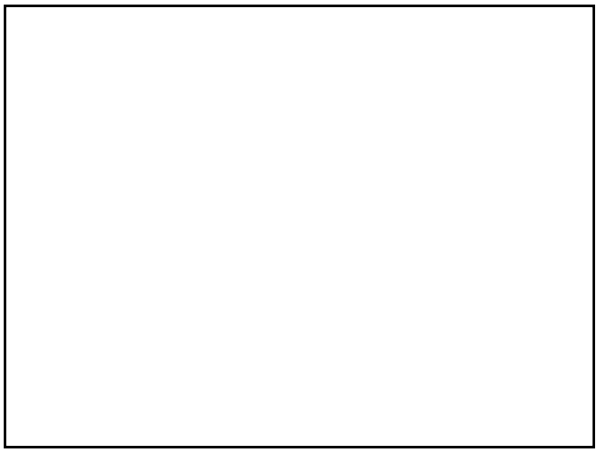
Persistent Pain

AGS

- *Older adults with DM should be assessed during the initial evaluation period for evidence of persistent pain. (IIIA)*
- At risk for neuropathic pain
- Pain may occur in as many as 50% of patients with DM
- Older adults with DM and pain are often under-treated (35%) and are often reluctant to report pain unprompted.
- *Evidence-based guideline: Treatment of painful diabetic neuropathy* (2011) provides further guidance on the treatment of painful diabetic neuropathy.







Standards of Medical Care in Diabetes – 2014

American Diabetes Association.

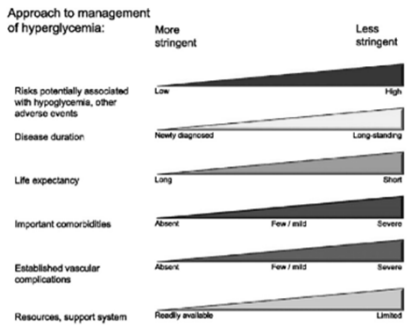
Guideline Focus

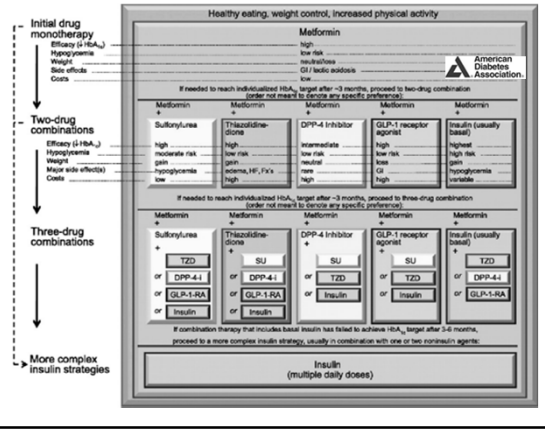
- Components of diabetes care
- General treatment goals
- Evaluation of quality of care
- Recommendations for screening, diagnosis, therapeutic actions

Type 1 diabetes

- Inform patient of opportunity to have relatives screened in the setting of clinical research (E)
- Most should be treated with MDI injections or CSII (A)
  - 3 – 4 prandial and basal insulin daily
- Educate on matching prandial insulin dose with carbohydrate intake, premeal BG, and anticipated activity (E)
- Screen for other autoimmune diseases as needed (B)

Glycemic Goals





BG Monitoring

- If meeting treatment goals
  - Monitor A1C ≤ biannually (E)
- If change in therapy or not meeting treatment goals
  - Monitor A1C quarterly (E)
- POC testing allows for timely treatment changes (E)

Hypoglycemia

- Leading limitation in insulin-managed DM patients
- For those at risk, inquire about symptomatic and asymptomatic hypoglycemia at each encounter (C)
- Treatment (E):
  - 15 – 20 gm glucose preferred treatment in a conscious patient
  - After 15 min of treatment, SMBG shows hypoglycemia, repeat above
  - Once BG normalizes, patient should eat meal or snack to prevent recurrence
  - Glucagon should be prescribed to patients at significantly high risk of severe hypoglycemia

Hypoglycemia Unawarenes

- Reassess regimen with hypoglycemia unawareness or ≥1 episode of severe hypoglycemia (E)
- In patients with hypoglycemia unawareness treated with insulin, loosen glycemic goals for several weeks to attempt to reverse hypgoglycemia unawareness and ↓ risk of recurrence (A)

Macrovascular Management: Dyslipidemia Hypertension

Prediabetes

- Consider testing in overweight or obese adults (BMI ≥25 kg/m^2) with ≥1 risk factors (without risk factors, age 45) (B)
  - Physical inactivity
  - 1st-degree relative with DM
  - High-risk ethnicity
  - Women who delivered >9 lb baby or diagnosed with GDM
  - Hypertension or treatment
  - HDL <35 mg/dL and/or TG >250 mg/dL
  - Women with PCOS
  - A1C ≥5.7%, IGT or IFG
  - Other conditions associated with insulin resistance
  - History of CVD

Prediabetes

- If tests are normal, repeat ≤every 3 years (E)
- Screen and treat other CVD risk factors (B)
- Refer to program to target 7% weight loss
- ↑ Dietary fiber (14 gm fiber/ 1000 Cal) (B)
- ≥150 mg/week of moderate-intensity activity (e.g. walking)
- Consider metformin for prevention, especially if BMI >35 kg/m^2, <60 years old, women with hx GDM(A)
- ≤ Annually monitor for diabetes (E)

Lifestyle Therapy

- Cardiovascular disease prevention. Monotherapy if mild ↑BP (B)
  - DASH-diet with ↓ sodium intake (<1.5 gm/day)
  - ↓ Body weight
  - ↑ Fruits, vegetables (8 – 10 servings/day)
  - ↑ Low-fat dairy (2 – 3 servings/day)
  - Limit EtOH servings:
    - ≤2/day for males
    - ≤1/day for females
  - ↑ Physical activity

Hypertension Pharmacologic Therapy

- Lifestyle therapy AND pharmacologic therapy if BP ≥140/90 (B)
  - ACE inhibitors (C)
  - ARBs (C)
  - β-blockers
  - Diuretics
  - Calcium channel blockers
- Antihypertensive should consist of ACE inhibitor or ARB C)
- Usually ≥2 antihypertensives required to achieve BP goal (B)

Hypertension Pharmacologic Therapy

- Antihypertensive should consist of ACE inhibitor or ARB C)
- Usually ≥2 antihypertensives required to achieve BP goal (B)
- Give ≥1 antihypertensive at bedtime (A)
- Monitor potassium and SCr/eGFR if any of following used (E):
  - ACE inhibitors
  - ARBs
  - Thiazide diuretics

Microvascular Management: Neuropathy Nephropathy

Neuropathy

- Screen for initial distal symmetric polyneuropathy (DPN)
- T1DM patients
  - 5 years after diagnosis (B)
- T2DM patients
  - At diagnosis (B)
- After initial screen, annually thereafter with simple clinical tests

Retinopathy

- Optimize BG and BP control to reduce/slow progression (A)
- T1DM patients
  - Initial dilated and comprehensive eye exam by ophthalmologist/optometrist within 5 years of diagnosis (B)
- T2DM patients
  - Initial dilated and comprehensive eye exam by ophthalmologist/optometrist shortly after diagnosis (B)
- After initial exam, repeat annually to biennially depending on presence of retinopathy (B)

Foot Care

- Educate on foot self-care (B) with daily visual inspection
- Annual comprehensive foot exam for risk factors for (B)
  - Ulcers
  - Amputations
- Assess (B)
  - Foot pulses
  - Loss of protective sensation (LOPS) using
    - 10 gm monofilament WITH testing using
      - 128 Hz tuning fork
      - Pinprick sensation
      - Ankle reflexes
      - Vibration perception threshold

Nephropathy

- Optimize BG and BP control to reduce/slow progression (A)
- Annual screen of albuminuria in T1DM patients with DM ≥5 years and in ALL T2DM starting from diagnosis (B)
- ACE inhibitor or ARB = primary prevention of diabetic kidney disease (B)
  - Recommended in patients with moderate albuminuria 30 mg/24 hr (C) or higher >300 mg/24 hr (A)
  - Not recommended in patients with normal BP and albuminuria <30 mg/24 h (B)
- Monitor SCr and potassium when ACE inhibitor, ARB, or thiazide used (E)

Albuminuria

- Nomenclature changes
  - Emphasizes albuminuria as a continuous risk factor
  - Normal albumin
    - <30 mg/24 hr
  - Albuminuria
    - 30 - >300 mg/24 hr

Comorbidities

- Consider assessing and addressing for comorbidities that complicate DM management (B)
  - Depression
  - OSA
  - Fatty liver disease
  - Cancer
  - Fractures
  - Cognitive impairment
  - Low testosterone in men
  - Periodontal disease

Medical Nutrition Therapy

- Recommended for all patients with prediabetes or DM (A)
- Reduce energy intake and improve dietary habits (A)
- Modest weight loss can provide clinical benefits (A)

Medical Nutrition Therapy

- Monitoring carbohydrates:
  - Carbohydrate counting or estimation based on experience (B)
  - Dietary fiber over other sources of carbohydrates (B)
  - Low vs. high-glycemic index foods may improve glycemic control (C)
  - Avoid or limit intake of sugar-containing beverages to avoid weight gain and worsening cardiometaboolic risk (B)
- Monitoring dietary fat

Medical Nutrition Therapy

- Monitoring dietary fat
  - Fat quality over quantity (B)
  - Mediterranean-style, MUFA-rich diet may improve glycemic control over low-fat but high carbohydrate diet (B)
  - Long-chain n-3 fatty acids recommended (B) but not routine supplementation (A) to prevent CV events

Medical Nutrition Therapy

- Alcohol serving limitations (E):
  - ≤2/day for males
  - ≤1/day for females
- Sodium restriction (B)
  - <2.3 gm/day as in general population
  - With both DM and HTN, further restriction as needed

Diabetes Self-Management Education and Support

- Provides ongoing skill-development and knowledge for patients to manage their prediabetes and diabetes
- Should receive DSME/S according to National Standards or Diabetes Self-Management Education at diagnosis and as needed after (B)
- Self-management and quality of life are cornerstone to DSME/S and should be assessed (C)

Physical Activity

- Shown to improve glycemic control, weight loss, and
- Exercise ≥150 min of moderate-intensity (50-70% max HR) aerobics weekly (A)
  - ≥3 times weekly
  - No more than 2 consecutive days without exercise
- ≥Biweekly resistance training (A)
- In T1DM, insulin deprivation (12-24 hrs) and ketosis can worsen hyperglycemia and ketosis

Physical Activity

- Caution in setting of long-term complications of DM:
  - Retinopathy
    - Risk of vitreous hemorrhage or retinal detachment
  - Peripheral neuropathy
    - Risk of skin breakdown and infection
  - Autonomic neuropathy
    - Risk of ↓ cardiac response, syncope, impaired thermoregulation
  - Albuminuria and nephropathy
    - Risk acute ↑ albuminuria

Psychosocial Assessment

- Can include (E):
  - Attitudes about illness
  - Expectations for management and outcomes
  - Mood
  - Quality of life
  - Resources
  - Psychiatric history

Psychosocial Assessment

- Routinely screen for (B):
  - Depression
  - Distress
  - Anxiety
  - Eating disorders
  - Cognitive impairment

Psychosocial Assessment

- Can include (E):
  - Attitudes about illness
  - Expectations for management and outcomes
  - Mood
  - Quality of life
  - Resources
  - Psychiatric history

Bariatric Surgery

- Has been shown to normalize completely/nearly glycemia in 40 - 95% of patients with T2DM
- In less severely obese patients, could cause remission of T2DM
- Can be considered for BMI >35 kg/m^2 and T2DM especially when DM and comorbidities are difficult to control (B)
- Post-surgery, patients require lifelong lifestyle support and medical monitoring (B)
  - Nutritional deficiencies and supplementation required

Immunization

- Influenza vaccine (C)
  - Annually to all ≥6 months
- Pneumococcal polysaccharide vaccine (C)
  - To all ≥2 years old
  - One time revaccination for patients >65 years old immunized >5 years ago
- Hepatitis B vaccine (C)
  - To all 19 – 59 years old
  - Consider for patients ≥60 years old

DM Complications and Management

American Diabetes Association.

Cardiovascular Disease

- Hypertension
- Dyslipidemia
- Antiplatelet use
- Smoking cessation
- Screening

American Association of Clinical Endocrinologists' Comprehensive Diabetes Management Algorithm 2013 Consensus Statement

Guideline Focus

- **Type 2 DM**
- **Obesity**
- **Prediabetes**
- Non-pharmacologic hyperglycemia management
- Pharmacotherapy and insulin
- Hypertension management
- Dyslipidemia management
- Other risk-reduction strategies

Prediabetes

- 1st: Weight reduction
- Antihyperglycemic treatment
  - 1st: metformin or acarbose
  - Last-line: TZD, GLP-1
- CVD risk

Antihyperglycemic Therapy Goals

1. To achieve clinical and biochemical glucose targets
2. To avoid hypoglycemia
3. To avoid weight gain in those who are obese and to assist with weight loss
4. To reduce or prevent CVD risk

Antihyperglycemic Therapy

- Monotherapy: A1C <7.5%
  - Metformin (1.5 – 2 gm/day)
  - Continue in eGFR ≥45 mL/min/1.73 m^2
    - Review use when eGFR 30 – 44 mL/min/1.73 m^2
    - Discontinue when eGFR <30 mL/min/1.73 m^2
  - Intolerant to metformin: alternatives:
    - GLP- agonists, DPP-3 inhibitors, alpha-glucosidase inhibitors, SGLT2 inhibitors
    - Use with caution: TZDs, SU, glinides due to hypoglycemia, weight gain

Antihyperglycemic Therapy

- Combination therapy: A1C >7.5%
  - Metformin AND another agent
  - If metformin intolerant, use 2 agents with differing MOAs
  - Oral combination tablets exist
    - Decrease pill burden
    - Improve adherence

Insulin

- Long-acting > intermediate-acting
  - No peak
  - Less hypoglycemia
- Rapid-acting > regular-acting
  - More predictable
- Combined with incretins (GLP-1 agonists, DPP-4 inhibitors)
  - Decreases FBG and PPBG
  - May minimize weight gain, hypoglycemia

Pharmacologic Treatment

A1C <7.5%

- Lifestyle therapy and monotherapy with:
- 1st: metformin
- Alt: GLP-1 agonists, DPP4-I, AG-I
- Caution: SGLT-2, TZD, SU/GLN

A1C ≥7.5%

- Lifestyle therapy and dual therapy with metformin/Alt AND:
- GLP-1 agonists, DPP4-I, AG-I, colesevelam, bromocriptine
- Caution: SGLT-2, TZD, SU/GLN, basal insulin

Pharmacologic Treatment

A1C >9% - symptoms

- Dual therapy or
- Triple therapy

A1C >9% + symptoms

- Insulin ±
- Other therapy

Macrovascular Management: Dyslipidemia Hypertension

Obesity

- Evaluate for complications and stage
  - Cardiometabolic disease or biomechanical complications
- No complications (BMI 25 – 26.9 or BMI ≥27) or BMI ≥27 with complications – stage severity (low, medium, high)
  - Choose therapeutic targets to prevent complications, treatment, intensity of weight loss
    - Lifestyle modification: MD/RD counseling, remote program, multidisciplinary program
    - Pharmacologic treatment: phentermine, orlistat, lorcaserin, phenterime/topiramate ER
    - Surgery if BMI ≥35: lap band, gastric sleeve, gastric bypass

Obesity

- Choose therapeutic targets to prevent complications, treatment, intensity of weight loss
  - Lifestyle modification: MD/RD counseling, remote program, multidisciplinary program
  - Pharmacologic treatment: phentermine, orlistat, lorcaserin, phenterime/topiramate ER
  - Surgery if BMI ≥35: lap band, gastric sleeve, gastric bypass
- Intensify lifestyle/pharmacologic treatment/surgery if targets not met

Dyslipidemia

- Non-statin LDL-lowering therapies
  - Ezetimibe
  - Bile-acid sequestrants
  - Fibrates
  - Niacin
  - Fish-oil, prescription

Dyslipidemia

Non-statin LDL-lowering therapy	Apo B	Non-HDL-C	LDL-C	LDL-P	HDL-C	TG
Ezetimibe	↓	↓	↓			↓
Bile-acid sequestrants			↓	↓		↑*
Fibrates						↓
Niacin	↓		↓		↑	↓
Fish oil (prescription)			↓			

Dyslipidemia

- Using lipid panel assess CVD risk
- 1st: Statin treatment
  - If intolerant: try another statin, change dose/frequency, or add non-statin LDL-lowering therapy

Hypertension Lifestyle Therap

- Weight loss
- Sodium restriction including DASH diet
- Limit alcohol intake
- Moderate-intensity exercise

Hypertension Pharmacologic Treatment

- Monotherapy
  - ACE inhibitor or ARB
- When BP >150/100 mmHg
  - Dual therapy with ACE inhibitor or ARB AND
  - Thiazide or β-blocker or Calcium channel blockers
- Triple therapy with above AND next agent from above
- Other choices: alpha-blockers, centrally acting agonists, vasodilators, spironolactones

Hypertension

- When BP >150/100 mmHg
  - Start with ≥2 antihypertensive agents
- Goal BP <140/80 mmHg
- BP 130 – 135 mmHg acceptable
  - Caution: SBP <130 mmHg target organ heterogeneity. Balance risk of serious adverse effects and lack of cardiac, renal, retinal beneefit
- SBP <120 mmHg considered in high stroke-risk patients

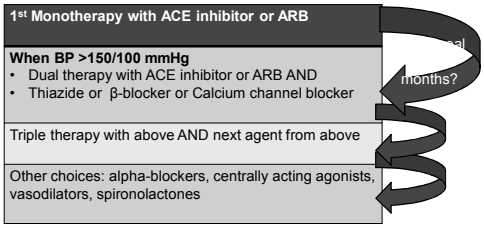
Hypertension Lifestyle Therapy

- Weight loss
- Sodium restriction
  - <2.3 gm/day with DASH diet
- Potassium
  - With normal renal function: 4.7 gm/day from fruits, vegetables
- Alcohol
  - ≤2 drinks/day (24 oz beer, 10 oz wine, 3 oz of 80-proof liquor)
    - <14 drinks/week for men or 9 drinks/week for women
- Physical activity
  - Moderate-intensity (brisk walking) 30 – 45 min most days of week

Hypertension Pharmacologic Treatment

- Achieving target BP goal is more important than the sequential additional of specific agents
- 1st line: ACE inhibitors = ARBs, Calcium channel blockers = diuretics
- Comorbidities
  - CHF – benefit from B-blockers
  - Proteinuria – benefit from ACE inhibitors or ARBs
  - Prostatism – benefit from alpha-blockers
  - CAD – benefit from B-blockers or CCBs

Hypertension



Dyslipidemia

- Statins are drug class of choice in CVD prevention
- Intensity statin therapy
  - Increase dose
  - Use more potent statin

Hypertriglyceridemia

- Treat TG first when >500 mg/dL
  - Avoid pancreatitits
- Fibrates used for CV benefit in patients with moderate dyslipidemia
  - TG >200 mg/dL
  - HDL <40 mg/dL
- Niacin considered in patients with high TG and low HDL

Microvascular Management: Neuropathy Nephropathy

2011

Neuropathy

- Prevalence 5 – 100% depending on diagnostic criteria
- Large-nerve fiber neuropathies
  - Sensory or motor nerve involvement
  - Present with glove and stocking sensory loss
  - Incoordinate, ataxic, 17x more likely to fall than nonneuropathic patients
- Small-nerve fiber neuropathies
  - Usually presents early without objective signs of nerve damage

2011

Retinopathy

- Diabetic retinopathy* = leading cause of blindness
- About 50% of T1DM patients develop nonproliferative retinopathy >7 years of diagnosis
  - Most have form of retinopathy >20 years
- In most T2DM patients, retinopathy develops with several years of poor glycemic control

2011

Nephropathy

- Microalbuminuria develops within 5 – 15 years of DM onset and progresses to albuminuria ~10 years
- Microalbuminuria: 30 – 299 mg/24 hr albumin excretion
- Albuminuria: ≥300 mg/24 hr albumin excretion
- May be earliest sign of diabetic nephropathy in T1DM and can appear within 5 years of diagnosis
- May be sign of underlying cardiovascular disease when microalbuminuria (often present) at diagnosis in T2DM patients

2011

Nephropathy

- Counsel on optimal control (Grade D; BEL 4)
  - BG
  - BP
  - Dyslipidemia
- Counsel on smoking cessation (Grade D; BEL 4)

Lifestyle Therapy

- Smoking cessation
- Increased physical activity, weight loss
- Dietary modifications to lower LDL-C
  - Limit saturated fat to <7% of calories (full-fat dairy, bacon, sausage, ribs, fatty meats, pastries)
  - Limit cholesterol to <200 mg/day (organ meats, egg yolks, excessive meat/dairy products)
  - Increase viscous (water-soluble) fiber to 10 – 25 gm/day to reduce bile acid reabsorption
  - Increase plant stanols/sterols to 2 gm/day to prevent intestinal cholesterol intake

Lifestyle Therapy

- Dietary modifications to lower TG
  - Physical activity 5 days/week for >30 min (>60% HR)
  - ↓ Calories if overweight
    - 5 – 10% weight loss ≈ ↓ 20% TG
  - ↓ Simple carbohydrates/sugars (sucrose, fructose, starch)
  - ↓ High-fat foods
  - ↑ Unsaturated fat
  - Eliminate trans fat
  - ↓ Saturated fat
  - ↑ marine-based omega-3 ethyl esters
  - Restrict alcohol to <20 – 30 gm/day

Depression

- Untreated causes difficulties with DM management due to
  - ↓ Self-care
  - ↓ Treatment adherence
  - ↓ Glycemic control
- Depression and DM associated with ↑ All-cause and CVD mortality

Sleep Disorders

- Daytime drowsiness is most obvious manifestation of a sleep disorder and is associated with
  - ↑ Accidents
  - ↓ Judgment and performance
- Sleep deprivation is a risk factor for CVD
  - Restless leg syndrome can be secondary
- Sleep apnea
  - Numerous cycles of breathing cessation followed by awakening due to deprivation of oxygen

Sleep Disorders

- Sleep apnea
  - Numerous cycles of breathing cessation followed by awakening due to deprivation of oxygen
  - Obstructive sleep apnea is most common and commonly diagnosed in
    - Obese patients
    - Men
    - Elderly
  - Treatment can provide ≥ glycemic control than oral agents

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Outline

- Classification
- Pathophysiology
- Diagnosis
  - FBG
  - 2-hour OGTT
  - Random
  - Hbga1c
- Goals of therapy
  - Stringent glycemic control
    - What's the expected time horizon for benefit from therapy? Will the patient live long enough to benefit? (microvascular (retinopathy, nephropathy) 8 yrs vs. macrovascular (HTN, DLP) 2 – 3 yrs)
  - Non-stringent glycemic control
- Diabetes self-management education and support
  - Covered under Medicare Part B (initial and annual)
- Non-pharmacologic treatment
  - Diet
  - Exercise
- Pharmacologic treatment
  - Oral treatment
    - Metformin
    - Sulfonylureas
    - Dipeptidyl peptidase-4 inhibitors
    - Thiazolidinediones
  - Injectable treatment
    - Insulin
    - GLP-1 receptor agonists
- Macrovascular management (AGS emphasis)
  - Cardiovascular disease prevention
    - Aspirin
      - AGS recommends 81 – 325 mg/d for overt CVD (i.e. MI, stroke)
        - No evidence that higher dose is more effective than lower
      - AGS no longer recommends for primary prevention
    - Smoking cessation

Stock chart

AGS	American Diabetes Association	AACE

Stock symbols

AGS	American Diabetes Association	AACE
♀♂ ¤ ≥ ≤ § ß ˜ ‡ † ↑ ↓ ≈ *		

Stock chart

AGS	American Diabetes Association.	AACE

Type 1 diabetes

American Diabetes Association.

Inform patient of opportunity to have relatives screened in the setting of clinical research (E)