Updates in Diabetes Management

Virginia Society of Health-System Pharmacists
Annual Spring Seminar
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Disclosure Statement

- Conflict of Interest
  - Nothing to Disclose
Learning Objectives

• Discuss diabetes prevalence and costs
• Discuss the 2015 Standards of Medical Care in adults with diabetes
• Discuss the appropriate care of pediatric patients with Type 2 Diabetes
• Recognize the newest agents available for the treatment of Type 2 Diabetes
• Describe the risks and benefits of the sodium-glucose co-transporters
• Demonstrate the appropriate use of inhaled insulin
PREVALENCE & COST
Prevalence

- 25.8 million people in the U.S. have DM (8.3% of the US population)
  - 18.8 million diagnosed
  - 7.0 million undiagnosed
  - 1.9 million new diagnoses over the age of 20 in 2010
- Leading cause of kidney failure, non-traumatic lower limb amputation, and new cases of blindness in adults in the US
- Major cause of heart disease and stroke
- 7th leading cause of death in the US
- 79 million Americans (estimated) older than 20 had pre-diabetes in 2010

Prevalence

Prevalence in adults by age and race:
- 65 years of age and older: 10.9 million (26.9%)
- 20 years of age or older: 25.6 million (11.3%)
- Men: 13.0 million (11.8%) over the age of 20
- Women: 12.6 million (10.8%) over the age of 20
- Non-Hispanic whites: 15.7 (10.2%) over the age of 20
- Non-Hispanic Blacks: 4.9 million (18.7%) of the age of 20.
- American Indians and Alaska Natives: 16.1%
  - Alaskan Native: 5.5%
  - American Indian: 33.5%

Prevalence After population Age adjustment Based on 2007-2009 Survey

<table>
<thead>
<tr>
<th>Race</th>
<th>Percent diagnosed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Hispanic White</td>
<td>7.1%</td>
</tr>
<tr>
<td>Asian American</td>
<td>8.4%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>11.8%</td>
</tr>
<tr>
<td>Cuban, Central and South American</td>
<td>7.6%</td>
</tr>
<tr>
<td>Mexican</td>
<td>13.3%</td>
</tr>
<tr>
<td>Puerto Rican</td>
<td>13.8%</td>
</tr>
<tr>
<td>Non-Hispanic Black</td>
<td>12.6%</td>
</tr>
</tbody>
</table>

*This is based on population 20 years of age and older

Prevalence < 20 years of age

- 208,000 Americans diagnosed type 1 or 2 (0.25%)

- 2008 – 2009: 18,436 estimated newly diagnosed with Type 1 Diabetes, 5,089 estimated newly diagnosed with Type 2 Diabetes

Rate of new cases of type 1 and type 2 diabetes among youth ages younger than 20 years, by race/ethnicity, 2002–2005

Source: SEARCH for Diabetes in Youth Study
NHW=non-Hispanic whites; NHB=non-Hispanic blacks; H=Hispanics/Latinos; API=Asian/Pacific Islander Americans; AI=American Indian
Cost of Diabetes

• Direct Cost
  • Direct medical expenditure in 2012 is $176 billion
    • In-patient hospital care: $75.7B
    • Medication cost to treat complications of DM: $31.7B
    • Diabetic medications and supplies: $21.1B
    • MD Office visits: $15.8B
    • Nursing home care: $14.1B
  • Average medical expenditures for a patient diagnosed with DM: $13,700 ($7,900 attributed to DM)
• Indirect Cost
  • Indirect medical expenditures in 2012 is $69 billion
    • Missed days from work: $5B
    • Reduced productivity at work: $20.8B
    • Reduced productivity for those not working: $2.7B
    • Disability: $21.6B
    • Early Mortality: $18.5B

Diabetes cost in specific populations

- Patients without insurance have fewer office visits and are prescribed fewer medications than those with insurance coverage
  - Caveat: 55% more emergency room visits
- Per-capita health care expenditures
  - Hispanics (lowest): $5,930
  - Non-Hispanic blacks (highest): $9,540
- Non-Hispanic blacks have the highest rate of emergency department visits
  - Per-capita hospital costs are 41.3% higher among non-Hispanic blacks compared with non-Hispanic whites
  - Per-capita hospital costs are 25.8% lower among Hispanics compared to non-Hispanic whites

Virginia and Diabetes

- Prevalence: 6.80%
- Population: 564,200
- Cost:
  - Total: $6.19 billion
  - Direct Medical Cost: $4.43 billion
  - Indirect Cost: $1.77 billion
2015 STANDARDS OF MEDICAL CARE IN DIABETES
Strategies for Improving Care

• Utilization of a patient-centered education style

• Treatment decisions should be timely and founded on evidence-based guidelines

• Chronic Care Model (CCM)

• Team-based care

Diagnosis of Diabetes

- Hemoglobin A1c Criteria
  - $\geq 6.5\%$

- Plasma glucose criteria
  - Fasting
    - $\geq 126$ mg/dL
  - 2 hour plasma glucose
    - $\geq 200$ mg/dL

- Patients with symptoms of hyperglycemia
  - $\geq 200$ mg/dL

Categories of Increased Risk for Diabetes

- Testing should be considered to assess risk for future diabetes in asymptomatic adults who are
  - Overweight or obese (BMI ≥ 25 kg/m² or ≥ 23 kg/m² in Asians) and
  - Have more than 1 additional risk factor for diabetes
- Any adult over the age of 45
- Screen for DM every 3 years
  - Hb1AC
  - FPG
  - Oral Glucose Tolerance Testing
- In patients with prediabetes
  - Screen, identify and treat CVD risk factors

Initial Evaluation and Diabetes Management Planning

- Medical evaluation
  - Classify diabetes
  - Detect diabetes complications
  - Review of previous treatments and risk factor control in patients with established diabetes
  - Formulate a management plan
  - Provide a basis for continuing care

- Management Plan
  - A team based approach

Foundations of Care: Diabetes Self-Management and Support

• Patients should receive diabetes self-management education (DSME) and diabetes self-management support (DSMS)

• Outcomes should be measured and monitored as part of care

• DSME and DSMS should address psychosocial issues

• DSME and DSMS should be adequately reimbursed by third-party payers

Foundations of Care: Medical Nutrition Therapy

• Goals
  • Promote and support healthful eating patterns
  • Address nutritional needs
  • Maintain the pleasure of eating
  • Provide practical tools for day-to-day meal planning

• Carbohydrate management

• Weight loss

Foundations of Care: Medical Nutrition Therapy

- Protein
- Dietary fat
- Alcohol
- Sodium
- Micronutrients and herbal supplements

Foundations of Care: Physical Activity

- At least 150 minutes of moderate-intensity aerobic activity per week

- Reduce sedentary time, particularly by breaking up extended amounts of time spent sitting

- Resistance training twice per week (if not otherwise contraindicated)

Foundations of Care: Smoking Cessation

- Advise all patients to not smoke or use tobacco products

- Include smoking cessation counseling as a routine component of diabetes care
Foundations of Care: Psychosocial Assessment and Care

- Include assessment of patient’s psychological and social situation as an ongoing part of medical management

- Routinely screen for psychosocial problems

Foundations of Care: Immunizations

- Influenza vaccine annually

- Pneumococcal polysaccharide vaccine 23 (PPSV23) to all diabetic patients ≥ 2 years of age

- Pneumococcal conjugate vaccine 13 (PCV13)
  - ≥ 65 years of age and not previously vaccinated should receive PCV13, followed by PPSV23 6-12 months after initial vaccination
  - ≥ 65 years of age and previously vaccinated with PPSV23, should receive a follow-up ≥ 12 months with PCV13

- Hepatitis B
  - All diabetic patients 19-59 years of age
  - Consider in patients ≥ 60 year old

Prevention or Delay of Type 2 Diabetes

- Patients with impaired glucose tolerance, impaired fasting glucose or an HgbA1c 5.7-6.4% should be referred to an intensive diet and physical activity behavioral counseling program
  - Metformin may be considered especially for those with a BMI > 35kg/m², age <60 years, and women with prior gestational diabetes
- Annual monitoring
- Screen for modifiable risk factors
- DSME and DSMS programs are appropriate

Glycemic Targets

- Assessment of glycemic control
  - Self-monitored blood glucose (SMBG) may help guide treatment decisions of patients using less frequent insulin injections or noninsulin therapy
  - Patients should receive ongoing instruction and regular evaluation of their SMBG technique
  - Patients on multiple daily doses of insulin should perform SMBG more frequently

Glycemic Targets

• HgbA1c testing
  • At least 2 times per year in patients who are at their treatment goals
  • Quarterly in patients whose regimen has changed or not meeting their treatment goals
  • Use of point-of-care testing provides the opportunity for more timely treatment changes

• HgbA1c goals
  • <7%

• Hypoglycemia

Approaches to Glycemic Treatment

- Metformin, if tolerated and not contraindicated, is preferred as initial therapy.
- In newly diagnosed patients who are markedly symptomatic and/or elevated blood glucose or HgbA1c, consider initiating insulin therapy (with or without oral agents).
- If noninsulin monotherapy at maximum tolerated dose does not achieve or maintain target HgbA1c over 3 months, add a 2nd oral agent, glucagon like peptide 1 receptor agonist (GLP-1 RA), or insulin.
- Patient centered approach.
- Insulin therapy is eventually indicated for many patients with T2DM.

Cardiovascular Disease and Risk Management

- Hypertension/blood pressure control
  - Screen at every visit
  - Goal <140/90
- Treatment
  - Lifestyle modifications
  - Angiotension Converting Enzyme Inhibitor or Angiotension receptor blocker
    - Note: most patients will require multiple agents to reach target

Cardiovascular Disease and Risk Management

• Dyslipidemia/Lipid Management
  • Screen a lipid profile at diagnosis, initial medical evaluation, and/or age of 40 years.
• Treatment
  • Lifestyle modifications
  • Triglycerides (TG) ≥ 150 mg/dL and/or high density lipoprotein (HDL) <40 mg/dL (men) <50 mg/dL (women) – intensify lifestyle therapy and optimize glycemic control
  • Fasting TG ≥ 500 mg/dL – evaluate for secondary causes and consider treatment
  • Overt cardiovascular disease (CVD) – High intensity statin
  • < 40 years + additional CVD risk – consider moderate intensity statin
  • 40-75 years without additional CVD risk consider moderate-intensity statin therapy
  • 40-75 years with additional CVD risk consider High-intensity statin therapy

Cardiovascular Disease and Risk Management

- **Dyslipidemia/Lipid Management**
  - Treatment (Cont’d)
    - >75 years without additional CVD risk factors consider moderate-intensity statin
    - >75 years with additional CVD risk factors consider moderate-intensity or high intensity statin
    - Cholesterol testing may be helpful to monitor adherence
    - Combination lipid therapy has not been shown to provide additional benefit

- **Antiplatelet**
  - Consider aspirin therapy (75-162 mg/day) as primary prevention in patients with increased cardiovascular risk (10 yr risk >10%)
    - Women >60 year or men >50 years with 1 additional major risk factor
  - Aspirin (75-162 mg/day) as secondary prevention in patients with DM and a history of CVD
Cardiovascular Disease and Risk Management

- Coronary Heart Disease
  - Patients with known prior MI – beta blockers should be continued for at least 2 years following event
  - Patients with stable heart failure – metformin may be used if renal function is normal
  - Patients with symptomatic heart failure – thiazolidinedione treatment should not be used.
Older Adults

• Recommendations
  • Older adults who have significant life expectancy should receive diabetes care with goals similar to younger adults
  • Glycemic goals may be more relaxed
  • Screening for complications should be individualized
  • Other cardiovascular risk factors should be treated with consideration of risk vs. benefit

MANAGEMENT OF TYPE 2 DIABETES IN PEDIATRICS
Type 2 Diabetes Mellitus per American Academy of Pediatrics

- First Line TLC (Therapeutic Lifestyle Modification)
  - Nutrition
  - Physical activity
    - 60 minutes daily
    - Limit non-academic screen time to < 2 hours
  - Exceptions
    - Unclear Type 1 vs Type 2 - Insulin
    - Random BG ≥ 250mg/dL or A1C > 9% or ketotic/DKA - Insulin
- Initiate metformin at time of diagnosis
- HgbA1c q3mo – target < 7%
  - Intensify if not at treatment goals
  - Self Monitoring of Blood Glucose
    - Insulin or risk of hypoglycemia
    - Initiating or changing regimen
    - Not at goal
    - Sickness

Type 2 Diabetes Mellitus per American Academy of Pediatrics

• Metformin 1st Line
  • Watch for GI SE
    • Start low and titrate q1-2wks
    • Max dose 2000mg daily
• Some children need to maintained with insulin and an oral agent
  • Insulin + melgitinide
• Goal FPG: 70-130mg/dL

NEW AGENTS
# Newly Approved Medications Since 2010

<table>
<thead>
<tr>
<th>Glucagon-like peptide-1 Receptor Agonists</th>
<th>Approval Date</th>
<th>Indication</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bydureon (exenatide)</td>
<td>1/2012</td>
<td>T2DM &gt;18 y/o</td>
<td>2mg SC weekly</td>
</tr>
<tr>
<td>Tanzeum (albiglutide)</td>
<td>4/2014</td>
<td>T2DM &gt;18 y/o</td>
<td>30mg SC weekly</td>
</tr>
<tr>
<td>Trulicity (dulaglutide)</td>
<td>9/2014</td>
<td>T2DM &gt;18 y/o</td>
<td>0.75mg SC weekly</td>
</tr>
<tr>
<td>Saxenda (liraglutide)</td>
<td>12/2104</td>
<td>Weight loss</td>
<td>3mg SC Daily</td>
</tr>
</tbody>
</table>

Gohil K and Enhoffer D. Diabetes market grows ever more crowded. P&T 2014; 39(12): 877-80
Newly Approved Medications Since 2010

<table>
<thead>
<tr>
<th>Dipeptidyl peptidase 4 Inhibitors</th>
<th>Approval Date</th>
<th>Indication</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tradjenta (linagliptin)</td>
<td>5/2011</td>
<td>T2DM &gt;18 y/o</td>
<td>5mg PO Daily</td>
</tr>
<tr>
<td>Nesina (alogliptin)</td>
<td>1/2013</td>
<td>T2DM &gt;18 y/o</td>
<td>6.25-25mg PO Daily</td>
</tr>
</tbody>
</table>

# Newly Approved Medications Since 2010

<table>
<thead>
<tr>
<th>Insulin</th>
<th>Approval Date</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alfreeza (human insulin)</td>
<td>6/2014</td>
<td>T1DM or T2DM &gt;18 y/o</td>
</tr>
<tr>
<td>Toujeo (Insulin glargine U-300)</td>
<td>2/2015</td>
<td>T1DM or T2DM &gt;18 y/o</td>
</tr>
</tbody>
</table>

## Newly Approved Medications Since 2010

<table>
<thead>
<tr>
<th>Sodium-Glucose Co-transport 2 Inhibitors</th>
<th>Approval Date</th>
<th>Indication</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invokana (canagliflozin)</td>
<td>3/2013</td>
<td>T2DM &gt;18y/o</td>
<td>100-300mg PO Daily</td>
</tr>
<tr>
<td>Farxiga (dapagliflozin)</td>
<td>1/2014</td>
<td>T2DM &gt;18y/o</td>
<td>5-10mg PO Daily</td>
</tr>
<tr>
<td>Jardiance (empagliflozin)</td>
<td>8/2014</td>
<td>T2DM &gt;18y/o</td>
<td>10-25mg PO Daily</td>
</tr>
</tbody>
</table>

Gohil K and Enhoffer D. Diabetes market grows ever more crowded. P&T 2014; 39(12): 877-80
## Newly Approved Medications Since 2010

<table>
<thead>
<tr>
<th>Combination Therapy</th>
<th>Approval Date</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Juvisync (sitagliptin/simvastatin)</td>
<td>10/2011</td>
<td>T2DM &gt;18 y/o</td>
</tr>
<tr>
<td>Jentadueto (linagliptin/metformin)</td>
<td>2/2012</td>
<td>T2DM &gt;18 y/o</td>
</tr>
<tr>
<td>Kazano (alogliptin/metformin)</td>
<td>1/2013</td>
<td>T2DM &gt;18 y/o</td>
</tr>
<tr>
<td>Oseni (alogliptin/pioglitazone)</td>
<td>1/2013</td>
<td>T2DM &gt;18 y/o</td>
</tr>
<tr>
<td>Xigduo XR (dapagliflozin/metformin)</td>
<td>10/2014</td>
<td>T2DM &gt;18 y/o</td>
</tr>
<tr>
<td>Glyxambi (empagliflozin/linagliptin)</td>
<td>2/2015</td>
<td>T2DM &gt;18 y/o</td>
</tr>
</tbody>
</table>
## Medications in the Pipeline

<table>
<thead>
<tr>
<th>Drug</th>
<th>Class</th>
<th>Status</th>
<th>Expected Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>LY2605541 (insulin peg lispro)</td>
<td>Insulin</td>
<td>Phase 3</td>
<td>2015</td>
</tr>
<tr>
<td>Lyxumia (lixisenatide)</td>
<td>GLP1-RA</td>
<td>Phase 3</td>
<td>2015</td>
</tr>
<tr>
<td>Semaglutide</td>
<td>GLP1-RA</td>
<td>Phase 3</td>
<td>2016</td>
</tr>
<tr>
<td>Omarigliptin</td>
<td>DDP-4 inhibitor</td>
<td>Phase 3</td>
<td>2016</td>
</tr>
<tr>
<td>Tofogliflozin</td>
<td>SGLT-2 inhibitor</td>
<td>Phase 3</td>
<td>2016</td>
</tr>
<tr>
<td>Tresiba (insulin degludec-ultra-LA)</td>
<td>Insulin</td>
<td>Phase 3</td>
<td>2016</td>
</tr>
<tr>
<td>LY2409021</td>
<td>Glucagon receptor agonist</td>
<td>Phase 2</td>
<td>2017</td>
</tr>
</tbody>
</table>

The Newest Class on the Block

• Sodium-Glucose Co-transport 2 Inhibitors
  • Canagliflozin (Invokana®), dapagliflozin (Farxiga®), emepagliflozin (Jardiance®)

http://www.uspharmacist.com/CMSImagesContent/2013/10/USP1310-SLGT2-F1.gif  Accesed 3/10/15
WAIT…WE CAN INHALE INSULIN NOW?
Administration of Inhaled Insulin

Step 1:

Push Cartridges to Remove

Remove a cartridge from the strip by pressing on the clear side to push the cartridge out. Remove the right number of cartridges for your dose. Pushing on the cup will not damage the cartridge. AFREZZA cartridges left over in an opened strip must be used within 3 days.

## Administration of Inhaled Insulin

### Step 2: Loading a cartridge

#### Hold Inhaler

Hold the inhaler level in one (1) hand with the white mouthpiece on the top and purple base on the bottom.

#### Open Inhaler

Open the inhaler by lifting the white mouthpiece to a vertical position.

Before you put the AFREZZA cartridge in your inhaler, make sure it has been at **room temperature for 10 minutes**.

#### Place Cartridge

Hold the cartridge with the cup facing down.

Line up the cartridge with the opening in the inhaler. The pointed end of the cartridge should line up with the pointed end in the inhaler.

Place the cartridge into the inhaler. Be sure that the cartridge lies flat in the inhaler.

---

Administration of Inhaled Insulin

Close Inhaler

Lower the mouthpiece to close the inhaler (this will open the drug cartridge).

You should feel a snap when the inhaler is closed.

Step 3: Inhaling AFREZZA

Remove the Mouthpiece Cover

Important: Keep the inhaler level during and after removal of the purple mouthpiece cover.

Before use, cartridges and inhaler should be at room temperature for 10 minutes.

Administration of Inhaled Insulin

Keep Level Once Loaded!
Now that the cartridge is loaded, keep the inhaler level from this point forward to avoid loss of drug powder.

DO NOT turn inhaler upside down.  DO NOT point the mouthpiece down.  DO NOT shake or drop the inhaler.

This can result in loss of drug powder.

If any of these occur, throw away the cartridge and load a new cartridge.

Administration of Inhaled Insulin

Exhale
Hold the inhaler away from your mouth and fully blow out (exhale).

Position Inhaler in Mouth
Keeping your head level, place the mouthpiece in your mouth and tilt the inhaler down towards your chin, as shown.
Close your lips around the mouthpiece to form a seal.
Tilt the inhaler downward while keeping your head level.

Inhale Deeply and Hold Breath
With your mouth closed around the mouthpiece, inhale deeply through the inhaler.
Hold your breath for as long as comfortable and at the same time remove the inhaler from your mouth. After holding your breath, exhale and continue to breathe normally.
Administration of Inhaled Insulin

[Diagram showing steps for removing a used cartridge:]

Step 4: Removing a used cartridge

Replace Mouthpiece Cover
Place the purple mouthpiece cover back onto the inhaler.

Open Inhaler
Open the inhaler by lifting up the white mouthpiece.

Remove Cartridge
Remove the cartridge from the purple base.

Throw away the Cartridge
Throw away the used cartridge in your regular household trash.

Source:
Administration of Inhaled Insulin

**Multiple cartridge dosing**

If you need more than one (1) AFREZZA cartridge for your dose,
See the AFREZZA dosage chart above (Figure B).

Repeat steps 2 through 4 for each AFREZZA cartridge you need for your prescribed AFREZZA dose.
Inhaled Insulin Storage

• **Storage**
  - **Sealed Foil Packages**
    - Refrigerated: until marked expiration date
  - **Opened Foil Packages**
    - Room temperature
      - Sealed Blister Cards and Strips: 10 days
      - Open Strips: 3 days
  - **Replace Inhaler every 15 days**
Contact Information

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