Diabetes Epidemiology and Prevention: Lessons Learned Towards Healthy People 2020

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Objectives

• Understand trends in the prevalence of diabetes mellitus (DM) in the US and abroad.

• Explain emergent risk factors for the development of diabetes chronic complications and the impact of glycemic control among those with DM.

• Identify strategies in subjects with prediabetes that may delay type 2 DM development.

• Review strategies to prevent complications and preserve functionality in older adults with DM.
Diabetes: A global pandemic

Prevalence of Diabetes (Diagnosed and Undiagnosed) in the U.S. Adult Population

Prevalence (%)

Age group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Undiagnosed</th>
<th>Diagnosed</th>
</tr>
</thead>
<tbody>
<tr>
<td>20+</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>20-44</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>45-64</td>
<td>7</td>
<td>12</td>
</tr>
<tr>
<td>65+</td>
<td>27</td>
<td>29</td>
</tr>
</tbody>
</table>

2011 National Diabetes Fact Sheet; www.cdc.gov/diabetes
Prevalence of Diabetes in U.S. Older Adults (Age ≥ 65) According to Alternative Definitions

Projected Number of Cases of Diagnosed Diabetes for Total- and Older Adults in the United States: 2005 to 2050

* Percent contribution of older adult numbers to the total numbers projected

HP 2020: Reduce the disease and economic burden of diabetes mellitus

- Reduce the rate of all-cause mortality and **cardiovascular disease** mortality in those with diabetes.
- Reduce the rate of lower extremity amputations in persons with diabetes.
- Improve **glycemic control** among the population with diagnosed diabetes.
- Improve the blood pressure and lipid control in the populations with diabetes.

[healthypeople.gov/2020](http://healthypeople.gov/2020)
Incidence (per 1000) of Major Diabetes Complications According to Age among Adults with Diabetes, 2009

- Hyperglycemic death
- Amputation
- ESRD
- ER Hypoglycemia
- Stroke
- IHD
- CHF

Colors:
- 20-44
- 45-64
- 65-74
- 75+

National Diabetes Surveillance System; www.cdc.gov/diabetes
Diabetes-related Hospitalizations And Hospital Costs Among Adult Patients

Menzin et al, J Manag Care Pharm 2010;16:264-275
Prevention of Cardiovascular Disease in Older Adults with Diabetes

- Death
- Prior CVD
- Clinical Disease
- No prior CVD
- ACCORD
- VADT
- ADVANCE
- UKPDS
- First of Onset of Hyperglycemia
## Comparison of Recent Cardiovascular Trials in Older Patients with Diabetes

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ACCORD</th>
<th>ADVANCE</th>
<th>VADT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62.2</td>
<td>66</td>
<td>60.4</td>
</tr>
<tr>
<td>DM duration (years)</td>
<td>10</td>
<td>8</td>
<td>11.5</td>
</tr>
<tr>
<td>A1c at baseline</td>
<td>8.1</td>
<td>7.2</td>
<td>9.4</td>
</tr>
<tr>
<td>% Prior CVD</td>
<td>30</td>
<td>32</td>
<td>40</td>
</tr>
<tr>
<td>Intensive Rx A1c(%)</td>
<td>6.4(6.1-7)</td>
<td>6.4(6-6.8)</td>
<td>6.9(6.5-7.4)</td>
</tr>
<tr>
<td>Standard Rx A1c(%)</td>
<td>7.5(7-8.1)</td>
<td>7(6.5-7.9)</td>
<td>8.4(7.6-9.1)</td>
</tr>
<tr>
<td>Follow-up (years)</td>
<td>3.4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Primary Outcome, Hazard Ratio (95%CI)</td>
<td><strong>0.9</strong> (0.78-1.04)</td>
<td><strong>0.94</strong> (0.84-1.06)</td>
<td><strong>0.87</strong> (0.73-1.04)</td>
</tr>
<tr>
<td>Mortality, Hazard Ratio (95%CI)</td>
<td>1.22 (1.01-1.46)*</td>
<td>0.93 (0.83-1.06)</td>
<td>1.07 (0.80-1.42)</td>
</tr>
</tbody>
</table>

**ACCORD**, Action to Control Cardiovascular Risk in Diabetes.  
**ADVANCE**, Action in Diabetes & Vascular Disease Controlled Evaluation;  
**VADT**, Veterans Affairs Diabetes Trial
UK General Practice: Association Between A1c and All Cause Mortality (Follow-up ~ 5yrs)

Low and High mean A1c values were associated with increased mortality

Predictors of Poor Outcomes in the VA Diabetes Trial

Diabetes Duration Predicts Mortality in the VA Diabetes Trial

Duration of Diabetes & Processing Speed
Compared to subjects without diabetes

Saczynski & Launer (2006)

-0.45
-0.4
-0.35
-0.3
-0.25
-0.2
-0.15
-0.1
-0.05
0

P for trend = .002

<1 year
1-6 years
7-14 years
15+ years
Unknown diabetic

P_{trend diabetes} < .001

p < .001

p < .01

Saczyenski & Launer (2006)
Cardiovascular Events in Low and High Arterial Calcium (AC) Categories according to VADT Treatment Group

HR = 0.08 (95% CI 0.008-.77), P = 0.03

Reaven P et al. VADT Res Group Diabetes 2009
HP 2020: Increase prevention behaviors in persons at high risk for diabetes

- Reduce the new cases of diabetes in the population
- Increase the proportion of persons with prediabetes who report:
  - increasing their levels of physical activity
  - trying to lose weight
  - reducing the amount of fat or calories in their diet
- Increase the proportion of physician office visits with counseling or education related to nutrition or weight.
- Improve the quality of life for all persons who have, or are at risk for diabetes.

healthypeople.gov/2020
### U.S. Diabetes Prevention Program (DPP): Effect of Interventions on Diabetes Incidence

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Metformin</th>
<th>Lifestyle</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incidence of diabetes (percent per year)</strong></td>
<td>11.0%</td>
<td>7.8%</td>
<td>4.8%</td>
</tr>
<tr>
<td><strong>Reduction in incidence compared with placebo</strong></td>
<td>----</td>
<td>31%</td>
<td>58%</td>
</tr>
<tr>
<td><strong>Number needed to treat to prevent 1 case in 3 years</strong></td>
<td>----</td>
<td>13.9</td>
<td>6.9</td>
</tr>
</tbody>
</table>

The DPP Research Group, *NEJM* 346:393-403, 2002
U.S. Diabetes Prevention Program: Mean Change in Leisure Physical Activity

The DPP Research Group, *NEJM* 346:393-403, 2002
Diabetes Incidence Rates by BMI

Body Mass Index (kg/m²)

Cases/100 person-yr

- 24 - < 30 (n=1045)
- 30 - < 35 (n=995)
- ≥ 35 (n=1194)

The DPP Research Group, NEJM 346:393-403, 2002
Benefits of Healthy Lifestyle in Older Patients

<table>
<thead>
<tr>
<th>Treatment</th>
<th>25 – 44 Years</th>
<th>45 – 59 Years</th>
<th>60 – 85 Years</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>11.0</td>
<td>10.8</td>
<td>10.3</td>
<td>0.71</td>
</tr>
<tr>
<td>Metformin</td>
<td>6.7</td>
<td>7.7</td>
<td>9.3</td>
<td>0.07</td>
</tr>
<tr>
<td>ILS</td>
<td>6.3</td>
<td>4.9</td>
<td>3.3</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Results are cases per 100 person-years

- Lifestyle change was very effective at preventing diabetes in older patients (71% risk reduction).
- Limited effectiveness of Metformin in older persons may reflect age-related differences in insulin action and secretion.

U.S. Diabetes Prevention Program: Long-Term Effects on Diabetes Incidence

Delay in diabetes onset after 10 yr follow-up:
- 4 years for Lifestyle
- 2 years for Metformin

Graph showing cumulative incidence (%) vs year since DPP Randomization.

DPP Research Group, Lancet 2009; 374:1677-86
US Diabetes Prevention Program: Weight Change Over Time

- Placebo
- Metformin
- Lifestyle
Interventions for Diabetes Prevention in Subjects with Prediabetes

<table>
<thead>
<tr>
<th>% Reduction in Risk of Diabetes</th>
<th>NON-TZDs</th>
<th>INTENSIVE LIFESTYLE</th>
<th>TZDs</th>
</tr>
</thead>
<tbody>
<tr>
<td>STOP-NIDDM: Acarbose</td>
<td>25</td>
<td>58</td>
<td>56</td>
</tr>
<tr>
<td>DPP: Metformin</td>
<td>31</td>
<td>58</td>
<td>75</td>
</tr>
<tr>
<td>XENDOS: Xenical</td>
<td>36</td>
<td>58</td>
<td>62</td>
</tr>
<tr>
<td>FDPS: Lifestyle</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DPP: Lifestyle</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRIPOD: Troglitazone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DPP: Troglitazone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DREAM: Rosiglitazone</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Changes in Physical Function & General Health: Intensive Lifestyle (ILS) better than Placebo (PLA) or Metformin (MET)

*p<0.05 (ILS vs. PLA/MET)

Florez H et al. SGIM 2012
Metabolic Syndrome Increases with Age in Zulia-Venezuela and in the US

Diabetes Prevention in Venezuela: Flow Chart of Study Subjects

Step 1: Risk factors questionnaire

Step 2: Evaluation of metabolic syndrome components and oral glucose tolerance test

Step 3: Cardiovascular evaluation

Participants

1159

262 Excluded (22.6%)
- 72 Diabetes (self-report)
- 190 Other diseases/medications

897

755 Excluded (65.1%)
- 62 Diabetes
- 580 Normoglycemia
- 74 Uncontrolled hypertension
- 32 TG>600 mg/dl
- 7 Fracture/other

142

70 intensive lifestyle (ILS)

140

Randomization

70 controls (standard of care)

Florez H et al. AHA Epi 2012
Diabetes Prevention in Venezuela: Control Group - Standard of Care

- Information about the benefits of healthy lifestyle for the reduction of diabetes risk (group sessions of 20-30 min)
- Recommendations were provided specifically on:
  1. Healthy diet: using the food pyramid.
  2. Healthy weight: benefits of 5-7% intentional weight reduction
  3. Physical activity: 30 minutes/ 5 days a week
  4. Eliminate alcohol and tobacco use
  5. Report of adverse events
During 24 weeks ILS participants received group training with modules adapted from the core curriculum proposed by the U.S. Diabetes Prevention Program, such as:

1. Changing lifestyle
2. Watching what you eat
3. Reduce your fat intake
4. Watching your physical activity
5. Increasing physical activity
6. No barriers to exercise
7. Eating at home and outside
8. Problem solving

Florez H et al. AHA Epi 2012
Diabetes Prevention in Venezuela: The ILS Health Coach

REGIONAL SPORT INSTITUTE IN ZULIA STATE
Management of Subjects in the Intensive Lifestyle Group (n=70)

Physical Activity Module
Supervised training (>150 min/week)
Moderate activity and strategies for start and maintenance

Nutritional Module
Food intake and calorie counts

Psychology Module
Motivation and strategies for behavioral changes and stress management

Florez H et al. AHA Epi 2012
Diabetes Prevention in Venezuela: 
Piloto Study in Maracaibo, Zulia

Regional Sport Arenas (IND/ FUNDAIDEM)

Florez H et al. AHA Epi 2012
Diabetes Prevention in Venezuela: Weight reduction by treatment group (Intensive Lifestyle vs. Control)

* \( p<0.00001 \) (ILS vs. Con)

ILS participants adhered to \( \geq 80\% \) of physical activity and nutritional goals (DPP guidelines)

Florez H et al. AHA Epi 2012
Diabetes Prevention in Venezuela: Changes in fasting and postprandial glucose by treatment group (ILS vs. Con)

* * *

Florez H et al. AHA Epi 2012
Diabetes Prevention in Latin America: 2-year improvement in metabolic variables

<table>
<thead>
<tr>
<th>Metabolic Variables</th>
<th>Baseline in controls</th>
<th>Baseline in ILS</th>
<th>2-year in controls</th>
<th>2-year in ILS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting plasma glucose (mg/dl)</td>
<td>103.1 ±7.8</td>
<td>102.4 ±9</td>
<td>100 ±17.4</td>
<td>95 ±14.3 *</td>
</tr>
<tr>
<td>HOMA-insulin resistance</td>
<td>7.9 ± 7.7</td>
<td>8.3 ± 9.4</td>
<td>6.9 ± 5.4</td>
<td>3.5± 2.7***</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>149 ±77.5</td>
<td>148 ±81</td>
<td>130.3 ±24</td>
<td>119.8 ±36*</td>
</tr>
<tr>
<td>HDL-cholesterol (mg/dl)</td>
<td>41.7 ±10.7</td>
<td>41.5 ±10</td>
<td>46.2 ± 4.5</td>
<td>49 ±5.5**</td>
</tr>
</tbody>
</table>

*p<0.05; **p<0.01; ***p<0.0001; ILS, intensive lifestyle intervention; HOMA, homeostasis model assessment; HDL, high density lipoprotein

Florez H et al. AHA Epi 2012
Diabetes Prevention in Venezuela; Changes in C-Reactive Protein by treatment group (ILS vs. Con)

Florez H et al. AHA Epi 2012
Diabetes Prevention in Venezuela; Changes in total and LDL cholesterol by treatment group (ILS vs. Con)

Cholesterol (mg/dl)

*p<0.05 (ILS vs. Con)

Florez H et al. AHA Epi 2012
AHA 2020: Cardiovascular (CV) Health Promotion and Disease Prevention

• Ideal CV health behaviors:
  – Nonsmoking
  – Achieving normal weight (BMI<25 kg/m²)
  – Enough physical activity (150 min/week)
  – Healthy diet: fiber, veggies/fruits, low fat, complex CHO

• Ideal CV health factors:
  – Total cholesterol<200 mg/dl
  – Blood pressure< 120/80 mmHg
  – Fasting blood glucose<100 mg/dl

Global Cardiovascular Health in Venezuelan Men and Women

Age groups (years)

20-29 30-39 40-49 50-59 60-69 70+

Men
Women
Overall

P<0.001 for age
P<0.001 for interaction sex*age

Florez H et al. AHA Epi 2012

Florez H et al. AHA Epi 2012
Global Cardiovascular Health Improves with Lifestyle Intervention in Latino Men and Women

Follow-up (months)

Florez H et al. AHA Epi 2012
Older Adults with Complex Health Status by Age: Health and Retirement Study

Blaum et al, Medical Care 2010: 48;327
Diabetes Challenges in the Aging Population

Modifiers: A1c, blood pressure, lipids, physical activity, treatment

Outcomes: Geriatric syndromes, Disability, Mortality

Complications:
- Macrovascular
- Microvascular

Impairments:
- Cognitive
- Affective
- Neurologic
- Physical function

IR, obesity

Diabetes
Prevalence of Inability to Do Physical Tasks and ADLs/IADLs (NHANES III)

Depression and Glycemic Control ($A_{1c} \geq 8\%$)

- No Depression
  - $N = 47$
  - Mean age: 61.3

- Minimal to Mild
  - $N = 92$
  - Mean age: 56.0

- Moderate to Severe
  - $N = 70$
  - Mean age: 55.7

Depression and Incidence of Adverse Outcomes in Older Adults With Diabetes

Duration and severity of diabetes associated with worse strength per mass

**Diabetes Duration**
(< 6 yrs vs. ≥ 6 yrs)

**Glycemic Control**
(A1c <8% vs. ≥ 8%)

* *P < 0.05 compared with subjects with diabetes < 6 years.*

**Fig. 1.** Leg (A) and arm (B) muscle quality in subjects without diabetes (□), diabetic subjects with duration < 6 years (■), and diabetic subjects with duration ≥ 6 years (■).

**Fig. 2.** Leg (A) and arm (B) muscle quality in subjects without diabetes (□), diabetic subjects with A1C ≤ 8.0% (■), and diabetic subjects with A1C > 8.0% (■).

*Diabetes 55:1813–1818, 2006*
Risk of Hip Fractures with Diabetes: Analysis from 3 Prospective Studies in Community-Dwelling Older Adults

Men

Women

JAMA. 2011;305(21):2184-2192
Healthy Aging Regional Collaborative (HARC)
It helps South Florida older adults to apply evidence-based prevention and management programs.

Enhance Fitness (EF)
An evidence-based exercise program that helps older adults to become more active, energized, and empowered to sustain independent lives.
Peer-Leader Activated Care & Telehealth (PACT): Diabetes Prevention & Management

Older Adults Pre-DM/DM

Better Health Outcomes

Caregivers

Primary Care Providers

Pharmacy/Nutritionist

Specialists

Peer Leaders

Monitoring

Education

Survey

Support Technologies

T-Care Team: Care Coordination
Miami VA GRECC Telehealth-Care Reduces Cardiovascular Risk

Dang S,..., Florez H. Diabetes Technology & Therapeutics 2010
Peer-led and Telehealth Interventions for Diabetes Prevention and Management

PACT Recruitment
Miami VAHS
UM-FIU-HARC network

Random assignment & baseline testing

Peer-led care alone

Telehealth + Peer-led care

Usual care

Outcomes (3, 6, & 12 months)
Weight, BP, A1c, lipids, self-efficacy, QoL, physical function, and health costs
Chronic Disease Epidemiology: Common Pathways

**Immediate Causes**
- Energy Consumption
- Physical Activity
- Metabolic Stress
- Inflammatory Biomarkers
  - Hyperinsulinemia
  - Insulin Resistance

**Underlying Causes**
- Basic Causes
  - Social Structure
  - Urbanization
  - Culture
  - Political Structure
- Education and Self-Management
- Lifestyles
- Resource Availability

**Basic Causes**
- Genetic Factors
- Obesity

**Chronic Disease**
- Cardiovascular Diseases
  - Dyslipidemias
  - Diabetes
  - Hypertension
- Cancer and Autoimmune Disorders
- Fractures and Functional Decline
Genetic risk profile for diabetes: TCF7L2 polymorphisms

Placebo group

Lifestyle group

TT vs. CC genotype: HR=1.81
(95% C.I.: 1.21-2.70)

TT vs. CC genotype: HR=1.15
(95% C.I.: 0.68-1.94)

“Intervention can mitigate the risk conferred by genetic background”
Diabetes Prevention Among Veterans: From MOVE to MVP Health Care:

Pilot in 2005
MOVE!

Diabetes Prevention Among Veterans:
From MOVE to MVP Health Care:

Miami Veterans Affairs Healthcare System

2007 2008 2009 2010 2011

Sep 2008
HARC

Feb 2009
EF Miami

Jun 2009
EF Broward

May 2011
A partnership with Veterans

Miami Million Veterans Program (MVP):
To enroll 20,000 Veterans in South Florida
(~3,000 currently enrolled)
“Diabetes & Healthier Aging” Forecasting?

Health Determinants
- Genetics
- Environment
- Behavior

Generic Pathways
- Oxidative Stress
- Immunology & Inflammation
- Development & Senescence
- Regeneration & Repair
- Hormones & Vitamins

Collaborative for Healthier Aging, Management & Prevention (CHAMP)

MILLER SCHOOL OF MEDICINE
UNIVERSITY OF MIAMI

GRECC
Conclusions and Perspectives

• Diabetes mellitus (DM) has reached epidemic (pandemic) proportions in both developed and developing countries.
• Cardiovascular and hypoglycemic-related ER visits/hospital admissions are major burden in older adults with DM.
• Lifestyle intervention is the most effective strategy to reduce diabetes risk with feasible and innovative approaches underway in Latin America and the US healthcare system.
• Efforts to promote healthier aging in older adults with DM require better prevention and management strategies with collaborative participation of medical and public health teams.
Team Support

- University of Miami (DRI, EDM, Geriatrics, and DEPH)
- VA-GRECC, diabetes team, HPDP, HARC/FIU
- University of Zulia (Clinical Research Institute, INZU-DIABETES)

Project Support

- UM/CTSA
- NIH/NIDDK (DPP/DPPOS, GRADE)
- HHS/NIH (R18-PACT)
- VA-CSP (VADT, MVP)
- PAHO and FONACIT
- IDF-BRIDGES