Diabetes in Older Adults

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Incidence (per 1,000) of major diabetes complications among adults with diabetes, by age, 2009.

Jeffrey B. Halter et al. Diabetes 2014;63:2578-2589
Impaired Glucose Tolerance (Prediabetes)

Undiagnosed Type 2 Diabetes

Diagnosed Type 2 Diabetes

Prevalence of Type 2 Diabetes, Undiagnosed Diabetes, and IGT

Adapted from Harris MI. Consultant 1997;37(Suppl):S9.
One in every two people age 65 and older have diabetes or pre-diabetes.
Why Diabetes Risk Increases With Age?
Type 2 Diabetes in Aging

Insulin Resistance

- β Cell Failure
- Low Physical Act.
- Sarcopenia
- Decreased Insulin Action
- Visceral Adiposity
Effect of Age on Insulin Secretion

- Young
- Older Normal Glucose Tolerant
- Old Impaired Glucose Tolerant

Blood Glucose (mg/dl)

Insulin (mU/ml)
Metabolic Signaling Pathways in Aging

- **Glucose**
  - GLUT4
  - mTOR
  - Ribosome (Synthesis)
  - Proteasome (Breakdown)

- **Insulin**
  - IRS
  - Akt
  - MuRF1
  - Atrogin

- **TLR4**
  - TNF-R

- **Fatty Acids**
  - Lipids

- **Mitochondrial Dysfunction**
  - ROS
  - Ub
  - Ub

- **IKK-NFκB**
Effect of Age on Insulin Sensitivity

Insulin Sensitivity (M)

Young
BMI=23.8

(27 years)

Older
BMI=25.1

(70 years)

Petersen, Science, 2003
Effect of Age on Lipid Content

Magnetic Resonance Spectroscopy

Intramyocellular Lipid Content

EMCL-CH₂
IMCL-CH₂
EMCL-CH₃
IMCL-CH₃
PPM

Young (27 years)
Older (70 years)

Petersen, Science, 2003
Effect of age on Mitochondrial ATP Production

Luciferase assay (ATP synthesis rate)

*P<0.05 vs. older group.
Effect of aerobic exercise on Mitochondrial ATP production in older subjects

- Before exercise
- After exercise

ATP synthesis rate (nmol/mg protein/min)

S+R: Succinate + Rotenone; G+M: Glutamate + Malate; P+M: Pyruvate + Malate

*, P<0.05 vs. older group before exercise.
Factors involved in mitochondrial biogenesis

Modified from Vina et al Adv Drug Del Rev. 2009
LPS Concentration in Aging

Ghosh et al, J Geron (2014)
Intestinal Barrier Dysfunction and Aging

Rera, PNAS (2012)

Intestinal Barrier Dysfunction Predicts Death
How should older adults be treated for diabetes?
Goals of Treatment (Tight Control?)

Consider:

1) Functional Status
2) Life expectancy
3) Cognitive Function
4) Clinical Heterogeneity (prone to complications?)
Does every diabetic person develop (mv) complications?
   No - approximately 20-40%

How long does it take to develop (mv) diabetic complications?
   15 years, on average

How much does the A1c level matter?
   It matters - a lot
How long does it take to develop diabetic complications?
How much does the A1c level matter?

Relationship of HbA₁C to Risk of Microvascular Complications

Diabetes Control and Complications Trial (DCCT)

Kaplan-Meier Survival Curves by Frailty Status

Espinoza, Hazuda (SALSA)
Recommendations (ADA, AGS)

Goals of Treatment (Tight Control?)

- Functional, Cognitively Intact, Significant Life Expectancy:
  - Similar Goals as Younger Person
  - A1c ~ 7%
Goals of Treatment (Tight Control?)

Decreased Function/Cognition, Short Life Expectancy:

- **Glycemic Control can be Relaxed**
- **Avoid Hyperglycemic Complications!**
Antihyperglycemic therapy T2DM (ADA Standards, 2016)

Healthy eating, weight control, increased physical activity, and diabetes education

<table>
<thead>
<tr>
<th>Metformin</th>
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<tbody>
<tr>
<td>high</td>
</tr>
<tr>
<td>low risk</td>
</tr>
<tr>
<td>neutral / loss</td>
</tr>
<tr>
<td>GI / lactic acidosis</td>
</tr>
<tr>
<td>low</td>
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If A1C target not achieved after ~3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference—choice dependent on a variety of patient- and disease-specific factors):

- **Metformin +**
  - **Sulfonylurea**
    - high
    - moderate risk
    - gain
    - hypoglycemia
    - low
  - **Thiazolidinedione**
    - high
    - low risk
    - gain
    - edema, HF, fx
    - low
  - **DPP-4 inhibitor**
    - Intermediate
    - low risk
    - neutral
    - rare
    - high
  - **SGLT2 inhibitor**
    - Intermediate
    - low risk
    - loss
    - GL, dehydration
    - high

If A1C target not achieved after ~3 months of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference—choice dependent on a variety of patient- and disease-specific factors):

- **Metformin +**
  - **Sulfonylurea**
    - high
    - moderate risk
    - gain
    - hypoglycemia
    - low
  - **Thiazolidinedione**
    - high
    - low risk
    - gain
    - edema, HF, fx
    - low
  - **DPP-4 inhibitor**
    - Intermediate
    - low risk
    - neutral
    - rare
    - high
  - **SGLT2 inhibitor**
    - Intermediate
    - low risk
    - loss
    - GL, dehydration
    - high
  - **GLP-1 receptor agonist**
    - highest
    - high risk
    - gain
    - hypoglycemia
    - variable

If A1C target not achieved after ~3 months of triple therapy and patient (1) on oral combination, move to injectables; (2) on GLP-1-RA, add basal insulin; or (3) on optimally titrated basal insulin, add GLP-1-RA or mealtimes insulin. In refractory patients consider adding TZD or SGLT2-i:

- **Metformin +**
  - **Basal insulin +**
  - **Mealtime insulin** or **GLP-1-RA**
Remaining Questions About DM in Older Adults

- Epidemiology of diabetes and complications
- Etiology
- Screening and diagnosis
- Preventative strategies (lifestyle and pharmacological)
- Treatment – goals, target, and interventions
- Clinical trials for prevention and treatment
- DM complications