Individualized Diabetes Treatment for the Elderly

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Extremely Relevant – Baby Boomers are aging!

- ¼ of people ≥ age 65 have diabetes
- ½ of people ≥ 65 have pre-diabetes
Hawaii Seniors
Average Lifespan: 82 years old
In next 20 years 1/3 of Hawaii’s population > 60 years old
Elderly patients with type 2 diabetes at risk for:

- Premature death
- Functional disability
- Accelerated muscle loss
- Stroke

Common geriatric syndromes
- Polypharmacy
- Cognitive impairment

Key Point #1: Individualize Glycemic Targets and Treatment Plans

ONE SIZE DOES NOT FIT ALL

A1C < 7
The elderly population is extremely heterogeneous
Assess multiple domains to set targets for elderly patients.
How do we set glycemic targets?
UK Prospective Diabetes Study (UKPDS)

- **Study design**: 5,102 patients with newly diagnosed Type 2 diabetes
  - Randomized controlled clinical trial
  - Followed for 10 years
  - Intensive vs. conventional therapy

- **Primary aim**: Determine effect of intensive glycemic control on complication rate
Intensive Insulin Therapy Decreases Microvascular Complications in Type 2 Patients

UKPDS=United Kingdom Prospective Diabetes Study

Evidence: High
Long Term Follow Up

- In post-trial monitoring, 3,277 patients were asked to attend annual UKPDS clinics for 5 years.
- Relative risk reductions at 10 years remained for diabetes-related end point (9%, \( p=0.04 \), and microvascular disease 24%, \( p=0.001 \)).
- Clinically relevant post-trial risk reductions emerged over time for myocardial infarction (15%, \( p=0.01 \)) and death from any cause (13%, \( p=0.007 \)).
But...

• UKPDS EXCLUDED patients over the age of 65!
Population - middle age to older patients with type 2 DM - higher risk for CV events than UKPDS - mean age at enrollment 60s - DM 8-11 years

ACCORD Glucose (Action to Control Cardiovascular Risk in Diabetes — Glucose-lowering arm)
National Heart, Lung, and Blood Institute
ACCORD telebriefing prepared remarks; February 6, 2008

• Goal:
  To test whether an intensive strategy that targets HbA$_{1c}$ levels <6.0% reduces the rate of CV events more than a standard strategy that targets an HbA$_{1c}$ of 7.0% to 7.9%

• Population and treatment:
  10,000 patients with type 2 diabetes and either heart disease or two risk factors for heart disease
  Randomly assigned to intensive blood sugar lowering or to standard blood sugar lowering

• Primary outcome:
  A composite of fatal and nonfatal major CV events
ACCORD Trial: Stopped at 3 years

**Death from Any Cause**

22% increase in all-cause mortality in intensive arm

NNH=95

Achieved at 1 year A1c of 6.4% vs. 7.5%


**Evidence: High**
Increase in mortality seen in younger patients < 65 years old

- Older Patients had increase in hypoglycemia
- Increase in medication related side effects
Target A1c 6.0% too tight in elderly
• Goal: Build upon knowledge of UKPDS and evaluate an A1c target of 6.5% improves micro and macrovascular risk

• Patient Population: 11,400 patients, average age 66, type 2 diabetes for average 8 years, history of major micro or macrovascular disease and 1 CV risk factor

A1c 6.3% vs 7.4%
ADVANCE

- No increase in mortality in intensive group
- A1c reduction to 6.5% no significant effect on macrovascular disease
- 20% reduction in diabetic nephropathy
Nuances from ADVANCE

• Large number of patients from Asia
• Used conventional agents (sulfonylurea, metformin, insulin)
• Decreased a1c gradually, stepwise approach over 2 years
• Increase in hypoglycemia in intensive group
What’s the Danger of Intensive Treatment Regimens?

- Hypoglycemia
- Excess mortality for patients with Type 2 diabetes and cardiovascular disease
- Precipitates major vascular events such as MI or CVA
- Weight gain
Glycemic Targets – 3 “Buckets”

**SELECT POPULATION**
- Short duration of diabetes
- Treated with lifestyle or metformin only
- Long life expectancy
- No significant cardiovascular disease

**MOST NON-PREGNANT ADULTS**
- Longer life expectancy
- Minimal complications

**COMORBIDITIES / LIMITED LIFESPAN**
- Severe hypoglycemia
- Limited life expectancy, advanced microvascular complications
- Extensive comorbid conditions, or …
- Longstanding diabetes for which goal is difficult to achieve despite multiple therapies

<table>
<thead>
<tr>
<th>A1C &lt; 6.5</th>
<th>A1C &lt; 7</th>
<th>A1C &lt; 8-9</th>
</tr>
</thead>
<tbody>
<tr>
<td>SELECT POPULATION</td>
<td>MOST NON-PREGNANT ADULTS</td>
<td>COMORBIDITIES / LIMITED LIFESPAN</td>
</tr>
</tbody>
</table>

DCCT

UKPDS
Bucket #1: Healthy Patients with Good Functional Status

- Mrs. Yamashiro is a 68 year female with type 2 diabetes for 8 years.
- PMH: hypertension
- She is on metformin 500 mg bid. She and her husband play tennis daily and she is active in her community
What is her A1c Target?
Healthy Patients with Good Functional Status

Treat similarly to younger patient population

**SELECT POPULATION**
- Short duration of diabetes
- Treated with lifestyle or metformin only
- Long life expectancy
- No significant cardiovascular disease

**MOST NON-PREGNANT ADULTS**
- Longer life expectancy
- Minimal complications

**ADVANCE**

**DCCT**

**UKPDS**
Bucket #2: Patients with Complications and Reduced Functionality

• Mrs. Young is a 73 year old female with history of hypertension, CAD, hyperlipidemia, CKD 4 and type 2 DM for 13 years.

• She lives alone, but has family who comes to help her.

• She is not very physically active and has fallen once this year.
Less Stringent Targets: American Geriatrics Society’s ‘Choosing Wisely’

- Multiple comorbidities
- Life expectancy < 10 years
- ESRD
- CAD

Most trials take 5 years to show microvascular benefit and 10+ years to show macrovascular benefit

- Increase in polypharmacy
- Increase in hypoglycemia
- More complex medication regimens
- Increase mortality
Bucket #3: Frail Elderly

Mrs. Camara is a 89 year female with type 2 diabetes for 26 years
PMH: hypertension, CAD s/p 2 stents, hyperlipidemia, gout, CKD 3, osteoporosis, R hip fracture
She lives in a nursing facility and is not very mobile
Bucket #3: Less Stringent Targets American Geriatrics Society’s ‘Choosing Wisely’

- Care Group 4
- Life expectancy < 2-3 years
- Multiple comorbidities
- Medically fragile
- Severe hypoglycemia

Goal is to avoid short term complications of diabetes
- Dehydration
- Electrolyte disturbances
- HHNK
- Polypharmacy
- Hypoglycemia

Most trials take 5 years to show microvascular benefit and 10+ years to show macrovascular benefit
How to best approach each of our 3 buckets?
Assess multiple domains to set targets for elderly patients

Medical Psychological Social Functional

A1C = ?????
Bucket #1: Healthy Patients with Good Functional Status

- Mrs. Yamashiro is a 68 year female with type 2 diabetes for 8 years.
- PMH: hypertension
- She is on metformin 500 mg bid. She and her husband play tennis daily and she is active in her community.
Mrs. Yamashiro continued

• Her metformin over the next year is increased to 1000 mg bid and she is placed on glipizide 10 mg bid with her A1c at 7.0%
• The next time you see her, her husband brings her in.
• He notes she sprained her ankle playing tennis and became less active
• She spends more time alone at home
• Husband notes that she seems a little more forgetful and sleeping more than usual.
• Her a1c increases to 8.2%
What is the best next step?

• A: Add on basal insulin to the metformin 1000 mg bid
• B: Send her for intensive physical therapy to rehab her sprained ankle
• C: Screen for depression and mild cognitive impairment
• D: Add on liraglutide 1.8 mg SQ daily to help her lose weight
Screening for early detection of mild cognitive impairment or dementia and depression is indicated for adults 65 years of age or older at the initial visit and annually as appropriate.

**MINI MENTAL STATE EXAMINATION (MMSE)**

**Mini Mental State Exam**

- Please name the:
  - Year?
  - Season?
  - Date?
  - Day of Week?
  - Month?
- Orientation to time /5
- Where are we? State?
  - City?
  - Suburb?
  - Hospital?
  - Floor/Ward?
- Orientation to place /5
- “I am going to test your memory” Name 3 objects. Ask them to repeat all 3. 1 point for each object remembered. Repeat until all 3 so that recall can be tested.
- Registration /3
- Serial 7s “please count backwards from 100 in sevens” 93, 86, 79, 72, 65
  - alternatively Spell WORLD backwards D L R O W
- Attention and Calculation /5

**“Please repeat the 3 objects I asked you to remember”**

Recall /3

**“Please name these objects”**

Point to a wristwatch and a pencil

Naming /2

**“Please repeat the following phrase”**

“No ifs, ands or buts”

Repetition /1

**“Please follow this command”**

“Take this paper in your right hand, fold it in half and place it in your lap”

Complex command /3

**Please read and obey the following command CLOSE YOUR EYES**

**“Please write a sentence”**

Must have a noun, verb and make sense

**“Please copy the following drawing”**

24-30 normal range
18-23 moderate cognitive impairment
6-17 marked cognitive impairment

1 point each for the last 3 commands /3

**TOTAL /30**

**PATIENT HEALTH QUESTIONNAIRE - 9**

<table>
<thead>
<tr>
<th>Over the last 2 weeks, how often have you been bothered by any of the following problems?</th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Little interest or pleasure in doing things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Feeling down, depressed, or hopeless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Trouble falling or staying asleep, or sleeping too much</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Feeling tired or having little energy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Poor appetite or overeating</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7. Trouble concentrating on things, such as reading the newspaper or watching television</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>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</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>9. Thoughts that you would be better off dead or of hurting yourself or some way</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

*Note: Each problem is scored 0 = Not at all, 1 = Several days, 2 = More than half the days, 3 = Nearly every day.*

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

<table>
<thead>
<tr>
<th>Not difficult at all</th>
<th>Somewhat difficult</th>
<th>Very difficult</th>
<th>Extremely difficult</th>
</tr>
</thead>
</table>

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Assess Multiple Domains

- Medical
- Psychological
- Social
- Functional
Back to Mrs. Yamashiro

• You screen her for both depression and cognitive impairment
• She has mild cognitive impairment and moderate depression
• She sees psychiatry and is placed on Lexapro 10 mg daily.
How would you best tailor her regimen given the mild cognitive impairment?

• A: Simplify her medications to once daily dosing
• B: Avoid medications that can cause hypoglycemia
• C: Provide clear, simple instructions for self-management
• D: Include her husband in management plans
• Over the next year, she improves!
• Depression lifts on Lexapro
• Medication regimen; Metformin 1000 mg XR and Linagliptin 5 mg daily
• She starts walking 3 x a week with husband
• She develops carpal tunnel, and starts wearing a brace
• A1c 7.3%
• Her husband says he has seen a medication on TV called that helps you urinate out the glucose, and is this appropriate for her?
Assess Multiple Domains
SGLT-2 Inhibitors

• Initial efficacy and safety data in elderly
• Limited Long term data
• Pros; once daily dosing
• Limited hypoglycemia

Elderly: Higher incidence of adverse reactions related to volume depletion and reduced renal function

Caution; UTIs, yeast infections, hypotension, GFR, electrolyte disturbances
Mrs. Yamashiro notes she has gained weight since stopping tennis.

• She has also seen on TV that there is a medication called Victoza that can control your diabetes and help you lose weight
• Is this something she can use?
GLP-1 in Elderly

- Age had no effect on the pharmacokinetics of VICTOZA® based on a pharmacokinetic study in healthy elderly subjects (65 to 83 years) and population pharmacokinetic analyses of patients 18 to 80 years of age.
- Side effects; nausea, vomiting, pancreatitis, c-cell tumors similar to younger patients.
Assess Multiple Domains
Diabetes medications in the Elderly

- Metformin first line if GFR $\geq$ 30. Caution in impaired hepatic function or CHF
- Sulfonylureas
- DPP-IV inhibitors
- GLP-1 agonists
- SGLT2-Inhibitors
You don’t hear from Mrs. Yamashiro for over a year.
She is brought in by her son.
Mr. Yamashiro had a massive MI and passed away 6 months ago.
Mrs. Yamashiro is living alone and has not been exercising or taking her medications. 
Mr. Yamashiro used to help her organize her pills weekly and remind her to take them.
Son notes she has left the stove on several times and cannot handle the bills.

A1c is 9.1%
What is next best step?

• A: Start Lantus insulin and Humalog with meals
• B: Get her social services with meals on wheels
• C: Have her move in with her son
• D: Consider assisted living
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Son notes she has left the stove on several times and cannot handle the bills.

A1c is 9.1%. BP 155/91
Assess Multiple Domains

- Medical
- Psychological
- Social
- Functional
<table>
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<tr>
<th>Functional Healthy Patient</th>
<th>Patient with Multiple Co-Morbidities</th>
<th>Frail Elderly</th>
</tr>
</thead>
<tbody>
<tr>
<td>• BP &lt; 140/80</td>
<td>• BP &lt; 140/80</td>
<td>BP: &lt;150/90 mm Hg</td>
</tr>
<tr>
<td>• Statin unless not tolerated or contraindicated</td>
<td>• Statin unless not tolerated</td>
<td>Lipids: consider potential statin benefit (focus on secondary prevention)</td>
</tr>
</tbody>
</table>
Summarize: Elderly needs EVOLVE over time

- Situations can change rapidly

Medical: GFR, hypoglycemia, polypharmacy
Social: Who cooks, exercise, social and community, death or spouses
Psychological: depression in elderly
Functional: Medications, pens, once daily regimens
Summarize: Set Individualized Treatment Targets

A1C = ?????
Assess multiple domains to set targets and treatment for elderly patients

Medical

Psychological

Social

Functional
Thank You!