Overcoming the challenges of managing chronic diseases in persons with dementia

Management of Diabetes

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Diabetes and Dementia

* What is the effect of diabetes on dementia?
  * Risk of dementia and progress of dementia
  * **Major identified concern is hypoglycaemia**

* What is the effect of dementia on diabetes?
  * Impact on management
    * To reduce the risk of hypoglycaemia
    * To provide a practical regimen in dementia

* How should diabetes be managed in the presence of cognitive impairment/dementia?
  * Treatment goals
  * Treatment selection
Factors affecting dementia and cognitive impairment mediated by diabetes mellitus

Rhee SY Endocrinol Metab 2017; 32: 195-199
Diabetes was associated with

- lower age at dementia diagnosis, OR 0.97 [CI 0.97-0.98]
- male sex, OR 1.41 [1.27-1.55]
- vascular dementia, OR 1.17 [1.01-1.36]
- mixed dementia, OR 1.21 [1.06-1.39]

In diabetes, it was less common for

- dementia with Lewy bodies, OR 0.64 [0.44-0.94]
- Parkinson disease dementia, OR 0.46 [0.28-0.75]
- treatment with antidepressants, OR 0.85 [0.77-0.95]

Patients with diabetes who had Alzheimer disease obtained significantly less treatment with cholinesterase inhibitors (0.78 [0.63-0.95]) and memantine (0.68 [0.54-0.85]).

Risk of hypoglycaemia in older veterans with dementia and cognitive impairment

- Cross-sectional database analysis of veterans, 65 years +, n = 497,900
- Prevalence of combined dementia and cognitive impairment
  - 13.1% for individuals aged 65 to 74
  - 24.2% for those aged 75 and older.
- The proportion of participants taking insulin was higher in those with dementia or cognitive impairment (30%) than in those with neither condition (24%).
- Of all participants taking insulin, more with dementia (26.5%) and cognitive impairment (19.5%) were hypoglycaemic than of those with neither condition (14.4%).
- ORs for hypoglycaemia were 2.42 (95% CI 2.36-2.48) for dementia and 1.72 (95% CI = 1.65-1.79) for cognitive impairment;
- Adjusted ORs for hypoglycaemia were 1.58 (95% CI = 1.53-1.62) for dementia and 1.13 (95% CI = 1.08-1.18) for cognitive impairment.

Do severe episodes of hypoglycemia increase subsequent risk of dementia in older patients with type 2 diabetes?

Evaluation of 16,667 older patients with type 2 diabetes

There was a 2.39% increase in absolute risk of dementia per year of follow-up (95% CI, 1.72%-3.01%) for patients with history of hypoglycaemia, compared those without

At least 1 episode of hypoglycemia was diagnosed in 8.8% and dementia was diagnosed in 11% during follow-up.

Compared with patients with no hypoglycemia, patients with single or multiple episodes had a graded increase in risk of dementia with fully adjusted hazard ratios (HRs):

- 1 episode (HR, 1.26; 95% CI, 1.10-1.49);
- 2 episodes (HR, 1.80; 95% CI, 1.37-2.36);
- 3 or more episodes (HR, 1.94; 95% CI, 1.42-2.64).

This study suggests that hypoglycaemic episodes severe enough to require hospitalization or an ED visit are associated with increased risk of dementia, particularly for patients who have a history of multiple episodes.

Hypoglycaemic episodes and risk of dementia in diabetes mellitus: 7-year follow-up study

- $n = 15,404$ without prior dementia and a mean age of 64.2 years
- 2% of participants had at least one episode of hypoglycaemia over 3 yrs
- Over 7 years 7.2% of patients with diabetes developed dementia.
- The incidence rate of dementia was higher in diabetic subjects with hypoglycaemic episodes
  - With: 29.9 per 1000 person-years (95% CI 22.1–39.2)
  - Without: 11.1 per 1000 person-years (95% CI 10.3–11.8)]
- The RR for dementia in diabetes with vs without hypoglycaemia: 2.76
  - age- and gender-adjusted RR 1.60
- Cox proportional hazards analysis: hypoglycaemia, older age, female gender and insulin use were independent predictors of dementia.

Lin C-H, Sheu W H-H. Journal of Internal Medicine, 2013, 273; 102–110
Kaplan–Meier curves for probability of developing dementia in relation to hypoglycaemia in diabetes

Lin C-H, Sheu W H-H. Journal of Internal Medicine, 2013, 273; 102–110
Prospective population-based, 1997-, aged 70 to 79 years, baseline Modified MMSE scores of 80+, n =793 with diabetes, 12 yrs follow-up

- 7.8% had a hypoglycaemic event, and 18.9% developed dementia.

- Those who experienced a hypoglycaemic event had a 2-fold increased risk for developing dementia compared with those who did not have a hypoglycaemic event: 34.4% vs 17.6%, P < .001
  - multivariate-adjusted HR, 2.1; 95% CI, 1.0–4.4).

- Older adults with DM who developed dementia had a greater risk for having a subsequent hypoglycaemic event compared with participants who did not develop dementia (14.2% vs 6.3%, P < .001;
  - multivariate-adjusted hazard ratio, 3.1; 95% CI, 1.5–6.6).

K-M curves for dementia with hypoglycaemia, and hypoglycaemia with dementia

Health, Aging, and Body Composition Study

There were significant cross-sectional associations between both cognitive impairment and dementia and hypoglycaemia.

Independent risk factors for future health service use for hypoglycaemia included:
- dementia (HR 3.00, 95% CI 1.06-8.48)
- inability to self-manage medications (HR 4.17, 95% CI 1.43-12.13).

Dementia is an important risk factor for hypoglycaemia requiring health service utilisation.

We found no evidence that hypoglycaemia contributes to cognitive impairment in older patients with diabetes.

Hypoglycaemia risk is higher in the patients using insulin (OR 2.17, 95% CI 1.16–4.08, P = 0.015) and lower in patients who were being treated with dipeptidyl peptidase-4 inhibitors (OR 0.47, 95% CI: 0.25–0.89, P = 0.019).

Patients with lower variability in blood glucose had a significantly lower hypoglycaemia risk (OR 0.87, 95% CI: 0.83–0.91, P< 0.0001), and patients with a lower average blood glucose level had a significantly higher risk (OR 1.09, 95% CI: 1.06–1.12, P< 0.0001).

In patients aged ≥ 65 years with type 2 diabetes, higher glucose variability and lower average glucose levels indicate a greater hypoglycaemia risk.

Continuous glucose monitoring reveals hypoglycaemia risk in elderly patients with type 2 diabetes mellitus

Summary of links between diabetes, hypoglycaemia and dementia

- Diabetes and dementia are associated
- More dementia in diabetes with hypoglycaemia
- More hypoglycaemia increases risk of dementia
- Insulin use in dementia is associated with more hypoglycaemia
- Hypoglycaemia in dementia requires more health service use
Diabetes: Management Principles

* render and maintain asymptomatic
* avoid acute complications
  * ketoacidosis, hyperosmolar hyperglycaemic state, hypoglycaemia
* reduce/remove risk of developing chronic complications
* treat and stop advance of established chronic complications if present
* promote psychological well-being and self-care
* promote near-normal lifestyle
# Risk Factor Modification: recommended targets

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diet</strong></td>
<td>Encourage healthy eating</td>
</tr>
<tr>
<td><strong>Body mass index</strong></td>
<td>At least 5-10% weight loss if overweight or obese</td>
</tr>
<tr>
<td><strong>Physical activity</strong></td>
<td>≥ 30 minutes of moderate physical activity on most if not all days</td>
</tr>
<tr>
<td><strong>Smoking</strong></td>
<td>No cigarettes</td>
</tr>
<tr>
<td><strong>Alcohol</strong></td>
<td>≤ 2 standard drinks/day</td>
</tr>
<tr>
<td><strong>Lipids</strong></td>
<td>TC &lt; 4.0 mmol/L, HDL-C ≥ 1.0 mmol/L, LDL-C &lt; 2.0 mmol/L, non-HDL-C &lt; 2.5 mmol/L, TG &lt; 2.0 mmol/L</td>
</tr>
<tr>
<td><strong>Blood pressure</strong></td>
<td>130/80 mmHg</td>
</tr>
<tr>
<td><strong>Waist circumference</strong></td>
<td>≤ 94 cm in men, ≤ 80 cm in women</td>
</tr>
<tr>
<td><strong>HbA1c</strong></td>
<td><strong>Individualise</strong>; generally ≤ 7%, range 6.5-7.5% (≤ 53 mmol/mol, range 48-58 mmol/mol)</td>
</tr>
</tbody>
</table>
2 Australian management algorithm for lowering blood glucose level in people with type 2 diabetes*

Lifestyle measures: diet, exercise, weight control
Determine the individual’s HbA1c target: this will commonly be \( \leq 53 \) mmol/mol (see text and UKPDS\(^1\)). If not at target, move down the algorithm.

First line: Metformin is the usual first-line therapy unless contraindicated or not tolerated
- Metformin
- Sulfonylurea
- DPP-4 inhibitor
- SGLT2 inhibitor
- Insulin
- Acarbose
- TZD

Second line: If metformin was not used at first line, add it now if not contraindicated
Sulfonylureas are the recommended initial agent to add to metformin
If sulfonylureas are contraindicated or not tolerated, another agent is recommended
- Sulfonylurea
- DPP-4 inhibitor
- GLP-1RA
- SGLT2 inhibitor
- Insulin\(^\d\)
- Acarbose
- TZD

Third line: Consider triple oral therapy or addition of GLP-1RA or insulin
- DPP-4 inhibitor
- Sulfonylurea
- GLP-1RA
- Insulin\(^\d\)
- SGLT2 inhibitor
- Acarbose
- TZD

Then:
- If receiving triple oral therapy:
  Switch \( \geq 1 \) oral agent to:
  GLP-1RA or insulin or another oral agent\(^\d\)
  OR
  Change to: premixed or basal insulin
  OR
  If receiving a GLP-1RA:
  Add: premixed or basal insulin
- If receiving insulin:
  Intensify Insulin: basal–bolus insulin or basal plus\(^\d\)

*Gunton et al
MJA 2014; 201: 650-653
Factors influencing choice of glucose-lowering treatment

Include:

- Preventing CV disease and complications
- Achieving sustained and effective glucose reduction over time
- Controlling weight
- Choosing well-tolerated medication
- Minimising the risk of hypoglycaemia
- Considering the effect of age
- Considering the effect of renal dysfunction
- Offering a convenient dosing regimen, reducing the ‘pill burden’
- Choosing PBS-listed medication
- Accounting for the patient’s social function

Individualised strategy for glycaemic control: Set the right target

Patient attitude and expected treatment efforts
Risk potentially associated with hypoglycaemia, and other adverse events
Disease duration
Life expectancy
Important comorbidities
Established, vascular complications
Resources, support system

Matching the Glycaemic Control Target to the Patient Characteristics

<table>
<thead>
<tr>
<th>Target HbA₁c</th>
<th>More Intensive Approach</th>
<th>Standard Approach</th>
<th>Less Intensive Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.0-6.5%</td>
<td></td>
<td>&lt;7%</td>
<td>7.5-8.0%</td>
</tr>
</tbody>
</table>

**Conditioning Factors**

| Patient attitude and expected treatment efforts | Highly motivated, adherent, excellent self-care capabilities | Less motivated, non-adherent, poor self-care capabilities |
| Disease duration | Newly diagnosed | Long-standing |
| Life expectancy | Long | Short |
| Important comorbidities | Absent | Few/mild | Severe |
| Established vascular complications | Absent | Few/mild | Severe |
| Resources, support system | Readily available | | Limited |

Develop a patient-specific approach with agreed realistic targets

Adapted from Inzucchi et al. 2012 Diabetes Care;35:1364-1379.
<table>
<thead>
<tr>
<th>Drug</th>
<th>Causes hypoglycemia?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha-glucosidase inhibitor</td>
<td>No</td>
</tr>
<tr>
<td>Dipeptidyl peptidase-4 (DPP-4) inhibitors</td>
<td>No</td>
</tr>
<tr>
<td>Glucagon-like peptide-1 (GLP-1) agonists</td>
<td>No</td>
</tr>
<tr>
<td>Insulin</td>
<td>Yes (highest risk with regular insulin and NPH insulin)</td>
</tr>
<tr>
<td>Meglitinides</td>
<td>Yes (low risk)</td>
</tr>
<tr>
<td>Metformin</td>
<td>No</td>
</tr>
<tr>
<td>Sodium-glucose linked transporter 2 (SGLT2) inhibitors</td>
<td>No</td>
</tr>
<tr>
<td>Sulfonylureas</td>
<td>Yes (highest risk with glyburide and lower risk with gliclazide)</td>
</tr>
<tr>
<td>Thiazolidinediones (TZDs)</td>
<td>No</td>
</tr>
</tbody>
</table>
Effect of the treatment of Type 2 diabetes mellitus on the development of cognitive impairment and dementia

- Review of randomised controlled trials which compared two or more different treatments for Type 2 diabetes mellitus and in which cognitive function was measured at baseline and after treatment.
- Seven eligible studies were identified but only four provided data we could include in efficacy analyses.
- *We found no good evidence that any specific treatment or treatment strategy for Type 2 diabetes can prevent or delay cognitive impairment.*
- The best available evidence related to the comparison of intensive with standard glycaemic control strategies. Here there was moderate-quality evidence that the strategies do not differ in their effect on global cognitive functioning over 40 to 60 months.

No evidence demonstrates benefits of tight glycemic control for older adults who are frail, have dementia, or have a limited life expectancy.

Individualizing therapy, including glycemic targets, to goals of care and time to benefit is good practice.

A systematic review suggests that deprescribing antihyperglycemic agents is feasible and safe in those with a low hemoglobin A1c level or those taking glyburide (glibenclamide), with monitoring and response to blood glucose levels that risk rising above target, although the quality of evidence was very low.

Farrell B et al  Can Fam Physician 2017;63:832-43
Deprescribing antihyperglycaemic agents in older persons:
Evidence-based clinical practice guideline

- Deprescribing antihyperglycaemic agents
  - lowering doses, switching to a safer medication, or stopping medications.
- Antihyperglycaemic medications known to contribute to hypoglycaemia should be deprescribed in older adults at risk, or in situations where antihyperglycaemic medications might be causing other adverse effects.
- Future research should address
  - optimal glycemic targets
  - optimal deprescribing regimens
  - patient preferences
  - short- and long-term benefits and harms of continuing versus deprescribing antihyperglycaemic medications; and cost effects.

Farrell B et al  Can Fam Physician 2017;63:832-43
Metformin vs sulfonylurea use and risk of dementia in US veterans aged ≥65 years with diabetes

* Retrospective cohort study of 17,200 new users of metformin and 11,440 new users of sulfonylureas.
  * Mean age was 73.5 years, mean HbA1c was 6.8%.
* Over 5 years, 4,906 cases of dementia were diagnosed
* Crude hazard ratio [HR] for any dementia
  * metformin vs sulfonylurea users was 0.67 (95% confidence interval [CI] 0.61-0.73)
* A lower risk of dementia was also seen in the subset of younger veterans:
  * who had HbA1C values ≥7% (HR 0.76; 95% CI 0.63-0.91),
  * had good renal function (HR 0.86; 95% CI 0.76-0.97),
  * and were white (HR 0.87; 95% CI 0.77-0.99).

Orkaby AR et al Neurology 2017; 89: 1877-1885.
The DIMORA Study

* 2258 patients with type 2 diabetes (dementia n = 1138, no dementia n = 1120).
* Patients had a mean age of 82 years, BMI of 25.4, HbA1c of 7.1%
* Severe hypoglycemia was more prevalent in patients with dementia (18%) compared to patients without dementia (8%).
* In patients with dementia, for severe hypoglycaemia
  * rapid- and long-acting insulin analogs were associated with reduced OR 0.333, and OR 0.248, respectively
  * sulphonylureas were associated with increased OR 8.805; and sulphonylurea + metformin OR 6.639

A.M. Abbatecola et al. JAMDA 2015; 16: 349.e7e - 349.e12
Severe Hypoglycemia Is Associated With OHA Treatment Compared With Insulin Analogs

**The DIMORA Study**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Unadjusted OR (95% CI)</th>
<th>P</th>
<th>Model AOD† OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>0.859 (0.565–1.306)</td>
<td>.480</td>
<td>0.678 (0.380–1.210)</td>
<td>.189</td>
</tr>
<tr>
<td>Sulphonylurea</td>
<td>4.931 (3.186–7.630)</td>
<td>&lt;.001</td>
<td>8.805 (4.260–18.201)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Metformin + sulphonylurea</td>
<td>2.931 (1.796–4.782)</td>
<td>&lt;.001</td>
<td>6.639 (3.273–14.710)</td>
<td>.001</td>
</tr>
<tr>
<td>Glinides</td>
<td>0.458 (0.164–1.281)</td>
<td>.137</td>
<td>1.486 (0.401–5.508)</td>
<td>.554</td>
</tr>
</tbody>
</table>

| Insulin rapid              | 0.548 (0.355–0.848)    | .007  | 0.333 (0.184–0.602)    | <.001 |
| Insulin intermediate*      | 1.306 (0.537–3.175)    | .556  | 0.812 (0.211–3.123)    | .762  |
| Insulin long acting        | 0.414 (0.148–1.154)    | .092  | 0.248 (0.070–0.882)    | .031  |

A.M. Abbatecola et al.  JAMDA 2015; 16: 349.e7e - 349.e12
In NH with highly trained expert staff regarding diabetes treatment, the use of rapid insulin analogs may be adjusted according to irregular eating habits often found in patients with dementia.

Additional use with long-acting insulin analogs helps maintain basal glycaemic control.

Our findings suggest that these insulin analogs may be good alternatives for preventing severe hypoglycaemia in patients with dementia in a controlled setting.

A.M. Abbatecola et al. JAMDA 2015; 16: 349.e7e - 349.e12
90 elderly patients with T2DM combined with AD enrolled to participate in this study.

Randomly divided into 3 groups: control group, the strength group, and the mitigation group.

- **control group**: only treated with diet and exercise,
- **strength group**: treated with oral hypoglycemic medications, subcutaneous insulin infusion or continuous infusion by micropump to achieve pre-meal ≤ 7.0 mmol/L, 2 hours postmeal glucose ≤ 12.0 mmol/L and HbA1c ≤ 7.0%
- **mitigation group**: personalized treatment programs were adopted to control the pre-meal blood glucose at ≤ 10.0 mmol/L (within 3 to 6 months) and also to control 2 hours post-meal blood glucose at ≤ 20.0 mmol/L

Average follow-up 3 years

Effect of different blood glucose intervention plans on elderly people with type 2 diabetes mellitus combined with dementia

### Table II. Comparison of occurrence rate of new-onset dementia and progressive rate of dementia.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Number of cases</th>
<th>New-onset dementia</th>
<th>Progressive rate of dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>30</td>
<td>11 (36.7)</td>
<td>10 (33.3)</td>
</tr>
<tr>
<td>Strength group</td>
<td>30</td>
<td>9 (30.0)</td>
<td>8 (26.7)</td>
</tr>
<tr>
<td>Mitigation group</td>
<td>30</td>
<td>3 (10.0)</td>
<td>2 (6.7)</td>
</tr>
<tr>
<td>χ²</td>
<td></td>
<td>6.074</td>
<td>6.686</td>
</tr>
<tr>
<td>p</td>
<td></td>
<td>0.048</td>
<td>0.035</td>
</tr>
</tbody>
</table>

### Table I. Comparison between glucose target rate of diabetes and occurrence rate of diabetes related complications.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Number of cases</th>
<th>Target rate</th>
<th>Hypoglycemia</th>
<th>Diabetic hyperosmolar coma</th>
<th>New-onset target organ injury</th>
<th>Occurrence rate of total complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>30</td>
<td>–</td>
<td>1 (3.3)</td>
<td>10 (33.3)</td>
<td>4 (13.3)</td>
<td>15 (50.0)</td>
</tr>
<tr>
<td>Strength group</td>
<td>30</td>
<td>16 (53.3)</td>
<td>8 (26.7)</td>
<td>4 (13.3)</td>
<td>2 (6.7)</td>
<td>14 (46.7)</td>
</tr>
<tr>
<td>Mitigation group</td>
<td>30</td>
<td>24 (80.0)</td>
<td>1 (3.2)</td>
<td>2 (6.7)</td>
<td>3 (10.0)</td>
<td>6 (20.0)</td>
</tr>
<tr>
<td>χ²</td>
<td></td>
<td>4.800</td>
<td></td>
<td>11.554</td>
<td>0.021</td>
<td>0.033</td>
</tr>
<tr>
<td>p</td>
<td></td>
<td>0.028</td>
<td></td>
<td></td>
<td>0.021</td>
<td>0.033</td>
</tr>
</tbody>
</table>
Summary of risk of hypoglycaemia and dementia with various treatments

- Less hypoglycaemia with metformin than a sulphonylurea

- More hypoglycaemia with insulin

- Less hypoglycaemia with rapid and long acting insulin than intermediate and mixed insulin in nursing home patients

- Less hypoglycaemia with fair glycaemic control than either tight control or minimal control
What works for whom in the management of diabetes in people living with dementia: a realist review

- Involving PLWD in self-management
- Person-centred approaches to care planning
- Developing skills to provide tailored and flexible care
- Regular planned contact
- Family engagement
- Usability of assistive technology

Involving PLWD in self-management

- confidence and a sense of control appeared to be important mechanisms that could lead to increased engagement in self management (SM) activities for PLWD

- supporting service users and carers to become more functional, independent and resilient was preferable to a purely clinical focus on managing or treating medical symptoms

Person-centred approaches to care planning

- PLWDD have two chronic life-limiting conditions with different trajectories.
- Dementia generally has a progressive or stepwise pattern of progression, whereas diabetes may have a more constant course with longer periods in which to adapt.
- The trajectory of each is likely to have an impact on the other.
- Delivering appropriate and sustainable care for PLWDD from early stage to advanced dementia is a difficult clinical enterprise that requires a change from a curative, biomedical strategy to a more person-centred approach where patient priorities are at the forefront.
Developing skills to provide tailored and flexible care

* tailoring advice and support to individual needs and goals for diabetes SM. Clinical guidelines on diabetes recommend that target HbA1c levels be relaxed for older people who are frail or have comorbidities and/or dementia

* For example, a Best Clinical Practice statement recommends that, for PLWD, clinicians should aim to achieve a fasting blood glucose 6–9 mmol/L, range (HbA1c 53–64 mmol/mol; 7–8%)

* Despite this, many older people with diabetes are potentially overtreated

* Because SM support does not fit with a biomedically-focused ethos, it is not embedded in the day-to-day work of primary care
Regular planned contact

- needed in order for HCPs to anticipate transitions and help PLWDD and their family carers to manage changes in function and SM capabilities.
- This is particularly important for PLWD where the dementia may progress in an uneven pattern of decline and where the transition from autonomy to delegation or to caregiver-led management may be particularly difficult.
- Dementia as a comorbidity may challenge a diabetes specialist, and a dementia specialist may lack appropriate diabetes knowledge.
  - Ensuring that all professionals have expertise in diabetes and dementia would be difficult, and a collaborative practice is likely to be necessary for people with both conditions.
- Most care given by GPs, nurses, occupational therapists, psychologists and Certified Diabetes Educators (CDEs).
Family engagement

* There is a great deal of evidence that family members often provide significant SM support for people with diabetes particularly when dementia affects a person’s ability to undertake self-care

* Family carers often feel undervalued or excluded from decision making

* Family carers may be ill prepared to take on responsibility for SM.

* Qualitative studies looking at SM for PLWD and for people with diabetes (not dementia) argue that it is important to involve carers in the development of SM skills alongside the person they care for.
Usability of assistive technology (AT)

* any product or service designed to enable independence for disabled and older people
* AT such as biometric monitoring, medicine management reminders and sensors and alarms to track movement is seen as one way of maintaining autonomy for PLWD
* Technology in itself is unlikely to solve the problem of independent living for older people, particularly for those living with dementia. Technology appears to be most effective when it augments or involves face-to-face contact.

* Improvement in continuous glucose monitoring technology
  * Abbott FreeStyle Libre flash glucose monitoring device
Treatment of diabetes in dementia

* Avoidance of hypoglycaemia
  * Treatment goals should be less stringent
  * Selection of agents with lower hypoglycaemia risk

* Integrated care
  * Patient and carer
  * GP, practice nurse, diabetes educator
  * Geriatrician, neurologist, endocrinologist
Thank you for your attention
### GLUCOSE-LOWERING OPTIONS (NON-INSULIN)

#### RISK OF HYPOGLYCAEMIA

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Risk of hypoglycaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>Low in monotherapy&lt;br&gt;Increased risk when combined with insulin/SU&lt;sup&gt;1,2&lt;/sup&gt;</td>
</tr>
<tr>
<td>SUs</td>
<td>Yes (common)&lt;sup&gt;3,4&lt;/sup&gt;</td>
</tr>
<tr>
<td>SGLT2 Inhibitors</td>
<td>Low in monotherapy&lt;br&gt;Increased risk when combined with insulin/SU&lt;sup&gt;4,5&lt;/sup&gt;</td>
</tr>
<tr>
<td>DPP-4 Inhibitors</td>
<td>Low in monotherapy&lt;br&gt;Increased risk when combined with insulin/SU&lt;sup&gt;5,6&lt;/sup&gt;</td>
</tr>
<tr>
<td>TZDs</td>
<td>Low in monotherapy&lt;br&gt;Increased risk when combined with insulin/SU&lt;sup&gt;1,7&lt;/sup&gt;</td>
</tr>
<tr>
<td>GLP-1 Agonists</td>
<td>Low in monotherapy&lt;br&gt;Increased risk when combined with insulin/SU&lt;sup&gt;1,2&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

- **Use with caution**
- **Likelihood of adverse events**

**References:**

1. Inzucchi SE *et al.*, 2015.
2. Garber AJ *et al.* 2013
3. RACGP Guidelines, 2014-15
5. Thynne *et al.* 2014
6. NPS RADAR February 2013
<table>
<thead>
<tr>
<th>Mode of Action</th>
<th>Key adverse events/side effects</th>
<th>Risk of hypoglycaemia</th>
<th>Effect on weight</th>
<th>Renal impairment (eGFR)</th>
<th>Cardiovascular outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>Lactic acidosis, gastro-intestinal, weight gain</td>
<td>Low in monotherapy, increased risk when combined with insulin/SU</td>
<td>Neutral or slight loss</td>
<td>Stop when &lt;60 (as per PI)</td>
<td>Likely to reduce CV events in the overweight</td>
</tr>
<tr>
<td>SUs</td>
<td>Hypoglycaemia, weight gain</td>
<td>Yes (common)</td>
<td>Gain</td>
<td>Stop when &lt;30</td>
<td>Unclear - possible increase CV risk</td>
</tr>
<tr>
<td>SGLT2 inhibitors</td>
<td>Genital infections, UTI, postural hypotension</td>
<td>Low in monotherapy, increased risk when combined with insulin/SUs</td>
<td>Loss</td>
<td>Stop when &lt;45 for Empagliflozin</td>
<td>No evidence of increased risk</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Stop when &lt;60 for Dapagliflozin</td>
<td>(Trials ongoing)</td>
</tr>
<tr>
<td>DPP-4 inhibitors</td>
<td>Potential risk of pancreatitis</td>
<td>Low in monotherapy, increased risk when combined with insulin/SUs</td>
<td>Neutral</td>
<td>Dose adjustments (except linagliptin)</td>
<td>No evidence of increased risk (CHF signal investigation)</td>
</tr>
<tr>
<td>TZDs</td>
<td>Oedema, CHF, fracture</td>
<td>Low in monotherapy, increased risk when combined with insulin/SU</td>
<td>Gain</td>
<td>No dose adjustment</td>
<td>Increased CHF/Decrease MI</td>
</tr>
<tr>
<td>GLP-1 agonists</td>
<td>Nausea vomiting and potential risk of pancreatitis</td>
<td>Low in monotherapy, increased risk when combined with insulin/SU</td>
<td>Loss</td>
<td>Stop when &lt;30</td>
<td>No evidence of increased risk (trials ongoing)</td>
</tr>
</tbody>
</table>
Figure 1 | Antihyperglycemics Deprescribing Algorithm

Does your elderly (>65 years of age) patient with type 2 diabetes meet one or more of the following criteria:
- At risk of hypoglycemia (e.g., due to advancing age, tight glycemic control, multiple comorbidities, drug interactions, hypoglycemia history or unawareness, impaired renal function, or on sulfonylurea or insulin)
- Experiencing, or at risk of, adverse effects from antihyperglycemic
- Uncertainty of clinical benefit (due to: frailty, dementia or limited life-expectancy)

- Set individualized A1C and blood glucose (BG) targets (otherwise healthy with 10+ years life expectancy, A1C < 7% appropriate; considering advancing age, frailty, comorbidities and time-to-benefit, A1C < 8.5% and BG < 12mmol/L may be acceptable; at end-of-life, BG < 15mmol/L may be acceptable) (good practice recommendation)
- Address potential contributors to hypoglycemia (e.g., not eating, drug interactions such as trimethoprim/sulfamethoxazole and sulfonylurea, recent cessation of drugs causing hyperglycemia – see reverse)

Recommend Deprescribing
• **Reduce dose(s) or stop agent(s)**
  - most likely to contribute to hypoglycemia (e.g. sulfonylurea, insulin; strong recommendation from systematic review and GRADE approach) or other adverse effects (good practice recommendation)

• **Switch to an agent**
  - with lower risk of hypoglycemia (e.g. switch from glyburide to gliclazide or non-sulfonylurea; change NPH or mixed insulin to detemir or glargine insulin to reduce nocturnal hypoglycemia; strong recommendation from systematic review and GRADE approach)

• **Reduce doses**
  - of renally eliminated antihyperglycemics (e.g. metformin, sitagliptin; good practice recommendation) – See guideline for recommended dosing

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**Monitor daily for 1-2 weeks after each change (TZD – up to 12 weeks):**

- For signs of hyperglycemia (excessive thirst or urination, fatigue)
- For signs of hyperglycemia and/or resolution of adverse effects related to antihyperglycemic(s)

Increase frequency of blood glucose monitoring if needed

A1C changes may not be seen for several months

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If hypoglycemia continues and/or adverse effects do not resolve:
- Reduce dose further or try another deprescribing strategy

If symptomatic hyperglycemia or blood glucose exceeds individual target:
- Return to previous dose or consider alternate drug with lower risk of hypoglycemia

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Farrell B et al  *Can Fam Physician* 2017;63:832-43