Update on Diabetes
Canadian Society of Internal Medicine
Oct 11, 2018

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Conflict Disclosures

I have the following conflicts to declare:

- Speaker honoraria from Servier Canada Inc.
Objectives


2. Write an appropriate exercise prescription for a patient living with diabetes.

3. Discuss the role of newer antihyperglycemic therapies in hospital.

4. Describe the role of medical and surgical therapies in managing obesity in diabetes and utilize practical clinical tips when managing a patient with diabetes who undergoes bariatric surgery.

5. Compare medical and surgical approaches to achieving type 2 diabetes remission.
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5. Compare medical and surgical approaches to achieving type 2 diabetes remission.
What’s New?

2018 Clinical Practice Guidelines Committees

The following committee members contributed to the development of the Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada.

Executive Committee

Robyn L. Houlden MD FRCPC
Chair
Professor and Chair
Division of Endocrinology and Metabolism, Department of Medicine, Queen’s University, Kingston, ON

Lori Berard RN CDE
Advisor
Diabetes Educator
Clinical Research Consultant, Winchester, MD

Ron Goldenberg MD FRCPC FACE
Sub-Group Chair, Diagnosis & Classification
Consultant Endocrinologist
North York General Hospital and LMC Diabetes & Endocrinology, Thornhill, ON

Doreen Rabi MD MSc FRCPC
Co-Chair, Methods
Associate Professor
Department of Medicine, Community Health and Epidemiology


What’s New?

• Greater focus on 3 key areas
  1. Reducing complications
  2. Patient safety
     ◆ New section on driving and diabetes
  3. Self-management

• Increased diversity on Expert Committee:
  • Greater representation from allied health/interprofessional stakeholders
  • Involvement of informed people with diabetes
  • Involvement of indigenous authors, health-care providers and organizations
Mr. Sweet is a 54 year old man, who was recently diagnosed with type 2 diabetes 1 year ago. His HbA1C at diagnosis was 8.8%. He is currently managed on metformin 1g BID and empagliflozin 25 mg daily. His past medical history is significant for hypertension, managed with perindopril 4 mg daily. He is otherwise high-functioning. What is your target HbA1C for this patient?

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>A</td>
<td>&lt; 6 %</td>
</tr>
<tr>
<td>B</td>
<td>&lt; 6.5%</td>
</tr>
<tr>
<td>C</td>
<td>&lt; 7 %</td>
</tr>
<tr>
<td>D</td>
<td>&lt; 8 %</td>
</tr>
</tbody>
</table>
### Targets for glycemic control

<table>
<thead>
<tr>
<th>A1C%</th>
<th>Targets</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤6.5</td>
<td>Adults with type 2 diabetes to reduce the risk of CKD and retinopathy if at low risk of hypoglycemia*</td>
</tr>
<tr>
<td>≤7.0</td>
<td><strong>MOST ADULTS WITH TYPE 1 OR TYPE 2 DIABETES</strong></td>
</tr>
<tr>
<td>7.1</td>
<td>Functionally dependent*: <strong>7.1-8.0%</strong></td>
</tr>
<tr>
<td></td>
<td>Recurrent severe hypoglycemia and/or hypoglycemia unawareness: <strong>7.1-8.5%</strong></td>
</tr>
<tr>
<td>8.5</td>
<td>Limited life expectancy: <strong>7.1-8.5%</strong></td>
</tr>
<tr>
<td></td>
<td>Frail elderly and/or with dementia†: <strong>7.1-8.5%</strong></td>
</tr>
<tr>
<td></td>
<td>Avoid higher A1C to minimize risk of symptomatic hyperglycemia and acute and chronic complications</td>
</tr>
</tbody>
</table>

*Functionally dependent* refers to individuals who have limited ability to perform self-care activities.

* * based on class of antihyperglycemic medication(s) utilized and the person’s characteristics

† see Diabetes in Older People chapter, p. S283

End of life: A1C measurement not recommended. Avoid symptomatic hyperglycemia and any hypoglycemia.
Updated Targets for Glycemic Control

ADVANCE

- Randomized 11 000+ patients over 55 with T2DM (mean duration 8 years), microvascular or macrovascular disease and 1 CV risk factor

- Intensive versus standard control

- Significant decrease in incidence of microvascular disease at 8 years with intensive (A1C 6.5%) vs standard control (7.3%)

- Incidence of nephropathy 4.1% in intensive versus 5.2% in standard groups

Updated Targets for Glycemic Control

ACCORD

- Randomized 10,000+ patients (mean age 62) with T2DM (mean duration 10 years) and CVD or multiple risk factors
- Intensive versus standard control (< 6 vs 7-7.9%)
  - Stopped early due to increased CV death at 3.5 years (257 vs 203)
- No difference in CV outcomes overall
- Observational follow-up at median of 8.8 years shows neutral long-term effect on mortality and CV outcomes
- Etiology unclear – increased incidence of severe hypoglycemia (10.5 vs 3.5%) versus difference in medications

Updated Targets for Glycemic Control

Consider if:

- Shorter duration of diabetes
- Can use agents that are less likely to cause hypoglycemia
- At low risk of hypoglycemia

Avoid if:

- Older/frail individuals
- Longer duration of diabetes
- Advanced coronary artery disease (CAD)
- Known history of severe hypoglycemia
Ms. Candy, a 70 year old lady, was recently admitted to hospital with an NSTEMI. She was previously healthy, though she saw her physician infrequently. While in hospital, she was diagnosed with T2DM with an A1C of 9.2%. She was initiated on metformin 1g BID. You are following up with her 2 months later. Her home glucose readings remain above target. She has been attending cardiac rehab. Her BMI is 33kg/m2 and GFR is 52. What agent would you add next to her management?

- Gliclazide MR 30 mg daily
- Sitagliptin 50 mg daily
- Canagliflozin 100 mg daily
- Liraglutide 0.6 mg daily
Blood glucose-lowering therapies (type 2 diabetes)

**At diagnosis of type 2 diabetes**
Start healthy behaviour interventions (nutritional therapy, weight management, physical activity) +/- metformin

<table>
<thead>
<tr>
<th>A1C &lt;1.5% above target</th>
<th>A1C ≥1.5% above target</th>
<th>Symptomatic hyperglycemia and/or metabolic decompensation*</th>
</tr>
</thead>
<tbody>
<tr>
<td>If not at glycemic target within 3 months, Start/Increase metformin</td>
<td>Start <strong>metformin</strong> immediately Consider a second concurrent antihyperglycemic agent</td>
<td>Initiate insulin +/- metformin</td>
</tr>
<tr>
<td>If not at glycemic target</td>
<td></td>
<td>If not at glycemic target</td>
</tr>
</tbody>
</table>

Clinical CVD?

<table>
<thead>
<tr>
<th>Clinical Considerations</th>
<th>Choice of Agent</th>
<th>Add additional antihyperglycemic agent best suited to the individual based on the following:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoidance of hypoglycemia and/or weight gain with adequate glycemic efficacy</td>
<td>DPP-4 inhibitor, GLP-1 receptor agonist or SGLT2 inhibitor</td>
<td></td>
</tr>
<tr>
<td>Other considerations: Reduced eGFR and/or albuminuria Clinical CVD or CV risk factors Degree of hyperglycemia Other comorbidities (CHF, hepatic disease†) Planning pregnancy‡ Cost/coverage Patient preference</td>
<td></td>
<td>See Table below</td>
</tr>
</tbody>
</table>

Start antihyperglycemic agent with demonstrated CV benefit empagliflozin (Grade A, Level 1A) liraglutide (Grade A, Level 1A) canagliflozin 1 (Grade C, Level 2)
If not at glycemic target

Clinical CVD?

YES

Add additional antihyperglycemic agent best suited to the individual based on the following:

**Clinical Considerations**

- Avoidance of hypoglycemia and/or weight gain with adequate glycemic efficacy
- Other considerations:
  - Reduced eGFR and/or albuminuria
  - Clinical CVD or CV risk factors
  - Degree of hyperglycemia
  - Other comorbidities (CHF, hepatic disease†)
  - Planning pregnancy‡
  - Cost/coverage
  - Patient preference

**Choice of Agent**

- DPP-4 inhibitor, GLP-1 receptor agonist or SGLT2 inhibitor

NO

If not at glycemic target

Start antihyperglycemic agent with demonstrated CV benefit empagliflozin (Grade A, Level 1A) liraglutide (Grade A, Level 1A) canagliflozin† † (Grade C, Level 2)
EMPA-REG OUTCOME

- 7,020 patients with T2DM (most > 5 years) and clinical CVD
- Randomized to empagliflozin vs placebo

CV events 10.5% versus 12.1% at median 3.1 years

Hazard ratio, 0.86 (95.02% CI, 0.74–0.99)
P=0.04 for superiority
LEADER

- ~9 300 patients with T2DM (median duration 12.8 years), majority over 50 with at least 1 CV condition
- Randomized to liraglutide or placebo

CV events 13% versus 14.9% at median 3.8 years

Hazard ratio, 0.87 (95% CI, 0.78–0.97)
P<0.001 for noninferiority
P=0.01 for superiority

CANVAS

• 10 000+ patients with T2DM (mean duration 13.5 years), age 30+ AND symptomatic CVD or 50+ AND 2 CV RFs

• Randomized to canagliflozin versus placebo

  • CV events 26.5 vs 31.5 per 1000 pt years at median 2.9 years

  • Increased rate of genital infections (68.8 vs 17.5 per 1000 pt years) – Similar to other trials

    ❖ Increased fracture rate (15.4 vs 11.9 per 1000 pt years)

    ❖ Increased risk of lower extremity amputation (6.3 vs 3.4 per 1000 pt years)
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Department of Medicine, Community Health and Policy
Diabetes and Driving

• “All drivers with diabetes should undergo a medical examination at least every 2 years to assess fitness to drive. Commercial drivers should undergo an assessment at the time of application for a commercial license and as per provincial requirements thereafter.

• People with diabetes should play an active role in assessing their fitness to drive.”
Driving and Diabetes

Reduce Driving Risk

- EDUCATE patients to drive safely with diabetes
  - **Prepare** Keep fast-acting sugar within reach and other snacks nearby
  - **Be Aware** of blood glucose (BG) before driving and every 4 hours during long drives. If BG is below 4 mmol/L, treat
  - **Stop** driving and treat if any symptoms appear
  - **After** treating a low, **wait** until BG is above 5 mmol/L to start driving again. Note: Brain function may not be fully restored until 40 minutes after hypoglycemia is resolved

If a patient is unaware of symptoms of hypoglycemia, he/she must check their BG before driving and every 2 hours while driving, or wear a real-time continuous glucose monitor
Objectives


2. Write an appropriate exercise prescription for a patient living with diabetes.

3. Discuss the role of newer antihyperglycemic therapies in hospital.

4. Describe the role of medical and surgical therapies in managing obesity in diabetes and utilize practical clinical tips when managing a patient with diabetes who undergoes bariatric surgery.

5. Compare medical and surgical approaches to achieving type 2 diabetes remission.
Which of the following activities should be part of your exercise prescription for diabetes?

150 minutes per week of moderate-high intensity aerobic exercise.

Resistance training 2-3 times per week.

Breaking up sedentary time.

Use of pedometers to monitor and increase daily step-count.

All of the above.

None of the above.
Physical Activity and Diabetes

Aerobic exercise:

- Improves A1C in T2DM, especially duration > 150 mins/week
  - Meta-analysis: A1C reduction 0.89% in >150 min group vs 0.36% in < 150 min
  - Higher intensity exercise results in lower A1C than lower intensity
    - Meta-analysis (small): Weighted mean difference in A1C - 0.22%
- Improves CV and overall mortality, lipids, BP, weight, CV fitness, peripheral neuropathy in T1 and T2DM
- Consider aquatic exercise if barriers, such as osteoarthritis

Physical Activity and Diabetes

Interval Training:

- Leads to improvement in CV fitness compared to continuous, moderate-intensity exercise
- Lower A1C in some studies
  - Meta-analysis: A1C↓ 0.31%, weight↓ 1.3kg, FBG ↓0.92mmol/L
- Lower risk of hypoglycemia during activity in T1 diabetics

Physical Activity and Diabetes

Resistance exercise

• Lowers A1C and decreases insulin resistance in type 2 diabetes
  • RCT 2002 – Progressive resistance training over 16 weeks resulted in 1.1% reduction in A1C in older adults
  • Improvements in muscle mass, strength and BMD
• Lower risk of hypoglycemia in T1 diabetics

Can J Diabetes. 2018;42:S1-S325
Physical Activity and Diabetes

Pedometers

- More steps per day associated with lower CV events, all-cause mortality and A1C in T2DM

  - NAVIGATOR trial - cohort study of 9300+ patients
    - Increasing steps by 2000/day associated with 8% reduction in mortality at 6 years
  
  - SMARTER trial – 275 patients randomized to pedometer-based prescription versus standard care
    - A1C 0.38% lower and step count 1200/day higher in intervention group

Physical Activity and Diabetes

Minimizing sedentary time

- Sedentary behaviours associated with increased mortality, A1C, central obesity, BMI and other metabolic risk factors

- Breaking up sitting associated with better glycemic control, insulin sensitivity and postprandial glucose

- Duvivier et al. – small randomized study:
  - Breaking up sitting with frequent light exercise > 24 hour glucose > structured exercise

Can J Diabetes. 2018;42:S1-S32
Recommendations

1. People with diabetes should ideally accumulate a minimum of 150 minutes of moderate-to-vigorous-intensity aerobic exercise each week, spread over at least 3 days of the week, with no more than 2 consecutive days without exercise, to improve glycemic control [Grade B, Level 2, for adults with type 2 diabetes and children with type 1 diabetes]; and to reduce risk of CVD and overall mortality [Grade C, Level 3, for adults with type 1 diabetes and type 2 diabetes].

Can J Diabetes. 2018;42:S1-S32
2. People with diabetes (including elderly people) should **perform resistance exercise at least twice a week and preferably 3 times per week** [Grade B, Level 2] in addition to aerobic exercise [Grade B, Level 2]. Initial instruction and periodic supervision by an exercise specialist are recommended [Grade C, Level 3]

3. In addition to achieving physical activity goals, people with diabetes should **minimize the amount of time spent in sedentary activities** and periodically break up long periods of sitting [Grade C, Level 3]
4. **Interval training** (short periods of vigorous exercise alternating with short recovery periods at low-to-moderate intensity or rest from 30 seconds to 3 minute each) **can be recommended** to people willing and able to perform it to increase gains in cardiorespiratory fitness in type 2 diabetes [Grade B, Level 2] and to reduce risk of hypoglycemia during exercise in type 1 diabetes [Grade C, Level 3]

5. **Step count monitoring** with a pedometer or accelerometer can be considered in combination with physical activity counselling, support and goal-setting **to support and reinforce increased physical activity** [Grade B, Level 2]
Case Study

Mr. Calorie, a 52 year old man, is referred to your Adult Diabetes Program for management of type 2 diabetes. He was diagnosed with diabetes 2 months ago with an A1C of 8.2%. He is presently not on any pharmacotherapy. His BMI is 30 kg/m². He works in insurance at a desk job.

- How would you discuss exercise with this patient?
- What key items would you include in your “exercise prescription?”
- How is exercise best performed?
- What should you consider and assess for prior to recommending moderate-vigorous aerobic exercise in your patient?
Which of the following statements is true?

When poll is active, respond at PollEv.com/csimm2018diab323

Text CSIM2018DIAB323 to 22333 once to join

All patients with type 2 diabetes mellitus should undergo exercise tolerance testing prior to initiation of regular exercise.

Patients with severe peripheral neuropathy should refrain from regular exercise.

Patients with proliferative retinopathy should be treated prior to initiation of vigorous exercise.

All of the above.

None of the above.
Exercise Prescription

- Consider investigating for underlying CAD in symptomatic patients only
- Treat retinopathy prior to initiation of vigorous exercise
- Educate patients with neuropathy about proper foot care
Online Tools

Guidelines
Executive Summary
Full Guidelines
2016 Interim Update
Quick Reference Guide

Key Messages
Screening & Diagnosis
Vascular Protection
Blood Glucose Lowering
Self-Management Education
Team & Organizing Care
Special Populations

For Healthcare Providers
Healthcare Provider Tools
Slides and Videos
Webinars

For Patients
Patient Resources

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Physical Activity Interactive Decision Tool

Healthcare Provider Tool

Complete this tool to help assess your patient's physical ability and level of motivation to start and/or progress through a physical activity program.

When your patient is succeeding at being physically active you can encourage progression through an increase in the duration of physical activity followed by a progression in intensity, provided they are not limited by angina or other medical issues. The recommendations and programs from the use of this tool should be reassessed at regular intervals - every 6 - 12 months.

▼ STEP 1: Pre-Activity Screening

Does your patient currently have symptoms of angina that would limit participation in physical activity (such as chest pain or severe pressure on physical exertion)?

☐ Yes  ☐ No

▼ STEP 2: Physical Activity Level and Participation

Please complete step 1

▼ STEP 3: Physical Activity Program Recommendation

Please complete step 2
Exercise Prescription

• Aerobic Exercise
  - Walk at comfortable pace for 5-15 minutes at a time
  - Increase over 12 weeks to up to 50 minutes of brisk walking per session

• Resistance Exercise
  - Choose 6-8 exercises that target major muscle groups
  - Increase resistance until you can perform 3 sets of 8-12 repetitions for each exercise
Exercise Prescription

Diabetes and Physical Activity

Your Exercise Prescription

Patient Name: ___________________________ Date: ___________________________

As your healthcare provider, I recommend that you follow the physical activity prescription ticked below (choose all that apply):

☐ 1. Increase physical activity in your day and reduce sedentary time. Limit sedentary recreational time to no more than 2 hours per day.

☐ 2. Begin regular aerobic exercise*: _____ minutes _____ times per week. (Goal is to build to 150 minutes per week, but some people may have to start with as little as 5 to 10 minutes per day and build gradually.)

☐ 3. Begin resistance exercise** 2 days per week.

☐ 4. Continue to do regular aerobic exercise* 5 days per week for a minimum of 30 minutes per session.

☐ 5. Continue to do regular resistance exercise** 3 or more days per week.

*Aerobic exercise is continuous exercise such as walking, bicycling or jogging that elevates breathing and heart rate.

**Resistance exercise involves brief repetitive exercises with weights, weight machines, resistance bands or one’s own body weight to build muscle strength.
Smarter Step Count Prescription

<table>
<thead>
<tr>
<th>Health-Care Provider Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suggest step count increments at each clinic visit to reach goal (an increase of 3,000 steps per day above the baseline step count within 1 year).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Steps per day at baseline</th>
<th>Clinic Visit 1 (0 months)</th>
<th>Clinic Visit 2 (3 months)</th>
<th>Clinic Visit 3 (6 months)</th>
<th>Clinic Visit 4 (9 months)</th>
</tr>
</thead>
</table>

Start Date:  
Patient's Name:  
Baseline Step Count:  
Clinic Visit Number:  
Recommended Step Count:  
Start Date for Step Increase:  

Patient Step Count Prescription

<table>
<thead>
<tr>
<th>Today's Date:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient's Name:</td>
</tr>
<tr>
<td>Please try to complete at least ______ steps per day until your next visit.</td>
</tr>
<tr>
<td>Please record your step counts in your log sheets at the end of each day.</td>
</tr>
<tr>
<td>Please bring your log sheets to the next clinic visit which will be in about three months.</td>
</tr>
</tbody>
</table>

Physician's Name:  
Physician's Signature:  

Can J Diabetes. 2018;42:S1-S32
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5. Compare medical and surgical approaches to achieving type 2 diabetes remission.
Mr. Treat is a 68 year old type 2 diabetic, who is being admitted to hospital for an unprovoked pulmonary embolus. He is presently on metformin 1g BID, empagliflozin 25 mg daily and sitagliptin 100 mg daily. His last A1C was 6.3% and he has not been monitoring his glucose regularly at home. He is dyspneic and requiring 2L of oxygen to maintain a saturation > 90. Otherwise, he feels well. GFR is 84. How would you manage his diabetes in hospital?

- Discontinue his regular medications and start a basal-bolus + correction insulin regimen.
- Continue his regular home medications.
- Discontinue his regular medications and start correction insulin.
- Hold metformin. Continue empagliflozin and sitagliptin.
Newer Antihyperglycemic Agents in Hospital

- Provided that their medical conditions, dietary intake and glycemic control are stable, people with diabetes should be maintained on their pre-hospitalization non-insulin antihyperglycemic agents or insulin regimens [Grade D, Consensus]
In-Hospital Management of Diabetes

- Hyperglycemia in hospital contributes to:
  - Increased complications & mortality
  - Longer length of stay

- Targets (if can be achieved safely without hypoglycemia):
  - Non-critically III with DM: 5-8 mmol/L pre-prandial, random < 10 mmol/L
  - Critically III with DM: 6-10 mmol/L

- Insulin (basal-bolus + correction) is cornerstone of therapy

- Newer oral hypoglycemic agents largely unstudied in hospital
Sitagliptin In Hospital

- Pasquel et al.
  - 277 patients with T2DM, ages 18-80
  - Previously diet-controlled, on oral agents or on total daily insulin dose < 0.6u/kg
  - Randomly assigned to basal-bolus versus basal-sitagliptin
  - All other antihyperglycemic agents were discontinued
  - No difference in mean daily blood glucose concentration
  - Limitation: Glucose higher in insulin group than in other trials

SGLT-2 Inhibitors

Modified from: https://www.medscape.org/viewarticle/842673_2
Which of the following adverse effects are most likely to occur when starting or continuing an SGLT2-inhibitor in hospital?

<table>
<thead>
<tr>
<th>Significant hypoglycemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Euglycemic diabetic ketoacidosis</td>
</tr>
<tr>
<td>Volume depletion</td>
</tr>
<tr>
<td>Acute infectious cystitis</td>
</tr>
</tbody>
</table>
Hypoglycemia with SGLT-2 Inhibitors

- Minimal risk of hypoglycemia, as mechanism of action is insulin-independent
  - In EMPA-REG and CANVAS trials, no difference in overall hypoglycemic events or in severe hypoglycemic events
  - Meta-analyses have showed no risk of hypoglycemia associated with use unless given with insulin or an insulin secretagogue
- Monitor for hypoglycemia in hospital if concurrent use of insulin or secretagogue

Diabetic Ketoacidosis with SGLT-2 Inhibitors

- Euglycemic DKA has been described
  - Peters et al. – 13 cases of euglycemic DKA – three cases occurred post-op
  - Erondu et al. – 12 cases DKA out of 17500+ patients on canagliflozin, 1 occurred post-op
  - EMPA-REG – 3% vs 1% in SGLT2 vs placebo groups
  - Recent meta-analysis: no increased risk of DKA in 13000+ patients

Diabetic Ketoacidosis with SGLT-2 Inhibitors

- Risk factors for DKA with SGLT-2 inhibitors:
  - Infection
  - Low carbohydrate diet
  - Reduced calorie intake
  - Reduction or discontinuation of insulin or insulin secretagogues
  - Concurrent diuretic use may exacerbate contraction alkalosis
  - Delay recognition of DKA with SGLT-2 inhibitors

https://www.fda.gov/Drugs/DrugSafety/ucm446845.htm
Renal Impairment and SGLT-2 Inhibitors

- SGLT2 inhibitors are renally dosed and cleared
  - Should be cautious with worsening kidney function
- Reports of AKI, which may be exacerbated in hospital
- Diuretic and BP lowering effects may predispose to hypovolemia and hypotension
  - Significant increase in hypovolemia and osmotic diuresis in CANVAS but not in EMPA-REG
- Caution if concurrent diuretic use

Infection and SGLT-2 Inhibitors

- Increased rates of yeast infections, which may be compounded by factors in hospital

- May also be associated with increased risk of UTI

  - EMPA-REG
    - Genital infections 64 vs 17% in females and 89 vs 25% in males
    - No difference in UTI

  - CANVAS
    - Genital infections 68.8 vs 17.5% in females and 34.9 vs 10.8% in males
    - No difference in UTI

Summary: SGLT2-inhibitors In Hospital

- May be safe to continue or initiate in stable patients
- Potential for hypoglycemia in patients on insulin or insulin secretagogue
- Risk of DKA is small, but may be additional risk factors in hospital
  - Assess for DKA if unexplained AGMA, nausea or vomiting
- Withhold SGLT2-inhibitors if:
  - Risk of AKI, volume depletion or hypotension
  - High risk of genital infections
  - Poor oral intake
Objectives


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3. Discuss the role of newer antihyperglycemic therapies in hospital.

4. Describe the role of medical and surgical therapies in managing obesity in diabetes and utilize practical clinical tips when managing a patient with diabetes who undergoes bariatric surgery.

5. Compare medical and surgical approaches to achieving type 2 diabetes remission.
Obesity – Medical Management

1. For people with overweight or obesity who have or are at risk for diabetes, an **interprofessional weight management program is recommended** to prevent weight gain and improve CV risk factors (Grade A, Level 1A)

2. Weight management medication may be considered in people with diabetes and overweight or obesity to promote weight loss and improved glycemic control (Grade A, Level 1A)

3. In adults with type 2 diabetes and overweight and obesity, the **effect of antihyperglycemic agents on body weight** should be considered when selecting pharmacotherapy (Grade D)
Ms. Glycemia is a 48 year old type 2 diabetic with an A1C of 8.4%. She is presently on metformin 1g BID. Her BMI is 34kg/m2 and she continues to struggle with weight loss. She has been participating in a structured exercise program and dietary intervention offered by your chronic disease management clinic. She has lost about 3 lbs in the past 2 months. What would you do next to manage her diabetes?

Add gliclazide MR 60 mg daily.

Add liraglutide 0.6 mg daily.

Add empagliflozin 10 mg daily.

Refer for bariatric surgery.
## Obesity – Medical Management

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Effect on Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGLT2 Inhibitor</td>
<td>↓</td>
</tr>
<tr>
<td>GLP-1 Agonist</td>
<td>↓</td>
</tr>
<tr>
<td>Orlistat</td>
<td>↓</td>
</tr>
<tr>
<td>DPP4 Inhibitor</td>
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<tr>
<td>Metformin</td>
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<tr>
<td>Meglitinide</td>
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<tr>
<td>Thiazolidinediones</td>
<td>↑</td>
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</tbody>
</table>
Obesity – Medical Management

• Consider pharmacotherapy if BMI >= 27kg/m² AND unsuccessful with lifestyle therapy

• Two drugs approved for weight management in Canada
  
  • Orlistat and Liraglutide

  • Improve glycemic control and facilitate weight loss, especially in combination with lifestyle changes

• Delay progression to type 2 diabetes if pre-diabetes

• GI side effects are barrier with orlistat
Obesity – Bariatric Surgery

- Consider if BMI $\geq 40\text{kg/m}^2$ OR $35-39.9\text{kg/m}^2$ with comorbidities and unable to achieve weight loss with lifestyle
  - Roux-en-Y gastric bypass (RYGB) vs sleeve gastrectomy vs biliopancreatic diversion (BPD)

- Mingrone $et$ $al.$ (2012)
  - 60 patients ages 30-60 with BMI $> 35$ and type 2 diabetes (duration $> 5$ years, A1C $> 7\%$)
  - Randomized to conventional medical therapy vs RYGB vs BPD
  - At 2 years, A1C $= 7.69\pm 0.57\%$ in medical-therapy group, $6.35\pm 1.42\%$ in RYGB and $4.95\pm 0.49\%$ in BPD
Bariatric Surgery: Post-op

- Increased risk of hypoglycemia given low caloric intake
- Also, potential for remission of DM
- Consider following:
  - Discontinue insulin secretagogues & adjust insulin doses postoperatively (Grade D)
  - Continue metformin and incretin-based agents until demonstrate prolonged resolution of diabetes (Grade D)
  - Encourage self-monitoring of blood glucose post-op to confirm normalization of glycemic targets
  - Use insulin in hospital to achieve glycemic targets (basal-bolus + correction) (Grade D)

Objectives


2. Write an appropriate exercise prescription for a patient living with diabetes.

3. Discuss the role of newer antihyperglycemic therapies in hospital.

4. Describe the role of medical and surgical therapies in managing obesity in diabetes and utilize practical clinical tips when managing a patient with diabetes who undergoes bariatric surgery.

5. Compare medical and surgical approaches to achieving type 2 diabetes remission.
Do you discuss management options to promote remission of diabetes with your patients?

Yes

No
Remission of Diabetes – Mediterranean Diet

- Esposito *et al.* (2014)
  - 215 patients, overweight (mean BMI 29kg/m2), middle-aged (mean age 52)
  - Randomized to low carb Mediterranean diet versus low fat diet
  - Remission rates higher in Mediterranean diet (A1C < 6.5%)
    - 14.7% versus 4.1% at 1 year
    - 5% versus 0% at 6 years

Remission of Diabetes – Intensive Lifestyle Intervention

- LOOK AHEAD trial
  - 5100+ patients, ages 45-76 with type 2 diabetes
  - Randomized to intensive lifestyle intervention (ILI) versus standard care/education
    - ILI: 1200-1800 calorie diet + 175 minutes of physical activity per week
    - Remission rates higher in intensive lifestyle intervention group (A1C < 6.5%)
      - 11.5% versus 2% at 1 year
      - 7.3% versus 2% at 4 years

Remission of Diabetes – Caloric Restriction

• Lean et al. (2017)
  • 306 patients ages 20-65 with type 2 diabetes (diagnosed within past 6 years) and BMI 27-45 kg/m²
  • Randomized to intensive, ~800 calorie diet, with discontinuation of meds versus standard care
  • At 12 months, diabetes remission (A1C < 6.5% x 2 months) achieved in 46% of intervention group versus 4% of control group
  • 86% of patients who lost >15kg achieved remission

Remission of Diabetes – Caloric Restriction

A

Fisher’s exact p<0.0001

Proportion achieving ≥35kg weight loss at 12 months (%)

Control group 0%
Intervention group 24%

B

Odds ratio 19.7, 95% CI 7.8–49.8; p<0.0001

Proportion achieving remission at 12 months (%)

Control group 4%
Intervention group 46%

C

Odds ratio per kg weight loss 1.32, 95% CI 1.23–1.41; p<0.0001

86%

Remission of Diabetes – Bariatric Surgery

- Mingrone et al. (2012)
  - 60 patients ages 30-60 with BMI > 35 and type 2 diabetes (duration > 5 years, A1C > 7%)
  - Randomized to conventional medical therapy vs RYGB vs BPD
  - At 2 years, diabetes remission (A1C < 6.5%, FBG < 5.6mmol/L) occurred in:
    - No patients in medical therapy group
    - 75% of RYGB group
    - 95% of BPD group

Key Messages

• New clinical practice guidelines offer stronger recommendations for lower glycemic targets and a new algorithm for pharmacotherapy

• Consider exercise prescriptions to promote physical activity in diabetics

• SGLT2 inhibitors may be used cautiously in hospital

• Consider a multifaceted approach to manage obesity in diabetics, including non-pharmacologic, pharmacologic and surgical options

• Remission of diabetes is possible…
Objectives


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5. Compare medical and surgical approaches to achieving type 2 diabetes remission.
References/Resources


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