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Farrell B, Black CD, Thompson W, McCarthy L, Rojas-Fernandez C, Lochnan H, Shamji S, Welch V, Bouchard M, Upshur R. 2016. Evidence-based clinical practice guideline for deprescribing antihyperglycemics. Unpublished manuscript.



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## Antihyperglycemics and Hypoglycemia Risk

Drug	Causes hypoglycemia?
Alpha-glucosidase inhibitor	No
Dipeptidyl peptidase-4 (DPP-4) inhibitors	No
Glucagon-like peptide-1 (GLP-1) agonists	No
Insulin	Yes (highest risk with regular insulin and NPH insulin)
Meglitinides	Yes (low risk)
Metformin	No
Sodium-glucose linked transporter 2 (SGLT2) inhibitors	No
Sulfonylureas	Yes (highest risk with glyburide and lower risk with glimepiride)
Thiazolidinediones (TZDs)	No

## Drugs affecting glycemic control

- Drugs reported to cause hyperglycemia (when these drugs stopped, can result in hypoglycemia from antihyperglycemic drugs) e.g. quinolones (especially ciprofloxacin), beta-blockers (except carvedilol), thiazides, atypical antipsychotics (especially olanzapine and clozapine), corticosteroids, calcineurin inhibitors (such as cyclosporine, sirolimus, tacrolimus), protease inhibitors
- Drugs that interact with antihyperglycemics (e.g. trimethoprim/sulfamethoxazole with sulfonylureas)
- Drugs reported to cause hypoglycemia (e.g. alcohol, MAOIs, salicylates, quinolones, quinine, beta-blockers, ACEIs, pentamidine)

## Engaging patients and caregivers

- Some older adults prefer less intensive therapy, especially if burdensome or increases risk of hypoglycemia
- Patients and/or caregivers may be more likely to engage in discussion about changing targets or considering deprescribing if they understand the rationale:
  - Risks of hypoglycemia and other side effects
  - Risks of tight glucose control (no benefit and possible harm with A1C < 6%)
  - Time to benefit of tight glucose control
  - Reduced certainty about benefit of treatment with frailty, dementia or at end-of-life
- Goals of care: avoid hyperglycemic symptoms (thirst, dehydration, frequency, falls, fatigue, renal insufficiency) and prevent complications (5-10 years of treatment needed)
- Many countries agree on less aggressive treatment of diabetes in older persons
- Reviewing options for deprescribing, as well as the planned process for monitoring and thresholds for returning to previous doses will help engage patients and caregivers

## Hypoglycemia information for patients and caregivers

- Older frail adults are at higher risk of hypoglycemia
- There is a greater risk of hypoglycemia with tight control
- Symptoms of hypoglycemia include: sweating, tachycardia, tremor BUT older patients may not typically have these
- Cognitive or physical impairments may limit older patient's ability to respond to hypoglycemia symptoms
- Some drugs can mask the symptoms of hypoglycemia (e.g. beta blockers)
- Harms of hypoglycemia may be severe and include: impaired cognitive and physical function, falls and fractures, seizures, emergency room visits and hospitalizations

## Tapering advice

- Set blood glucose & A1C targets, plus thresholds for returning to previous dose, restarting a drug or maintaining a dose
- Develop tapering plan with patient/caregiver (no evidence for one best tapering approach; can stop oral antihyperglycemics, switch drugs, or lower doses gradually e.g. changes every 1-4 weeks, to the minimum dose available prior to discontinuation, or simply deplete patient's supply)
- Doses may be increased or medication restarted any time if blood glucose persists above individual target (12-15 mmol/L) or symptomatic hyperglycemia returns

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