Quarterly Medication Review Deprescribing Focus

LONG TERM CARE

Hypertension Management

October to December 2022

Background

- The key benefit of treating high blood pressure is to reduce the risk of cardiovascular events (e.g. MI and stroke) from occurring.[2] However, it is unclear whether the cardiovascular benefits of reduced blood pressure extends to the frail older population.
- The LTC population is often excluded from trials that assess the benefits of antihypertensive treatment or involve treating to specific blood pressure targets.[3]
- Significant side effects and potential harms are associated with antihypertensive medications.[2]
- Hypertension management and blood pressure targets require an individualized approach, taking into consideration the resident's comorbidities, degree of frailty, goals of care, and the potential risk of harms with treatment.[4]

! For the quarterly medication reviews from October to December 2022, reassess all residents on antihypertensive medications to determine whether they are candidates for deprescribing.

- Review the resident's blood pressure trend over the past three months and determine an individualized blood pressure target for the resident:
  - ◊ Systolic blood pressure of 150 mmHg or less may be an appropriate target for many LTC residents (*see Figure 1, page 3*). Lower blood pressure targets may be appropriate for residents who are younger or have a longer life expectancy than the average LTC resident.
  - ◊ Individualize the blood pressure target based on the resident's goals of care, comorbidities, frailty, and the risk of harms and adverse effects associated with treatment.
- Consider the following reasons to support deprescribing antihypertensives (e.g. decreasing the dose or discontinuing an antihypertensive):
  - ◊ Resident is experiencing adverse effects due to antihypertensive medications (*see page 6, Table 2 Antihypertensive Adverse Events*).
  - ◊ Resident has orthostatic hypotension and/or history of falls or is at risk of falls.
  - ◊ There has been changes in their renal function that require adjustment of the antihypertensive dose.
  - ◊ Resident's goals of care have changed and/or the resident/family's preference is for comfort over active treatment.
- For residents taking multiple antihypertensives, identify if any are being used to treat comorbidities other than hypertension. Begin with medications being solely used for blood pressure lowering effects or antihypertensive medications not recommended for use in the older population.
- Determine whether the medication needs to be tapered off slowly to avoid rebound hypertension or other adverse effects.
- When discontinuing or decreasing the dose of antihypertensives, regular blood pressure monitoring is recommended.
  - ◊ Measure the resident's blood pressure 1-2 times per week for four weeks after discontinuing or decreasing the dose of the antihypertensive medication, then reassess.

QMR Contents:

Attachments included with QMR:

- Price Comparison of Commonly Prescribed Antihypertensive Medications in Manitoba 2022 → Cardiovascular Agents

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Blood Pressure Targets — Guidelines and Trials

- There are conflicting recommendations in the guidelines regarding blood pressure (BP) targets in older adults, and very limited guidance specific to frail older adults and those in residing in long term care (LTC) facilities. Trials have had conflicting findings in terms of the benefit of intensive blood pressure lowering in older individuals.
- **HYVET**[7] trial showed cardiovascular benefit when treating to a targeted SBP of less than 150 mmHg compared to no treatment for people 80 years and older.
- **SPRINT**[8] trial compared an intensive targeted SBP of less than 120 mmHg to targets of less than 140 mmHg in people with high cardiovascular risk including those 75 years; more cardiovascular benefit with a SBP of less than 120 mmHg shown.
- While the HYVET[7] and SPRINT[8] trials showed that older adults with hypertension benefited from blood pressure reduction regardless of age and baseline frailty, these trials excluded institutionalized individuals and individuals requiring nursing care.
- In both trials, less than 30% of the participants were identified as being frail.[9] It is uncertain whether the results of these trials can be generalized to individuals residing in LTC.

Guideline	Recommendations
Hypertension Canada Guidelines	• 2020 guidelines for individuals with high cardiovascular risk, including those 75 years and older, the goal is to target to BP less than 120/80 mmHg[5]. However it is noted in the guidelines that intensive blood pressure lowering cannot be generalized to institutionalized patients due to lack of evidence in this population. • Recommendations specific to frailty and advanced age have not been made since the 2016 guidelines. In the 2016 guidelines, a target SBP of less than 150 mmHg for those 80 years and older was recommended.[6] • In 2017, recommendations for advanced age and frailty were removed based on the results of the HYVET[7] and SPRINT[8] trials.
NICE Guidelines[10]	BP targets of less than 150/90 mmHg in those 80 years and older and less than 140/90 mmHg for those under 80 years old
2017 ACC/AHA Guidelines[11]	Target systolic BP for noninstitutionalized, ambulatory, community-living adults 65 years of age and older while highlighting that "in the very old, frailty and higher risk of medication side effects complicate treatment. Additional knowledge of the effects of antihypertensive treatment for patients with dementia and patients who reside in long-term-care facility settings is needed."
AHA Hypertension Management in Older and Frail Older Patients[3]	Target SBP of 130-150 mmHg as a safety range for older adults with loss of function and autonomy for activities of daily living, and limited life expectancy. (*see Figure 1 on page 3*)
American College of Physicians and the American Academy of Family Physicians[12]	Target SBP less than 150 mmHg in those 60 years and older, while considering a target SBP less than 140 mmHg in those with history of stroke or transient ischemic attack or others at high cardiovascular risk.
2018 ESC/ESH Guidelines[13]	Target of 130-139/80 mmHg and avoid treating to a SBP of less than 130 mmHg in those 65 years and older.
2020 International Society of Hypertension[14]	Target of less than 140/90 mmHg in patients 65 years and older and to "consider an individualized BP target in the context of frailty, independence, and likely tolerability of treatment."
Geri-RxFiles[15]	"Consider a less aggressive, more expansive BP target (140-159/90mmHg) in older adults at risk for adverse events, with limited life expectancy, and for those in whom aggressive pursuit of treatment targets does not align with their goals of care"

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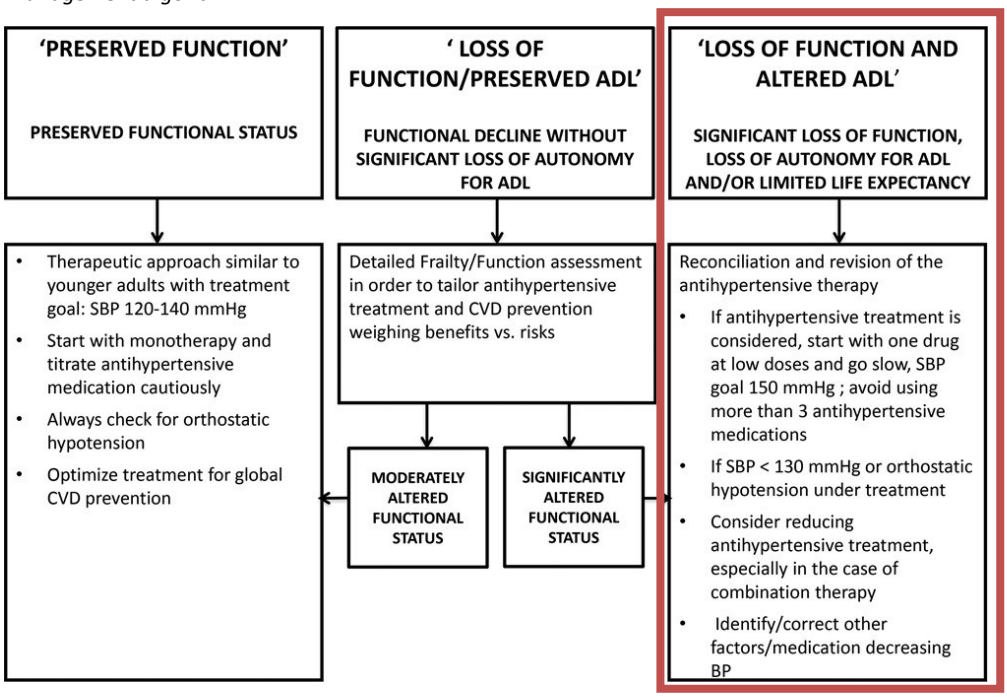
Blood Pressure Targets — Guidelines and Trials continued...

- **PARTAGE study**[17] was a longitudinal study assessing all-cause mortality in nursing home residents over 80 years of age with a SBP less than 130 mmHg taking two or more antihypertensives compared to all other participants
  - ◊ There was a higher risk of mortality in those with SBP less than 130 mmHg and taking two or more antihypertensives – unadjusted hazard ratio = 1.81 (95% CI 1.36-2.41), adjusted hazard ratio = 1.78 (95% CI 1.34-2.37), both P < 0.001
  - ◊ Those with low blood pressure and multiple medications had a more frequent history of cardiovascular disease which may also have contributed to observed increased risk of mortality

Blood Pressure Target Recommendations

- Since there is very limited guidance on blood pressure targets in frail older adults and for those residing in long term care, individualization of targets is required.
- Blood pressure targets in LTC should be selected based on comorbidities, frailty, resident/family preference and goals of care, adverse events associated with treatment, fall risk, life expectancy, and quality of life.
- **Systolic blood pressure of 150 mmHg or less is an appropriate target for many LTC residents** (*see Figure 1 Hypertension management algorithm*)
- Lower blood pressure targets may be appropriate for residents who are younger or have a longer life expectancy than the average LTC resident.

Figure 1. Hypertension management algorithm[3]



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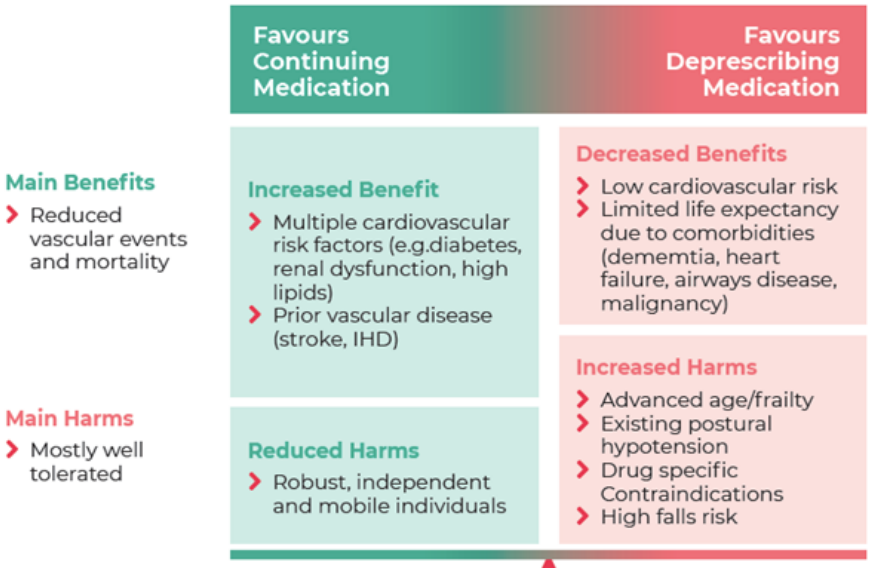
Goals of Care for LTC Residents with Hypertension

- Individualize BP goals based on resident-specific factors such as frailty and life expectancy due to comorbidities
- Consider resident/family values and preferences for goals of care
- Assess if the benefits of treatment outweigh the harms associated with treatment (*see Figure 2 Benefits and harms of antihypertensives*[22])
- Prevent potential adverse events of medications (*see page 6, Table 2 Antihypertensive Adverse Events*)
- Prevent exacerbation of other comorbidities (e.g. heart failure, airways diseases)
- Prevent orthostatic hypotension and risk of falls and modify treatment if either are occurring
- For older individuals with uncomplicated hypertension and no other compelling indications, utilize medications that are considered first line treatments (*see Table 1 First Line Agents for Uncomplicated Hypertension With No Other Compelling Indications*[5]

Table 1. First Line Agents for Uncomplicated Hypertension With No Other Compelling Indications[5,15]

Diastolic hypertension with or without systolic hypertension	• Thiazide/thiazide-like diuretics (e.g. hydrochlorothiazide, chlorthalidone and indapamide) • Chlorthalidone and indapamide have better evidence for reduction of cardiovascular morbidity and mortality in older adults • ACE Inhibitors (ACEi) (although not recommended as monotherapy for black individuals) • Angiotensin Receptor Blockers (ARBs) • Long acting calcium channel blockers (CCBs)
Isolated systolic hypertension (ISH)**	• Thiazide/thiazide-like diuretics • Angiotensin Receptor Blockers (ARBs) • Long acting dihydropyridine CCBs (e.g. nifedipine, amlodipine, felodipine) **While ISH is more common in older people, ISH treatment recommendations are based on studies that did not include frail elderly patients*

Figure 2. Benefits and harms of antihypertensives[22]



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Rationale for Deprescribing Antihypertensives

- **Changing goals of care for resident or harms of treatment outweighs the benefits**
  - ◊ Resident/family preference to reduce or stop active treatment and prioritize quality of life or minimize treatment burden.
  - ◊ Harms of treatment outweigh benefit (*see page 4, Figure 2: Benefits and harms of antihypertensives*)[22]
- **Adverse events**
  - ◊ To help improve quality of life, deprescribing may be warranted when residents are experiencing side effects that could be caused by antihypertensives.
  - ◊ Refer to *Table 2: Antihypertensive Adverse Events*[3] (page 6) for potential side effects associated with antihypertensives.
- **Orthostatic hypotension and fall risk**
  - ◊ Older adults are at risk of orthostatic hypotension due to age-related changes to the baroreceptor compensatory mechanisms when standing as well as other changes to the autonomic nervous system.[18]
  - ◊ Antihypertensives can further contribute to the risk of orthostatic hypotension.[15]
  - ◊ Orthostatic hypotension increases the risk for syncope, falls with subsequent hospitalization, and functional impairment. Orthostatic hypotension also increases the risk of cardiovascular and non-cardiovascular mortality[3]
  - ◊ Per ISMP, cardiac medications are among the top medication groups associated with falls or increased risk of falls.[19]
- **Pharmacokinetic and pharmacodynamic changes with aging**
  - ◊ Renal function: Decline in renal function with increasing age may support deprescribing certain antihypertensives for either efficacy or safety reasons.
    - ⇒ Thiazide diuretics are less effective if creatinine clearance is below 30 mL/min[15]
    - ⇒ Dose adjustments are required for ACEi and ARBs with reduced renal function.
  - ◊ Age-related changes to the renin-angiotensin system can increase the risk of fluid imbalance, electrolyte abnormalities, and chronic kidney disease, all of which may warrant adjustments to antihypertensive medications.[20]
    - ⇒ Hyponatremia or hypokalemia can occur with thiazide diuretics, hyperkalemia with ACEi/ARBs.
- **Polypharmacy and frequent medication pass times**
  - ◊ As many LTC residents are on multiple antihypertensive agents, these medications can contribute to high overall pill burden and nursing workload during medication passes.
  - ◊ Polypharmacy has been associated with increased risk of adverse drug events, drug interactions, functional decline, and falls.[21]
- **Resident is taking a medications not considered a first line medication for hypertension in older adults**
  - ◊ For more information on determining appropriateness of antihypertensives in older individuals, refer to BEERS Criteria, START/STOPP Tool, MedStopper
  - ◊ Examples of agents not recommended as first line monotherapy in older adults if no other compelling indications:[15]
    - ⇒ Beta blockers in those 60 years and older - could increase the risk of fatigue, cognitive impairment, confusion
    - ⇒ Furosemide - could increase the risk of orthostatic hypotension, electrolyte imbalances, gout
    - ⇒ Alpha blockers (e.g. terazosin, doxazosin, prazosin) - could increase the risk of syncope and falls, risk of heart failure and stroke
- **To prevent or reduce incidence of prescribing cascades**
  - ◊ Prescribing cascades occur when a medication is prescribed, then the patient experiences an adverse effect of that medication, then another medication is prescribed to address the adverse effect.[4]
  - ◊ Examples: amlodipine → peripheral edema → diuretic; NSAID analgesic → hypertension → antihypertensive
  - ◊ Refer to: *Therapeutics Letter (Jul-Aug 2022) Reducing prescribing cascades*
- **Switching to lower cost alternatives within the same medication class**
  - ◊ Refer to: *Price Comparison of Commonly Prescribed Medications in Manitoba* (attached)

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Table 2. Antihypertensive Adverse Events[3,24,25]

Thiazide/Thiazide-Like Diuretics **Examples**: hydrochlorothiazide Indapamide chlorthalidone	**ACE Inhibitors (ACEi)** **Examples:** ramipril lisinopril perindopril enalapril	**Angiotensin Receptor Blockers (ARBs)** **Examples:** candesartan irbesartan losartan telmisartan valsartan	**Calcium Channel Blockers (CCBs)** **Examples**: Dihydropyridine (DPH) : nifedipine, amlodipine, felodipine Non-dihydropyridine (non-DHP): verapamil, diltiazem	**Beta blockers** **Examples:** metoprolol bisoprolol atenolol propranolol
• Hypokalemia • Hyponatremia • Hypomagnesemia • Hyperuricemia, gout • Hyperglycemia • Lipid disturbances • Rash • Photosensitivity reaction • Dehydration/volume depletion	• Dry cough • Hyperkalemia • Renal impairment • Rash • Angioedema • Fatigue • Headache	• Hyperkalemia • Renal impairment • Rash • Angioedema (less than with ACE inhibitors) • Fatigue • Headache	• Peripheral edema • Headache • Flushing (especially with DHP) • Heart failure (with non-DHP) • Tachycardia (with DHP) • Bradycardia (with non-DHP) • Constipation (especially with verapamil) • Gingival hyperplasia	• Fatigue • Dizziness • Postural hypotension • Bradycardia • Bronchospasm • Peripheral vasoconstriction

Evidence for Deprescribing Antihypertensives

OPTIMISE Trial[16]

- Randomized clinical trial comparing medication reduction to usual care for short-term blood pressure control in those 80 years or older taking 2 or more antihypertensives.
- **Medication reduction (stopping one medication) was non-inferior to usual care (continuing both medications) in maintaining blood pressure below 150 mmHg over 12 weeks—adjusted relative risk 0.98 (97.5% 1-sided confidence interval [CI] 0.92 to infinity)**.
- Mean change in systolic BP was 3.4 mmHg higher in the medication reduction group compared to usual care (95% CI 1.1-5.8 mmHg).

COSMOS Study[23]

- Randomized controlled trial where patients 65 years and older in Norwegian nursing homes were randomized to systematic medication review or usual care.
- Deprescribing of antihypertensives was significantly higher in the intervention group.
- **Intervention group had an increase in systolic blood pressure with deprescribing of antihypertensives (from baseline 128 +/- 19.5 mmHg to 143 +/- 25.5 mmHg at 4 months), although blood pressure was back to baseline values by 9 months (mean 134 mmHg).**
- Higher number of hospitalizations in control group at 4 and 9 months

Recommendations for Deprescribing Antihypertensives

- For residents taking more than one antihypertensive, determine which one(s) would be suitable for deprescribing. Give consideration to:
  - ◊ Medications requiring more than once a day dosing
  - ◊ Medications contributing to adverse effects
  - ◊ Medications being used for uncomplicated hypertension that are not first line choices for older individuals
  - ◊ High cost medications that could be switched to lower cost alternatives within the same medication class. Refer to: *Price Comparison of Commonly Prescribed Medications in Manitoba* (attached)

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Recommendations for Deprescribing Antihypertensives continued...

- Assess if the antihypertensive is being used for indications other than blood pressure control
  - ◊ Deprescribing agents that are being used for other indications may cause worsening of those conditions[10]
  - ◊ For example:[15,22]
    - ⇒ Beta blockers being used for heart failure, atrial fibrillation, or coronary artery disease
    - ⇒ ACEi being used for heart failure, diabetes + kidney disease, or secondary prevention of stroke or MI
    - ⇒ Alpha blockers being used for benign prostatic hypertrophy
- Consider whether the goal is to decrease the dose or to discontinue completely. Assess if tapering is required based on the class of medication, current dose, blood pressure, and if the resident is currently experiencing or is at risk of harms.
  - ◊ Certain antihypertensives must be tapered to reduce the risk of withdrawal syndromes.[26]
    - ⇒ Abrupt cessation of clonidine is associated with acute rebound hypertension.[26]
    - ⇒ Withdrawal of beta blockers can result in rebound hypertension, tachycardia, arrhythmia, angina, and MI[26,27]
  - ◊ A general tapering recommendation for beta blockers is to decrease the dose by 25-50% every 1-2 weeks[28]
  - ◊ Withdrawal effects of other classes (ACEi/ARBs, CCBs, thiazides) include exacerbation of the underlying conditions[27]

Monitoring of Blood Pressure

- Discontinuation of antihypertensives may result in:
  - ◊ Asymptomatic increase in BP to pre-treatment BP levels
  - ◊ Symptomatic increase in BPs. BPs may become higher than pre-treatment levels.[26] Symptoms of hypertension may include headaches, blurred vision, chest pain, palpitations, dizziness, fatigue, difficulty breathing
  - ◊ Acute symptomatic rebound hypertension
- Measure the resident's blood pressure 1-2 times per week for four weeks after discontinuing or decreasing the dose of the antihypertensive medication, then reassess. Weekly reassessment by the prescriber is recommended if tapering off clonidine or a beta-blocker to assess for rebound hypertension.

Nursing tip: Document the position of the resident when measuring blood pressure (e.g., sitting, laying down, standing). Assess for orthostatic hypotension regularly.

- If blood pressure trends show a rise above the resident's individualized target and/or the resident becomes symptomatic:
  - ◊ Increase the antihypertensive dose to the previous dose, or restart the antihypertensive if it was completely stopped. Restart either at the previous dose or at a lower dose, depending on how far above target the resident's blood pressure is.
  - ◊ Continue routine BP monitoring and reassess whether medications need to be added back, the dose increased further, or if there is the opportunity for further deprescribing.
  - ◊ If restarting an antihypertensive or increasing the dose, the resident should be monitored regularly for orthostatic hypotension.

Assessing Orthostatic Hypotension[15]

- Intermittently assess residents on antihypertensives for orthostatic hypotension
- Have resident sit for 1-2 minutes or lie down for 5 minutes and measure blood pressure and heart rate
- Have resident stand and measure blood pressure and heart rate after 1 minute and again after 3 minutes of standing
- **Orthostatic hypotension = systolic BP decrease by more than 20 mmHg or diastolic BP decrease by more than 10 mmHg within 3 minutes of standing**
- Also assess for symptoms of orthostatic hypotension including dizziness, light-headedness, weakness, fatigue, etc.

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