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Promoting higher blood pressure targets for frail older adults: A consensus guideline from Canada

ABSTRACT

The authors, who are members of the Dalhousie Academic Detailing Service and the Palliative and Therapeutic Harmonization program, recommend that antihypertensive treatment be less intense in elderly patients who are frail. This paper reviews their recommendations and the evidence behind them.

KEY POINTS

For frail elderly patients, consider starting treatment if the systolic blood pressure is 160 mm Hg or higher.

An appropriate target in this population is a seated systolic pressure between 140 and 160 mm Hg, as long as there is no orthostatic drop to less than 140 mm Hg upon standing from a lying position and treatment does not adversely affect quality of life.

The blood pressure target does not need to be lower if the patient has diabetes. If the patient is severely frail and has a short life expectancy, a systolic target of 160 to 190 mm Hg may be reasonable.

If the systolic pressure is below 140 mm Hg, antihypertensive medications can be reduced as long as they are not indicated for other conditions.

In general, one should prescribe no more than two antihypertensive medications.

FRAIL OLDER ADULTS deserve guidelines that take frailty into account while assessing the potential benefit and risks of treatment.

Specifically, our group—the Dalhousie Academic Detailing Service (ADS) and the Palliative and Therapeutic Harmonization (PATH) program—recommends that physicians strive to achieve more liberal treatment targets for elderly frail patients who have high blood pressure,¹ as evidence does not support an aggressive approach in the frail elderly and the potential exists for harm.

This article reviews the evidence and reasoning that were used to develop and promote a guideline for drug treatment of hypertension in frail older adults. Our recommendations differ from other guidelines in that they focus as much on stopping or decreasing therapy as on starting or increasing it.

■ FRAILTY INCREASES THE RISK OF ADVERSE EFFECTS

The word *frail*, applied to older adults, describes those who have complex medical illnesses severe enough to compromise their ability to live independently.² Many have multiple coexisting medical problems for which they take numerous drugs, in addition to dementia, impaired mobility, compromised functional

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How we developed the guideline

To improve awareness of frailty when making treatment decisions and to develop specific recommendations for treating hypertension in the frail elderly, two groups came together—PATH^{27,28} and Dalhousie ADS.²⁹

The Palliative and Therapeutic Harmonization program

The PATH program^{27,28} aims to help health professionals, patients, and families consider frailty when making treatment decisions. In a series of three steps, patients referred to PATH undergo a comprehensive assessment of frailty and health status (step 1), receive information about the findings of the assessment (step 2), and engage in a discussion about treatment options (step 3). The goal is to empower patients or families to develop care plans that consider the impact of frailty and preserve quality of life.³⁰

We believe the program reduces inappropriate care. In a cohort of 150 individuals participating in the PATH program,²⁷ 71 frail patients were initially scheduled to undergo 77 procedures such as surgery, invasive tests, or hemodialysis. After completing the PATH program, patients or their substitute decision-makers declined 75% of these procedures. In conjunction with other groups, PATH is developing evidence-informed, frailty-specific guidelines for common health conditions.

The Dalhousie Academic Detailing Service

The ADS^{29,31} operates through the Office of Continuing Professional Development at Dalhousie University and is funded by the Nova Scotia Department of Health and Wellness, which does not influence its content. It develops evidence-based educational messages about the treatment of common medical conditions. The messages are then disseminated to family physicians and other health professionals throughout Nova Scotia in one-on-one or small-group sessions.

Guideline committee

The guideline committee consisted of members of the Dalhousie ADS and PATH programs and other health professionals with expertise in drug treatment or frailty. In total, it included two family physicians, two internist geriatricians, and four pharmacists, who achieved 100% consensus in developing the guideline.

ability, or a history of falling.

Frailty denotes vulnerability; it increases the risk of adverse effects from medical and surgical procedures,³ complicates drug therapy,⁴ prolongs hospital length of stay,⁵ leads to functional and cognitive decline,⁶ increases the risk of institutionalization,⁷ and reduces life expectancy⁸—all of which affect the benefit and harm of medical treatments.

Guidelines for treating hypertension^{9–11} now acknowledge that little evidence exists to support starting treatment for systolic blood pressure between 140 and 160 mm Hg or aim-

ing for a target of less than 140 mm Hg for “very old” adults, commonly defined as over the age of 80. New guidelines loosen the treatment targets for the very old, but they do not specify targets for the frail and do not describe how to recognize or measure frailty.

RECOGNIZING AND MEASURING FRAILTY

A number of tools are available to recognize and measure frailty.¹²

The Fried frailty assessment¹³ has five items:

- Unintentional weight loss
- Self-reported exhaustion
- Weakness in grip
- Slow walking speed
- Low physical activity and energy expenditure.

People are deemed frail if they have three or more of these five. However, experts disagree about whether this system is too sensitive¹⁴ or not sensitive enough.^{15,16}

The FRAIL questionnaire¹⁷ also has five items:

- Fatigue
- Resistance (inability to climb stairs)
- Ambulation (inability to walk 1 city block)
- Illness (more than 5 major illnesses)
- Weight loss.

People are deemed frail if they have at least three of these five items, and “prefrail” if they have two.

These and other tools are limited by being dichotomous: they classify people as being either frail or not frail^{18–20} but do not define the spectrum of frailty.

Other frailty assessments such as the Frailty Index²¹ identify frailty based on the number of accumulated health deficits but take a long time to complete, making them difficult to use in busy clinical settings.^{22–24}

The Clinical Frailty Scale⁷ is a validated scale that categorizes frailty based on physical and functional indicators of health, such as cognition, function, and mobility, with scores that range from 1 (very fit) to 9 (terminally ill).^{7,12}

The Frailty Assessment for Care-planning Tool (FACT) uses scaling compatible with the Clinical Frailty Scale but has been developed for use as a practical and interpretable frailty screening tool for nonexperts (**TABLE 1**). The FACT assesses cognition, mobility, function, and the social situation, using a

TABLE 1

Frailty Assessment for Care-planning Tool (FACT)

Score	Mobility	Social situation	Function	Cognition
1	Very fit, exercises regularly (among fittest for age)	In charge of organizing social events	Still working at high-level job or hobby	Recalls 3 of 3 items, has no subjective cognitive complaints, and regularly performs high-level cognitive tasks
2	Fit, active occasionally (seasonally)	Socializes weekly and would have a caregiver if needed	No impairment (ie, still does everything on own)	Recalls 2 or 3 items, has no subjective cognitive complaints
3	Not regularly active beyond routine walking	Socializes weekly and might have a caregiver if needed	Subjective impairment (ie, does everything on own, but finds things more difficult)	Recalls 2 or 3 items, has subjective complaints, but family is not concerned about memory
4 (vulnerable)	Starting to slow down, and often tired during the day	Socializes less than weekly and might have a caregiver if needed	Not dependent on others but symptoms often limit activities	Recalls 0 or 1 item but can recall current events, OR Recalls 2 or 3 items and can recall current events, but clock-drawing is abnormal
5 (mild)	Walking slower and regularly uses (or needs to use) a cane or walker	Socializes rarely and might have a caregiver if needed, or might not have a caregiver	Needs help with some instrumental acts of daily living (IADLs) (eg, someone else does finances or housework)	Vague or incorrect recall of current events, but can recall name of current US president
6 (moderate)	Needs help of another person when going up or down stairs, walking on uneven ground, or getting in or out of bath, OR Has fallen more than once in the past 6 months, excluding slip on ice	Mostly housebound and might have a caregiver if needed	Needs cueing with basic activities of daily living (BADLs) such as dressing (eg, help choosing what to wear)	Incorrect recall of name of current US president, can recall names of children or spouse
7 (severe)	Always needs help when moving around, OR Unable to propel self in manual wheelchair	Housebound and isolated, with caregiver stress or no caregiver available	Needs hands-on help with BADLs (eg, bathing, toileting, dressing)	Vague or incorrect recall of names of children or spouse
8 (very severe)	Bed-bound, unable to participate in transfers	Unable to participate in any social exchange, even when visited	Dependent for all aspects of daily life	Limited language skills with fewer than 10 words verbalized
9	Terminally ill with a life expectancy of 6 months or less, regardless of function, cognition, or mobility status			

For each column, the assessor indicates the patient's baseline status. Information about mobility, the social situation, and function should come from a collateral source (family or caregiver). For details about how to complete the FACT cognitive assessment, please see PATHclinic.ca—Guidelines and Resources. The FACT or Clinical Frailty Scale score is the highest number in any column.

COMPATIBLE WITH ROCKWOOD K, SONG X, MACKNIGHT C, ET AL. A GLOBAL CLINICAL MEASURE OF FITNESS AND FRAILTY IN ELDERLY PEOPLE. CMAJ 2005; 173:489–495 AND REISBERG B, FERRIS SH. BRIEF COGNITIVE RATING SCALE (BCRS). PSYCHOPHARMACOL BULL 1988; 24:629–636.

TABLE 2

Results of antihypertensive therapy in elderly patients

Outcome	Event rate		ARR (ARI)	RRR (RRI)	NNT for 4.5 years	95% CI
	Placebo	Drug				
Elderly (≥ age 60)						
Total mortality rate	15%	14%	1.1% ^a	10%	91	53–333
Cardiovascular mortality and morbidity	21%	14%	4.3% ^a	18%	23	16–42
Fatal and nonfatal stroke	7.1%	4.2%	1.9% ^a	44%	53	42–77
Coronary heart disease mortality and morbidity	4.8%	3.7%	0.9%	21%	111	67–250
Very elderly (≥ age 80)					NNT for 2.2 years	
Total mortality rate	16%	19%	(2%) ^{a,b}	(20%) ^b	NS	
Cardiovascular mortality and morbidity	14%	10%	2.8% ^a	25%	36	23–71
Fatal and nonfatal stroke	7.9%	4.6%	1.8% ^a	44%	56	36–125
Coronary heart disease mortality and morbidity	3.5%	3.4%	0.3% ^a	14%	NS	

^a Results calculated by Dalhousie Academic Detailing Service from data provided in publication using the meta-analysis program Comprehensive Meta-analysis. ARR values are calculated by doing meta-analysis of ARRs from all studies and not from subtracting event rates in drug group from placebo group. NNTs are calculated from ARRs in the table.

^b The event rate in drug group is higher than in placebo group, so values are absolute and relative risk increase.

Total mortality means deaths from all causes; cardiovascular morbidity and mortality includes coronary heart disease plus fatal and nonfatal stroke, plus aneurysm, congestive heart failure, and transient ischemic attack; coronary heart disease morbidity and mortality includes fatal and nonfatal myocardial infarction and sudden or rapid cardiac death; fatal and nonfatal stroke is reported separately.

ARI = absolute risk increase; ARR = absolute risk reduction; CI = confidence interval; NNT = number needed to treat; NS = not statistically significant; RRI = relative risk increase; RRR = relative risk reduction

DATA FROM MUSINI VM, TEJANI AM, BASSETT K, WRIGHT JM. PHARMACOTHERAPY FOR HYPERTENSION IN THE ELDERLY. COCHRANE DATABASE SYST REV 2009; CD000028.

combination of caregiver report and objective measures. To assess cognition, a health care professional uses items from the Mini-Cog²⁵ (ie, the ability to draw an analog clock face and then recall three unrelated items following the clock-drawing test) and the memory axis of the Brief Cognitive Rating Scale²⁶ (ie, the ability to recall current events, the current US president, and the names of children or spouse). Mobility, function, and social circumstance scores are assigned according to the caregiver report of the patient's baseline status.

The FACT can be completed in busy clinical settings. Once a caregiver is identified, it takes about 5 minutes to complete.

Our guideline^{27–31} is intended for those with a score of 7 or more on the Clinical Frailty Scale or FACT,^{7,12} a score we chose because it describes people who are severely frail with shortened life expectancy.⁸ At this level, people need help with all instrumental activities of daily living (eg, handling finances, medication management, household chores, and shopping) as well as with basic activities of daily living such as bathing or dressing.

REVIEWING THE LIMITED EVIDENCE

We found no studies that addressed the risks and benefits of treating hypertension in frail older adults; therefore, we concentrated on studies that enrolled individuals who were chronologi-

TABLE 3

Systolic blood pressure achieved in studies in the elderly

Study	No. of patients	Duration (years)	Systolic blood pressure achieved (mm Hg)			Benefit
			Control	Active	Difference	
Drug treatment trials						
EWPHE ³⁴	840	4.6	172	150	22	Yes
CW ³⁵	884	4.4	180	162	18	Yes
SHEP ³⁶	4,736	4.5	170	143	27	Yes
STOP ³⁷	1,627	2.1	186	167	19	Yes
MRC ³⁸	4,396	5.8	165	156	9	Yes
Syst-Eur ³⁹	4,695	2.0	161	151	10	Yes
Syst-China ⁴⁰	2,394	3.0	160	151	9	Yes
SCOPE ⁴¹	4,937	3.7	148	145	3	Partial ^a
HYVET ⁴⁴	3,845	2.1	159	144	15	Yes
Treat-to-target trials						
JATOS ⁴²	4,418	2.0	146	136	10	No
VALISH ⁴³	3,079	3.7	142	137	5	No

^a Significant benefits of more active treatment were limited to some secondary end points.

CW = Coope and Warrender; EWPHE = European Working Party on High Blood Pressure in the Elderly; HYVET = Hypertension in the Very Elderly Trial; JATOS = Japanese Trial to Assess Optimal Systolic Blood Pressure in Elderly Hypertensive Patients; MRC = Medical Research Council; SCOPE = Study on Cognition and Prognosis in the Elderly; SHEP = Systolic Hypertension in the Elderly Program; STOP = Swedish Trial in Old Patients with Hypertension; Syst-China = Systolic Hypertension in China; Syst-Eur = Systolic Hypertension in Europe; VALISH = Valsartan in Elderly Isolated Systolic Hypertension

Lacking studies of frail elderly, we looked at studies in individuals who were chronologically old but not frail

cally old but not frail. We reviewed prominent guidelines,^{9–11,32,33} the evidence base for these guidelines,^{34–44} and Cochrane reviews.^{45,46} A detailed description of the evidence used to build our recommendation can be found online.³¹

When we deliberated on treatment targets, we reviewed evidence from two types of randomized controlled trials⁴⁷:

Drug treatment trials randomize patients to different treatments, such as placebo versus a drug or one drug compared with another drug. Patients in different treatment groups may achieve different blood pressures and clinical outcomes, and this information is then used to define optimal targets. However, it may be difficult to determine if the benefit came from lowering blood pressure or from

some other effect of the drug, which can be independent of blood pressure lowering.

Treat-to-target trials randomize patients to different blood pressure goals, but the groups are treated with the same or similar drugs. Therefore, any identified benefit can be attributed to the differences in blood pressure rather than the medications used. Compared with a drug treatment trial, this type of trial provides stronger evidence about optimal targets.

We also considered the characteristics of frailty, the dilemma of polypharmacy, and the relevance of the available scientific evidence to those who are frail.

Drug treatment trials

A Cochrane review⁴⁵ of 15 studies with approximately 24,000 elderly participants found

**After age 80,
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that treating hypertension decreased the rates of cardiovascular morbidity and mortality as well as fatal and nonfatal stroke in the “elderly” (defined as age ≥ 60) and “very elderly” (age ≥ 80). However, in the very elderly, all-cause mortality rates were not statistically significantly different with treatment compared with placebo. The mean duration of treatment was 4.5 years in the elderly and 2.2 years in the very elderly (TABLE 2). Of importance, all the trials enrolled only those individuals whose systolic blood pressure was at least 160 mm Hg at baseline.

None of the studies were treat-to-target trials—patients were assigned either active medication or placebo. Thus, these trials provide evidence of benefit for treating hypertension in the elderly and very elderly but do not identify the optimal target. All of the drug treatment trials showed benefit, but none achieved a systolic pressure lower than 140 mm Hg with active treatment (TABLE 3). Therefore, these studies do not support a systolic target of less than 140 mm Hg in the elderly.

Treat-to-target trials: JATOS and VALISH

The Japanese Trial to Assess Optimal Systolic Blood Pressure in Elderly Hypertensive Patients (JATOS)⁴² and the Valsartan in Elderly Isolated Systolic Hypertension (VALISH) study⁴³ each enrolled more than 3,000 people age 65 or older (mean age approximately 75). Patients were randomized to either a strict systolic target of less than 140 mm Hg or a higher (more permissive) target of 140 to 160 mm Hg in JATOS and 140 to 149 mm Hg in VALISH.

In both trials, the group with strict targets achieved a systolic pressure of approximately 136 mm Hg, while the group with higher blood pressure targets achieved a systolic pressure of 146 mm Hg in JATOS and 142 mm Hg in VALISH. Despite these differences, there was no statistically significant difference in the primary outcome.

Thus, treat-to-target studies also fail to support a systolic target of less than 140 mm Hg in the elderly, although it is important to recognize the limitations of the studies. Approximately 15% of the participants had cardiovascular disease, so the applicability of the findings to patients with target-organ damage is uncertain. In addition, there were fewer ef-

ficacy outcome events than expected, which suggests that the studies were underpowered.

When to start drug treatment

In each of the drug treatment and treat-to-target trials, the inclusion criterion for study entry was a systolic blood pressure above 160 mm Hg, with a mean blood pressure at entry into the drug treatment trials of 182/95 mm Hg.⁴⁶ Thus, data support starting treatment if the systolic blood pressure is above 160 mm Hg, but not lower.

Notably, in all but one study,⁴⁶ at least two-thirds of the participants took no more than two antihypertensive medications. Since adverse events become more common as the number of medications increases, the benefit of adding a third drug to lower blood pressure is uncertain.

Evidence in the ‘very elderly’: HYVET

With the exception of the Hypertension in the Very Elderly Trial (HYVET),⁴⁴ the mean age of elderly patients in the reported studies was between 67 and 76.

HYVET patients were age 80 and older (mean age 84) and were randomized to receive either indapamide (with or without perindopril) or placebo. The trial was stopped early at 2 years because the mortality rate was lower in the treatment group (10.1%) than in the placebo group (12.3%) (number needed to treat 46, 95% confidence interval 24–637, $P = .02$). There was no significant difference in the primary outcome of fatal and nonfatal stroke.

Notably, trials that are stopped early may overestimate treatment benefit.⁴⁸

Evidence in frail older adults

While the above studies provide some information about managing hypertension in the elderly, the participants were generally healthy. HYVET⁴⁴ specifically excluded those with a standing systolic blood pressure of less than 140 mm Hg and enrolled few patients with orthostasis (7.9% in the placebo group and 8.8% in the treatment group), a condition commonly associated with frailty. As such, these studies may be less relevant to the frail elderly, who are at higher risk of adverse drug events and have competing risks for morbidity and mortality.

Observational studies, in fact, raise ques-

tions about whether tight blood pressure control improves clinical outcomes for the very elderly. In the Leiden 85-plus study, lower systolic blood pressure was associated with lower cognitive scores, worse functional ability,^{49,50} and a higher mortality rate⁵¹ compared with higher systolic pressure, although it is uncertain whether these outcomes were indicative of underlying disease that could result in lower blood pressure or an effect of blood pressure-lowering.

The National Health and Nutrition Examination Survey⁵² found an association between blood pressure and mortality rate that varied by walking speed. For slower walkers (based on the 6-minute walk test), higher systolic pressures were not associated with a higher risk of death, suggesting that when older adults are frail (as indicated by their slow walking speed) they are less likely to benefit from aggressive treatment of hypertension.

People at high risk because of stroke

Because the evidence is limited, it is even more difficult to judge whether lowering blood pressure below 140 mm Hg is beneficial for frail patients who have a history of stroke, compared with the possibility that medications will cause adverse effects such as weakness, orthostasis, and falls. When reviewing the evidence to answer this question, we especially looked at outcomes that affect quality of life, such as nonfatal stroke leading to disability. In contrast, because the frail elderly have competing causes of mortality, we could not assume that a mortality benefit shown in nonfrail populations could be applied to frail populations.

The **PROGRESS trial** (Perindopril Protection Against Recurrent Stroke Study)⁵³ was in patients with a history of stroke or transient ischemic attack and a mean age of 64, who were treated with either perindopril (with or without indapamide) or placebo.

At almost 4 years, the rate of disabling stroke was 2.7% in the treatment group and 4.3% in the placebo group, a relative risk reduction of 38% and an absolute risk reduction of 1.64% (number needed to treat 61, 95% confidence interval 39–139). The relative risk reduction for all strokes (fatal and nonfatal) was similar across a range of baseline systolic

pressures, but the absolute risk reduction was greater in the prespecified subgroup that had hypertension at baseline (mean blood pressure 159/94 mm Hg) than in the normotensive subgroup (mean blood pressure 136/79 mm Hg), suggesting that treatment is most beneficial for those with higher systolic blood pressures. Also, the benefit was only demonstrated in the subgroup that received two antihypertensive medications; those who received perindopril alone showed no benefit.

This study involved relatively young patients in relatively good health except for their strokes. The extent to which the results can be extrapolated to older, frail adults is uncertain because of the time needed to achieve benefit and because of the added vulnerability of frailty, which could make treatment with two antihypertensive medications riskier.

PROFESS (Prevention Regimen for Effectively Avoiding Second Strokes),⁵⁴ another study in patients with previous stroke (mean age 66) showed no benefit over 2.5 years in the primary outcome of stroke using telmesartan 80 mg daily compared with placebo. This result is concordant with that of **PROGRESS**,⁵³ in which patients who took only one medication did not show a significant decrease in the rate of stroke.

A possible reason for the lack of benefit from monotherapy was that the differences in blood pressure between the placebo group and the treatment group on monotherapy were small in both studies (3.8/2.0 mm Hg in **PROFESS**, 5/3 mm Hg in **PROGRESS**). In contrast, patients on dual therapy in **PROGRESS** decreased their blood pressure by 12/5 mm Hg compared with placebo.

■ CURRENT HYPERTENSION GUIDELINES

Current guidelines make reference to the elderly, but we found none that made specific recommendations for the frail elderly.

JNC 8

In December 2013, members of the Eighth Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 8) released new recommendations.³² One significant revision was to support higher blood pressure targets for older adults (age 60 and older). Whereas JNC 7 stat-

People with a clinical frailty score of 7 are severely frail and need help with instrumental and basic activities of daily living

ed that lowering blood pressure below 140/90 mm Hg reduced cardiovascular complications,³³ JNC 8 now acknowledges that there is no strong evidence to support blood pressure targets below 150/90 mm Hg for hypertensive persons without kidney disease or diabetes age 60 and older. Thus, in the general population age 60 and older, JNC 8 recommends starting antihypertensive treatment when blood pressure is 150/90 mm Hg or higher, and treating to a goal blood pressure of less than 150/90 mm Hg. JNC 8 makes no recommendation about how to adjust blood pressure targets for frailty or how to measure blood pressure.

American College of Cardiology and American Heart Association

In 2011, the American College of Cardiology and American Heart Association published a consensus document on the management of hypertension in the elderly.⁹

They acknowledged that the generally recommended blood pressure goal of lower than 140/90 mm Hg in uncomplicated elderly patients is based on expert opinion rather than on data from randomized controlled trials, but nevertheless recommended a target systolic pressure lower than 140 mm Hg for older adults, except for octogenarians.

For those over age 80, systolic levels of 140 to 145 mm Hg can be acceptable if tolerated and if the patient does not experience orthostasis when standing. Systolic pressure lower than 130 mm Hg and diastolic pressures lower than 65 mm Hg should be avoided in this age group.

The document acknowledges that systolic pressure may have to remain above 150 mm Hg if there is no response to four “well-selected drugs” or if there are unacceptable side effects. In these cases, the lowest “safely achieved” systolic blood pressure should be the goal.

Canadian Hypertension Education Program

The 2014 Canadian Hypertension Education Program (CHEP) report makes several recommendations for the “very elderly,” a group they define as over the age of 80. The CHEP website and resources include the following recommendations¹⁰:

- For the very elderly without diabetes or target-organ damage, drug therapy should be initiated when systolic blood pressure is high-

er than 160 mm Hg to reach a systolic blood pressure target lower than 150 mm Hg. This is a grade C level recommendation, indicating that it is based on low-quality trials, unvalidated surrogate outcomes, or results from nonrandomized observational studies.

- For the very elderly with macrovascular target-organ damage, antihypertensive therapy should be considered if systolic blood pressure readings average 140 mm Hg or higher (grade D for 140 to 160 mm Hg; grade A for higher than 160 mm Hg), although caution should be exercised in elderly patients who are frail. (Grade D recommendations are the weakest, as they are based on low-powered, imprecise studies or expert opinion, whereas grade A recommendations are based on the strongest evidence from high-quality randomized clinical trials.)
- Decisions regarding initiating and intensifying pharmacotherapy in the very elderly should be based on an individualized risk-benefit analysis.

The European Society of Hypertension and European Society of Cardiology

The 2013 guidelines from the European Society of Hypertension and the European Society of Cardiology¹¹ recommend that for elderly patients under age 80, antihypertensive treatment may be considered at systolic values higher than 140 mm Hg and aimed at values lower than 140 mm Hg if the patient is fit and treatment is well tolerated.

For those over age 80 with an initial systolic pressure of 160 mm Hg or higher, the guidelines recommend lowering systolic pressure to between 150 and 140 mm Hg, provided the patient is in good physical and mental condition. In frail elderly patients, they recommend leaving decisions on antihypertensive therapy to the treating physician, based on monitoring of the clinical effects of treatment.¹¹

The ADS/PATH guidelines

When finalizing our recommendations,¹ we considered the characteristics of frailty and the following key points from the evidence:

- Although evidence from drug treatment trials indicates that there is benefit in treating healthy older adults who have hypertension, the benefit of treating frail older adults is unknown.

**We believe
our program
reduces
inappropriate
care**

- Major trials enrolled elderly patients only if they had systolic blood pressures of at least 160 mm Hg. Therefore, evidence supports initiating pharmacotherapy at a systolic pressure of 160 mm Hg or higher.
- No evidence from randomized controlled trials supports a systolic target lower than 140 mm Hg in the elderly, and there is some evidence that such a target does not benefit.
- The benefit of adding a third medication to lower blood pressure has not been studied.
- Frailty makes the potential benefits of strict blood pressure targets even less certain and increases the possibility of harm from adverse drug events.
- The only study of very old adults, HYVET,⁴⁴ enrolled relatively healthy older adults and few with orthostasis, while excluding those with a standing systolic blood pressure lower than 140 mm Hg.

■ OUR RECOMMENDATIONS

Based on the above, we advise against unnecessarily strict targets and recommend stopping antihypertensive medications that are used for the sole purpose of keeping the systolic blood pressure below 140 mm Hg. Our guidelines are unique in that they focus equally on when to stop and when to start medications. We concluded that without evidence of definitive benefit, “less is more” with frailty.⁵⁵ We believe that if physicians and health professionals understand the limitations of the evidence, they can be more confident in stopping medications that lower blood pressure to an unnecessarily low level.

We recommend the following (TABLE 4):

Before treating

- Carefully review the risks and the potential but unproven benefits of treatment.
- To avoid overtreatment, treatment decisions should be based on blood pressure measurements in the seated (not supine) position, while also considering the presence of orthostasis.
- To evaluate orthostasis, measure blood pressure in the supine position, then immediately on standing, and again after 2 minutes. Ask the patient if he or she feels light-headed or dizzy when standing.

TABLE 4

Treating hypertension in the frail elderly

Stop or decrease treatment

Taper and discontinue antihypertensive drugs if seated systolic blood pressure is less than 140 mm Hg, but:

- It is not certain whether to discontinue treatment if the patient has a history of stroke (see full guideline at <http://pathclinic.ca/resources/hypertension/>)
- The target seated systolic blood pressure can be adjusted upward if there is symptomatic orthostasis or if standing systolic blood pressure is less than 140 mm Hg,
- Before stopping, consider whether the medication is treating additional conditions such as atrial fibrillation or symptomatic heart failure

Start or increase treatment

Consider treatment if systolic blood pressure is 160 mm Hg or higher

Aim for a seated systolic blood pressure of 140 to 160 mm Hg

Use seated (not supine) blood pressure to make treatment decisions

In the very frail with short life expectancy, a target systolic blood pressure of 160 to 190 mm Hg is reasonable

In general, use no more than two medications

Intended for patients who are severely frail, with a Clinical Frailty Scale score of 7 or higher—who require assistance performing basic activities of daily living such as bathing or dressing (see TABLE 1).

Stop treatment

- If the seated systolic blood pressure is less than 140 mm Hg, medications can be tapered and discontinued to achieve the targets described below.
- Before discontinuation, consider whether the medications are treating additional conditions such as rate control for atrial fibrillation or symptomatic management of heart failure.
- It is uncertain whether to discontinue treatment when there is a history of stroke. Consider that treatment with two medications resulted in an absolute risk reduction for disabling stroke of 1.64% over approximately 4 years for adults with previous stroke and a mean age of 64,⁵⁷ an effect that may be more prominent at higher systolic pressures.

Start treatment

- Consider starting treatment when systolic pressure is 160 mm Hg or higher.

- Aim for a seated systolic pressure between 140 and 160 mm Hg if there are no adverse effects from treatment that affect quality of life.
- If there is symptomatic orthostasis or if standing systolic pressure is lower than 140 mm Hg, the target seated systolic pressure can be adjusted upwards.
- In the severely frail nearing the end of life, a target systolic pressure of 160 to 190 mm Hg is reasonable.
- The blood pressure target is the same in people with diabetes.
- In general, use no more than two medications.

Dissemination and implementation

The ADS/PATH guideline is intended for use by physicians and other health professionals (eg, pharmacists and nurses) who care for frail older adults or who work in long-term care facilities. Since creating our guideline, we have disseminated it to physicians, pharmacists, and other health professionals through academic detailing, large conferences, and interactive webinars.

While we do not have objective evidence of practice change, our evaluation data found that 34% of 403 family physicians who received academic detailing indicated that the guideline would change their practice, while 36% stated that the guideline confirmed their practice, an indication that family physicians are sensitive to the needs of the frail elderly.

Because health professionals may be wary of stopping medications and not meeting recommended targets, there may be barriers to adopting this guideline. However, our experi-

ence with the PATH program indicates that these barriers can be overcome using effective communication strategies between health professionals and consumers.

AN APPROACH APPROPRIATE TO FRAILTY

There is no direct evidence for systolic blood pressure targets in the frail elderly, so we applied evidence from the nonfrail elderly. Our recommendations differ somewhat from those of other groups, which recommend targets below 140 to 150 mm Hg for older adults, although some do advise caution in the elderly for whom a substantial fall in blood pressure might be poorly tolerated. Despite these messages, we believe that clearer guidance is needed to direct health practitioners toward models that acknowledge that frail patients are in a precarious balance of health and may be harmed by treatments that strive to lower blood pressure to unproven targets. For this reason, our guideline clearly indicates when to decrease or stop drug treatment.

After physicians and health professionals examine the evidence and more fully understand the benefits and harms of treating frail older adults, we are confident that they will be more comfortable stopping medications that lower blood pressure to an unnecessarily low level and instead use an approach that is more appropriate to frailty. We hope clinicians can use this guideline with the same enthusiasm applied to other guidelines, and we welcome discussion.

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Our guideline focuses as much on stopping treatment as on starting it

REFERENCES

1. **Palliative and Therapeutic Harmonization program.** Hypertension guidelines. Treating hypertension in frailty. <http://pathclinic.ca/resources/hypertension/>. Accessed May 2, 2014.
2. **Theou O, Rockwood MR, Mitnitski A, Rockwood K.** Disability and co-morbidity in relation to frailty: how much do they overlap? Arch Gerontol Geriatr 2012; 55:e1–e8.
3. **Makary MA, Segev DL, Pronovost PJ, et al.** Frailty as a predictor of surgical outcomes in older patients. J Am Coll Surg 2010; 210:901–908.
4. **Tinetti ME, Bogardus ST Jr, Agostini JV.** Potential pitfalls of disease-specific guidelines for patients with multiple conditions. N Engl J Med 2004; 351:2870–2874.
5. **Ekerstad N, Swahn E, Janzon M, et al.** Frailty is independently associated with short-term outcomes for elderly patients with non-ST-segment elevation myocardial infarction. Circulation 2011; 124:2397–2404.
6. **Theou O, Rockwood K.** Should frailty status always be considered when treating the elderly patient? Aging Health 2012; 8:261–271.
7. **Rockwood K, Song X, MacKnight C, et al.** A global clinical measure of fitness and frailty in elderly people. CMAJ 2005; 173:489–495.
8. **Searle SD, Mitnitski A, Gahbauer EA, Gill TM, Rockwood K.** A standard procedure for creating a frailty index. BMC Geriatr 2008; 8:24.
9. **Aronow WS, Fleg JL, Pepine CJ, et al; ACCF Task Force.** ACCF/AHA 2011 expert consensus document on hypertension in the elderly: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents. Circulation 2011; 123:2434–2506.
10. **The Canadian Hypertension Education Program (CHEP).** 2014 CHEP recommendations. www.hypertension.ca/en/. Accessed May 2, 2014.
11. **Mancia G, Fagard R, Narkiewicz K, et al.** 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J 2013; 34:2159–2219.
12. **Morley JE, Vellas B, van Kan GA, et al.** Frailty consensus: a call to action. J Am Med Dir Assoc 2013; 14:392–397.

13. Fried LP, Tangen CM, Walston J, et al; Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001; 56:M146–M156.
14. Ensrud KE, Ewing SK, Cawthon PM, et al; Osteoporotic Fractures in Men Research Group. A comparison of frailty indexes for the prediction of falls, disability, fractures, and mortality in older men. *J Am Geriatr Soc* 2009; 57:492–498.
15. Avila-Funes JA, Amieva H, Barberger-Gateau P, et al. Cognitive impairment improves the predictive validity of the phenotype of frailty for adverse health outcomes: the three-city study. *J Am Geriatr Soc* 2009; 57:453–461.
16. Bergman H, Ferrucci L, Guralnik J, et al. Frailty: an emerging research and clinical paradigm—issues and controversies. *J Gerontol A Biol Sci Med Sci* 2007; 62:731–737.
17. Morley JE, Malmstrom TK, Miller DK. A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. *J Nutr Health Aging* 2012; 16:601–608.
18. Strawbridge WJ, Shema SJ, Balfor JL, Higby HR, Kaplan GA. Antecedents of frailty over three decades in an older cohort. *J Gerontol B Psychol Sci Soc Sci* 1998; 53:S9–S16.
19. Matthews M, Lucas A, Boland R, et al. Use of a questionnaire to screen for frailty in the elderly: an exploratory study. *Aging Clin Exp Res* 2004; 16:34–40.
20. Salvi F, Morichi V, Grilli A, et al. Screening for frailty in elderly emergency department patients by using the Identification of Seniors At Risk (ISAR). *J Nutr Health Aging* 2012; 16:313–318.
21. Mitnitski AB, Mogilner AJ, Rockwood K. Accumulation of deficits as a proxy measure of aging. *ScientificWorldJournal* 2001; 1:323–336.
22. Kellen E, Bulens P, Deckx L, et al. Identifying an accurate pre-screening tool in geriatric oncology. *Crit Rev Oncol Hematol* 2010; 75:243–248.
23. Rolfson DB, Majumdar SR, Tsuyuki RT, Tahir A, Rockwood K. Validity and reliability of the Edmonton Frail Scale. *Age Ageing* 2006; 35:526–529.
24. Martin FC, Brighton P. Frailty: different tools for different purposes? *Age Ageing* 2008; 37:129–131.
25. Borson S, Scanlan J, Brush M, Vitaliano P, Dokmak A. The mini-cog: a cognitive 'vital signs' measure for dementia screening in multi-lingual elderly. *Int J Geriatr Psychiatry* 2000; 15:1021–1027.
26. Reisberg B, Ferris SH. Brief Cognitive Rating Scale (BCRS). *Psychopharmacol Bull* 1988; 24:629–636.
27. Moorhouse P, Mallery LH. Palliative and therapeutic harmonization: a model for appropriate decision-making in frail older adults. *J Am Geriatr Soc* 2012; 60:2326–2332.
28. Palliative and Therapeutic Harmonization Clinic (PATH). www.pathclinic.ca. Accessed May 2, 2014.
29. Dalhousie University Faculty of Medicine: Continuing Medical Education. <http://cme.medicine.dal.ca/ADS.htm>. Accessed January 8, 2014.
30. Mallery LH, Moorhouse P. Respecting frailty. *J Med Ethics* 2011; 37:126–128.
31. Dalhousie University Faculty of Medicine: Continuing Medical Education. Issues in hypertension 2011. <http://cme.medicine.dal.ca/files/Hypertension%20book.pdf>. Accessed May 2, 2014.
32. James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA* 2014; 311:507–520.
33. Chobanian AV, Bakris GL, Black HR, et al; National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA* 2003; 289:2560–2572.
34. Amery A, Birkenhäger W, Brixko P, et al. Mortality and morbidity results from the European Working Party on High Blood Pressure in the Elderly trial. *Lancet* 1985; 1:1349–1354.
35. Coope J, Warrender TS. Randomised trial of treatment of hypertension in elderly patients in primary care. *Br Med J (Clin Res Ed)* 1986; 293:1145–1151.
36. SHEP Cooperative Research Group. Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. Final results of the Systolic Hypertension in the Elderly Program (SHEP). *JAMA* 1991; 265:3255–3264.
37. Dahlöf B, Lindholm LH, Hansson L, Scherstén B, Ekblom T, Wester PO. Morbidity and mortality in the Swedish Trial in Old Patients with Hypertension (STOP-Hypertension). *Lancet* 1991; 338:1281–1285.
38. Medical Research Council trial of treatment of hypertension in older adults: principal results. MRC Working Party. *BMJ* 1992; 304:405–412.
39. Staessen JA, Fagard R, Thijs L, et al. Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. The Systolic Hypertension in Europe (Syst-Eur) Trial Investigators. *Lancet* 1997; 350:757–764.
40. Liu L, Wang JG, Gong L, Liu G, Staessen JA. Comparison of active treatment and placebo in older Chinese patients with isolated systolic hypertension. Systolic Hypertension in China (Syst-China) Collaborative Group. *J Hypertens* 1998; 16:1823–1829.
41. Lithell H, Hansson L, Skoog I, et al; SCOPE Study Group. The Study on Cognition and Prognosis in the Elderly (SCOPE): principal results of a randomized double-blind intervention trial. *J Hypertens* 2003; 21:875–886.
42. JATOS Study Group. Principal results of the Japanese trial to assess optimal systolic blood pressure in elderly hypertensive patients (JATOS). *Hypertens Res* 2008; 31:2115–2127.
43. Oparil S, Yarows SA, Patel S, Fang H, Zhang J, Satlin A. Efficacy and safety of combined use of amliskiren and valsartan in patients with hypertension: a randomised, double-blind trial. *Lancet* 2007; 370:221–229.
44. Beckett NS, Peters R, Fletcher AE, et al; HYVET Study Group. Treatment of hypertension in patients 80 years of age or older. *N Engl J Med* 2008; 358:1887–1898.
45. Musini VM, Tejani AM, Bassett K, Wright JM. Pharmacotherapy for hypertension in the elderly. *Cochrane Database Syst Rev* 2009; CD000028.
46. He FJ, MacGregor GA. Effect of longer-term modest salt reduction on blood pressure. *Cochrane Database Syst Rev* 2004; CD004937.
47. Allen M, Kelly K, Fleming I. Hypertension in elderly patients: recommended systolic targets are not evidence based [in French]. *Can Fam Physician* 2013; 59:19–24.
48. Guyatt GH, Briel M, Glasziou P, Bassler D, Montori VM. Problems of stopping trials early. *BMJ* 2012; 344:e3863.
49. Sabayan B, Oleksik AM, Maier AB, et al. High blood pressure and resilience to physical and cognitive decline in the oldest old: the Leiden 85-plus Study. *J Am Geriatr Soc* 2012; 60:2014–2019.
50. Sabayan B, van Vliet P, de Ruijter W, Gussekloo J, de Craen AJ, Westendorp RG. High blood pressure, physical and cognitive function, and risk of stroke in the oldest old: the Leiden 85-plus Study. *Stroke* 2013; 44:15–20.
51. Poortvliet RK, Blom JW, de Craen AJ, et al. Low blood pressure predicts increased mortality in very old age even without heart failure: the Leiden 85-plus Study. *Eur J Heart Fail* 2013; 15:528–533.
52. Odden MC, Peralta CA, Haan MN, Covinsky KE. Rethinking the association of high blood pressure with mortality in elderly adults: the impact of frailty. *Arch Intern Med* 2012; 172:1162–1168.
53. PROGRESS Collaborative Group. Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack. *Lancet* 2001; 358:1033–1041.
54. Yusuf S, Diener HC, Sacco RL, et al; PROFESS Study Group. Telmisartan to prevent recurrent stroke and cardiovascular events. *N Engl J Med* 2008; 359:1225–1237.
55. Garfinkel D, Mangin D. Feasibility study of a systematic approach for discontinuation of multiple medications in older adults: addressing polypharmacy. *Arch Intern Med* 2010; 170:1648–1654.

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