Treating New Patients for Hypertension?
The best evidence suggests low-dose thiazides as your first choice

Why choose low-dose thiazides as a first-line treatment for your patient?
ALLHAT, the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial, was a large NIH-funded study that randomized over 30,000 patients to a thiazide, an ACE inhibitor, or calcium channel blocker. It was one of several randomized, double-blind, active-controlled trials that examined the clinical outcomes of thiazides as first-line agents in patients with uncomplicated hypertension. The conclusion:

“Thiazide-type diuretics are superior in preventing one or more major forms of CVD and are less expensive. They should be preferred for first-step antihypertensive therapy.”
JAMA. 2002; 288: 2981–2997

1. Thiazides are effective and safe:
Compared to ACE inhibitors (ACE-Is), alpha blockers (α-blockers), and calcium channel blockers (CCBs), low-dose thiazide diuretics are as good or better at reducing stroke, heart attack or heart failure.

2. Low-dose thiazides are also as good or better at lowering blood pressure:

3. Thiazides are well-tolerated:
Patients taking thiazides had fewer adverse events requiring withdrawal as compared to patients taking other classes of medications.3

4. ... and your patient spends less:
Save your patient money when prescribing a thiazide compared to beta blockers, ACE inhibitors, ARBs or CCBs:

Thiazides are recommended as first-line agents for primary hypertension by the:
• Joint National Committee JNC7 (Google: “JNC7”)  
• Canadian Hypertension Society (Google: “CHEP 2004 therapy”)
Using Thiazides for First-Line Antihypertensive Therapy
Frequently Asked Questions (FAQs)

1. What have randomized trials found about thiazides as first-line antihypertensive therapy?
Several recent studies and a meta-analysis\(^1\) have shown that thiazides, as first-line therapy, are as effective as or more effective than other classes of antihypertensive drugs (ACE-Is, CCBs, ARBs, α-blockers, β-blockers) in lowering cardiovascular events in uncomplicated hypertension.

<table>
<thead>
<tr>
<th>Trial(^3)</th>
<th>Primary Agents</th>
<th>Population Studied</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALLHAT(^3)</td>
<td>doxazosin, amlopidine, lisinopril, chlorthalidone</td>
<td>High BP + 1 other risk factor</td>
<td>Chlorthalidone (thiazide): well tolerated, as or more effective in lowering CV events, and least expensive.</td>
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<tr>
<td>CAPPP(^4)</td>
<td>captopril, conventional Rx (e.g. atenolol, metoprolol or thiazide)</td>
<td>DBP&gt;100, BP 162/100 (captopril) BP 160/98 (conventional)</td>
<td>Captopril and conventional arms were equal in preventing CV events and mortality; conventional treatment reduced strokes as compared to captopril.</td>
</tr>
<tr>
<td>INSIGHT(^5)</td>
<td>nifedipine, hydrochlorothiazide/amlopidine</td>
<td>High BP and 1 other risk factor</td>
<td>Nifedipine and thiazide equal in preventing CV death, stroke and all MI. Fewer fatal MIs and heart failures in the thiazide arm.</td>
</tr>
<tr>
<td>STOP-Hypertension–2(^6)</td>
<td>1. conventional (thiazide or β-blocker) 2. felodipine or iridapril +/- β-blocker 3. enalapril or lisinopril</td>
<td>Elderly (mean: 76y), High BP 194/98</td>
<td>Conventional drugs were similar to the other two arms in CV mortality and in number of overall major CV events.</td>
</tr>
</tbody>
</table>

2. Do thiazides cause metabolic effects? – ALLHAT trial findings\(^5\):
- Potassium: Decreased by only 0.3 meq/L with thiazide compared to CCB and by 0.5 meq/L compared to ACE-I.
- Cholesterol: Increased by only 0.1 mmol/L with the thiazide compared to CCB or ACE-I.
- Fasting glucose: Increased by only 0.3 mmol/L with the thiazide compared to CCB and by 0.4 mmol/L compared to ACE-I.
Notably, these differences did **NOT** lead to a difference in clinical outcomes. This is consistent with other trials, such as CAPPP\(^4\) and INSIGHT\(^5\).
Metabolic effects are less with low-dose regimens (12.5 mg thiazide).

3. Are all thiazides equally effective and safe?
There is no study that directly compares one thiazide to another, head-to-head, in terms of major health outcomes. Among outcome studies that compare thiazides to other classes of drugs, the findings for different thiazides are consistent. This is indirect evidence suggesting that no thiazide is superior to another.

4. When might thiazides not be the first choice?
Post myocardial infarction, congestive heart failure, atrial fibrillation, severe renal failure and recurrent gout are conditions in which thiazide diuretics may not be the best first-choice therapy. Furthermore, because about 50% of the hypertensive population usually requires more than one drug for blood pressure control, in most cases a thiazide should be a part of any multi-drug antihypertensive regimen.\(^7\)

5. How do patients comply with thiazides as compared to other agents?
In randomized double-blind trials, compliance rates are as good or better with thiazides as with other drug classes.\(^14\)

6. What is the cost difference between thiazides and other agents?
Thiazides are the least expensive of all antihypertensive drugs available in British Columbia. See Antihypertensive Price Speedometer for cost information.

7. Whom can I contact if I have questions or want more information?
Please contact Dr. Malcolm Maclure at the School of Health Information Science, University of Victoria at (250) 405–4940.

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2. Rx Files. Hypertension update: is anyone leaving samples of thiazide diuretics? Table 4. 2003.