This passage is written by Martin Bohdal and is intended for healthcare decision-makers interested in the use of evidence in guidelines, educational materials, and decision support tools.

Guidelines: A comprehensive dose of the evidence should be prescribed at all times

Suppose that you have the opportunity to help guide a loved one's healthcare decisions. What might you do? How might you seek the best available evidence regarding treatment?

In my case, my parents would find me helpful in seeking information, accessing resources, and interpreting expert guidance. In the following passage, I hope to demonstrate that any reader is able to help guide well-informed healthcare decisions with a sincere approach and appreciation for the necessities of evidence-based guidance. To do so, I will summarize a scenario in which my father and mother are diagnosed with hypertension. In this scenario, I am led to make conflicting decisions given two sources of health evidence that are processed and presented differently. I expect evidence-based guidance to be meaningfully distilled from the best available evidence. This is not always true, and in cases where the evidence exists, discordance must be identified.

Hypertension is a condition in which blood pressure is elevated beyond particular threshold. The Canadian Hypertension Education Program (CHEP) produces guidelines that provide evidence-based guidance for blood pressure targets, treatment thresholds, and therapeutic choices for consumers. The Cochrane Hypertension review group edits and publishes systematic reviews to answer clinically relevant questions regarding hypertension. As an internationally recognized and methodologically acclaimed review group, Cochrane Hypertension provides evidence syntheses independent from industry affiliation.

Let's suppose that my father is 67 years old with a blood pressure of 170/105 mmHg (moderate hypertension) and my mother is 57 years old with a blood pressure of 150/92 mmHg (mild hypertension). Despite healthy lifestyle and diet modifications, their elevated blood pressure persists. I trust that they are diagnosed accurately as their doctors followed the recommended guidance for measuring blood pressure. Let's suppose that both Mom and Dad have done everything they can do to control their blood pressure without drug therapy. Accordingly, we want to understand how useful drug therapy might be and how appropriate blood pressure targets are in guiding care.

Evidence at first glance

The Canadian Hypertension Education Program (CHEP) Guidelines are evidence-based and updated annually. For several years, experts selected by Hypertension Canada have been meeting to vote on distillations of the evidence in the form of guiding statements for the diagnosis and treatment of high blood pressure. At first, my parents and I would likely agree that our treatment actions should align with the guidelines.

According to the most recent 2017 CHEP guidelines, dad should be first treated with 1 of 8 possible types of drugs[1]. I would read that the most promising and beneficial option is a combination pill where two types of antihypertensive drugs are combined into a single pill. Following the guidelines, I would hope that dad's treatment would begin with an angiotensin-converting enzyme (ACE) inhibitor + calcium channel blocker (CCB) combination medication. Next, the guidelines assert that additional drugs should be added if we don't achieve the target of less than 140/90. In this case, there are also recommendations on some of the most useful combinations. From the corresponding guideline and accompanying information, I am certain that a long-acting thiazide or thiazide-like diuretic is the best addition to my dad's hypertension therapy. This evidence urges the importance of "treating to target". Accordingly, we would likely use our judgement to add/substitute drugs for the remainder of my father's life with the goal of 140/90.

In my mother's case I learn that the Canadian Hypertension Education Program is yet to provide a simplified guideline regarding treatment of mildly elevated blood pressure for otherwise healthy people. However, the group writes, in the explanatory paragraphs for the 2016 guidelines, that drug therapy is beneficial for patients like my mom[2]. Here it is also written that if lifestyle risk management is unsuccessful, antihypertensive drug therapy should be considered just as in cases of moderate hypertension. This is true in the case of my mom who has limited her sodium intake, managed a healthy body weight and diet, and so on. We have tried our best to control her blood pressure without drug therapy.

Thus, within supplementary material, Canadian Hypertension Guidelines assert that my mom should be on antihypertensive drug therapy. And, according to the guidelines, she must also achieve a blood pressure below 140/90. Our likely decision would be to start with a single drug. We would be further advised to add another from the list of useful combinations if she fails to

achieve the target blood pressure. Accordingly, the guidelines would lead me to choose a long-acting CCB followed by an ACE inhibitor.

A more comprehensive look at the evidence

How might our decisions change if I explore evidence published in the Cochrane Library?

Reading the Cochrane Hypertension plain language summaries would lead me to the information that is most relevant to my father's case. I would find that the review titled "Pharmacotherapy for hypertension in the elderly"[3] is particularly relevant to my father's treatment decisions. Patients studied and accounted for within this systematic review were similar to my dad in age and condition.

The information in this review leads me to discern that the benefits of antihypertensive drug treatment outweigh the harms for people like my father. Given his moderate hypertension, antihypertensive drugs could save his life. We would learn that my father could enjoy a 4.3% reduced risk of cardiovascular events if he takes drug therapy. I could communicate this information in a variety of ways to help him understand. For example, I could describe that for every 24 people like my father, one will benefit from treatment. Such a benefit could result from one, two, or three drugs added progressively within five years.

Interestingly, from this review, I would learn that 35-40 % of treated participants failed to achieve blood pressure targets of less than 160/90. To me, this demonstrates that we would be misguided to "treat to target" with targets being pressures less than 140/90. Even if targets were higher at 160/90, this information shows that it is not necessary to achieve such a target in order to benefit from drug therapy.

At this point, Cochrane Hypertension evidence would inform an appreciation of the modest benefits of treatment. It would encourage our balanced understanding of blood pressure targets, treatment thresholds and other measures of benefit and risk as they are.

What can Cochrane Reviews teach me about the evidence for *choices* of drug therapy?

For my father, I would find several reviews to help guide our decisions.[4,5,6,7,8]
These reviews would inform me that low-dose thiazides or thiazide-like diuretics are the most effective drug therapy for people like my father as first-line treatment. I would learn that the evidence for reduction in cardiovascular events is second best for ACE inhibitors. Additionally, a recently published review would demonstrate that there is yet to be meaningful evidence that supports starting with combination therapy over single-agent therapy in my parents' cases.

Cochrane evidence would likely lead me to decide the following for my father.

a. He is not likely to benefit from a combo-pill medication as a first-line therapy.
b. He is likely to benefit most from a low-dose thiazide to start.
c. He could progress to take an ACE inhibitor if necessary.

Regarding Cochrane evidence to help guide treatment for my mom – I would find one highly relevant review titled "Pharmacotherapy for mild hypertension"[9].

From this review, I would learn that there is no proof of reduction in mortality or total cardiovascular events in people who take drug therapy for mild hypertension. I would learn that for people studied like my mom, antihypertensive therapy has yet to demonstrate a meaningful benefit. Because she is mildly hypertensive it is not known whether she is better off taking medication or not. The populations studied have mostly not been representative of my mother's condition.
Practically, the systematic review shows that more trials relevant to this population are to provide meaningful.

Acting on the Cochrane Evidence relevant to my mom, I would explain to her that it is not known whether drug therapy is more beneficial or harmful for her. I feel that it would be sensible to let her decide the course of action. In my case, without compelling evidence, I think my mom would decide against drug therapy.

Table 1. Summary of likely results when following two disparate sources of evidence

	CHEP Guidelines		Cochrane Hypertension	
	Mom	Dad	Mom	Dad
Targets/ Treatment Thresholds	<140/90 Treat to target	<140/90 Treat to target	Flexible within mild ranges	Treatment without pressure to achieve targets
Drug Therapy	Ramipril, Amlodipine	Ramipril, Amlodipine, Hydrochlorothiazide, Bisoprolol, …	None	Low-dose Hydrochlorothiazide, Lisinopril
Response from my parents	Worried	Discontent and focused on treating to target	Reassured and able to focus on lifestyle risk management	Understanding of the modest benefits of drug therapy

<u>So what?</u>
After closely reading the 2016 and 2017 guidelines and supplementary material for this exercise, I am not convinced that the Canadian Hypertension Education Program meaningfully conveys the best available evidence when guiding care for people like my mom and dad. I feel that the Canadian Hypertension Education Program lacks the transparency and rigorous methodology that any decision maker should expect from evidence-based treatment guidance. Four criticisms are worth pointing out in this regard.

1. It is unclear to me how evidence is searched for and selected for inclusion.

- While this information is available upon request, a greater effort to clarify inclusion/exclusion criteria would help a decision-maker appreciate the context in which the evidence is relevant.

2. Prescriptive guidance does not correspond with evidence grading.
   - Recommendations are graded on a four-point scale where grade-A recommendations are regarded to be of the strongest quality while a Grade-D recommendation could be included based on expert opinion alone. While this grading method is not necessarily problematic on it's own - it becomes so when statements are prescriptive. I think it is quite confusing to be told that several things "should be" prescribed, only to learn that the evidence for each option varies from A-D in power, subjectively. For me, this tactic obscures the information necessary to make a well-informed decision.

3. A guideline requires 70% approval of the CHEP committee to be published.
   - I would like to know if a guideline I am following had 24 of 81 experts not in favor.

4. CHEP summarizes new information more so than the most relevant information.
   - The supplementary writing attached to guidelines summarizes a narrow body of new findings with varied significance. As a reader, I'm encouraged to favour treatment that is new and hopeful. I am left to trust that evidence vetted in previous years is still valid.

<u>Reality check:</u>

I feel it is important to mention that friends of mine probably wouldn't make the time to assess guidelines if they had the opportunity to advise their parents on hypertension treatment. Instead, they might turn to the Mobile Guidelines App, CHEP outreach materials, and/or decision support applications[10,11]. Decision-makers must not fail to recognize that these tools are a further simplification of the guidelines. All information in these resources in particular appear to be selected from the guidelines in a completely undisclosed knowledge translation process.

While these products may play a role in education and engagement, they inevitably inform decisions. Accordingly, I expect producers of such products to follow rigorous methods. If not possible, every effort must be made to inform readers of the process followed and the utility promised. For now, I am well aware that the evidence-based label does not ensure truly evidence-based guidance. I encourage all readers to consider how your own decisions may vary according to the format and process in which evidence is distilled and presented. Meaningful guidance can still be provided in the absence of consensus or certainty.

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