

Finding the right blood pressure (BP) target for patients on hemodialysis

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Co-Investigators:

- Dr. Karthik Tennankore (*presenter*),
- Dr. David Collister



University
of Manitoba



Chronic Disease
Innovation Centre

Question for the Audience (*Clinicians*)

What blood pressure do you target in your patients who are on in-centre hemodialysis?

- **Pre-dialysis BP**
- **Post-dialysis BP**
- **Lowest intradialytic BP**

**Ambulatory / Home BPs: not available for most patients*

Question for the Audience (*Clinicians*)

What is your pre-dialysis BP target “for most patients”?

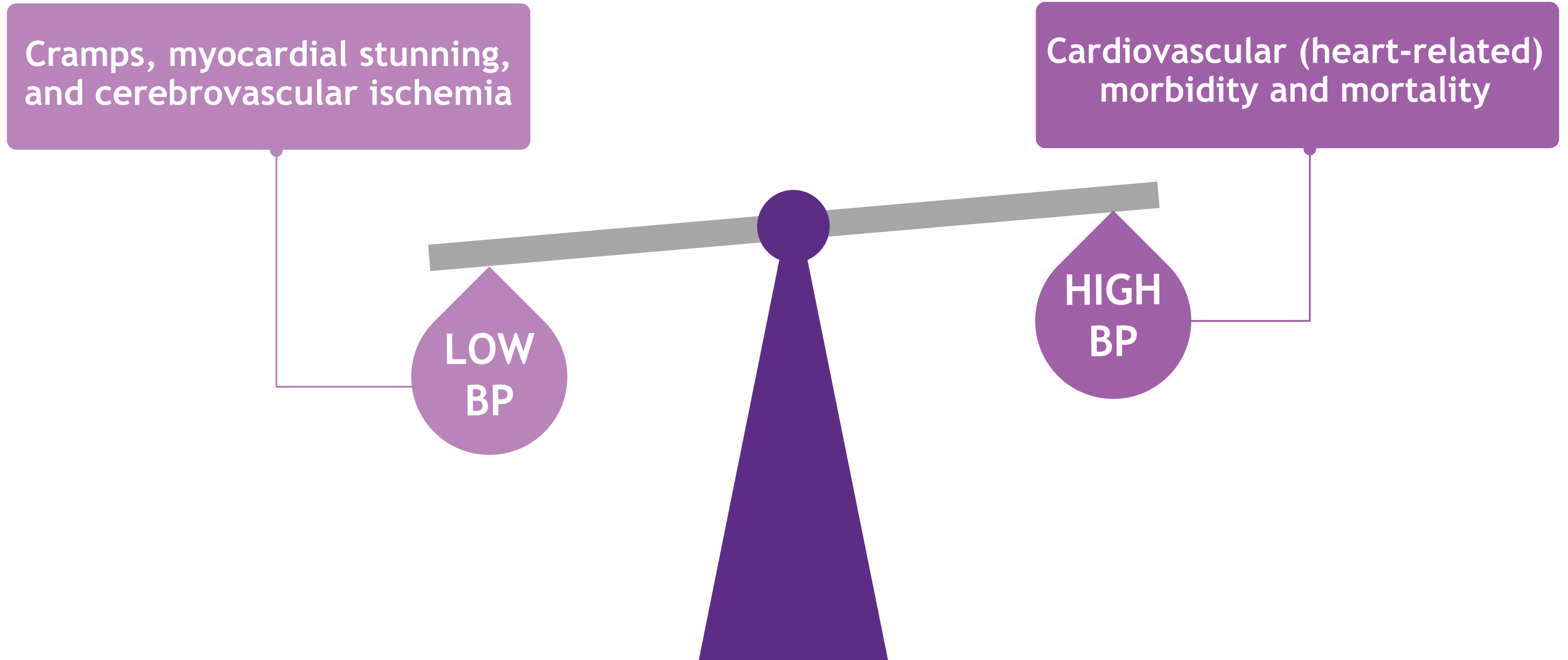
- <130/80
- <140/90
- <150/90
- <160/100
- Other

Question for the Audience (*Clinicians*)

Do you have a protocol in place in your in-centre hemodialysis unit to treat BP(target and/or medications)?

- **Yes**
- **No**
- **Unsure**

Blood Pressure (BP) in Hemodialysis



Patient Partner Perspectives

As someone receiving hemodialysis, how does blood pressure management affect you?



Cathy Du Val, Ontario

“If your pressures are too low you will feel very crappy. Bottoming out is not fun, you get the sweats and feel dizzy and nauseous. I have personally had this happen to me numerous times and it is not fun at all.”

“I have also been on the other end of the spectrum where my pressures ran so high for a bunch of years and that's not fun either. Some of the side effects for me included headaches and lack of sleep due to pounding in my head. When my pressures were that high they had me on all kinds of meds, I believe I was on 3 different kinds just for blood pressure. Again not fun as the pills would bring the pressures down but only temporarily.”

“Either way high or low it's not an easy road - I feel if you want to make it as a dialysis patient you must regulate your BPs and know your body and the signs it gives you in order to feel well.”

Michael Smith, Ontario: formerly on in-centre hemodialysis

Blood Pressure (BP) in Hemodialysis

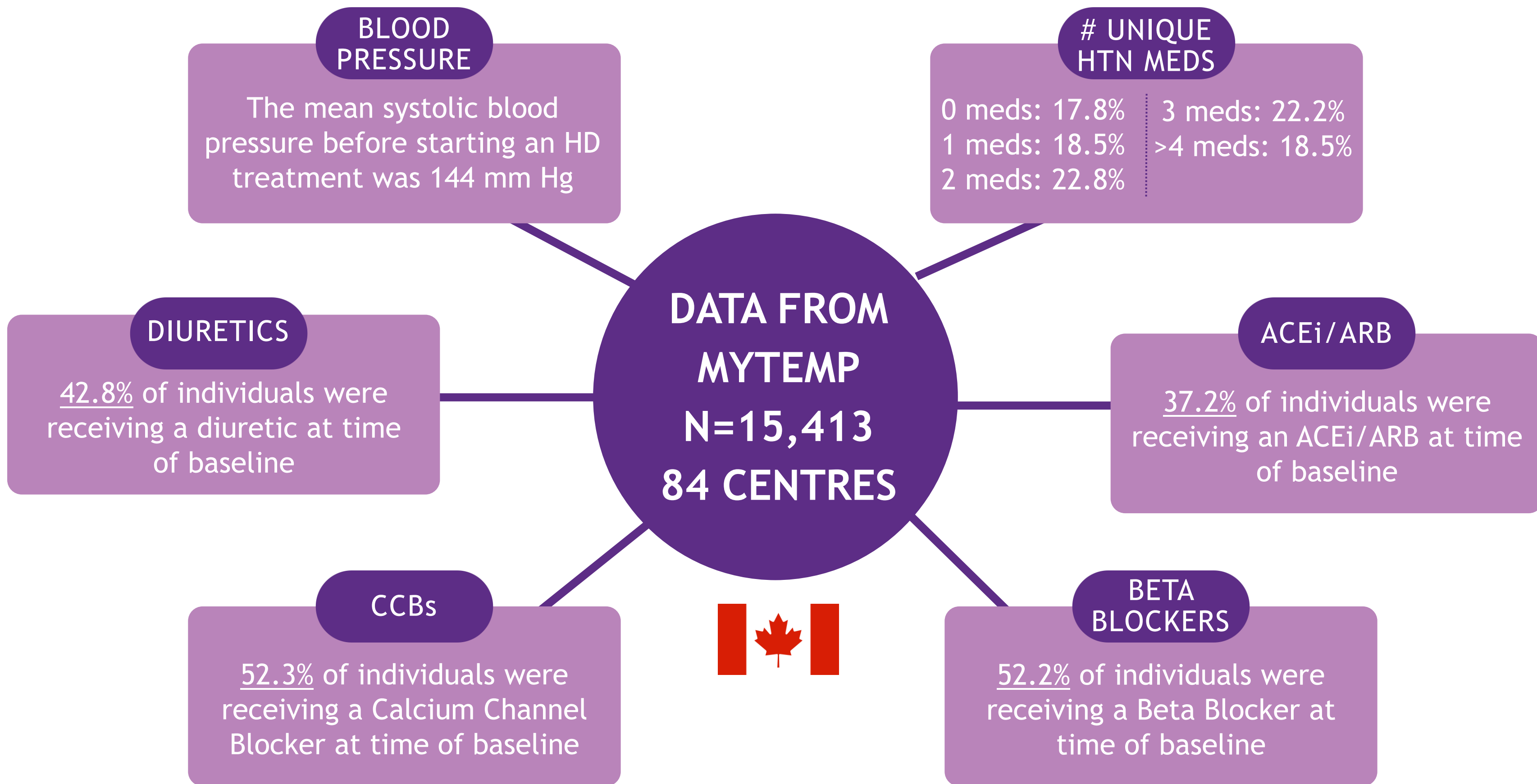
Even though BP management is an important part of care management in hemodialysis -- the “right” blood pressure target is unknown.

The Best Available Evidence

- Miskulin et al. (2018) : pilot randomized controlled trial of:
 - 126 individuals on in-centre hemodialysis
 - Randomized to a pre-dialysis standardized blood pressure of 155-165 mm Hg versus 115-140 mm Hg.
- A difference of **12.9 mm Hg** between the two study groups was achieved
- A signal towards higher incidence of adverse events and hospitalizations at one year in the intensive treatment arm

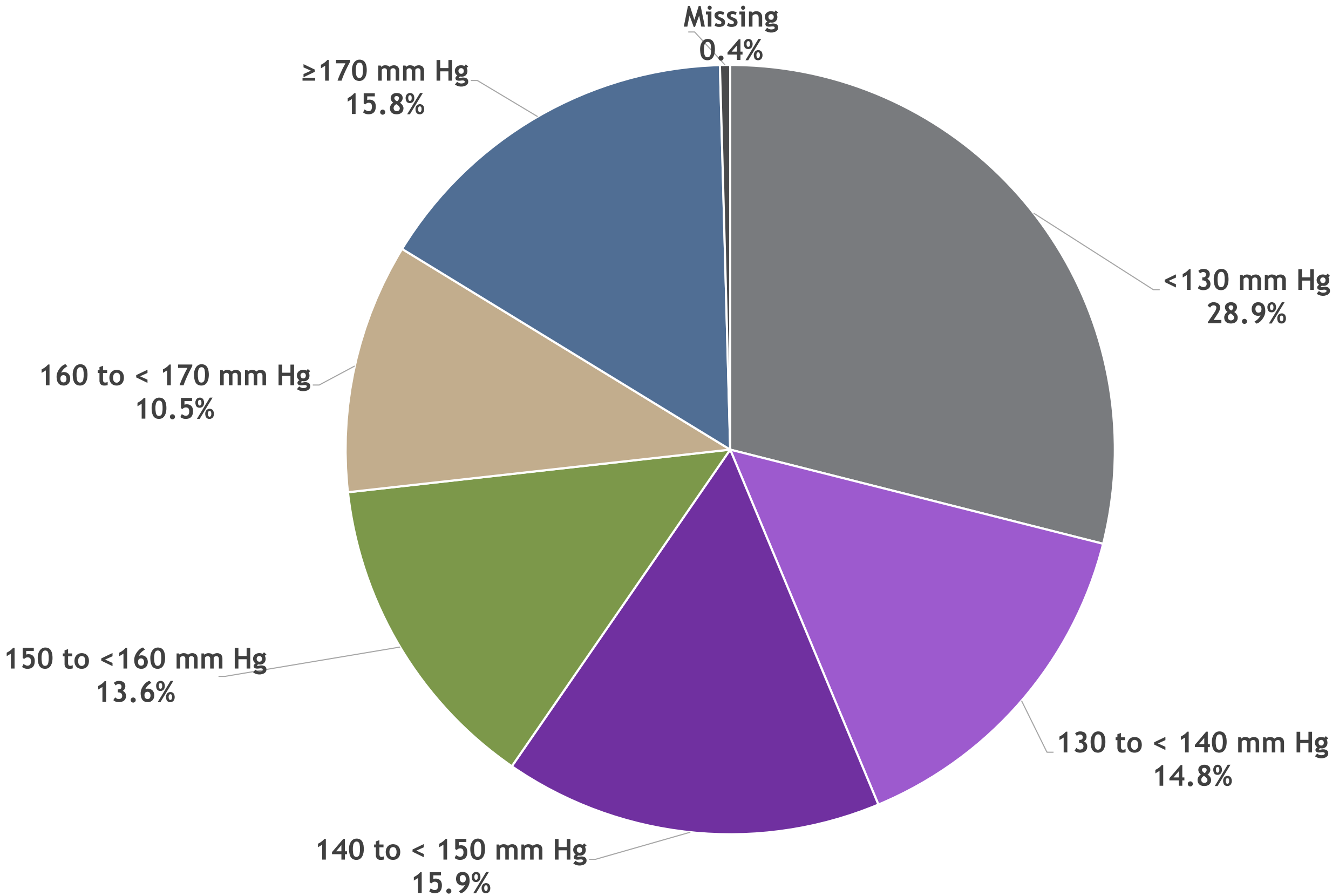
The current landscape of BP management in in-centre hemodialysis in Canada





**Baseline medication assessment restricted to patients with universal outpatient prescription drug coverage*

MyTEMP: Distribution of pre-dialysis systolic BP



Survey assessing current BP management

- One-time survey study
 - Distributed to the Principal Investigators / Nephrologists at sites participating in an ongoing national hemodialysis trial (Feb. 2023)
- Hemodialysis units with an established clinical trials framework / capacity
- **26 responses received** - 25 nephrologists, 1 administrator

Survey assessing current BP management



Survey assessing current BP management:

Does your in-centre hemodialysis unit have a standardized blood pressure management plan or protocol in place?

25 out of 26 respondents replied “no”

Most added that **individual physicians** (e.g. the rounding nephrologist) **make decisions regarding BP management for patients on hemodialysis**

Why do you not have a standardized BP plan?

Lack of Clear Evidence

- “Lack of clear guidelines on which to base a protocol and differing opinions by nephrologists”
- “Due to “lack of evidence” to inform practice and uncertainty from observational evidence on BP and the general population”
- “No tool in place”
- “Lack of evidence for BP targets or optimal therapeutic approach therefore clinician judgement/ discretion guides therapy”
- “No optimal BP target established - there is equipoise”

Individualized to Patient

- “Underlying medical conditions/ comorbidities determine BP targets”
- “Blood pressure control is adjusted based on patient characteristics, when required, and mostly based on home readings”
- “Would be hard given the complexity of this, frequent BP fluctuations, individualization, lack of clear targets and which BP on which to base the target”

Left up to Clinician Discretion

- “Physician discretion; generally follow guidelines extrapolated from CHEP (*Canadian Hypertension Education Program*)”
- “We have never considered standardized approach. Primary and rounding nephrologist address BP”
- “Pre/intra/post BP measurement is standardized but treatment is left up to individual physicians. Home BP measurement is encouraged”
- “Optimal management is left up to individual clinicians (nurse practitioners and nephrologists)”

Other

- “Hasn't been considered a priority for the HD unit”
- “We've not developed a protocol but most importantly we do not have man power resources such as NPs or pharmacist to actually implement the protocol”

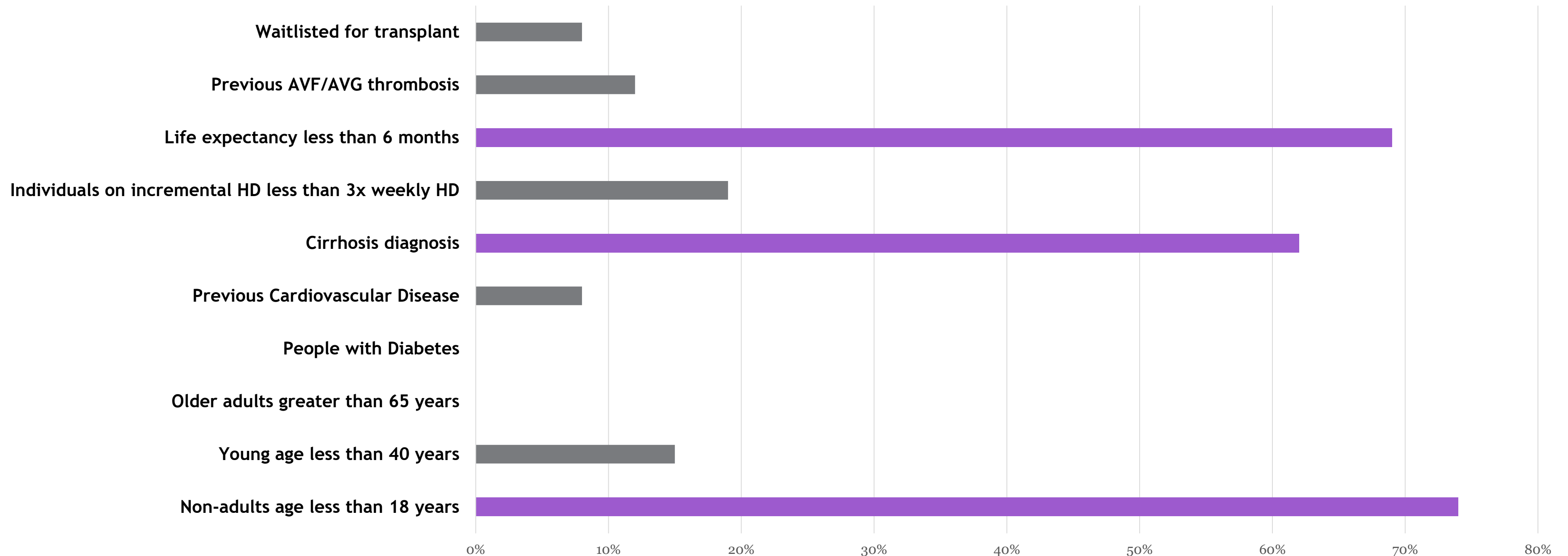
Survey assessing current BP management: If we were to conduct a national randomized trial - Would you be willing to have your in-centre hemodialysis unit randomized to:

- 1. A blood pressure target using a standardized protocol?**
- 2. A blood pressure agent (first-line, second-line) using a standardized protocol?**

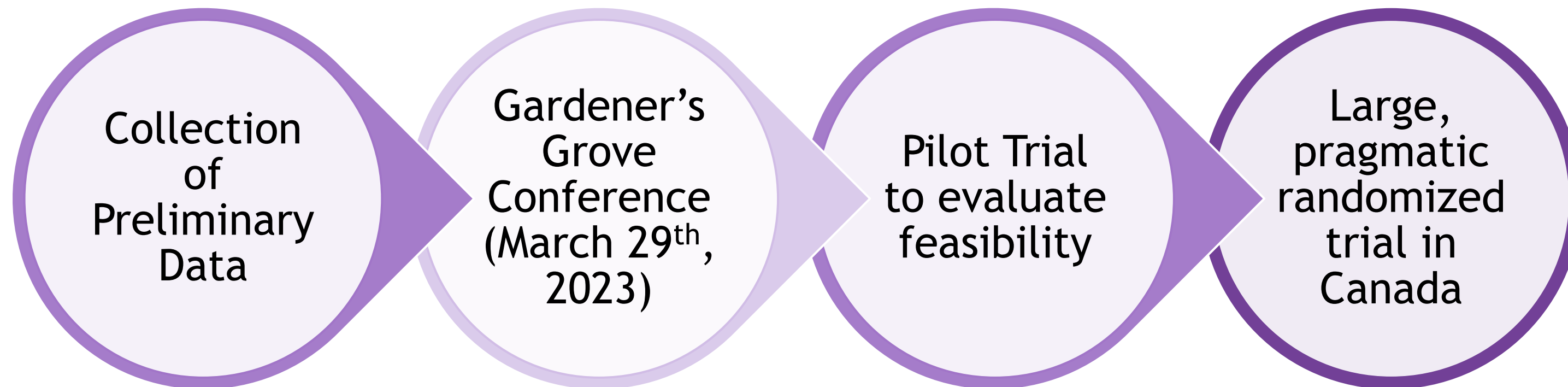
24 out of 25 nephrologists replied **yes** -> suggesting there is a willingness among this group of nephrologists to participate in a trial evaluating blood pressure targets in hemodialysis

From the **1 nephrologist** that replied **no** -> *“I would need agreement from ALL my local nephrology colleagues ... that's the only reason I said NO for both questions below.”*

What "type" of patient would you exclude from a cluster randomized trial of blood pressure targets? Check all that apply:

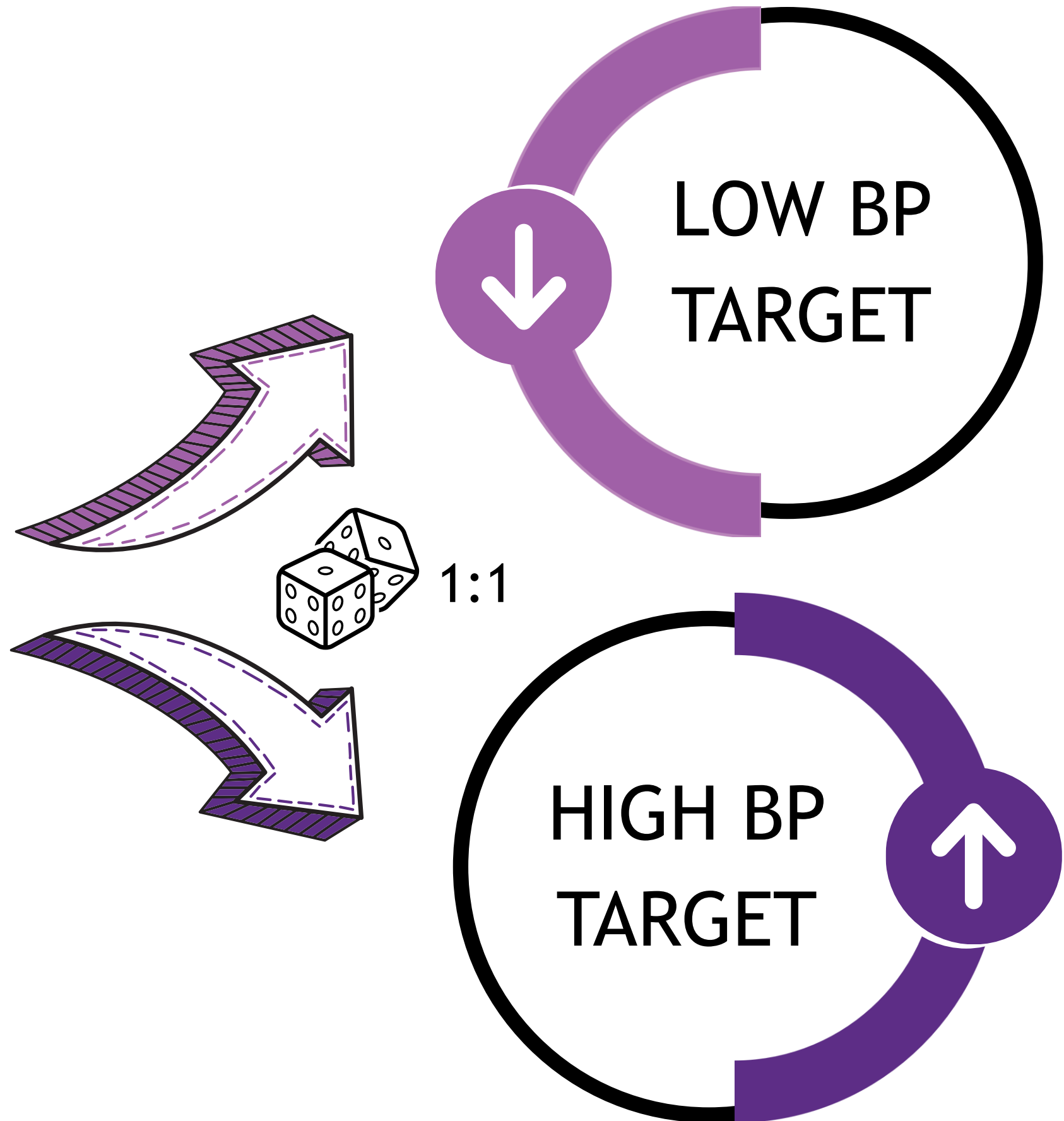


Next Steps - *Finding the “right” target*



FINDING THE RIGHT TARGET

Cluster
Randomized trial
at the level of the
in-centre
hemodialysis unit





**Proposed
Cluster
Randomized
Trial**

OF “CLUSTERS”

- **156 in-centre hemodialysis (HD) units**

DURATION

- **6 months implementation**
- **3 years of follow-up**

POPULATION

- **Adults (≥ 18 years old) on chronic in-centre HD**

INTERVENTION

- **BP target 155-165 mm Hg Systolic (pre-dialysis)**

CONTROL

- **BP target 135-145 mm Hg Systolic (pre-dialysis)**



PRIMARY

- **Composite of cardiovascular-related death or hospital admission with a major cardiovascular event**

SECONDARY

- A composite of all-cause mortality or cardiovascular-related hospitalization, all cause-mortality,
- Components of the primary outcome examined separately.
- All-cause emergency room visits and all-cause hospital admissions
- A hospital encounter with a major fall or fracture.
- Patient-reported symptoms (e.g., cramps, hypotensive episodes requiring fluid) in a subset of patients



OF UNITS

- 4 sites

DURATION

- 3 months

BP TARGETS

- Same as the proposed larger trial

PRIMARY OUTCOME

- A difference in pre-dialysis BP of >10 mm Hg

SECONDARY

- Patient adherence
- Unit adherence
- Adverse events

Sample Size / Power Calculation

- Applying estimates from previous cluster trials, we are able to assume the following:
 - The availability of 156 dialysis centres (78 per arm)
 - Event rate: 0.108/person-year for the primary cardiovascular outcome
 - A coefficient of variation (ratio of between-cluster variance to the average baseline hazard rate) of 0.2694, and a cluster harmonic total person-follow up time (assuming 3-year follow up) of 72.6 years, if we are targeting a hazard ratio of 0.80 we would have approximately 84% power to detect the primary cardiovascular outcome.

Why not randomize at an individual level?

- A well-powered trial would require:
 - 4421 individuals / 631 events (80% Power)
 - 5913 individuals / 844 events (90% Power)
- A pragmatic trial at the cluster (unit) level:
 - Would leverage existing infrastructure (e.g. MyTemp, Dial-Mag)
 - Not require dedicated full-time coordinators in each province
 - Use administrative databases for majority of outcome ascertainment

Question for the Audience (*Clinicians*)

Would you be willing to randomize your patients who are on in-centre hemodialysis to a BP target and/or a BP medication

- **Yes**
- **No**
- **Maybe - More discussion needed with colleagues**

Question for the Audience (*People with in-centre hemodialysis experience*)

As a patient - If your unit was randomized in a clinical trial, would you be agreeable to being assigned to a high BP target?

- **Yes**
- **No**
- **Maybe - More discussion needed with my care team**

Get in touch!

For questions, comments, and suggestions,
or if you are interested in participating as a pilot site:

Principal Investigator – ntangri@sogh.mb.ca

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