

Dial-Bicarb Trial: Lower vs. higher dialysate bicarbonate concentration in patients receiving hemodialysis

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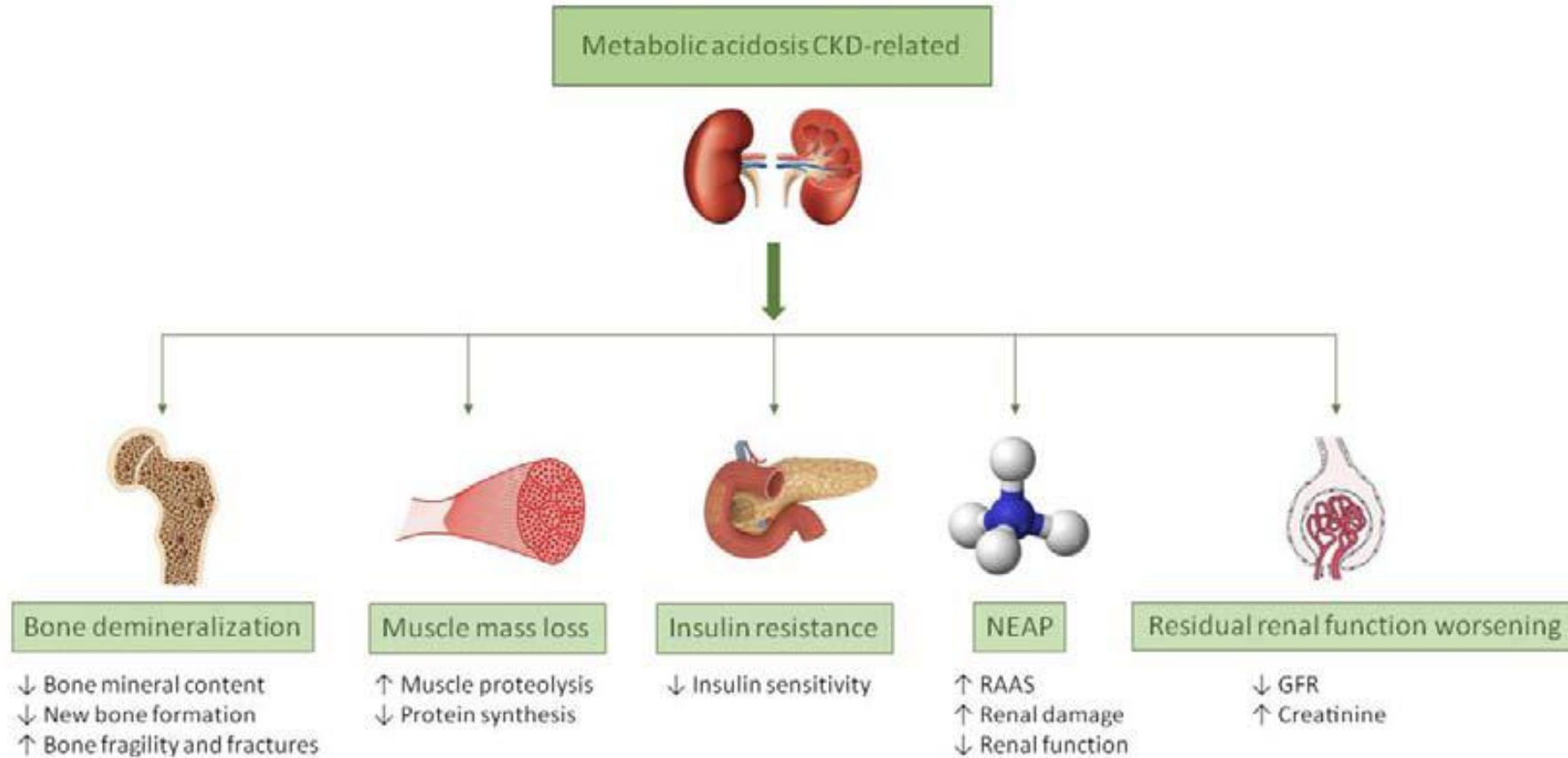
Research Question

In outpatients receiving maintenance hemodialysis, does providing a higher vs. lower dialysate bicarbonate concentration (32 mmol/L vs. 38 mmol/L) as a centre policy for 4 years alter the risk of:

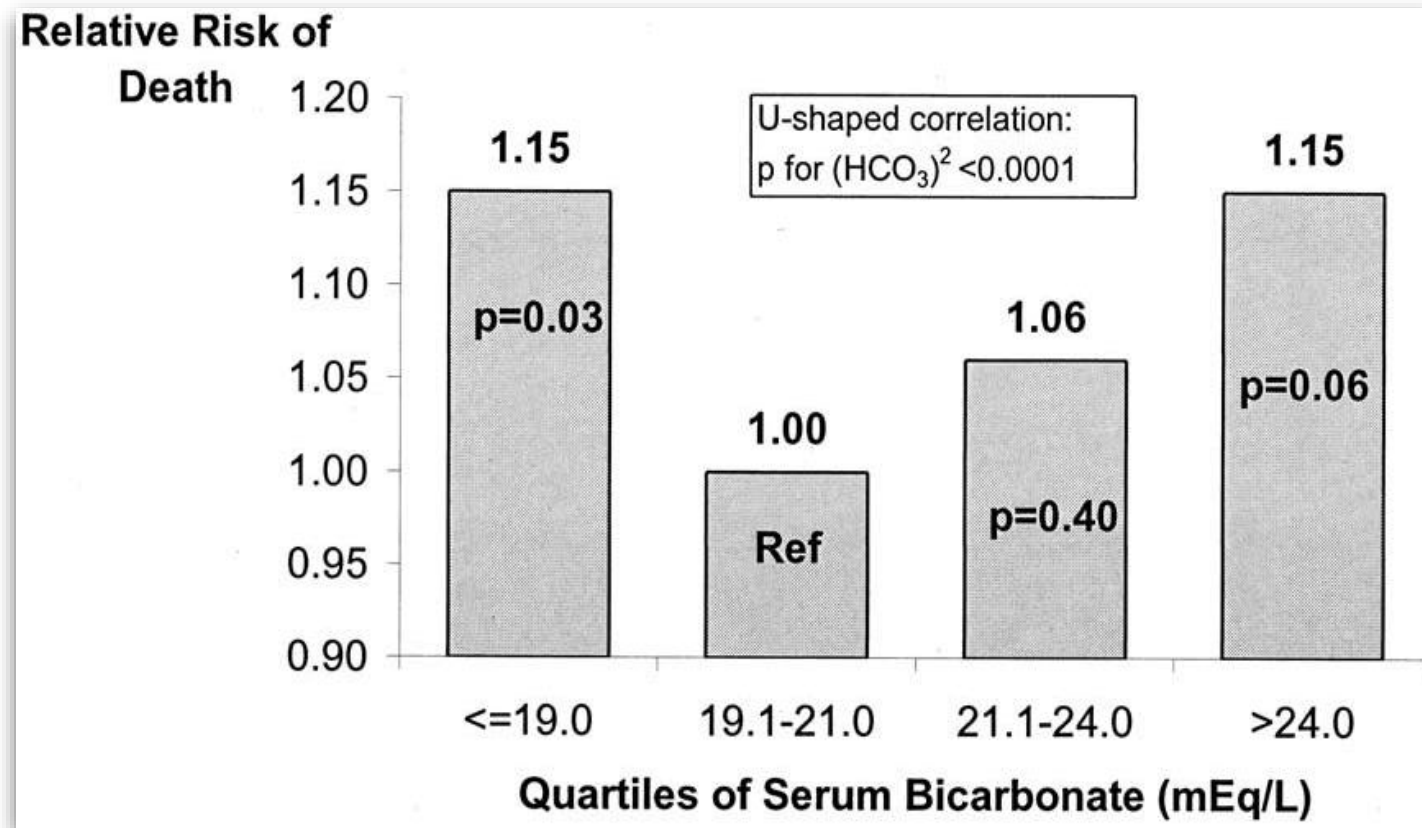
- i) all-cause (non-elective) hospitalization or all-cause mortality (primary composite outcome)

- ii) patient reported muscle cramps

Complications associated with metabolic acidosis



Summary of evidence for the benefit of correcting metabolic acidosis



Summary of evidence for the benefit of correcting metabolic acidosis

Randomized trials in patients on peritoneal dialysis

- Oral bicarbonate supplementation (n=60) or higher dialysate lactate (n=200)
 - Reduced hospitalizations and improved nutrition

Small interventional studies in patients on hemodialysis

- High dialysate bicarbonate (40 mmol/L) suppressed PTH secretion (n=8)
- High dialysate bicarbonate (30 vs. 40 mmol/L) increased triceps skin fold thickness (n=46)
- Correction of acidosis with oral sodium bicarbonate increased insulin sensitivity (n=8)
- Small studies have shown no difference in serum albumin

KDOQI Guideline Acid/base Recommendations

2000

Maintain the pre-dialysis serum bicarbonate ≥ 22 mmol/L

2020

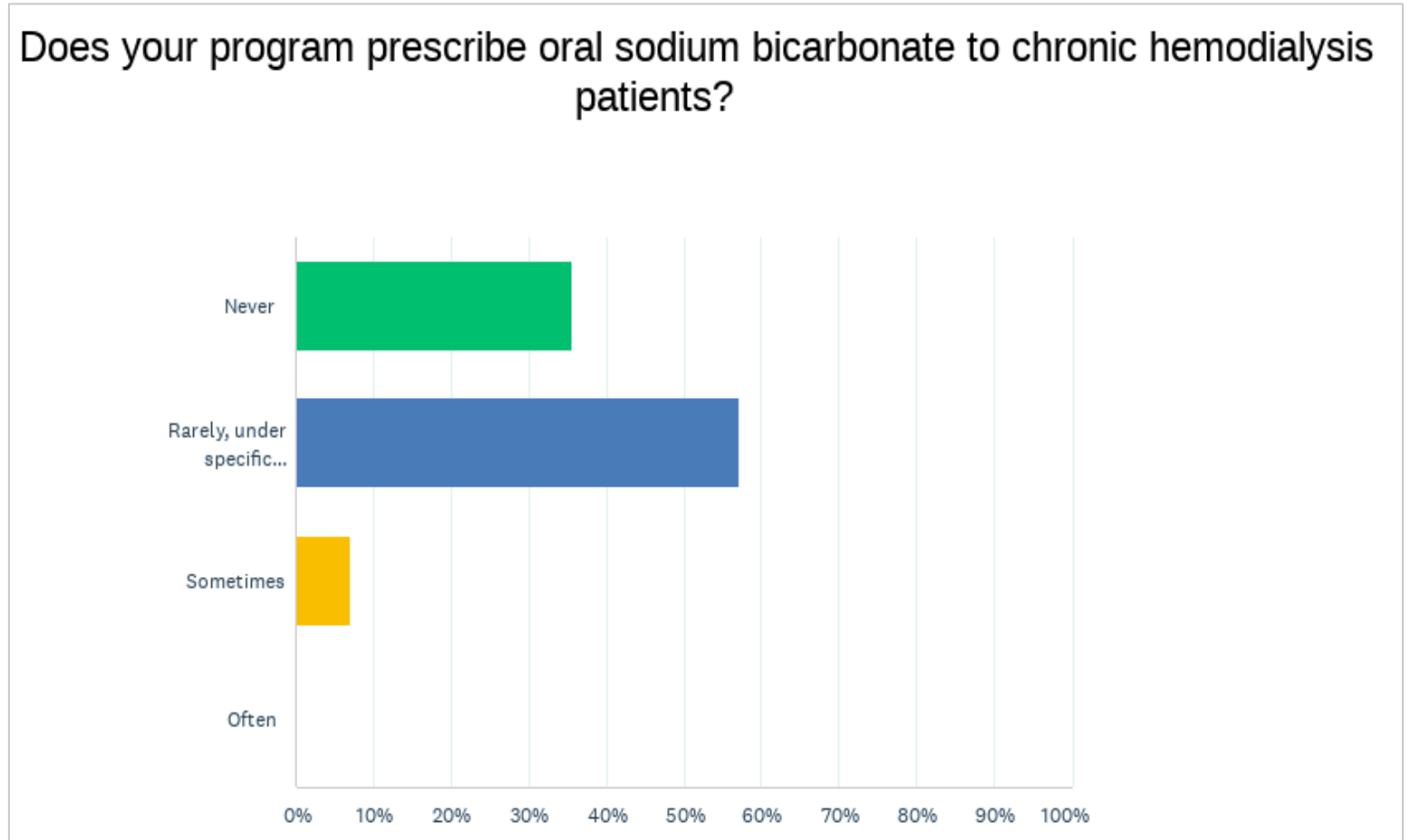
Bicarbonate Maintenance

6.1.2 In adults with **CKD 3-5D**, we recommend reducing net acid production (NEAP) through increased bicarbonate supplementation (1C) in order to reduce the rate of decline of residual kidney function.

6.1.3 In adults with **CKD 3-5D**, it is reasonable to maintain serum bicarbonate levels at 24 - 26 mmol/L (OPINION).

Alkali Replacement in Hemodialysis

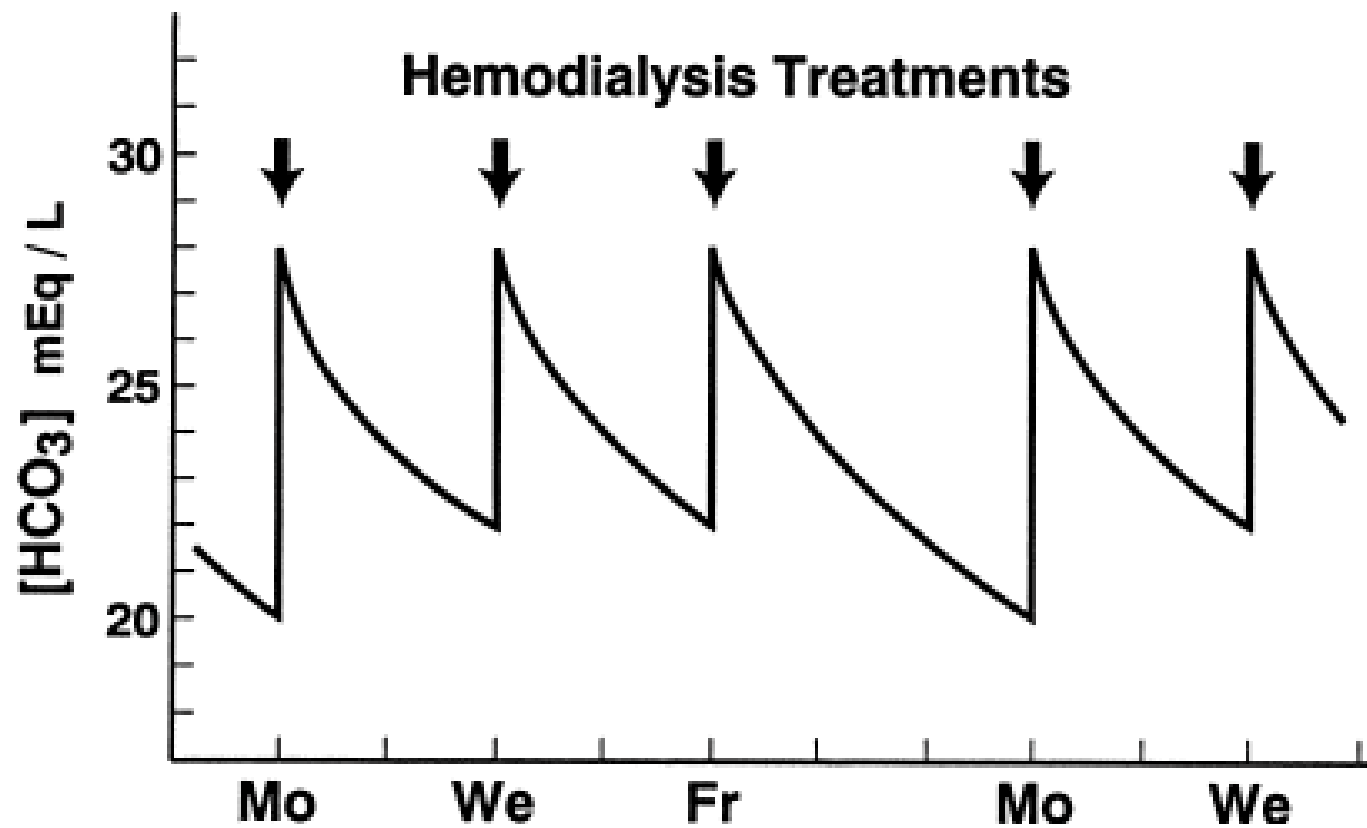
- Oral bicarbonate supplementation OR bicarbonate added to the dialysate



Polling Question #1

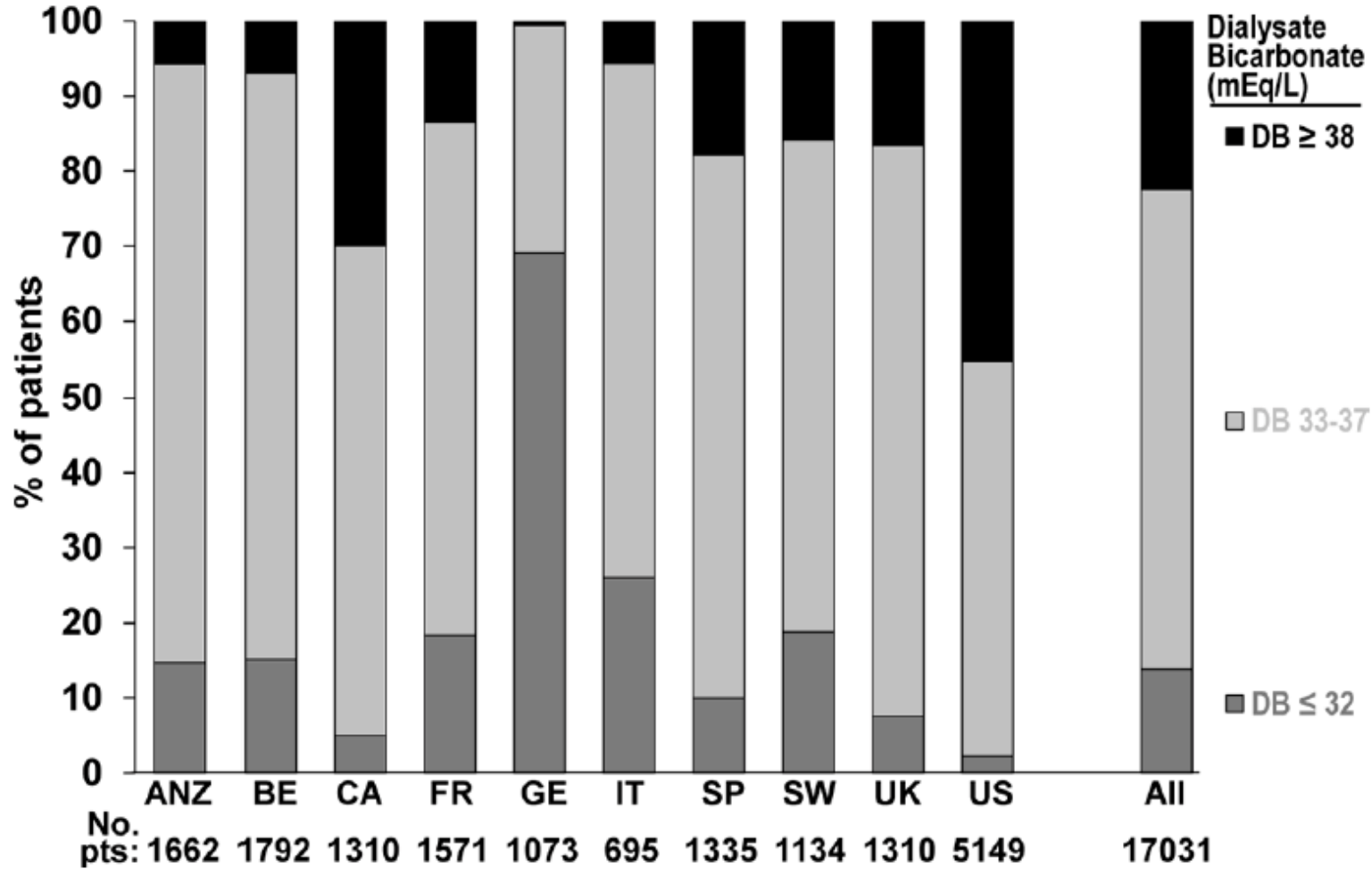


Correction of metabolic acidosis with hemodialysis

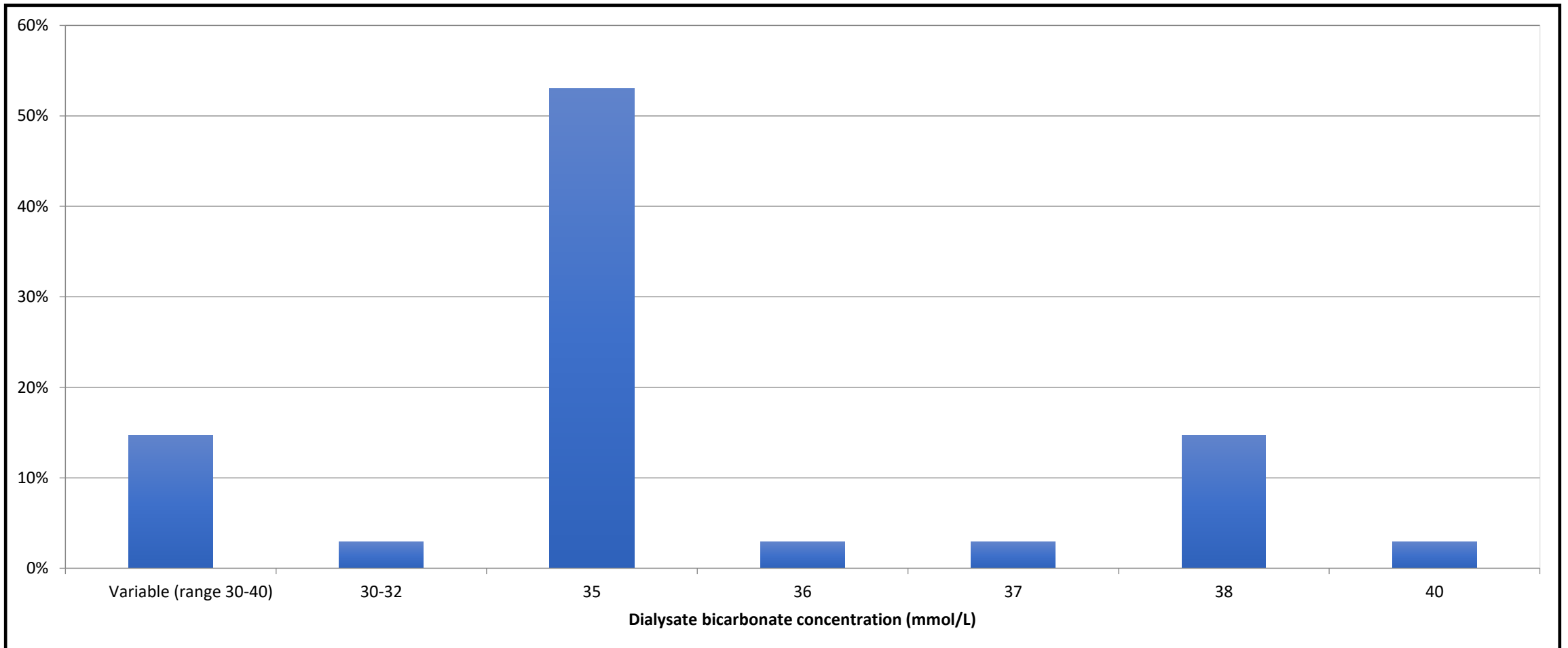


DOPPS-Dialysate Bicarbonate Practices

Mean 35.5



Dialysate Bicarbonate Practices- Canada



Polling Question #2



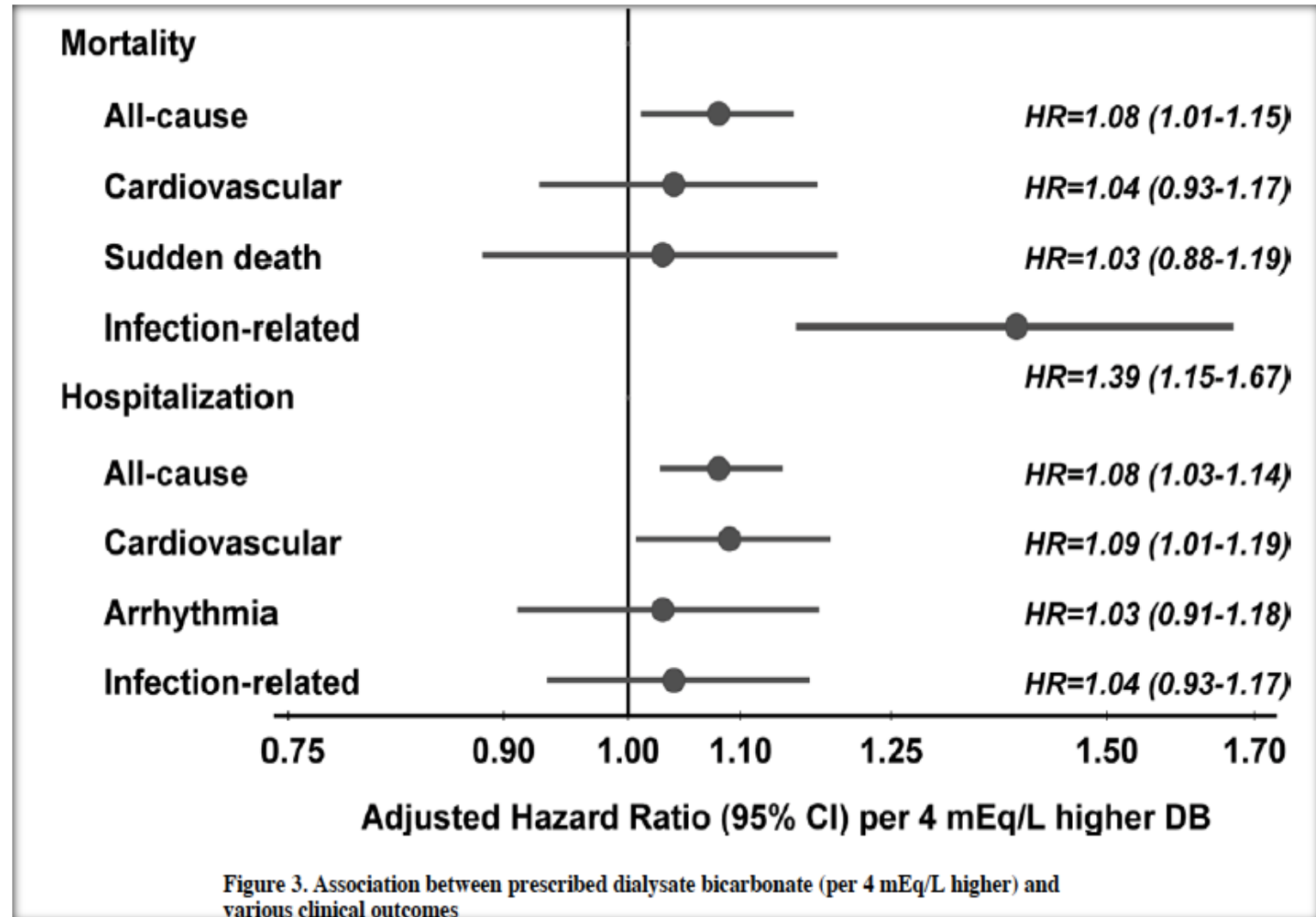
Dialysate Bicarbonate Concentration and Pre/Post-Dialysis pH and Serum Bicarbonate

	Dialysate bicarbonate (mEq/L)		
	25	30	35
Arterial pH		7.36±0.0	7.37±0.04
pre-dialysis	7.36±0.02	5	7.51±0.04
post-dialysis	7.48±0.05*	7.49±0.0*	
Arterial HCO ₃ ⁻ (mEq/L)		9*	
pre-dialysis	21.6±2.6		22.9±3.4
post-dialysis	27.4±1.5*	20.9±2.8	31.2±1.4*
		28.5±3.4* †	

HCO₃⁻, Serum bicarbonate.
 *p value<0.05 between pre-dialysis vs post-dialysis.
 †p value<0.05 between 35 mEq/L vs 30 mEq/L or 25 mEq/L.

DOPPS DATA

17,031 patients
11 countries, including
Canada



Higher dialysate bicarbonate and mortality

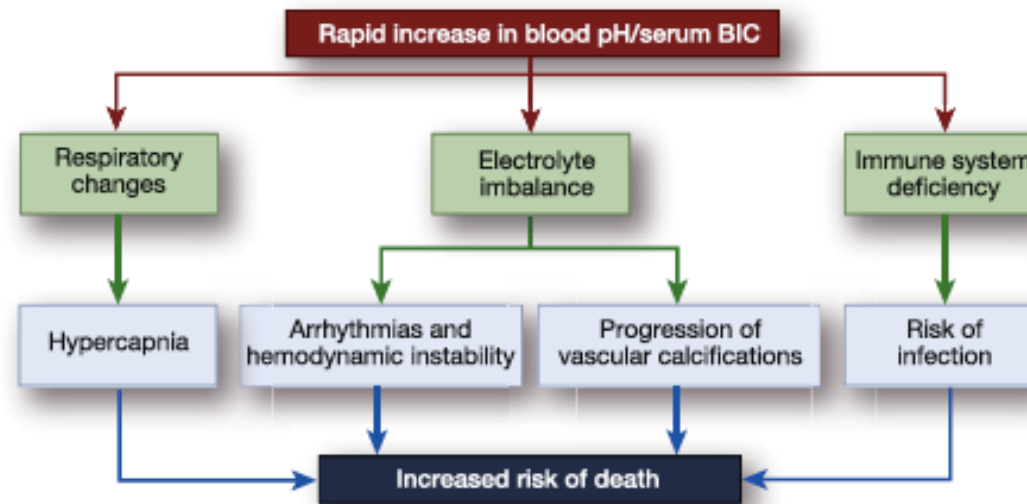


Figure 2 | The strict interplay of the main risk factors associated with a high predialysis blood pH/serum bicarbonate (BIC) leading to an increased risk of death in patients undergoing hemodialysis.

Background Summary

- Aiming for a pre-dialysis serum bicarbonate ≥ 22 mmol/L by increasing the dialysate bicarbonate concentration is not supported by high-quality evidence
- Use of a high dialysate bicarbonate concentration increases the risk for post-dialysis alkalosis
- Observational data show that a higher dialysate bicarbonate concentration is associated with harm
- The effect of dialysate bicarbonate on patient-prioritized outcomes and safety has not been tested in large, adequately powered randomized controlled trials

Research Question

In outpatients receiving maintenance hemodialysis, does providing a higher vs. lower dialysate bicarbonate concentration (32 mmol/L vs. 38 mmol/L) as a centre policy for 4 years alter the risk of:

- i) all-cause (non-elective) hospitalization or all-cause mortality (primary composite outcome)

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Methods

Open label
cluster-
randomization

Covariate constrained
randomization

Waived consent
model

Patients can opt out
of the intervention
and opt out of muscle
cramp data collection

Inclusion criteria

Receipt of HD at the
same centre for at
least 90 days

Exclusion criteria

In centre or frequent
HD

Intervention Groups- 32 mmol/L vs. 38 mmol/L

- Groups fall within the range of current standard of care in Canada
- Can be practically delivered by all dialysis machines
- Create maximal separation between the two groups
- Selected a range that would be acceptable to most nephrologists

Polling Question #3a



Polling Question #3b



Outcomes

Primary composite

- **All cause mortality and all cause hospitalizations**
- We will ascertain non-elective hospitalizations from the *CIHI-DAD*.

Patient-reported outcome

- **Muscle cramps on dialysis**
- This outcome is not available through routinely collected data and will be collected anonymously using the same approach as the ongoing Dial-Mag trial

Sample Size and Power



We assumed a common coefficient of variation (0.30) and a baseline rate of 1.18 events (hospitalizations and/or death) per person year in the higher bicarbonate group.



Anticipate 144 clusters across 5 provinces



4- year follow-up



Assuming a two-sided level of significance $\alpha=0.05$, we will have 80% power to detect a rate ratio of 0.85 for the primary composite outcome



Impact



If we show that a lower dialysate bicarbonate concentration is beneficial, this represents a simple, scalable intervention



The dialysate bicarbonate concentration can be easily adjusted at the level of the dialysis machine at no cost.



The results would be readily translatable into clinical practice

Decisions/Questions

- Refining the intervention
- Refining the outcome
 - Concerns about an all-cause outcome?
 - Concerns about including all-cause non-elective hospitalizations (recurrent event)?
 - Should alpha be spent for a patient-reported outcome?
 - Any other suggestions for a patient-reported outcome?

Polling Question #4

