It was the prior Work Group's opinion that a minimum treatment time of 3 hours reflected contemporary clinical practice and was an especially important threshold level in patients with low Kru (creatinine clearance $< 2$ mL/min). This opinion was largely based on the treatment time delivered within the standard-dose arm in the HEMO trial ($195 \pm 23$ minutes). Thus, 3 hours was selected as the "bare minimum." Since publication of the prior guideline, increasing evidence suggests that longer treatment times may offer clinical benefits beyond small-solute removal. Despite the opinion of many members of the Work Group who routinely initiate HD for 3.5 to 4 hours, the Work Group did not find sufficient evidence to warrant a change in the minimal treatment time recommendation. However, the Work Group acknowledged that many patients require more than 3 hours to achieve optimal volume and metabolic control and suggested that sodium and water balance, interdialytic weight gain, hemodynamic stability during HD, BP control, overall metabolic control (including ability to manage, eg, metabolic acidosis, serum phosphorus, and potassium), Kru, patient preference, and health-related quality of life also be considered when making a decision regarding HD treatment time. Longer treatment times may be required for patients with high interdialytic weight gain, high ultrafiltration rates, poorly controlled BP, difficulty achieving dry weight, or poor metabolic control.

## RATIONALE FOR GUIDELINE 4.2

Although hypertension affects 60% to 90% of HD patients, the clinical benefits of treatment of hypertension in patients undergoing HD have not been established. Observational cohort studies have also been unable to demonstrate evidence for a higher risk of death or CV events in patients undergoing maintenance HD with higher predialysis BPs. In contrast, observational data suggest higher risk of death in patients with low systolic BP, both pre- and post-HD.[169] It is difficult to make treatment recommendations based on these and other observational cohort studies. The inability to demonstrate a higher risk for death with higher BP in these observational studies likely reflects confounding from comorbid conditions like CV disease and protein-energy wasting. In at least one prospective study, higher mean arterial BP was associated with the development of progressive concentric LVH, de novo ischemic heart disease, and de novo congestive heart failure.[170] It is the opinion of the Work Group that control of BP is likely important to reduce the high CV risk of patients undergoing maintenance dialysis. While the ongoing Blood Pressure in Dialysis trial may provide further information about the effects of different BP targets in HD patients on cardiac morphology,[171] the current paucity of clinical trial data does not allow defining the target predialysis, postdialysis, or ambulatory BP for HD patients.

The prevalence and severity of hypertension in patients undergoing maintenance HD is in part attributable to sodium and water retention and ECV expansion.[172-174] No RCTs have tested the hypothesis that one method of BP control is superior to another in improving outcomes, but considering that ECV expansion is an important contributor to elevated BP, it is the opinion of the Work Group that reducing ECV should be the first line of treatment. Achievement of true dry weight, which still remains a largely clinical determination, is necessary for control of BP,[174-177] while failure to achieve target dry weight associates with higher all-cause and CV mortality.[178,179] In one small clinical trial, targeted reduction in ECV using bioimpedance guidance improved BP, LVH, and arterial stiffness when compared to usual-care assessment of dry weight and determination of ultrafiltration rate.[180] However, the effect of controlling BP and reducing LVH on patient-centered outcomes such as hospitalization, CV morbidity, and mortality remains unknown.

To improve control of ECV, reduction of dry weight should be accomplished gradually (over 4-12 weeks or longer) and with assessment of patient tolerability both on and off HD. The Dry Weight Reduction Intervention (DRIP) trial is the largest RCT demonstrating the effect of dry weight reduction on BP control.[181] In this study, 150 HD patients were randomized 2:1 to gradual dry weight reduction (0.1 kg reduction per 10 kg body weight) versus usual care. With an average weight loss of $\sim$1.0 kg, gradual dry weight reduction resulted in an additional $\sim$7 mm Hg greater reduction in ambulatory BP at 8 weeks.[181] However, adverse events including hypotension and seizures were noted with dry weight probing; thus, more gradual reductions may be better tolerated. Critically, whether there is a longer term benefit of this strategy on hard clinical outcomes remains unknown.

The safety and tolerability of the HD procedure is dictated in part by the ultrafiltration rate, which in turn is determined by the interdialytic weight gain and length of each session. No RCTs have tested the hypothesis that reducing interdialytic weight gains or reducing ultrafiltration rates can improve patient-centered outcomes. Observational studies suggest that both large interdialytic weight gain and high ultrafiltration rate are associated with higher mortality.[182-186] Mechanistically, these associations seem plausible, but given the observational nature of these studies, the results may be confounded, especially