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The information delivered in this document was provided by the panellists in the *ISN-KDIGO Webinar: BP Guidelines in CKD - 10th Dec 2021* as feedback to the numerous questions which could not be answered during the live event. Please note that the responses below are only provided for general information and education purposes and do not constitute any medical advice. Under no circumstances shall **The International Society of Nephrology (ISN)**, **Kidney Disease: Improving Global Outcomes (KDIGO)** and any of the panellists be held responsible for any errors or consequences incurred arising from the use of the information hereby provided.

- **What populations were studied before arriving at the target blood pressures? Where African populations part of the study? If no, how can you justify use of these BP targets, including targets in CKD and DM, be justified in African populations?**

From personal practice experience, the adoption of the bio-psycho-social care model with pre-eminence on patient-centred care is an effective management modality for addressing the issue of adherence.

- **Can both speakers offer their experiences and views on management of non-adherence (which can be very intractable in some patients)?**

Thank you for your questions. SPRINT was performed in the USA and Puerto Rico, and around 30% were classified as non-Hispanic African-American, but we both know that such participants may differ markedly from African populations, in terms of genetics, environment, nutrition, etc. So the answer to your question is that we cannot be as certain of the benefits of the SBP target in African populations. In my opinion, one should start from the assumption that (patho)physiology of hypertension is similar across the world: I know of no convincing studies pointing to important differences. It would however be wonderful to see studies done in African populations to confirm or refute the benefits of the SBP target. With respect to adherence, I share your opinion that patient-centred care, with individualised decisions based on the patient's values and preferences, is very important. Encouraging patients to be part of their own care (increasing 'activation') must be important, although studies proving that interventions that improve activation also improve adherence to BP-lowering treatment are lacking. There is however some evidence that home BP monitoring improves both.

- **Is Midodrine a good drug for patients having recurrent drop in blood pressure during dialysis? (having blood pressures of systolic 100-120mmhg in the inter dialytic period?)**

Thank you for your question. There have been studies of the use of Midodrine in haemodialysis patients with chronic hypotension (an infrequent but disabling complication



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of long-term dialysis) (e.g. Lin Y-F et al Am J Med Sci 2003; 325: 256-261), as well as in neurogenic postural hypotension. A systematic review shows that it can be of benefit in intradialytic hypotension (Prakash G et al Nephrol Dial Transplant 2004; 19: 2553-2558) but it was considered a third-line strategy in this review: Reeves PB et al Clin J Am Soc Nephrol 2018; 13: 1297-1303. It can cause urinary retention.

- **If the rate of eGFR falls more rapidly after targeting a lower (i.e. 120 target), in your opinion is that an indication to back off? If SBP is very high e.g. >180, how fast should you bring down the SBP to 120. Is rate of reduction a concern?**

In answer to the first, this depends on the timescale. An acute fall in GFR after initiation or up-titration is an expected consequence of decreased renal perfusion. In albuminuric CKD, this reduction in perfusion is thought to contribute to reduction of intraglomerular hypertension and to predict a slower rate of loss of GFR in the longer term. However, if GFR continues to fall at a faster rate than prior to intensification of BP lowering therapy after the first (say) three months (and there are enough measurements before and after to be sure of this), then, yes, I would consider reducing treatment. I would have more confidence in doing so I thought that the basic pathophysiology was of ischaemic nephropathy (with no albuminuria, and with evidence of extrarenal vascular disease) and less confidence in patients with marked albuminuria.

I don't have a firm answer to the second question. The only situation in which rapid BP reduction might be justified is accelerated hypertension. In all other situations, it makes more sense to titrate treatment slowly. As I mentioned in the Q&A session, there is evidence that it takes one week to achieve 50% of the maximum BP-lowering effect of a change in drug therapy, and up to 6 weeks for the full effects of a change in drug therapy to take effect (Lasserson Heart 2011; 97: 1771-1775). Titrating drug therapy upwards rapidly can therefore result in dangerous over-treatment.

- **Following on from the earlier question, in patients with progressive CKD, what is your strategy for managing hyperkalemia in patients on RAASi?**

RAASi have both CV and kidney benefits in many patients with CKD, so maintaining patients on them as long as possible makes sense. First step is to look at concurrent medication and to see if there is room to add or substitute a diuretic (e.g. Chlortalidone) for another BP-lowering drug (such as an alpha-blocker or calcium channel blocker). Second is to check for acidosis and correct if present (although there is little evidence to support this); sodium bicarbonate supplementation does not worsen fluid retention or exacerbate hypertension, in contrast to sodium chloride. The third option is changing rapidly, but depends on the setting. Until Patiromer and Sodium Zirconium Silicate became available (in some, mostly richer, parts of the world) the third step was dietary potassium restriction; but these drugs are likely to allow continuation of RAASi for longer, and studies are under way to show this.



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- **How to prevent use of nephrotoxic meds?**

It depends on what you mean by nephrotoxic. I hope that you don't mean ACEI and ARB (see <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6334116/>). If you mean truly nephrotoxic drugs such as aminoglycosides, amphotericin, some anti-virals, then a combination of education, restrictions on prescribing through formularies, pharmacist intervention, and use of electronic medical records to provide alerts to clinicians are all worth considering.

- **Why is there not a focus on MAP outside of children?**

I don't have a clear answer. As I mentioned in the course of my presentation, both AASK and MDRD used MAP targets, but all that happened when these trials started to influence practice was that clinicians 'translated' the MAP targets to SBP and DBP targets, and continued to use these to make clinical decisions. It would have, at the time, been more logical to stick to the available evidence and titrate treatment to MAP. The translation to SBP and DBP targets required (unjustifiable) assumptions about pulse pressure; as I also mentioned, a MAP of 92 is consistent with a BP of 125/75 but also of 140/68, 160/58, etc). I can only assume that most clinicians were too 'stuck in their ways' thinking about SBP and DBP to change their practice to include a calculation of MAP. However, I also don't know of any evidence that titrating therapy according to MAP in adults would generate better outcomes. Compared to current practice, a focus on MAP would result in patients with a wide pulse pressure (the elderly, those with CKD and other causes of stiff conduit arteries) being left with higher SBP: and we now that lowering SBP (even in those with relatively high pulse pressure, e.g. the lowest DBP quintile in SPRINT) is beneficial. So the short answer is that children don't have stiff arteries, but many adults do.

- **Can we use ARB in Ckd non- dialysis group?**

Yes, ARBs can be used in non-dialysis CKD. The KDIGO guidelines include recommendations that ACEI or ARB be used in diabetic and non-diabetic CKD with albuminuria (the strength of the recommendation varies with the degree of albuminuria and the presence or absence of diabetes). They also include a practice point stating "It may be reasonable to treat people with high BP, CKD and no albuminuria, with or without diabetes, with RASi (ACEI or ARB)". The guideline also specifically warns against combination of ACEI and ARB (dual therapy). This network meta-analysis <https://pubmed.ncbi.nlm.nih.gov/26597926/> concluded that the evidence favoured ACEI over ARB but this remains a subject of debate.



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- **How do you low blood pressure in hemodialysis under low resources setting with oral drugs?**

The management of hypertension in dialysis patients was not included in the scope of the KDIGO guideline discussed in the webinar, but I'm happy to give you a personal opinion, with the caveat that I have never practised nephrology in a low-resource setting. As you know, ensuring normovolaemia is the most important step in controlling hypertension in dialysis patients: however, this aim has to be balanced with the need to prevent intradialytic hypotension (by slowing the rate of ultrafiltration, though this may necessitate longer dialysis time if resources permit; and by the use of cool dialysate), But you asked about drug therapy. There have not been enough studies on this question – it's a difficult area to study, not least because of the difficulties in deciding on which BP measurement to use. As Dr Hiremath mentioned, BP measured during HD is the opposite of 'standardized'. BP tends to rise in the 4h prior to a dialysis session, so immediate pre-HD BP is not representative of BP at other times. Post-HD BP may be influenced by recent volume reduction. I reviewed this a few years ago now – see [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(09\)60213-0/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(09)60213-0/fulltext). This was a review of a meta-analysis <https://pubmed.ncbi.nlm.nih.gov/19249092/> - another one appeared at much the same time <https://pubmed.ncbi.nlm.nih.gov/19273737/> - both concluded that antihypertensive drug treatment conferred cardiovascular benefits in dialysis patients. Most nephrologists would want to avoid vasodilators because they might exacerbate intradialytic hypotension, and diuretics because they are probably ineffective in oliguric patients. Meta-analyses (but limited to the few available trials) have suggested that beta-blockers and RAAS inhibitors may be beneficial – so my advice would be to start with affordable drugs from these classes. Please see this KDIGO controversies conference report <https://kdigo.org/wp-content/uploads/2017/05/KDIGO-BP-Volume-in-Dialysis-FINAL.pdf>

- **What will you do if there's elevation of BP during dialysis but without symptoms?**

This is out of the scope of the KDIGO guideline so this is my personal opinion. My own approach would be to evaluate carefully for subclinical hypervolaemia, and to consider a reduction in target weight if that can safely be achieved without intradialytic hypotension – depending partly on what the BP is in the interdialytic interval, based on ambulatory or home measurements if available. If you're sure that volume and overall BP control are satisfactory, I would do nothing further for asymptomatic rises in BP during dialysis. Please see this KDIGO controversies conference report <https://kdigo.org/wp-content/uploads/2017/05/KDIGO-BP-Volume-in-Dialysis-FINAL.pdf>

- **What we experienced is the opposite of the first question especially in dialysis patients. They usually have very high systolic and Low diastolic BP. My question is what is the diastolic BP lower target that we shouldn't go lower than that ?**

The short answer is that we have no evidence to guide us. We worry about low diastolic BP because myocardial perfusion is dependent on blood flow to the heart muscle during diastole; so if diastolic pressure is very low, particularly in the presence of flow-limiting coronary artery stenosis, subendocardial ischaemia may result, causing ischaemic injury and subsequent fibrosis. Numerous analyses have demonstrated U-shaped or J-shaped curves relating DBP to poorer outcome, but none of these prove that lowering BP is harmful: they show that low DBP (with high pulse pressure) is a poor prognostic marker, because it is a result of arterial stiffening that usually reflects long-standing structural damage. This is, as you say, very common in dialysis patients, particularly those with a long history. But we don't have any clinical studies to show us what the safe lower limit for DBP is. The KDIGO guideline (for non-dialysis CKD) suggested a limit of 60 mm Hg and this might be reasonable for dialysis patients as well. This is a situation that demands individualised decision-making that takes into account the values and preferences of the patient and the clinical situation – the risks of stroke and heart failure from higher SBP versus the possible risk of MI from lower DBP.

Please see this KDIGO controversies conference report <https://kdigo.org/wp-content/uploads/2017/05/KDIGO-BP-Volume-in-Dialysis-FINAL.pdf>

- **Which type of calcium channel blocker preferred in CKD patients? Dihydropyridine or non dihydropyridine?**

In transplant patients, dihydropyridine CCBs are preferred for reasons explained in detail in the guideline. In non-transplant CKD, there is no strong evidence favouring one subclass over the other.

- **What are your views Beta blocker on CKD patients?**

The evidence suggests that beta-blockers are the preferred antihypertensive agents only when there is another indication for them – such as heart failure. From the limited available evidence, this also pertains in CKD. See this systematic review and meta-analysis <https://pubmed.ncbi.nlm.nih.gov/21884954/>

- **Which is better ACEI or ARB?**

It is difficult to answer this with certainty, because of the paucity of adequately powered head-to-head trials with hard outcomes. This network meta-analysis <https://pubmed.ncbi.nlm.nih.gov/26597926/> concluded that the evidence favoured ACEI over ARB but this remains a subject of debate.



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- **Is the HYPERTENSION in Hemodialysis always related to Volume overload,. If yes how to find the exact volume status in them? Is there any way to predict hyperkalemia due to ACE/ARBS. Please address the issue of Hypertension management in Dialysis pts.**

Some of these were partly answered during the Q&A session.

I don't know of any good way of predicting which patients with CKD will develop hyperkalaemia if treated with ACEI or ARB, other than the baseline eGFR and the baseline serum potassium.

Hypertension in dialysis patients is by no means always related to volume overload, but hypervolaemia is certainly a major cause of hypertension in these patients. There is no 'gold standard' method for finding the correct target weight; it's a matter of careful clinical assessment that includes clinical examination, looking at the pattern of BP response to fluid removal during dialysis, the change of haematocrit during dialysis, and, where resources permit, by assessments of inferior vena cava collapsibility, lung ultrasound, and bioimpedance and other technologies.

Hypertension in dialysis can also be caused by endothelin and angiotensin release, sympathetic activation, and loss of production of vasodepressor substances from the kidney, and many other factors. Hypertension in anephric patients is much more commonly due to pure volume overload, but such patients can still have stiff conduit arteries causing systolic hypertension even when normovolaemic.

Please see this controversies conference report: <https://kdigo.org/wp-content/uploads/2017/05/KDIGO-BP-Volume-in-Dialysis-FINAL.pdf>

- **How about beta blockers in CKD-HD?**

This question is outside the scope of the KDIGO guideline so I can only give you a personal opinion: which is that beta-blockers should be used in dialysis patients in clinical situations where there would a positive indication (such as heart failure) in the non-renal population. There is a good review of this question, with free full text, here <https://pubmed.ncbi.nlm.nih.gov/25359873/>. A small trial (n=200) suggested that atenolol-based therapy might be superior to lisinopril-based therapy in dialysis patients <https://pubmed.ncbi.nlm.nih.gov/24398888/> but this was based on non-prespecified primary endpoints.

The best review available is this controversies conference report: <https://kdigo.org/wp-content/uploads/2017/05/KDIGO-BP-Volume-in-Dialysis-FINAL.pdf>



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- **How to calculate cardiovascular risk in patients with progressive decline of CKD?**

This paper gives the most comprehensive answer:

[https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(20\)30296-0/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30296-0/fulltext)

But probably the best site to visit would be the CKD consortium website, which gives several risk models including the Kidney Failure Risk Equation and an equation that predicts various clinical outcomes including CV events and ESKD <https://www.ckdpcrisk.org>

- **What is the treatment for refracter hypertension in CKD?**

This is outside the scope of the KDIGO guideline.