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New Insights on the Ideal Blood Pressure Levels for Renal Protection

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The global prevalence and impact of chronic kidney disease (CKD) are significant and escalating. Representing a worldwide prevalence of 9.1%, there were 697.5 million documented cases of CKD across all stages in 2017 resulting in 1.2 million deaths and 2.6 million individuals requiring kidney replacement therapies. Notably, since 1990, the global all-age prevalence of CKD has risen by 29.3%.[1] Hypertension (HTN) affects 80%–85% of individuals with CKD, a considerably higher rate compared to the general populace thus highlighting the significant role CKD plays in worsening hypertensive conditions.[2] Diabetes is the leading cause of both CKD and end-stage kidney disease (ESKD), a condition that is primarily attributed to hyperglycemia, which leads to detrimental functional and structural alterations within the glomeruli.[3,4] Furthermore, HTN is observed twice as frequently in individuals with diabetes compared to the general population.[5] As the primary cause of morbidity and mortality among diabetic individuals, cardiovascular disease (CVD) is further exacerbated by the presence of HTN.[5]

For most of the CKD population, the risk of death from CVD exceeds the risk of developing ESKD. From 2002 to 2022, the number of newly registered ESKD cases in the United States experienced a substantial increase from 99,956 to 131,194, representing an increase of 31.3%.[6] Therefore, measures aimed at reducing the rate of cardiovascular events represent a cornerstone in the management of CKD patients, including effectively treating HTN.

The results of a large meta-analysis conducted with prospective observational studies in more than one million individuals without known CVD revealed that the risk of death from CVD (stroke and coronary heart disease) decreased progressively with lower blood pressure (BP) levels. This correlation was maintained even at BP levels considered normal (values of 115/75 mmHg) and in all age groups (between 40 and 89 years).[7]

All guidelines recommend a treatment strategy that seeks to adequately control all cardiovascular risk factors, especially type 2 diabetes mellitus (T2DM), and strict control of BP. Pursuing BP targets is essential to mitigate the prevalence of CKD. However, despite the results of different studies over the last two decades, the optimal target BP for renal protection in individuals with T2DM remains an unresolved issue, with major guidelines worldwide adopting different targets. Just to cite the three most recently published, the European Society of Hypertension recommends targeting BP <130/80 mmHg in under 65-year-old T2DM patients, and systolic BP (SBP) 130–139 mmHg in over 65-year-old patients.[8] The European Society of Cardiology and the American Diabetes Association, on the other hand, recommend an on-treatment BP goal of <130/80 mmHg if tolerated.[9,10]

Current disagreements in the clinical guideline recommendations stem from the outcomes of major trials conducted in the past decade. Numerous studies have failed to demonstrate additional renal protection from BP targets lower than those typically advised for individuals with diabetes and CKD. This phenomenon may be attributed to the potential for very low BP levels to decrease the glomerular filtration rate (GFR), thereby exacerbating renal function.[11] For instance, a substantial real-world cohort study analyzing clinical records of 29,923 patients with HTN and T2DM who exhibited normal renal function at baseline provides further insight into this complex issue. The results indicate that individuals in the apparent treatment-resistant HTN group experience a significantly increased risk of developing CKD or experiencing a substantial decline in GFR over a 4-year follow-up period. The relationship between achieved BP and renal function appears to follow a J-shaped curve, with adverse outcomes observed at very low SBP values (below 120 mmHg). Optimal SBP values were identified as being between 120 and 140 mmHg.[12] While it is generally anticipated that worsening heart failure leads to decreased BP and deteriorated renal function, this study did not detail the baseline prevalence of heart failure. Consequently, a direct correlation between worsening cardiac and renal function cannot be established from the provided data.

Other investigative trials, such as the ACCORD (Action to Control Cardiovascular Risk in Diabetes) study, investigated two groups of patients based on their target SBP: an intensive treatment group (target SBP <120 mmHg) versus a standard treatment group (target SBP <140 mmHg). The intensive treatment group achieved BP of 119/64 mmHg and the standard group 133/70 mmHg. There were no significant differences in cardiovascular events between the study groups, except for a reduced incidence of stroke in the intensive treatment group. However, the intensive treatment group was associated with a higher risk of adverse events (bradycardia, hypotension, hyperkalemia, and worsening of renal function).[13]

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Additionally, the ACCORD study was underpowered for a BP intervention group, and the results may have been biased due to the factorial design of the glucose intervention employed.[14]

In turn, the Systolic Blood Pressure Intervention Trial (SPRINT) tested SBP reduction targets similar to the ACCORD trial in non-diabetic subjects with a high cardiovascular risk. The intensive treatment group (SBP <120 mmHg) presented a 25% relative risk reduction in fatal and nonfatal cardiovascular events, and a 27% reduction in all-cause mortality.[15] The SPRINT Trial concluded prematurely and was insufficiently powered to conclusively determine its renal protective effects. A notable observation was the significant occurrence of acute kidney injury within the intensive treatment group.[16]

More recently, the BPROAD (Blood Pressure Control Target in Diabetes) trial revealed that the incidence of major cardiovascular events was significantly lower after applying intensive treatment (target SBP <120 mmHg) compared to standard treatment (target SBP <140 mmHg) in patients with T2DM. Nevertheless, no significant difference was observed for the renal end points (CKD progression and CKD development).[17]

Considering all factors, the study conducted by Olsen et al. represented a significant contribution to the understanding of reducing the risk of CVD by employing a lower SBP target for renal protection.[18] They aimed to investigate whether achieving an average SBP 130–139 mmHg or SBP < 130 mmHg would be related to renal protection compared to patients remaining at SBP ≥140 mmHg.[18] Data from 13,803 participants of the Valsartan Antihypertensive Long-term Use Evaluation (VALUE) trial were analyzed.[19] The study that took place between 1997 and 2004 compared the effects of two different antihypertensive treatment regimens (amlodipine and valsartan) on cardiac morbidity and mortality in high-risk hypertensive patients aged 50–80 years. The primary endpoint of this study was defined as the time to the first occurrence of a cardiac event. This composite endpoint included several critical cardiovascular outcomes: sudden cardiac death, fatal myocardial infarction (MI), death during or after coronary angioplasty or coronary artery bypass graft, death resulting from heart failure, and death associated with recent MI confirmed by autopsy. Additionally, it encompassed heart failure requiring hospital management, nonfatal MI, or emergency procedures performed to prevent an MI.[19] The outcomes showed no significant difference for the primary endpoint between valsartan and amlodipine. Subsequently, patients in the valsartan and amlodipine treatment arms were pooled for further analyses of the effects of lowering the BP on renal protection, including in a prespecified subgroup of 4,655 diabetic patients and 9,148 patients in the non-T2DM group. Olsen *et al*. reported the results for prespecified secondary kidney endpoints approved by the VALUE Trial expert Endpoint Committee, which were: worsened kidney function (an increase of 50% or more in serum creatinine from baseline confirmed on at least two occasions four weeks apart) and ESKD with the need for dialysis and/or kidney transplantation. They designated a group with an achieved average SBP ≥140 mmHg as the reference group. Adjusted Cox proportional hazards models with multiple covariates at baseline were used to analyze the endpoints for patients who achieved average SBP of 130–139 mmHg or SBP <130 mmHg up to the occurrence of a prespecified endpoint, or throughout the treatment period. Additionally, quartile analyses of achieved average SBP with the relationships to kidney endpoints were assessed by Cox regression with quartile one (highest SBP) as reference.[18]

In their analysis, the authors identified 502 kidney endpoints. Of these, 420 patients experienced worsened kidney function, and 82 progressed to ESKD. A significantly reduced hazard ratio for both worsening kidney function and ESKD was observed in patients who achieved an average SBP between 130 and 139 mmHg and those with SBP below 130 mmHg. However, it is notable that very few patients in the group with SBP below 130 mmHg reached the ESKD endpoint. The findings demonstrated consistency between the T2DM and non-T2DM cohorts. However, a notable exception was observed: statistical significance for ESKD could not be established in diabetic patients with SBP below 130 mmHg, a limitation attributed to the occurrence of only a single ESKD event within this specific subgroup. Also, for continuous and quartile-based analyses of achieved SBP, the lowest BP (specifically quartiles 3 and 4) found significant results for both kidney endpoints. Data suggest that an average SBP <130 mmHg is associated with renal protection in high-risk hypertensive patients, irrespective of whether they have T2DM or not. However, due to the limited number of renal endpoints in the study, a definitive conclusion regarding more substantial renal protection within this precise BP range cannot be firmly established.[18] Unlike randomized clinical trials (RCTs) such as BPROAD and ACCORD, which employ varied therapeutic targets, the findings from the Olsen et al. study originate from a secondary analysis of a large prospective study representing a primary limitation. Similarly, in the VALUE study, proteinuria was assessed qualitatively on only two occasions. This restricted evaluation weakens the robustness of the renal outcome definition and, consequently, the inferences drawn regarding the impact of target BP on these outcomes.

Despite the noted limitations, several strengths of the study warrant emphasis. Firstly, no significant differences were observed in the primary endpoints of the VALUE trial between the study groups. Secondly, the renal endpoint was prespecified and received approval from an ethics committee that included nephrologists, ensuring its rigorous definition. Thirdly, the trial incorporated a substantial number of individuals with diabetes (n = 4,655), enhancing the generalizability of its findings to this patient population. Fourth, the data analysis was rigorously adjusted for baseline differences in covariates across the various BP ranges and quartiles. Finally, the consistent trend observed across the quartiles further reinforced the findings related to the BP ranges.[18]

The results of the ongoing prospective OPTIMAL-DIABETES study are expected to show sufficient endpoints so that the investigators can finally demonstrate, in an extensive prospective study, the benefits of intensive treatment in renal protection of diabetics.[20] Given the relationship between kidney disease and cardiovascular events, as well as the prevalence of CKD in HTN

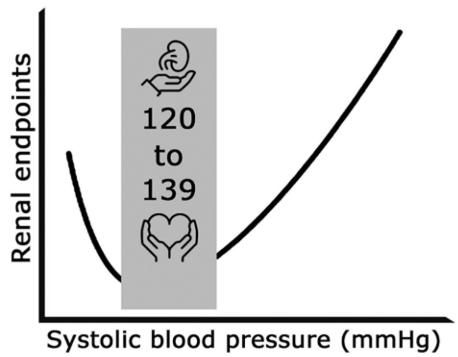

Figure 1. The figure shows that for high-cardiovascular-risk patients a systolic blood pressure range of 120–139 mmHg offers renal protection and cardiovascular events.

and T2DM, this evidence may be of great relevance. Moreover, recently published HTN guidelines recommend an SBP target of 120–129 mmHg to reduce cardiovascular events.[9]

This study concludes that an SBP target below 130 mmHg offers comparable renal protection to an SBP range of 130–139 mmHg. However, an analysis of the quartile trends suggests that SBP values under 130 mmHg might provide superior renal protection. Future randomized controlled trials (RCTs) are anticipated to definitively confirm these preliminary findings. While awaiting the results of such studies, an SBP target below 130 mmHg could be recommended for high-cardiovascular-risk patients, irrespective of their T2DM status. This approach aims to mitigate the risks of CKD, ESKD, and CVD, aligned with existing recommendations for reducing cardiovascular events and providing renal protection, as illustrated in Figure 1.

Conflict of Interest

The authors declared no conflict of interest.

REFERENCES

1. Deng L, Guo S, Liu Y, Zhou Y, Liu Y, Zheng X, Yu X, Shuai P. Global, regional, and national burden of chronic kidney disease and its underlying etiologies from 1990 to 2021: a systematic analysis for the Global Burden of Disease Study 2021. *BMC Public Health* 2025; 25:636.
2. Mills KT, Bundy JD, Kelly TN, Reed JE, Kearney PM, Reynolds K, Chen J, He J. Global disparities of hypertension prevalence and control. *Circulation* 2016; 134:441–450.
3. Gheith O, Farouk N, Nampoory N, Halim MA, Al-Otaibi T. Diabetic kidney disease: world wide difference of prevalence and risk factors. *J Nephropharmacol* 2016; 5:49–56.
4. Webster AC, Nagler EV, Morton RL, Masson P. Chronic kidney disease. *Lancet* 2017; 389:1238–1252.
5. Petrie JR, Guzik TJ, Touyz RM. Diabetes, hypertension, and cardiovascular disease: clinical insights and vascular mechanisms. *Can J Cardiol* 2018; 34:575–584.
6. National Institutes of Health (NIH). The United States Renal Data System (USRDS) 2024. Annual Data Report // End Stage Renal Disease // 1: Incidence, Prevalence, Patient Characteristics, and Treatment Modalities. https://usrds-adr.niddk.nih.gov/2024/end-stage-renal-disease/1-incidence-prevalence-patient-characteristics-and-treatment-modalities. Accessed 01 June 2025.
7. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R; Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* 2002; 360:1903–1913.
8. Mancia G, Kreutz Co-Chair R, Brunström M, Burnier M, Grassi G, Andrzej J, Muiesan ML, Tsioufis K, Agabiti-Rosei E, Algharably EAE, Azizi M, Benetos A, Borghi C, Hitij JB, Cifkova R, Coca A, Cornelissen V, Cruickshank JK, Cunha PG, Danser AHJ, Rosa Maria de P, Delles C, Dominiczak AF, Dorobantu M, Doumas M, Fernández-Alfonso MS, Halimi J-M, Járai Z, Jelaković B, Jordan J, Kuznetsova T, Laurent S, Lovic D, Lurbe E, Mahfoud F, Manolis A, Miglinas M, Narkiewicz K, Niiranen T, Palatini P, Parati G, Pathak A, Persu A, Polonia J, Redon J, Sarafidis P, Schmieder R, Spronck B, Stabouli S, Stergiou G, Taddei S, Thomopoulos C, Tomaszewski M, Van de Borne P, Wanner C, Weber T, Williams B, Zhang Z-Y, Kjeldsen SE. 2023 ESH Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Hypertension Endorsed by the European Renal Association (ERA) and the International Society of Hypertension (ISH). *J Hypertens* 2023; 41:1874–2071.
9. McEvoy JW, McCarthy CP, Bruno RM, Brouwers S, Canavan MD, Ceconi C, Christodorescu RM, Daskalopoulou SS, Ferro CJ, Gerdts E, Hanssen H, Harris J, Lauder L, McManus RJ, Molloy GJ, Rahimi K, Regitz-Zagrosek V, Rossi GP, Sandset EC, Scheenaerts B, Staessen JA, Uchmanowicz I, Volterrani M, Touyz RM; ESC Scientific Document Group. 2024 ESC guidelines for the management of elevated blood pressure and hypertension. *Eur Heart J* 2024; 45:3912–4018.
10. American Diabetes Association Professional Practice Committee. 10. Cardiovascular disease and risk management: standards of care in diabetes—2025. *Diabetes Care* 2025; 48:S207–S238.
11. Viazzi F, Leoncini G, Grassi G, Pontremoli R. Antihypertensive treatment and renal protection: is there a J-curve relationship? *J Clin Hypertens (Greenwich)* 2018; 20:1560–1574.
12. Viazzi F, Piscitelli P, Ceriello A, Fioretto P, Giorda C, Guida P, Russo G, De Cosmo S, Pontremoli R; AMD-Annals Study Group. Resistant hypertension, time-updated blood pressure values and renal outcome in type 2 diabetes mellitus. *J Am Heart Assoc* 2017; 6:e006745.
13. The ACCORD Study Group. Effects of intensive blood-pressure control in type 2 diabetes mellitus. *N Eng J Med* 2010; 362:1575–1585.
14. Tsujimoto T, Kajio H. Benefits of intensive blood pressure treatment in patients with type 2 diabetes mellitus receiving standard but not intensive glycemic control. *Hypertension* 2018; 72:323–330.
15. The SPRINT Research Group. A randomized trial of intensive versus standard blood-pressure control. *N Eng J Med* 2015; 373:2103–2116.
16. Cheung AK, Rahman M, Reboussin DM, Craven TE, Greene T, Kimmel PL, Cushman WC, Hawfield AT, Johnson KC, Lewis CE, Oparil S, Rocco MV, Sink KM, Whelton PK, Wright JT Jr, Basile J, Beddhu S, Bhatt U, Chang TI, Chertow GM, Chonchol M, Freedman BI, Haley W, Ix JH, Katz LA, Killeen AA, Papademetriou V, Ricardo AC, Servilla K, Wall B, Wolfgram D, Yee J; SPRINT Research Group. SPRINT Research Group. Effects of intensive BP control in CKD. *J Am Soc Nephrol* 2017; 28:2812–2823.
17. Bi Y, Li M, Liu Y, Li T, Lu J, Duan P, Xu F, Dong Q, Wang A, Wang T, Zheng R, Chen Y, Xu M, Wang X, Zhang X, Niu Y, Kang Z, Lu C, Wang J, Qiu X, Wang A, Wu S, Niu J, Wang J, Zhao Z, Pan H, Yang X, Niu X, Pang S, Zhang X, Dai Y, Wan Q, Chen S, Zheng Q, Dai S, Deng J, Liu L, Wang G, Zhu H, Tang W, Liu H, Guo Z, Ning G, He J, Xu Y, Wang W. BPROAD Research Group. Intensive blood-pressure control in patients with type 2 diabetes. *N Eng J Med* 2024; 392:1155–1167.
18. Olsen E, Søraas CL, Schmieder RE, Jamerson K, MacDonald TM, Mancia G, Heimark S, Mehlum MH, Liestöl K, Larstorp AN, Mariampillai JE, Mo R, Halvorsen LV, Rostrup M, Høieggen A, Kjeldsen SE, Weber MA. Low achieved systolic blood pressure related to kidney protection in diabetic and non-diabetic high-risk hypertensive patients. *Am J Hypertens* 2025. hpaf093. https://pubmed.ncbi.nlm.nih.gov/40397037/
19. Julius S, Kjeldsen SE, Weber M, Brunner HR, Ekman S, Hansson L, Hua T, Laragh J, McInnes GT, Mitchell L, Plat F, Schork A, Smith B, Zanchetti A; VALUE trial group. VALUE trial group. Outcomes in hypertensive patients at high cardiovascular risk treated with regimens based on valsartan or amlodipine: the VALUE randomised trial. *Lancet* 2004; 363:2022–2031.
20. Clinicaltrials.gov. Optimal Blood Pressure for the preventTIon of Major vAscuLar Events in Patients With DIABETES Mellitus (OPTIMAL-DIABETES). https://clinicaltrials.gov/study/NCT04040634. Accessed 2 June 2025.