International Society of Nephrology (ISN) submission to the second WHO consultation on the updated Appendix 3 of the Global action plan for the prevention and control of NCDs 2013–2030

August 2022

The International Society of Nephrology (ISN), as the leading, global organization dedicated to advancing kidney health, continues to build its global network and programs to facilitate and promote the provision of sustainable, equitable, ethical care for people with kidney disease in all regions and countries of the world. ISN therefore welcomes WHO's clear recognition of health and, specifically, the need to tackle the burden of non-communicable diseases (NCDs) as key priorities of the Global NCD Action Plan 2013–2020.

Kidney disease worldwide is an important, yet "neglected" NCD and raises important public health concerns. All-age mortality from Chronic Kidney Disease (CKD increased) 41.5% between 1990-2017 prevalence 9.1%. Global all-age prevalence increased by 29.3% since 1990 and most CKD burden is concentrated in lower quintiles of socio-demographic index (SDI).[1] The age standardized global prevalence of CKD in adults over 20 years is 10.4% in men and 11.8% in women, but the majority are unaware of the condition.[2] The prevalence of kidney disease in many low income countries remains unknown but is anticipated to be higher. Globally, 2.6 million people received dialysis in 2010, a number which is projected to rise to 5.4 million by 2030[3].

Although kidney disease is not among the NCDs specifically targeted by the WHO Global Action Plan (2013–2020), the ISN welcomes the fact that Appendix 1 recommends a comprehensive response to the prevention and control of NCDs considering "synergies between the 4 major communicable diseases and other diseases, including kidney disease".

Indeed, the major risk factors for CKD in developed countries are diabetes, age and hypertension, conditions which are all increasing and contributing to the rising prevalence of CKD globally. The important implications of CKD lie not only in the risk of End-Stage Kidney Disease (ESKD), which necessitates dialysis or transplantation for survival, but also in the significant multiplication of cardiovascular risk among patients with CKD that leads to many excess strokes and heart attacks yearly[4]. A frequently underappreciated fact is that CKD alone is a stronger risk factor for coronary than diabetes alone, and when the two conditions co-exist (occurs in 1 in 3 patients with diabetes), the risk of cardiovascular events and overall mortality is further multiplied[5],[6].

In view of the strong relationship between kidney disease, diabetes & cardiovascular disease (CVD), the ISN wishes to suggest a number of additional interventions to those currently listed in the **updated Appendix 3 presented on pages 15 -17 of the WHO Discussion Paper.**

---

[1] Global, regional, and national burden of chronic kidney disease, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017." Lancet, 2020 vol. 395,10225, pp 709-733.

[2] Mills et al., Kidney international, 2015, vol. 88,5, pp 950-7.

[3] Liyanage et al., Lancet, 2015, vol. 385,9981 (2015), pp 1975-82.

[4] European Kidney Health Alliance. Recommendations for sustainable kidney care. In: Alliance EKH, editor: European Kidney Health Alliance; 2015.

[5] Tonelli M, Muntner P, Lloyd A, et al. Risk of coronary events in people with chronic kidney disease compared with those with diabetes: a population-level cohort study. Lancet 2012; 380(9844): 807-14.;

[6] European Kidney Health Alliance. Recommendations for sustainable kidney care. In: Alliance EKH, editor.: European Kidney Health Alliance; 2015.

Cardiovascular disease

1. PROPOSED INTERVENTION (NEW)
"Identification and treatment of albuminuria with SGLT2 inhibitors and inhibitors of the renin angiotensin system (ACE-- inhibitors and ARBs) in patients with hypertension, diabetes and cardiovascular disease in order to reduce cardiovascular risk"
JUSTIFICATION
Protecting the kidney is essential to protecting the heart. Chronic kidney disease (CKD) is a very important risk factor for cardiovascular disease (CVD), especially when albuminuria is present. Dipstick positive albuminuria has been shown to be associated with CVD and dipstick testing can be implemented relatively cheaply. (Couser et al, Kidney Int., 2011, vol. 80(12), pp.1258-70). Screening for albuminuria and early intervention with angiotensin--converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) has been demonstrated to be cost effective in Europe as a measure to reduce CVD. (Vanholder et al, Nat Rev Nephrol, July 2017, vol 13, p 393) Furthermore, the use of ACE-- inhibitors and ARBs to treat albuminuria has also been shown to reduce the risk of heart failure in patients with CKD. (Anand et al, 2009, Circulation vol. 120,16, pp. 1577-84.). CKD, including albuminuria alone and/or reduced glomerular filtration rate (GFR), is as much of a risk factor for CVD as diabetes mellitus (DM) and should therefore be treated as such. (Couser et al, Kidney Int., 2011, vol. 80(12), pp.1258-70). The risk is further increased when DM and CKD co--exist (Tonelli et al, Lancet, 2012, vol. 380,9844, pp 807-14).
2. PROPOSED INTERVENTION (NEW)
"Recognition of reduced kidney function / glomerular filtration rate (GFR) as a high risk factor for adverse cardiovascular outcomes that can be attenuated with timely management: do not allow reduced kidney function to inappropriately preclude or delay investigations or treatments that are clinically indicated"
JUSTIFICATION

The phenomenon of "renalism" (Chertow et al, JASN, 2004 vol. 15,9, pp 2462-8)) demonstrates that patients with reduced kidney function / glomerular filtration rate (GFR) receive fewer interventions and tend to leave hospital with fewer of the guideline-recommended medications for secondary prevention. This phenomenon leads to higher mortality, suboptimal secondary prevention and increased risk of future cardiovascular disease (CVD) events.

In patients with a reduced GFR, invasive cardiovascular investigations and cardioprotective medications should, nevertheless, be utilized with appropriate caution to reduce kidney complications. (Leung et al., CJASN, 2014, vol. 9,11, pp 1840-8., Charytan et al., CJASN, 2009, vol. 4,6, pp. 1032-43.)

3. PROPOSED INTERVENTION (NEW)
"Routine assessment of kidney function and albuminuria in people with cardiovascular disease and diabetes to improve risk stratification and guide the use of additional preventive therapy"
JUSTIFICATION
Improved risk stratification and guidance for the use of additional preventive therapy

Diabetes

4. PROPOSED INTERVENTION (REVISION: CURRENT INTERVENTION D7)
D4. "Screening of people with diabetes for proteinuria and treatment with angiotensin-converting enzyme-inhibitor for the prevention and delay of renal disease" revised to: **D4. "Screening for albuminuria in people with diabetes and treatment with SGLT2 and angiotensin-converting enzyme-inhibitor inhibitor for the prevention and delay of kidney disease"**
JUSTIFICATION

Abnormal protein in the urine (proteinuria) is a cardinal manifestation of kidney disease and can be detected using several different laboratory tests. Many different kidney diseases can increase urinary protein excretion to pathological levels, usually in the form of albumin.
Abnormal albumin excretion is termed “albuminuria”. Evidence demonstrates that albuminuria is an important tool to help guide the investigation and management of known Chronic Kidney Disease (CKD), as well as identifying cases of CKD in people with diabetes or hypertension. It should also be noted that laboratory assays for proteinuria are more difficult to standardize and have poorer analytical precision when compared with assays for albuminuria. A detailed description of this evidence can be found in the attached paper.

It is recognized that the approach of looking for disease in a population with identified risk factors is more accurately described as “case-finding” rather than “screening”. As the term case-finding is not well understood by the healthcare community, alternative terminology such as “assessment” or “early detection” should therefore be considered.
(Martinez et al., JAMA, 2016, vol. 315,13, pp. 1343-4.).

In line with the WHO Global NCD Action Plan, which refers to ‘kidney disease’, rather than ‘renal disease’ (pages 57, 58), it is recommended that the terminology used in intervention D4 is harmonized. The ISN, together with the wider kidney community, recommends a consistent use of terminology when referring to ‘kidney disease’ to ensure the clarity of messages directed towards governments, patients and other relevant stakeholders. As already highlighted, around 1 in 10 people world-wide are living with CKD, but around 90% of those affected are unaware of the condition. ISN believes that increased awareness begins with consistent use of terminology by the international healthcare community.

Thank you for considering our contribution to this WHO Discussion Paper and we hope you find it useful in your ongoing reflections. Please do not hesitate to contact us should you require any further information at:
advocacy@theisn.org