Advancing kidney health worldwide. Together.

International Society of Nephrology - Advancing Clinical Trials (ISN-ACT) Statement on Trials and COVID-19

Clinical trials are essential in advancing treatment and care, but often exclude people with kidney diseases.[1] This means that a significant proportion of the global population is rarely represented in the kind of research that ensures evidence-informed clinical practice. The current COVID-19 crisis highlights the challenges that result from such exclusion.

Preliminary studies indicate that people with kidney diseases demonstrate a two- to sixteen-fold increased risk for developing severe COVID-19 symptoms[2–4] or dying from COVID-19.[5] Thus, the inclusion of people with kidney diseases is critical to understanding the full impact of the COVID-19 pandemic.

COVID-19 results in serious illness in approximately 5% of those affected. These patients require intensive care and organ support, including renal replacement therapy (RRT). 20% to 40% of patients hospitalized with COVID-19 in Europe and the United States require RRT, [3,6,7] and this risk is greater for those with pre-existing kidney disease. Some data suggests that up to 65% of patients have proteinuria and 42% have hematuria during the acute phase of the COVID-19 illness.[5,7] The longer-term implications of these findings are unknown.

Given that access to healthcare and, in particular, to intensive care and organ support is severely limited in many parts of the world, it is imperative that effective therapies are developed to prevent and treat COVID-19 in all patients, including those with kidney disease. Effective therapies for COVID-19 patients who have underlying kidney diseases may also reduce the burden on healthcare systems by preventing and reducing the need for hospitalizations and mechanical ventilator support in this high-risk population in the acute phase, and reducing accelerated progression in the longer term.

Contemporary trial design methodologies permit populations included in trials to better represent those most likely to benefit from the treatment being tested, thus improving the validity of the results. This may be achieved through broadening eligibility criteria or enriching trial populations with individuals with pre-existing kidney disease. These types of approaches are encouraged by regulatory agencies, including the US Food and Drug Administration (FDA).

The Kidney Health Initiative, a public-private partnership between the FDA and the American Society of Nephrology catalyzing innovation and the development of safe and effective patient-centered therapies for people living with kidney diseases, issued a similar statement calling for the inclusion of people with kidney disease in COVID-19-related trials.

The International Society of Nephrology urges all investigators and our Industry partners to include people with kidney diseases in research activities related to COVID-19. These activities include the development of vaccines, preventative therapies, or treatments for the infection or its sequelae. The inclusion of people with kidney diseases in clinical research will not only benefit these individuals but will have broader implications for health care systems.

References

1. Kidney Patients are Neglected in Clinical Trials. The American Society of Nephrology, the European Renal Association and the International Society of Nephrology. (July 2019). https://www.theisn.org/images/190709_Press_Release-ERA-ASN-ISN-Clinical_Trials-Nephrology_00000002.pdf

2. Henry, B. M. & Lippi, G. Chronic kidney disease is associated with severe coronavirus disease 2019 (COVID-19) infection. *Int Urol Nephrol* **52**, 1193–1194 (2020).

3. Richardson, S. *et al.* Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. *Jama* **323**, 2052 (2020).

4. Emami, A., Javanmardi, F., Pirbonyeh, N. & Akbari, A. Prevalence of Underlying Diseases in Hospitalized Patients with COVID-19: a Systematic Review and Meta-Analysis. *Archives Acad Emerg Medicine* **8**, e35 (2020).

5. Cheng, Y. *et al.* Kidney disease is associated with in-hospital death of patients with COVID-19. *Kidney Int* **97**, 829–838 (2020).

6. Ronco, C., Reis, T. & Husain-Syed, F. Management of acute kidney injury in patients with COVID-19. *Lancet Respir Medicine* (2020) doi: 10.1016/s2213-2600(20)30229-0.

7. Pei, G. *et al.* Renal Involvement and Early Prognosis in Patients with COVID-19 Pneumonia. *J Am Soc Nephrol Jasn* **31**, 1157–1165 (2020).