National Center for Health Statistics
Centers for Disease Control and Prevention
3311 Toledo Road
Hyattsville, Maryland 20782–2064
nchsicd10cm@cdc.gov

May 17, 2024

Dear ICD-10-CM Coordination and Maintenance Committee (Committee):

On behalf of the more than 37,000,000 Americans living with kidney diseases and the 21,655 nephrologists, scientists, and other kidney health care professionals who are members of the American Society of Nephrology (ASN), ASN writes in support of the proposal to implement International Classification of Disease, 10th Revision Clinical Modification (ICD-10-CM) codes related to APOL1- mediated kidney disease (AMKD), as discussed in the March 2024 ICD-10 Meeting.

We strongly urge the Committee to implement the proposed primary diagnosis code, "hereditary nephropathy, not elsewhere classified with APOL1-mediated kidney disease (AMKD)" (N07.B). We also support the creation of new codes related to tracking genetic susceptibility for AMKD (Z-codes). We recognize, however, that the creation of new genetic susceptibility Z-codes may be an area of ongoing discussion for the Committee. If the Committee defers action on the proposed genetic susceptibility Z-codes, we respectfully urge the Committee *not* to delay implementation of the AMKD primary diagnosis code and implement N07.B effective on October 1, 2024.

I. Unique Primary Diagnosis Code for AMKD (N-code)

There is a compelling need for a new primary diagnosis code to specifically identify individuals with AMKD. As the Committee knows, AMKD is a serious and progressive kidney condition. It is associated with specific inheritable mutations of the APOL1 gene, overwhelmingly affects people of Sub-Saharan African ancestry,[1] clinically manifests as a number of primarily kidney and kidney-associated pathologies,[2] and is believed to be a significant contributor to persistent health disparities in end-stage renal disease

[1] Patrick Dummer et al., APOL1 kidney disease risk variants – an evolving landscape , 35 Seminars in Nephrology 222 (2015).

[2] *See A.* Bajaj, et al. Phenome-wide association analysis suggests the APOL1 linked disease spectrum primarily drives kidney-specific pathways, 97 Kidney Int. 1032–1041 (2020).

(ESRD) in the United States.[3] In fact, individuals with AMKD progress to dialysis 10 to 14 years earlier than patients with chronic kidney disease due to other causes,[4] and the genetic mutations to the APOL1 gene that form the root cause of AMKD have been found to affect approximately 13% of African Americans (about 5 million people),[5] with the population of individuals developing AMKD roughly estimated to be as many as 800,000 people in the United States.[6]

The absence of a unique primary diagnosis code creates challenges for researchers and public health officials in fully tracking the incidence, prevalence, and epidemiology of this important condition. This is especially concerning given that AMKD disproportionately impacts African American patient populations that are already often under-represented in clinical research data. General public awareness of AMKD is growing, with the American Kidney Fund launching the first ever AMKD Awareness Day on April 30, 2024, during National Minority Health Month.[7] A primary diagnosis code is essential to ensure that clinicians, researchers, and payers can reliably capture, analyze, and process claims information related to an AMKD diagnosis.

A unique primary diagnosis code for AMKD also would facilitate research and development of treatments targeting the condition. Currently, there is no Food and Drug Administration (FDA) approved treatment specifically targeting the underlying cause of AMKD, but there are a number of treatments in development now. A unique primary diagnosis code for AMKD would play an important role in tracking and facilitating access to such technology, both for purposes of investigational clinical trials and also post-approval, if FDA ultimately approves a treatment for AMKD for use in the United States.

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[3] Patrick Dummer et al., APOL1 kidney disease risk variants – an evolving landscape , 35 Seminars in Nephrology 222 (2015).

[4] *See* O. Olabisi et al, Abstract: Design of a Phase 2 Trial, JUSTICE, Evaluating Baricitinib as Treatment for APOL1-Mediated Kidney Disease, INF007-TH (2023) (informational poster abstract at American Society of Nephrology Informational Poster Session, Nov. 2, 2023), *available at* https://www.asn-online.org/education/kidneyweek/2023/program-abstract.aspx?controlId=3965283.

[5] David Friedman & Martin Pollak, APOL1 Nephropathy: From Genetics to Clinical Applications, 16 Clin. J. Soc. Nephrology (2021); Patrick Dummer et al., APOL1 kidney disease risk variants – an evolving landscape , 35 Seminars in Nephrology 222 (2015).

[6] *See* ICD-10 March 2024 Topic Packet at 22, *available at* https://www.cdc.gov/nchs/data/icd/march-2024-topic-packet-final.pdf.

[7] *See* American Kidney Fund, April 30: Ne APOL 1 Aware Community Toolkit (2024), *available at* https://www.kidneyfund.org/sites/default/files/media/documents/2024%20AMKD%20Day%20Community%20ToolKit.pdf.

II. Genetic Susceptibility for AMKD Codes (Z-codes)

We also support the Committee's proposal to create new genetic susceptibility codes related to AMKD (Z-codes). Expression of AMKD is a function of both genetic factors *and* epigenetic factors. The epigenetic factors (e.g., infections or inflammatory responses) act as a "second hit" that interplays with genetic susceptibilities caused by G1/G2 APOL1 gene mutations to trigger AMKD.[8] As a consequence, comprehensive tracking related to AMKD would greatly benefit from the creation of both new primary diagnosis codes and genetic susceptibility codes that would allow for multi-integrated analysis into the role of genetic and environmental factors in the expression of the condition.[9]

At the March 2024 ICD-10 meeting, no stakeholders opposed the creation of specific genetic susceptibility codes for AMKD. We acknowledge, however, that there was discussion about whether widespread adoption of genetic susceptibility codes in other contexts could create new stresses on coding and claims processing systems. That said, there are important and unique reasons to consider the creation of genetic susceptibility codes specific to AMKD: APOL1 genetic variants are associated with much of the excess risk of chronic kidney disease, including kidney failure, with some estimates showing that the lifetime risk of kidney disease in APOL1 dual-high risk allele individuals is at least 15%.[10] In addition, there are published data demonstrating that patients with African ancestry with APOL1 high-risk genotypes have a higher odds of worse clinical outcomes, including kidney disease progression and death.[11] [12] Better tracking of genetic susceptibility for AMKD could play an especially important role in the ongoing development of treatment options, given the currently pending trials for AMKD investigational therapies.

As such, the Committee would have unique reasons to adopt AMKD-specific genetic susceptibility codes without necessarily being required to adopt genetic susceptibility codes for differentially situated genetic susceptibilities. That said, should the Committee delay action on AMKD genetic susceptibility codes, we strongly urge the Committee still to act promptly in creating a new primary diagnosis code for AMKD effective October 1, 2024. Even assuming the Committee wishes to continue to evaluate the need for genetic susceptibility codes, this would not be a basis for delaying implementation of a critically needed new primary diagnosis code for AMKD.

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[8] *See* George Vasquez-Rios et al., Novel Therapies in APOL1-Mediated Kidney Disease: From Molecular Pathways to Therapeutic Options, Kidney International Reports 1 (2023).

[9] Patrick Dummer et al., APOL1 kidney disease risk variants – an evolving landscape, 35 Seminars in Nephrology 222 (2015).

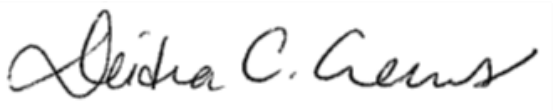
[10] *Id.*

[11] https://www.nejm.org/doi/full/10.1056/NEJMoa1310345

[12] https://www.nejm.org/doi/full/10.1056/NEJMoa1310345

ASN thanks the Committee for its consideration of our comments, and we reiterate our strong support for finalization of the codes related to AMKD. If you have any questions about this comment letter or we can provide any additional information that would assist the Committee, please do not hesitate to contact David White, ASN Regulatory and Quality Officer, dwhite@asn-online.org.

Sincerely,



Deidra C. Crews, MD, ScM, FASN

President