GUARDD
Genetic testing to Understand and Address Renal Disease Disparities

Summary of Evidence for Providers
APOL1 and CKD

Racial/Ethnic Differences in CKD

- African American/Black patients with hypertension face 2-3x increased risk of developing chronic kidney disease (CKD) and 5x increased risk for end stage renal disease (ESRD) compared with European Americans/White patients.
- Onset of ESRD (dialysis) occurs 10 years earlier in life in blacks compared with whites.

APOL1 and Kidney Disease[1] [2]

- Alleles of the APOL1 locus on Chr 22 confer risk for HTN-associated CKD/ESRD (a recessive model).
  - These risk alleles explain up to 70% of excess prevalence of ESRD in AA's.
  - Estimated lifetime ESRD risk is 2-3% with zero/ one copy and ~10% with 2 copies of APOL1 risk alleles.
  - 2 copies (APOL1+) progress to dialysis faster than 0 or 1 copies (Figure 1).
- Variants are nearly absent in populations of European and Asian ancestry (<0.5%), but commonly present in African ancestry populations (13-15%).
- Africans with mutations were protected against sleeping sickness in West Africa (like malaria/sickle cell).
  - This survival advantage increased mutation's frequency in parts of Africa.
  - 2 copies of Hb S uniformly produce sickle cell, but not all those with 2 APOL1 risk variants develop CKD.
  - Exact mechanism by which the risk alleles for APOL1 cause kidney disease is unclear.
- Black patients with 2 APOL1 risk alleles are also at increased risk for focal global glomerulosclerosis (FGGS), HIV-associated nephropathy, nephropathy related to sickle cell, and severe lupus nephritis with collapsing lesions.

Studies examining APOL1, race, and the development of kidney disease[3]

◦ ARIC study - AA without CKD followed for 20 yrs showed a 1.5x increased risk of CKD and 1.92x increased risk of ESRD with 2 APOL1 risk alleles.
◦ AASK study – Primary outcome of ESRD or doubling of serum creatinine occurred in 58.1% of AA patients with 2 risk alleles and in 36.6% of AA with 0-1 risk alleles.
◦ CRIC study – AA patients with 2 high risk alleles showed more rapid decline in eGFR among those with and without diabetes.

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[1] http://www.ncbi.nlm.nih.gov/pubmed/23766536
[2] http://www.ncbi.nlm.nih.gov/pubmed/?term=palmer+apol1+editorial
[3] http://www.ncbi.nlm.nih.gov/pubmed/24206458