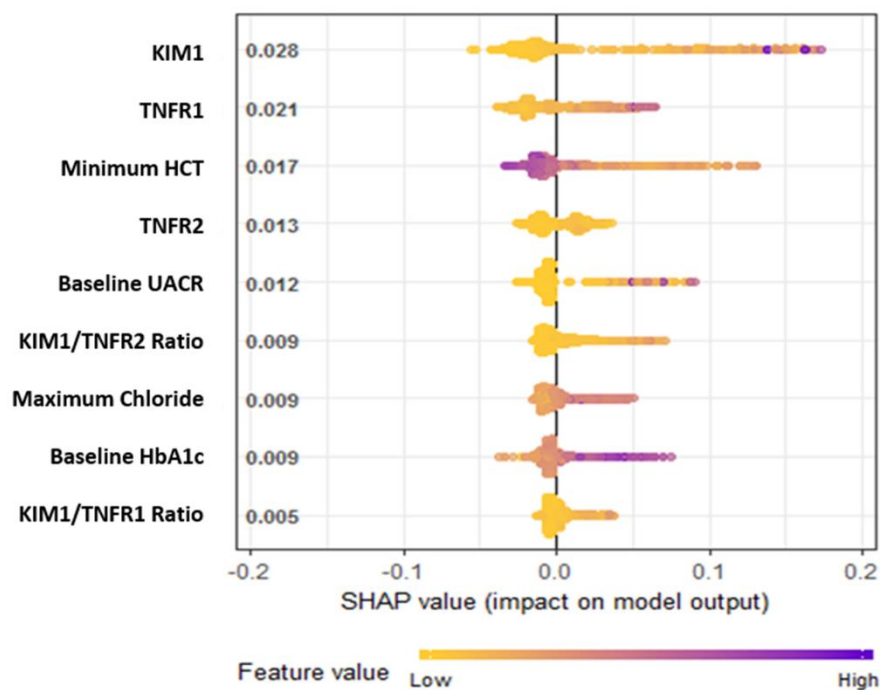
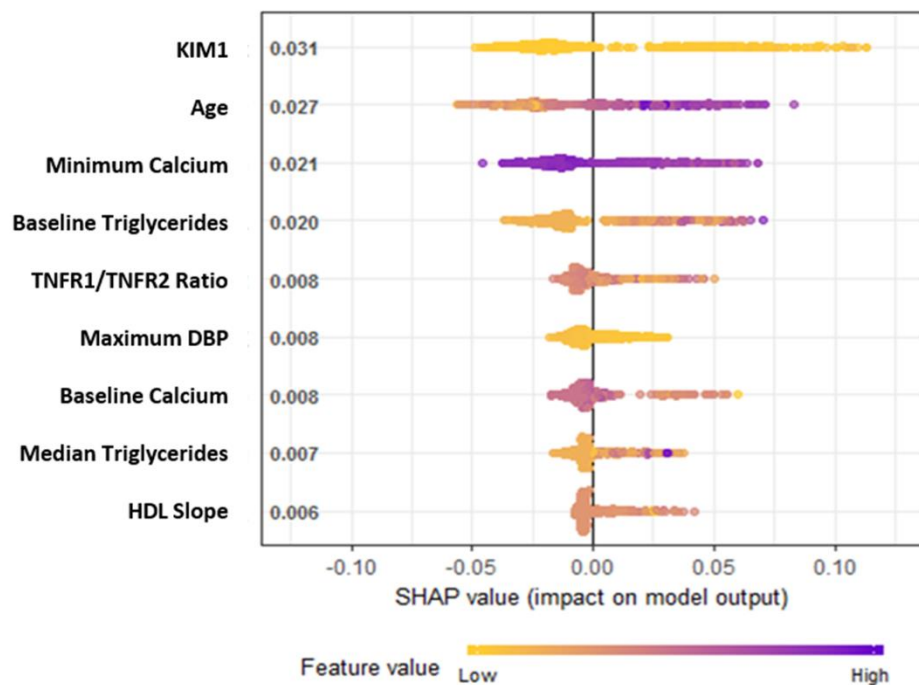


Supplemental Figures 1:

A. SHAP plots for feature importance in T2D population.



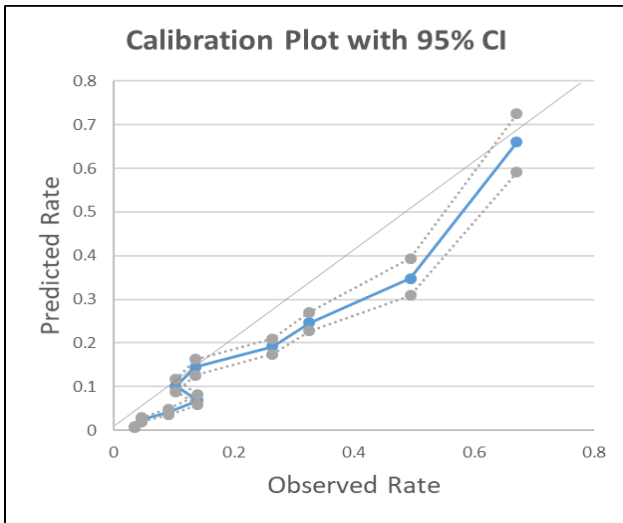
B. SHAP plots for feature importance in *APOL1*-HR population.



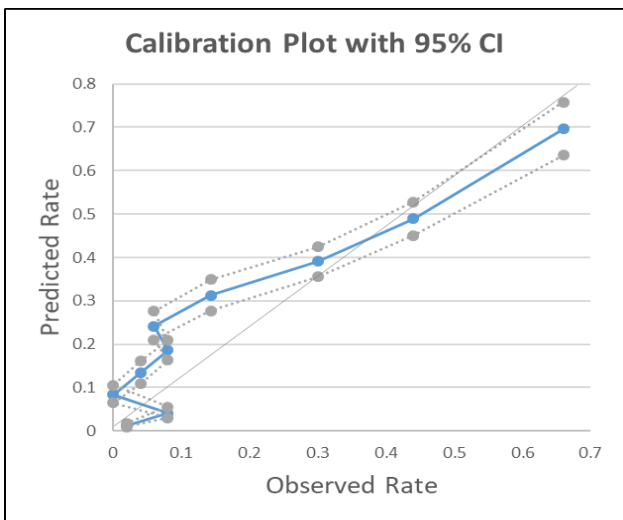
Legend: SHAP: SHapley Additive exPlanations – these plots quantify the magnitude and direction (positive or negative) of a feature’s effect on a prediction.

Supplemental Figure 2. Observed vs. Expected Plots (calibration plots) with 95% Confidence Interval in Patients with T2D (Panel A) and *APOL1*-HR Genotypes (Panel B)

A



B



Hosmer-Lemeshow goodness-of-fit test p-value 0.15 for T2D and 0.11 for *APOL1*-HR

Supplemental Table 1. Key Characteristics in Training and Test Datasets in T2D Cohort

	Train (n=696)	Test (n=175)
Age in years, Median [IQR]	60 [53 - 67]	59 [51 - 66]
Female, n (%)	411 (59%)	96 (54.9 %)
Race, n (%)		
African Ancestry	272 (39%)	74 (42.2%)
European American	48 (6.9%)	14 (8 %)
Hispanic Latino	337 (48.4%)	75 (42.9 %)
Others	39 (5.6)	1 (0.57 %)
Biomarkers, Median [IQR]		
TNFR1 (pg/mL)	6025 [4765 - 8105]	6250 [4812 - 9097]
TNFR2 (pg/mL)	6825 [5262 - 9763]	7429 [5712 - 10312]
KIM-1 (pg/mL)	313.11 [196.96 - 562.36]	379.3 [201.6 - 722.5]
eGFR in ml/min/1.73 m ² , Median [IQR]	70.04 [55.35 - 82.12]	68.27 [55.8 - 82]
Systolic BP in mm Hg, Median [IQR]	132 [120 - 146]	128 [120 - 140]
Diastolic BP in mm Hg, Median [IQR]	75 [67 - 83]	74 [66 - 80]

Supplemental Table 2. Key Characteristics in Training and Test Datasets in *APOL1*-HR Cohort

	Train (n=398)	Test (n=100)
Age in years, Median [IQR]	49 [39 - 59]	52 [43 - 62]
Female, n (%)	269 (67.6%)	68 (68%)
Race, n (%)		
African Ancestry	377 (95)	94 (94)
Hispanic Latino	9 (2.3)	4 (4)
Others	12 (3)	2 (2)
Biomarkers, Median [IQR]		
TNFR1 (pg/mL)	2467.7 [1989.7 - 3203]	2441 [1971 - 3397]
TNFR2 (pg/mL)	4254.8 [3231.9 - 5627.8]	4180 [3256 - 5675]
KIM-1 (pg/mL)	159.6 [96 - 275.5]	141.3 [96.2 - 236.7]
eGFR in ml/min/1.73 m ² , Median [IQR]	82 [68.3 - 98.5]	82.4 [66.1 - 99.3]
Systolic BP in mm Hg, Median [IQR]	130.2 [117 - 140]	131 [118.0 - 143]
Diastolic BP in mm Hg, Median [IQR]	76.8 [70 - 84.8]	79.5 [70 - 86]

Supplemental Table 3. AUCs for Random Forest Models with Clinical Features Alone and with Addition of Plasma Biomarkers and Ratios in Training and Test Cohorts

T2D			<i>APOL1</i>-HR		
Subgroup	Random Forest Model without Biomarkers ^a	KidneyIntelX (with Biomarkers)	Subgroup	Random Forest Model without Biomarkers ^b	KidneyIntelX (with Biomarkers)
Training (n=696)	0.78 (0.77-0.79)	0.81 (0.80-0.82)	Training (n=398)	0.84 (0.83-0.85)	0.86 (0.84-0.87)
Test (n=175)	0.72 (0.7-0.75)	0.77 (0.75-0.79)	Test (n=100)	0.78 (0.76-0.82)	0.80 (0.77-0.83)

^a Clinical features for the random forest model without biomarkers included minimum hematocrit, baseline hematocrit, baseline HbA1c, maximum serum glucose, median serum glucose, baseline BMI, median serum calcium, median serum chloride, and baseline UACR

^b Clinical features for the random forest model without biomarkers included age, baseline serum calcium, minimum serum calcium, baseline triglycerides, baseline diastolic blood pressure, and maximum diastolic blood pressure

Note: the features and hyperparameters for the random forest model without biomarkers are different than the features and hyperparameters used in the final fully integrated KidneyIntelX model with biomarkers (as shown in Supplemental Figures 1A and 1B).

Supplemental Table 4. KidneyIntelX Discrimination for the Individual Components of the Composite Kidney End Point

T2D (Test set, n=175)		APOL1-HR (Test set, n=100)	
Endpoint	AUC (95% CI)	Endpoint	AUC (95% CI)
Full composite outcome	0.78 (0.75-0.79)	Full composite outcome	0.80 (0.77-0.83)
RKFD alone	0.79 (0.78-0.80)	RKFD alone	0.80 (0.78-0.82)
Sustained 40% decline alone	0.82 (0.81-0.83)	Sustained 40% decline alone	0.84 (0.82-0.85)
“Kidney Failure” alone	0.94 (0.93-0.95)	“Kidney Failure” alone	NR*

NR= not reported

*there were only 5 events of kidney failure in the entire 498 participants in the APOL1-HR cohort, thus we could not calculate an AUC for this outcome in this cohort

RKFD= rapid kidney function decline (eGFR slope decline of ≥ 5 ml/min/1.73 m²/year)

Kidney Failure= sustained eGFR <15 ml/min/1.73 m² confirmed at least 30 days later, or long-term maintenance dialysis or kidney transplant (i.e. ESKD).