Cricket Health

Whitepaper

Machine Learning for Chronic Kidney Disease Detection & Risk Stratification

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Executive Summary

The purpose of this whitepaper is to describe the methodology and application of Cricket Health's predictive analytics capabilities for early detection and risk stratification of patients with chronic kidney disease (CKD). Though CKD is highly prevalent and represents a large economic burden in the United States, efforts to manage the condition at earlier stages, delay disease progression, and reduce complications have been fairly limited. Furthermore, a large proportion of persons with CKD remain undiagnosed, underdiagnosed, or unspecified. Because of this, Cricket Health saw a strong need to invest in developing machine learning (ML) models to predict estimated glomerular filtration rate (eGFR), which is a common proxy for kidney health. These models use claims data only to predict eGFR with a high degree of accuracy — no EHR or lab data is required to make a prediction. Utilizing in-house ML models in kidney care management ensures that Cricket Health is well-positioned to identify and risk-stratify misclassified CKD patients for risk-bearing entities with access to claims data.

Introduction

About Cricket Health

Cricket Health is a specialty provider of integrated kidney care for people with chronic kidney disease (CKD) and end stage renal disease (ESRD). We deliver technology-enabled clinical care by a multidisciplinary care team to improve outcomes for our members and reduce costs for our partners. We partner with payers and provider networks to keep members healthy and out of the hospital, accelerate access to kidney transplants, and increase home dialysis adoption.

Learn more at www.crickethealth.com or follow us @crickethealth.

Introduction

Chronic kidney disease (CKD) is a highly prevalent condition with a high economic burden. CKD is associated with increased mortality and morbidity, including greater risk of cardiovascular disease, hospitalization, premature death, and progression to ESRD. This is especially true in the aging population of the United States. Over 35 million persons are estimated to have CKD, and these persons contribute more than $100 billion in direct healthcare costs [1–5]. As patients progress through the stages of CKD, annual healthcare expenditures per patient increase dramatically [6]. In ESRD, when patients experience kidney failure, annual costs may exceed $200,000 per patient per year [7–8].

Early CKD identification and intervention can reduce disease burden and lower healthcare costs. Specifically, early detection allows opportunities to institute evidence-based care management strategies that reduce complications and can delay CKD progression [14–18, 23–24]. Despite this, CKD's underdiagnosis is well-documented, with fewer than 50% of late-stage patients diagnosed [5, 9–10]. Indeed, approximately half of all incident ESRD cases occur among people with minimal nephrology care prior to initiating dialysis. These suboptimal dialysis starts usually require hospitalizations that can cost tens of thousands of dollars more per patient and lead to worse health outcomes [11–13, 25].

Low awareness among patients affected by CKD is exacerbated by the fact that primary care providers are often unaware of and confused by guidelines for CKD management [27]. This issue is compounded by the fact that CKD remains largely asymptomatic until it has caused severe, irreversible damage, and fragmentation of care exacerbates the barriers to early detection. Moreover, lab testing to measure kidney health and actively screen for CKD in persons at risk is woefully inconsistent.

With the advent of electronic health records (EHR), there is great enthusiasm to leverage technology to detect persons with CKD [22, 26]. Several CKD detection algorithms requiring laboratory values have been published with good performance. However, the ability to implement these algorithms in practice is limited by the fact that EHR and/or laboratory values are often unavailable to payers or health systems. In addition, many persons at risk are never tested for CKD. We propose that an algorithm that is not based on laboratory testing can identify high-risk patients for whom additional testing is warranted to confirm their CKD status, determine their risk for complications, and allow Cricket Health to begin CKD management before kidney failure.

Our algorithm represents an important advance in CKD screening because it can be passively run at frequent intervals on large member populations at little to no marginal cost to payers. Care providers may also benefit from this innovation since patients can be screened with no direct time investment, allowing the care provider to engage patients more efficiently. When high risk of CKD is flagged, common blood and urine laboratory tests can be ordered to confirm CKD status and allow appropriate follow-up treatment and care. Identifying members with CKD in earlier stages could then lead to significant savings through highly targeted care management focused on engaging the highest risk patients in their own care plans.

Machine Learning Algorithm FAQ

Development: Who trained & developed the model?

Cricket Health's interdisciplinary data team, combining clinical, epidemiological, statistical, and data science expertise co-developed this model in 2019. This is the first of what we expect will be many predictive analytics projects geared towards impacting kidney health outcomes alongside Cricket Health's care platform and clinical team. The data team that worked on this project, and their roles at Cricket Health are listed below:

- Kunal Mishra, MPH, Data Scientist
- Carmen Peralta, MD, Chief Medical Officer
- Michelle Odden, PhD, Epidemiology & Biostatistics Consultant
- James Pesuit, Data Team Lead
- Rachel Clark, Data Scientist
- Jens Leerssen, Data Engineer

Development: How was the model trained?

We've trained and validated models using multiple linked claims and clinical datasets from diverse regions throughout the United States, leveraging learnings and calibration from nearly 5 million members. Predictors include factors such as patient demographics (i.e., age), health conditions derived from claims data (i.e., hypertension and diabetes), social determinants of health, and utilization patterns which are all readily available in claims datasets. We predicted estimated glomerular filtration rate by serum creatinine (eGFRcreat) and excluded race in the eGFR calculation to avoid potential racial bias. For internal validation, we utilized 5-fold cross validation on a 75%-25% training-test set. For external validation, we trained models using an entire population's data and validated in a separate payor population. Every model we build is an ensemble of both biostatistical and machine learning methods, to ensure the model is generalizable to other populations and interpretable to our data science teams and clinicians.

Deployment: Who are we interested in identifying?

Our predictive models have been calibrated to identify members with advanced CKD, defined as Stage 3b, 4, or 5. This corresponds to an eGFR of less than 45 mL/min/1.73m2.

Deployment: Who can be tested?

Our models, which feed into a proprietary screening algorithm, can be passively used over the entire member population of any health insurance payer using the data available to them. For deployment, no lab values are required for any of the members, so our screening is not limited to the subset of members who have been tested. For every member screened, our screening algorithm generates a predicted glomerular filtration rate (pGFR) value and the member's probability of having each individual CKD stage.

Deployment: What happens when the model indicates a high risk of CKD?

Cricket Health will work with the payer to implement an outreach strategy to alert the primary care provider or specialists engaged in the patients' care. As part of this outreach, the payer (or the primary care provider of the impacted members) will inform the identified member about the risks associated with undiagnosed CKD and provide decision support around ordering tests for CKD confirmation and further risk stratification. Typically, the tests include at least serum creatinine and urinary albumin to creatinine ratio and will inform the next steps for the member, which may include a referral to Cricket Health for CKD management.

Model Performance Metrics

Prior to this section, it may be helpful to reference **Appendix 1. Contextualizing Performance Metrics** to refresh on some statistical and epidemiological terminology.

Internal Validation

A key strength of our machine learning model is the ability to passively risk stratify an entire payer's population by selecting an appropriate risk score threshold that matches a partner's goals surrounding optimal health outcomes as well as member experience.

The key takeaways from the table below center around positive predictive value (PPV) and negative predictive value (NPV). Each of the prior risk scores — all of which required EHR or lab data — has excellent NPV. However, prior risk scores have faltered in their ability to positively predict — that is, given a positive test result, how likely it was that someone did have CKD.

	Sensitivity	Specificity	PPV	NPV	AUC
Bang, 2007 [28]	92%	68%	18%, CKD 3a+	99%	0.88, CKD 3a+
Peralta, 2016 [29]	~	~	~	~	0.87, CKD 3a+
Carillo-Larco, 2017 [30]	71%	69%	11%, CKD 3a+	98%	0.71, CKD 3a+

Cricket Health's contributions to the field are most apparent in the metrics below, where we examined three possible thresholds for risk stratification of predicted eGFR. The key difference between the three possible thresholds is the tradeoff between Sensitivity and PPV. We can positively identify the patients who are at extreme risk of having late-stage CKD (i.e., a nearly 100% probability of 3b+) or who are at extreme risk of having advanced CKD (i.e., a nearly 100% probability of 3a+), but that comes at the expense of identifying fewer total individuals at high risk of CKD. The low sensitivity metrics reflect this. Alternatively, we can choose a "high risk" threshold that optimizes both sensitivity and specificity, allowing our algorithm to have

clinically useful PPV/NPV values and to capture a large proportion of the overall population for which we are interested in identifying and confirming CKD.

	Sensitivity	Specificity	PPV	NPV	AUC
"Cricket Health, 2019 High Risk Threshold"	86%, CKD 3b+ 95%, CKD 4+ 98%, CKD 5+	91%	77%, CKD 3a+ 46%, CKD 3b+	99%	0.97, CKD 3b+, adjusted 0.95, CKD 3b+, raw
"Cricket Health, 2019 Very High Risk Threshold"	21%, CKD 3b+ 48%, CKD 4+ 98%, CKD 5+	99%	100%, CKD 3a+ 92%, CKD 3b+	92%	~
"Cricket Health, 2019 Extreme Risk Threshold"	16%, CKD 3b+ 41%, CKD 4+ 95%, CKD 5+	100%	100%, CKD 3a+ 100%, CKD 3b+	93%	~

Receiver Operating Characteristic (ROC) & Area Under Curve (AUC): See Appendix 2
Predictions by Stage & Comparison to Actual: See Appendix 3 & 4

External Validation

Each time we've received access to a new linked labs-claims dataset we've trained new models and conducted external validation using the new models and datasets. We've observed that external validation performance remains strong across a variety of diverse populations, even without additional calibration and iteration, and further solidifies our algorithm performance as industry-leading for screening for CKD.

	Payor Model					
Payor Dataset	**A**	**B**	**C**	**D**	**E**	**# of Members in Validation Set**
A	x	0.856	0.853	0.854	0.84	3,045
B	0.829	x	0.865	0.865	0.842	215,652
C	0.917	0.946	x	0.951	0.951	4,481,986
D	0.9	0.914	0.914	x	0.914	86,082
E	0.827	0.889	0.904	0.902	x	22,689
All combined	**0.902**	**0.93**	**0.922**	**0.949**	**0.934**	**400,000**

1. "All Combined" performance is calculated in an equally weighted random sample with replacement from each of the external payers for a given payer model

Conclusion

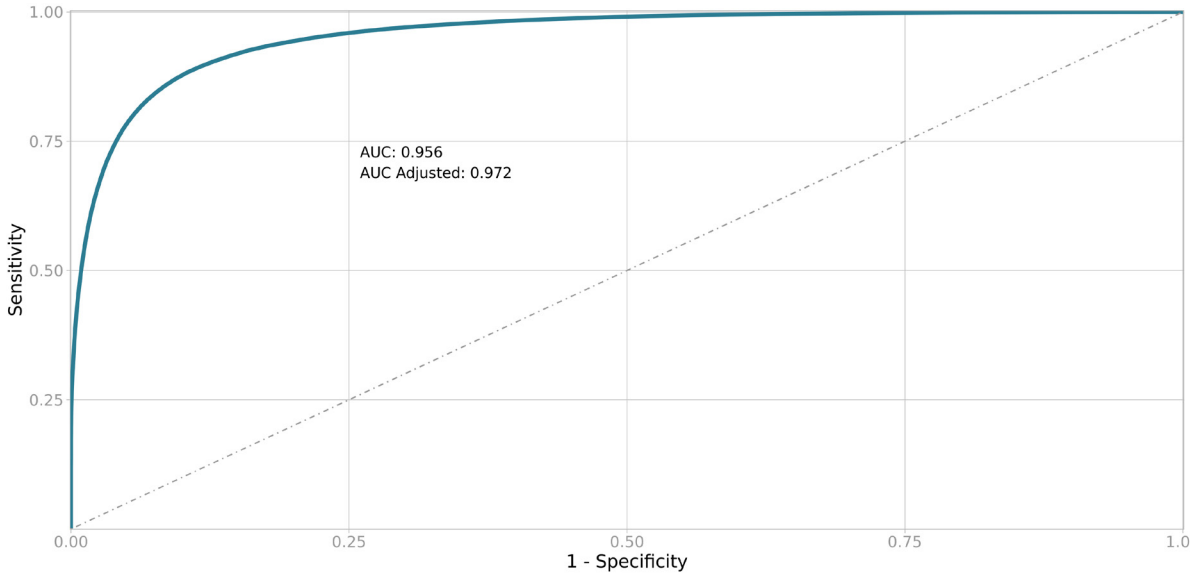
Cricket Health has developed the ability to predict eGFR as a proxy for kidney disease risk with a higher degree of accuracy than any previous literature that we are aware of. These machine learning models can be deployed on any "claims only" dataset without requiring access to EHR or laboratory data. Learn more at www.crickethealth.com or follow us @crickethealth.

Appendix 1. Contextualizing Performance Metrics

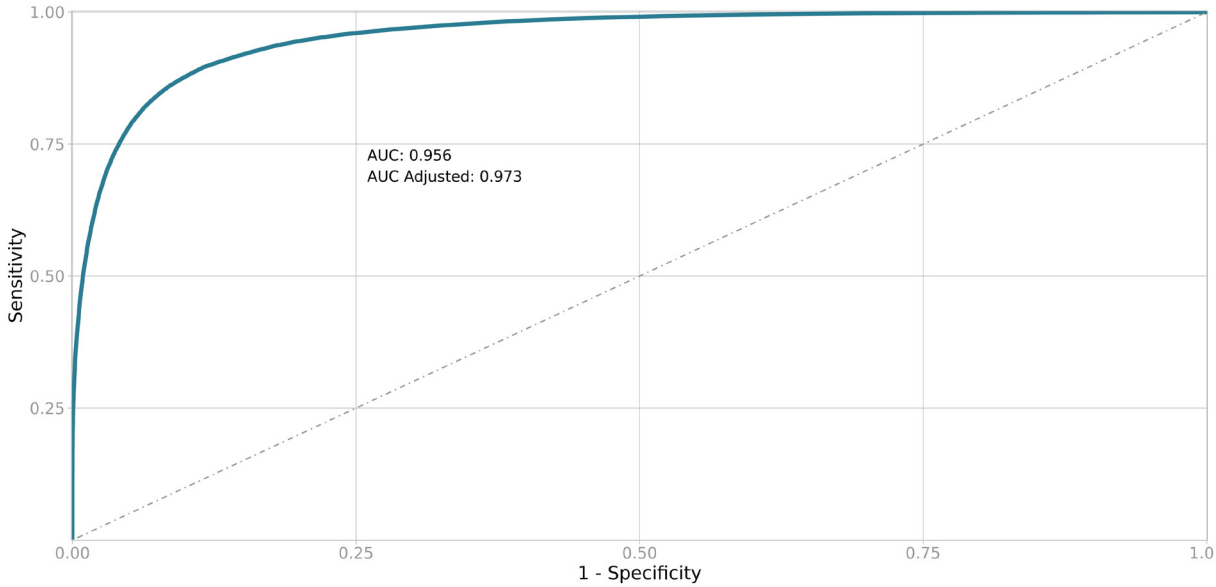
Metric	Definition + Context
Sensitivity	Defined as the proportion of truly positive CKD cases — the number of members who test positive for CKD 3b+ divided by the number who are truly positive. A value of 0 indicates that 0% of the population with CKD 3b+ was capturedby our model. A value of 1 indicates that 100% of the population with CKD 3b+ was captured by our model.
Specificity	Defined as the proportion of truly negative CKD cases — the number of members who are truly negative divided by the number who test negative for CKD 3b+. A value of 0 indicates that 0% of the healthy population was correctly classified by our model. A value of 1 indicates that 100% of the healthy population was correctly classified by our model.
Positive Predictive Value (PPV)	Defined as the probability that someone who tests positive is truly positive for CKD 3b+. A value of 0 indicates that 100% of members who test positive actually do not have CKD 3b+. A value of 1 indicates that 100% of members who test positive actually do have CKD 3b+.
Negative Predictive Value (NPV)	Defined as the probability that someone who tests negative is truly negative for CKD 3b+. A value of 0 indicates that 100% of members who test negative actually do have CKD 3b+. A value of 1 indicates that 100% of members who test negative actually do not have CKD 3b+.
Area Under Curve (AUC)	Defined as the probability that the predicted value of a true positive is greater than the predicted value of a true negative. This is identical to the area under the curve of a receiver operating characteristic (ROC) curve. Informally, AUC is a measure of discrimination — how well a model can separate positives from negatives. I servers as an all-encompassing classification metric that allows disparate models to be compared to each other. A value of 0.5 indicates the model is no better than a random guesser, while a value of 1 indicates the model is a perfect classifier.

Appendix 2. ROC Curves

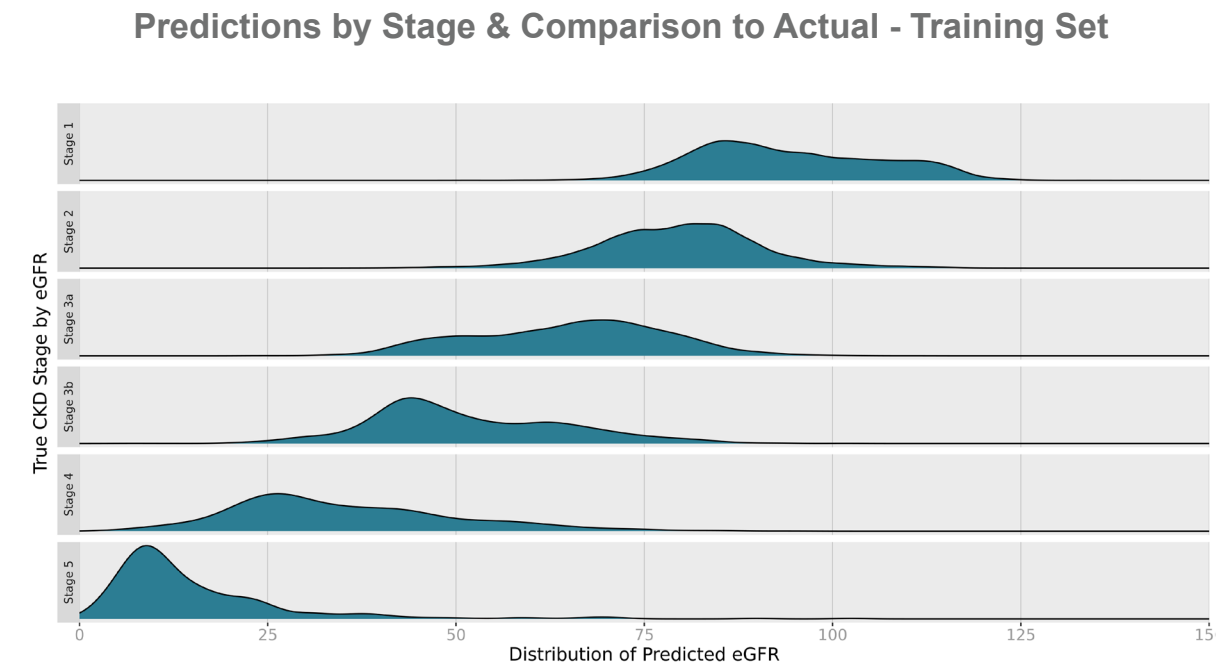
Receiver Operating Characteristic (ROC) & Area Under Curve (AUC) - Training Set

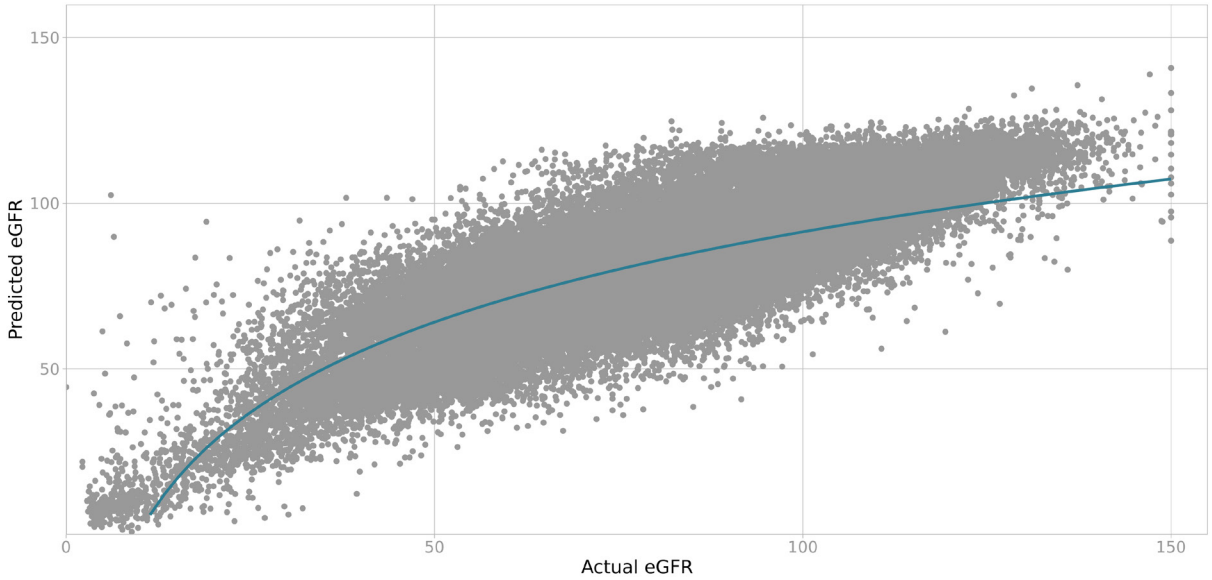


Receiver Operating Characteristic (ROC) & Area Under Curve (AUC) - Test Set

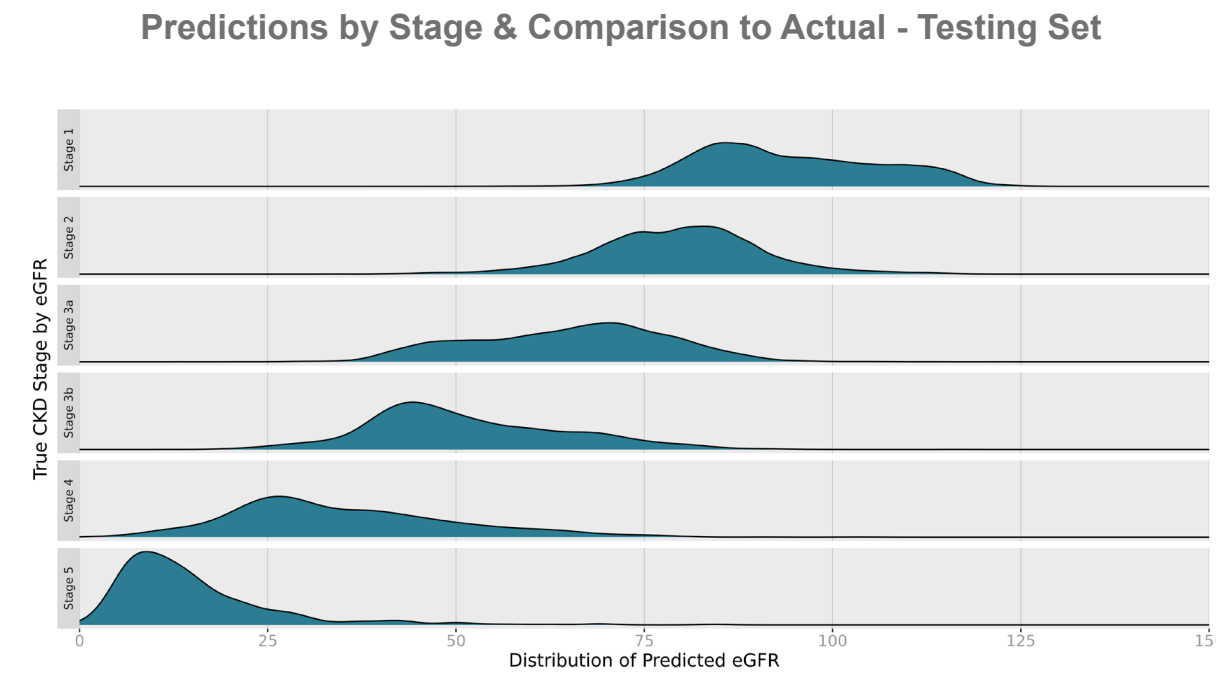


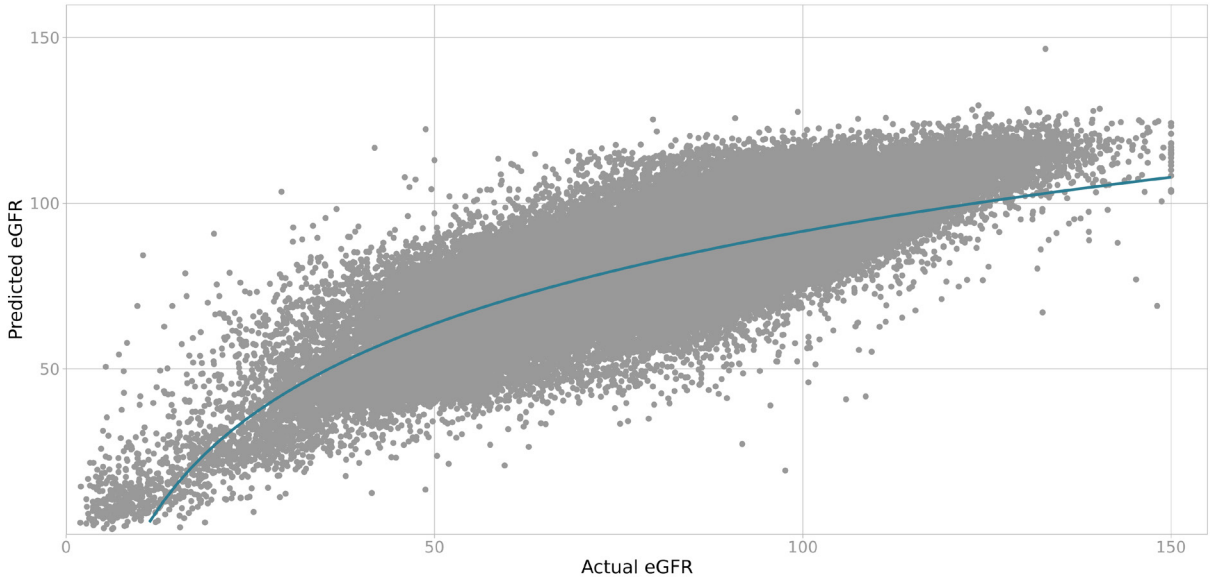
Appendix 3. Predictions by Stage & Comparison to Actual, Training Set





Appendix 4. Predictions by Stage & Comparison to Actual, Test Set





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