**Whitepaper |** Cricket Health

# Machine Learning for Chronic Kidney Disease Detection & Risk Stratification

Kunal Mishra MPH, Carmen Peralta MD, Michelle Odden PhD, James Pesuit, Rachel Clark, Jens Leerssen

# Table of Contents

# 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. 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 undiagnosed or 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 help 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.

## Background

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?

A multiyear dataset that linked claims and clinical data from over 40,000 members from an integrated healthcare system in the United States was used to train the model. Predictors include factors such as patient demographics (i.e., age) and health conditions derived from claims data (i.e., hypertension and diabetes) as well as utilization patterns which are all readily available in claims datasets. We predicted estimated glomerular filtration rate by serum creatinine (eGFRcreat). A 5-fold cross validation on a 75% training set, along with internal validation on a 25% test set with an ensemble of both biostatistical and machine learning methods, was utilized to ensure the model is generalizable to other populations.

## 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 [19] | 92% | 68% | 18%, CKD 3a+ | 99% | 0.88, CKD 3a+ |
| Peralta, 2016 [20] | ~ | ~ | ~ | ~ | 0.87, CKD 3a+ |
| Carillo-Larco, 2017 [21] | 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**<br><br>**High Risk Threshold** | … **86%** of Stage 3b+<br><br>… **95%** of Stage 4+<br><br>… **98%** of Stage 5+ | 91% | 77%, CKD 3a+<br>46%, CKD 3b+ | **99%** | 0.97, CKD 3b+, adjusted<br>0.95, CKD 3b+, raw |
| **Cricket Health, 2019**<br><br>**Very High Risk Threshold** | … 21% of Stage 3b+<br><br>… 48% of Stage 4+<br><br>… 98% of Stage 5 | 99% | **100%, CKD 3a+**<br>92%, CKD 3b+ | 92% | ~ |
| **Cricket Health, 2019**<br><br>**Extreme Risk Threshold** | … 16% of Stage 3b+<br><br>… 41% of Stage 4+<br><br>… 95% of Stage 5 | **100%** | 100%, CKD 3a+<br>**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

## 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.<br><br>A value of 0 indicates that 0% of the population with CKD 3b+ was captured by 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+.<br><br>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+.<br><br>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+.<br><br>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.<br><br>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.<br><br>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

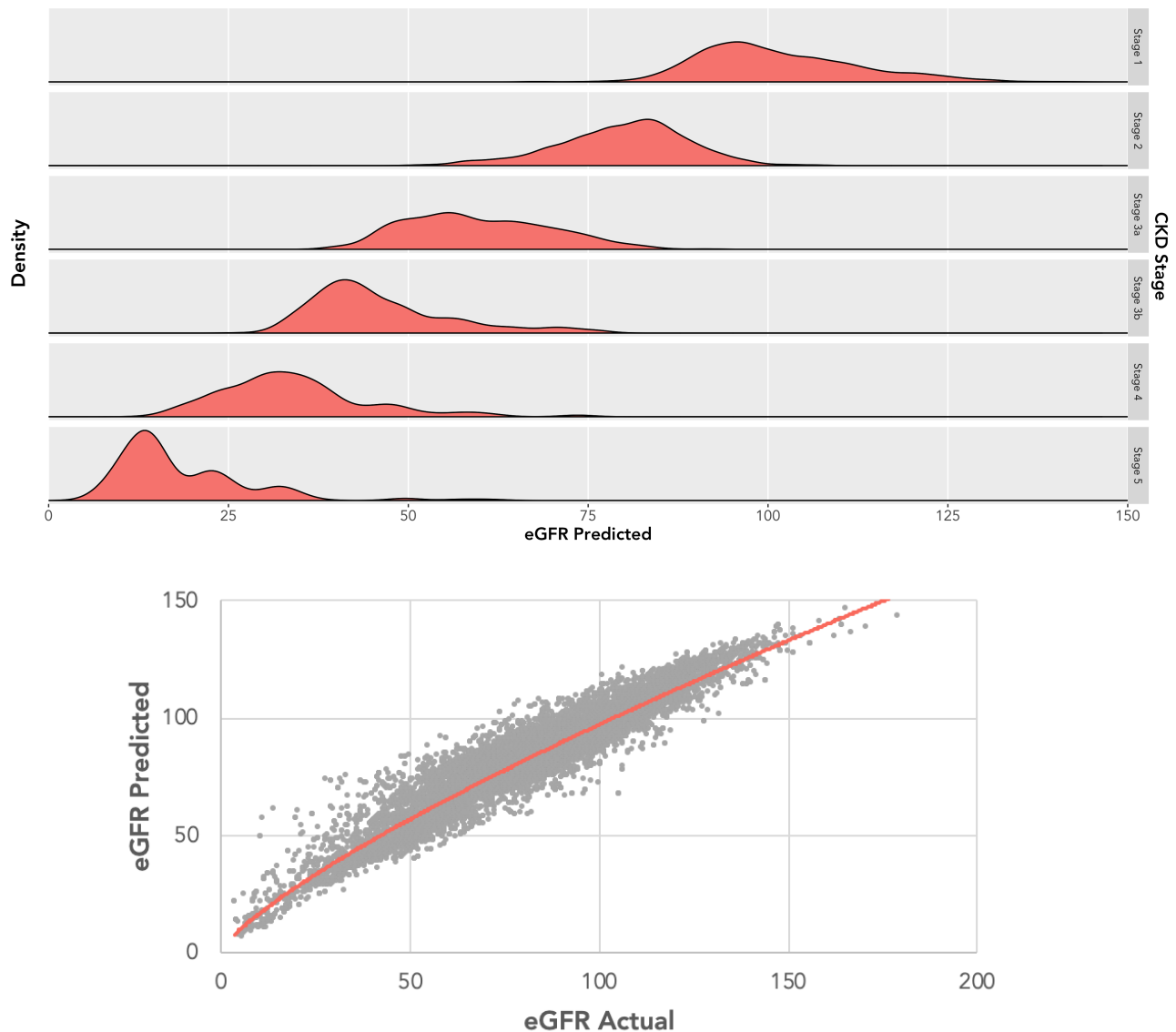### Receiver Operating Characteristic (ROC) & Area Under Curve (AUC) - Training Set



AUC: 0.986
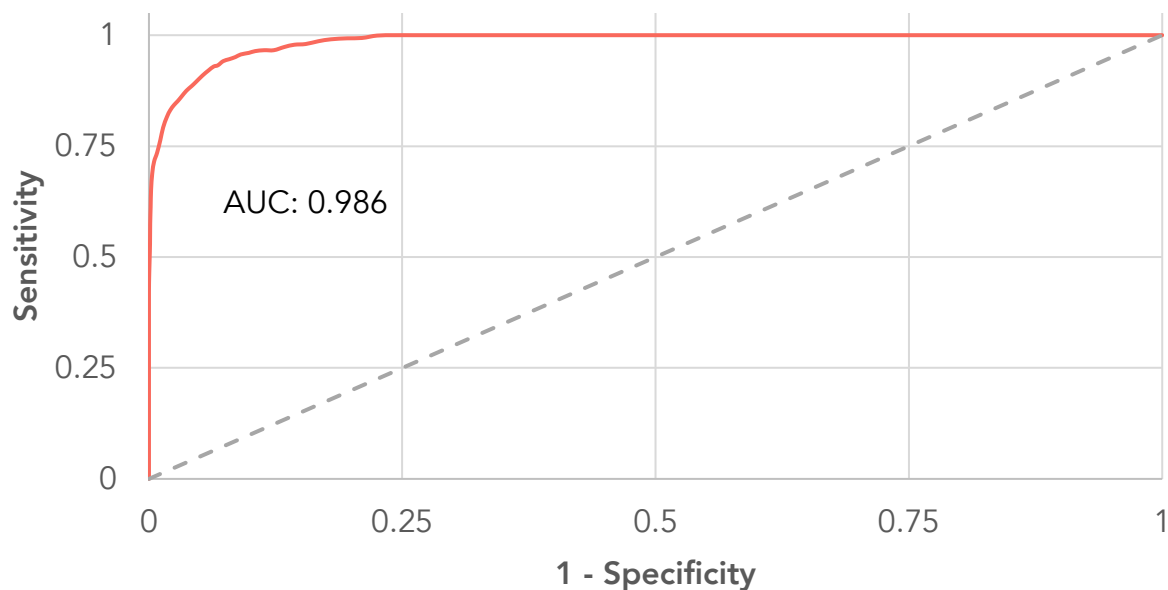
### Receiver Operating Characteristic (ROC) & Area Under Curve (AUC) - Test Set
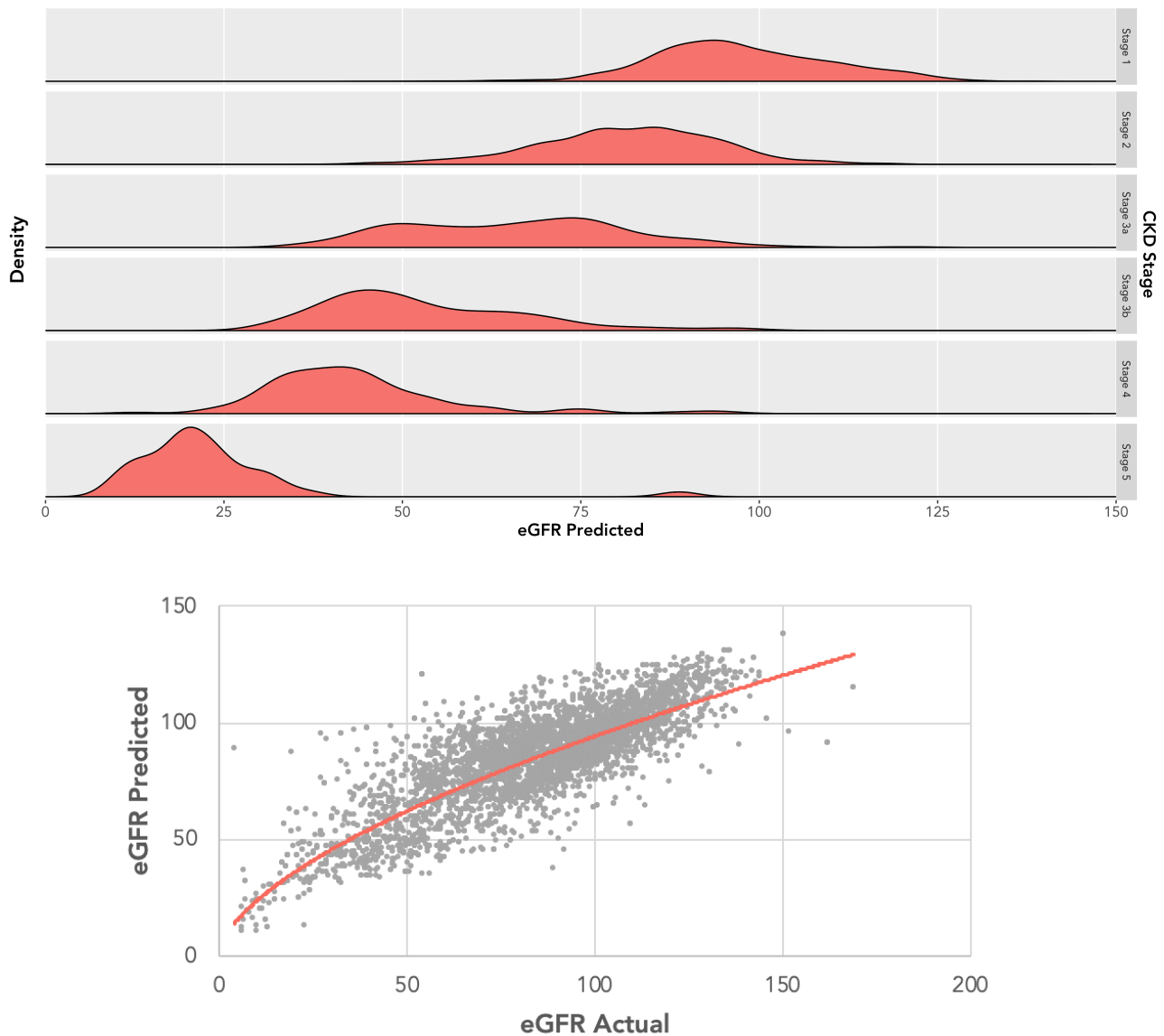


AUC: 0.947
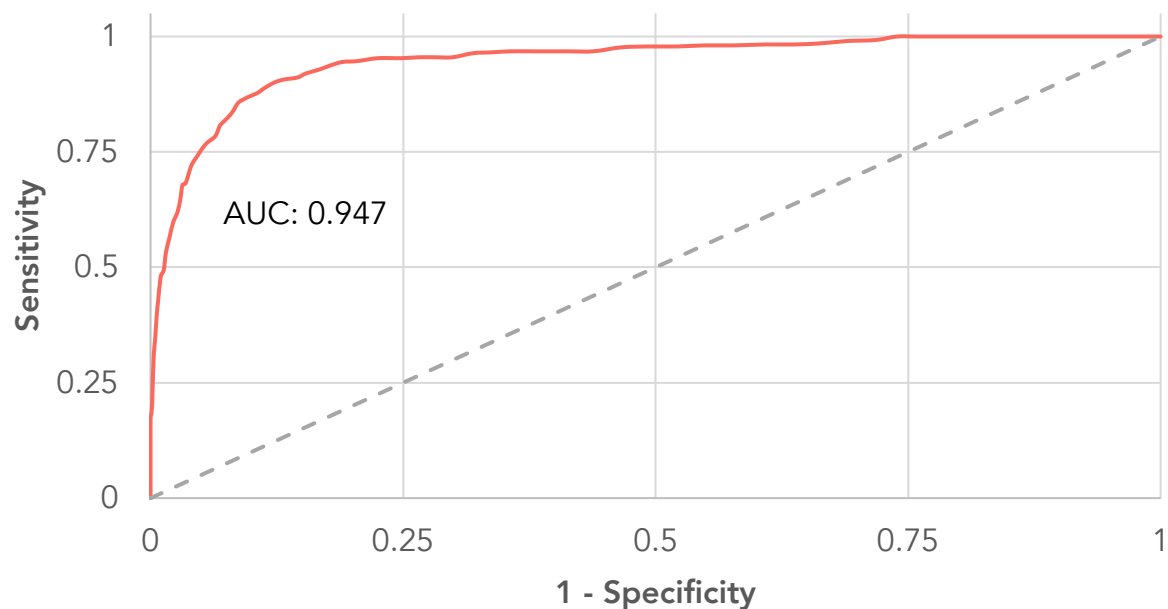
# Appendix 3. Predictions by Stage & Comparison to Actual, Training Set



Predictions by Stage & Comparison to Actual - Training Set

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

Predictions by Stage & Comparison to Actual - Testing Set

# References

1. "Kidney Disease: The Basics." National Kidney Foundation, August 12, 2014. https://www.kidney.org/news/newsroom/factsheets/KidneyDiseaseBasics.

2. Go, Alan S., Glenn M. Chertow, Dongjie Fan, Charles E. McCulloch, and Chi-yuan Hsu. "Chronic Kidney Disease and the Risks of Death, Cardiovascular Events, and Hospitalization." *New England Journal of Medicine* 351, no. 13 (September 23, 2004): 1296–1305. https://doi.org/10.1056/NEJMoa041031.

3. "FastStats," June 19, 2019. https://www.cdc.gov/nchs/fastats/kidney-disease.htm.

4. "Annual Data Report Highlights." Accessed August 28, 2019. https://www.usrds.org/adrhighlights.aspx.

5. "Chronic Kidney Disease Basics | Chronic Kidney Disease Initiative | CDC," March 13, 2019. https://www.cdc.gov/kidneydisease/basics.html.

6. Honeycutt, Amanda A., Joel E. Segel, Xiaohui Zhuo, Thomas J. Hoerger, Kumiko Imai, and Desmond Williams. "Medical Costs of CKD in the Medicare Population." *Journal of the American Society of Nephrology* 24, no. 9 (September 1, 2013): 1478–83. https://doi.org/10.1681/ASN.2012040392.

7. "V2 CH11 ESRD Costs of ESRD." Accessed August 28, 2019. https://www.usrds.org/2013/view/v2_11.aspx.

8. AJMC. "All-Cause Costs Increase Exponentially with Increased Chronic Kidney Disease Stage." Accessed November 4, 2019. https://www.ajmc.com/journals/supplement/2017/all-cause-costs-increase-exponentially-with-increased-chronic-kidney-disease-stage/all-cause-costs-increase-exponentially-with-increased-chronic-kidney-disease-stage-article.

9. Kuznar, Wayne. "Primary Care Physicians Underdiagnose Chronic Kidney Disease in Diabetic Patients," September 25, 2012. http://www.ahdbonline.com/issues/value-based-care-cardiometabolic-health/august-2012-vol-1-no-2/1104-article-1104.

10. Szczech, Lynda A., Rebecca C. Stewart, Hsu-Lin Su, Richard J. DeLoskey, Brad C. Astor, Chester H. Fox, Peter A. McCullough, and Joseph A. Vassalotti. "Primary Care Detection of Chronic Kidney Disease in Adults with Type-2 Diabetes: The ADD-CKD Study (Awareness, Detection and Drug Therapy in Type 2 Diabetes and Chronic Kidney Disease)." *PLOS ONE* 9, no. 11 (November 26, 2014): e110535. https://doi.org/10.1371/journal.pone.0110535.

11. "V2 CH1 Incidence, Prevalence, Patient Characteristics, and Treatment Modalities." Accessed November 4, 2019. https://www.usrds.org/2018/view/v2_01.aspx.

12. Brown, Pierre Antoine, Ayub Akbari, Amber O. Molnar, Shaurya Taran, Janice Bissonnette, Manish Sood, and Swapnil Hiremath. "Factors Associated with Unplanned Dialysis Starts in Patients Followed by Nephrologists: A Retropective Cohort Study." *PLOS ONE* 10, no. 6 (June 5, 2015): e0130080. https://doi.org/10.1371/journal.pone.0130080.

13. Hassan, Rana, Ayub Akbari, Pierre A. Brown, Swapnil Hiremath, K. Scott Brimble, and Amber O. Molnar. "Risk Factors for Unplanned Dialysis Initiation: A Systematic Review of the Literature." *Canadian Journal of Kidney Health and Disease* 6 (January 1, 2019): 2054358119831684. https://doi.org/10.1177/2054358119831684.

14. Kidney International Supplements (2013) 3, 134–135; https://doi.org/10.1038/kisup.2012.71

15. Drawz, Paul E, and Mark E Rosenberg. "Slowing Progression of Chronic Kidney Disease." *Kidney International Supplements* 3, no. 4 (December 2013): 372–76. https://doi.org/10.1038/kisup.2013.80.

16. "Slow Progression & Reduce Complications | NIDDK." National Institute of Diabetes and Digestive and Kidney Diseases. Accessed August 28, 2019. https://www.niddk.nih.gov/health-information/communication-programs/nkdep/identify-manage-patients/manage-ckd/slow-progression-reduce-complications.

17. Lin, Eugene, Glenn M. Chertow, Brandon Yan, Elizabeth Malcolm, and Jeremy D. Goldhaber-Fiebert. "Cost-Effectiveness of Multidisciplinary Care in Mild to Moderate Chronic Kidney Disease in the United States: A Modeling Study." *PLoS Medicine* 15, no. 3 (March 27, 2018). https://doi.org/10.1371/journal.pmed.1002532.

18. Raymond Vanholder, Lieven Annemans, Edwina Brown, Ron Gansevoort, Judith J. Gout-Zwart, Norbert Lameire, et al. "Reducing the Costs of Chronic Kidney Disease While Delivering Quality Health Care: A Call to Action." *Nature Reviews Nephrology* 13, no. 7 (July 2017): 393–409. https://doi.org/10.1038/nrneph.2017.63.

19. Bang, Heejung, Suma Vupputuri, David A. Shoham, Philip J. Klemmer, Ronald J. Falk, Madhu Mazumdar, Debbie Gipson, Romulo E. Colindres, and Abhijit V. Kshirsagar. "SCreening for Occult REnal Disease (SCORED): A Simple Prediction Model for Chronic Kidney Disease." *Archives of Internal Medicine* 167, no. 4 (February 26, 2007): 374–81. https://doi.org/10.1001/archinte.167.4.374.

20. Peralta, Carmen A., Paul Muntner, Rebecca Scherzer, Suzanne Judd, Mary Cushman, and Michael G. Shlipak. "A Risk Score to Guide Cystatin C Testing to Detect Occult Reduced Estimated Glomerular Filtration Rate." *American Journal of Nephrology* 42, no. 2 (2015): 141–47. https://doi.org/10.1159/000439231.

21. Carrillo-Larco, Rodrigo M., J. Jaime Miranda, Robert H. Gilman, Josefina Medina-Lezama, Julio A. Chirinos-Pacheco, Paola V. Muñoz-Retamozo, Liam Smeeth, William Checkley, Antonio Bernabe-Ortiz, and CRONICAS Cohort Study Group. "Risk Score for First-Screening of Prevalent Undiagnosed Chronic Kidney Disease in Peru: The CRONICAS-CKD Risk Score." *BMC Nephrology* 18, no. 1 (November 29, 2017): 343. https://doi.org/10.1186/s12882-017-0758-4.

22. Tummalapalli, Sri Lekha, and Carmen A. Peralta. "An Electronic CKD Phenotype: A Step Forward in Improving Kidney Care." *Clinical Journal of the American Society of Nephrology* 14, no. 9 (September 6, 2019): 1277–79. https://doi.org/10.2215/CJN.08180719.

23. Fishbane, Steven, Sofia Agoritsas, Alessandro Bellucci, Candice Halinski, Hitesh H. Shah, Vipul Sakhiya, and Leah Balsam. "Augmented Nurse Care Management in CKD Stages 4 to 5: A Randomized Trial." *American Journal of Kidney Diseases: The Official Journal of the National Kidney Foundation* 70, no. 4 (October 2017): 498–505. https://doi.org/10.1053/j.ajkd.2017.02.366.

24. Everett, Beverly, Liana D. Castel, Matthew McGinnis, Amy Beresky, Rudolph C. Cane, Tasha Cooper, Rajesh K. Davda, et al. "Economic and Clinical Outcomes Resulting From the Stage 4 Chronic Kidney Disease Case Management Quality Improvement Initiative." *Professional Case Management* 22, no. 6 (November 2017): 291–98. https://doi.org/10.1097/NCM.0000000000000253.

25. Mendelssohn, David C., Bryan Curtis, Karen Yeates, Serge Langlois, Jennifer M. MacRae, Lisa M. Semeniuk, Fernando Camacho, Philip McFarlane, and STARRT Study investigators. "Suboptimal Initiation of Dialysis with and without Early Referral to a Nephrologist." *Nephrology, Dialysis, Transplantation: Official Publication of the European Dialysis and Transplant Association - European Renal Association* 26, no. 9 (September 2011): 2959–65. https://doi.org/10.1093/ndt/gfq843.

26. JM, Norton, et al Clin J. Am Soc Nephrol 2019;doi:10 2215/CJN 00360119 August 19, and 2019. "EHR-Based Tool May Accurately Identify Patients Likely to Have CKD." Accessed September 30, 2019. https://www.healio.com/nephrology/chronic-kidney-disease/news/online/{0f6985f2-c774-448a-9efc-420bf69fb08f}/ehr-based-tool-may-accurately-identify-patients-likely-to-have-ckd.

27. Greer, Raquel C., Yang Liu, Kerri Cavanaugh, Clarissa Jonas Diamantidis, Michelle M. Estrella, C. John Sperati, Sandeep Soman, et al. "Primary Care Physicians' Perceived Barriers to Nephrology Referral and Co-Management of Patients with CKD: A Qualitative Study." *Journal of General Internal Medicine* 34, no. 7 (July 2019): 1228–35. https://doi.org/10.1007/s11606-019-04975-y.