Developing An Advisor Predicting Inpatient Hypokalemia: A Negative Study
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Introduction
Hypokalemia, defined as serum potassium ("K") levels below 3.5mEq/L, is important clinically. It can cause muscle weakness, renal tubular defects, arrhythmias, and even death. A complex buffering system regulates serum K levels. Diuretics, like furosemide, cause renally mediated K depletion [1]. A previous study detected hypokalemia (lowK) in 21% of inpatients taking furosemide [2]. Despite hypokalemia's significance, a search of PubMed reveals few articles that provide algorithms for forecasting lowK. With the ultimate goal of building an informatics advisor to help clinicians avoid lowK in their patients, authors reasoned that linear regression using recent K measurements might predict incipient hypokalemia, since serum K levels might fall at a different rate after K store depletion.

Methods
Vanderbilt University Hospital (VUH) is an academic, tertiary care hospital in Nashville, TN. Since 1995, VUH has maintained a locally developed electronic health record (EHR) that includes care provider order entry (CPOE) and patient data repository components. Authors completed a simple epidemiological analysis of the frequency of hypokalemia in patients receiving and not receiving furosemide. With the goal of correlating serum K levels and furosemide ordering, and with IRB approval, authors extracted anonymized data from the data repository systems spanning 8/1999-7/2003 inpatients whose admissions lasted at least 48 hours. Authors defined "simple lowK crossing" as sequential serum K measurements, first above, then below 3.5 mEq/L within a given time period, and "clinically significant lowK crossing" as a serum K measurement above 3.5mEq/L followed immediately by either one measurement below 3.2 mEq/L or followed by 2 or more measurements below 3.5 mEq/L.

Authors wrote a PERL script attempting to predict, using linear regression, lowK crossings at "starting points" of 48, 72, 96, 120, and 144 hours into a hospital admission. The linear regression used all measured K levels during the 48 hours prior to each starting point, and projected 24, 48, and 72 hours into the future (after the starting point). If the regression line crossed 3.5mEq/L from above to below, a forecast of "impending lowK" during that future 24-hour time interval was recorded. The regression predictions were compared to the "gold standard" of actual recorded lowK crossings of both types. Algorithm performance was measured through sensitivity, specificity, positive predictive value, and negative predictive value calculations.

Results
Data from the EHR system indicated 57,839 inpatients from 8/1999–7/2003 stayed at least 48 hours. Of those, 53,643 patients had at least one serum K measurement. A total of 18828 patients received furosemide (34%), and their relative risk of lowK (at any time, including admission) was 1.53. Approximately 10% of the 57,839 patients had initial (admission) K < 3.5mEq/L. Of patients not receiving furosemide, 17.5% had simple lowK crossings a median of 76 hours into the hospital stay; for patients receiving furosemide, 38.9% had such crossings at median 105 hours. On furosemide, the relative risk of simple lowK crossing after admission was 2.2.

For the patients receiving furosemide, using "simple lowK crossing" as the gold standard, the regression algorithm yielded sensitivities ranging from 52% to 55% (for 24, 48, and 72 hours into the future) and positive predictive value (PPV) ranging from 18% to 34%. Using "significant lowK crossings", the algorithm yielded sensitivities ranging from 54-57% and PPV ranging from 9% to 20%.

For patients who never received furosemide, using "simple lowK crossing" as gold standard, the algorithm yielded sensitivities ranging from 46% to 47%, with PPV ranging from 15% to 30%. Using "significant lowK crossing", the algorithm yielded sensitivities ranging from 46% to 48% and PPV ranging from 8% to 16%.

Analysis and Discussion
The algorithm's sensitivity for predicting lowK crossings improved 7-11% when applied to patients given furosemide versus not. Sensitivities further improve 2-4% using the gold standard of "significant lowK crossing." Thus, simple linear regression upon recent 48 hours of historical serum K measurements remains a poor predictor (not much better than measured prevalence) for lowK crossings at our institution. Further refinement to improve sensitivities of algorithm may include incorporating other patient variables such as other labs and medications. The same approach at different institutions (using local data) can produce different, locally appropriate monitoring recommendations. At present, our informatics advisor for hypokalemia prevention would recommend: measure serum K every 48 hours if initial value >= 4.0 mEq/L, and change monitoring to once every 24 hours if K < 4.0 or if furosemide started.

References:
Supported by NLM Grant R01-LM-007995.