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Placing clinical variables on a common linear scale of empirically-determined risk: a step toward construction of a general patient condition score from the Electronic Health Record

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Abstract

Objective: To explore the hypothesis that placing clinical variables of differing metrics on a common linear scale of all-cause post-discharge mortality provides risk functions that are directly correlated with in-hospital mortality risk.

Design: Cohort study of in-hospital and post-discharge mortality of patients over two 1-year periods.

Setting: An 805-bed community hospital in the southeastern United States.

Participants: 42,302 inpatients admitted for any reason, excluding obstetrics, pediatric and psychiatric patients.

Outcome Measures: All-cause in-hospital and post-discharge mortalities, and associated correlations.

Results: Pearson correlation coefficients comparing in-hospital risks with post-discharge risks for creatinine, heart rate and a set of twelve nursing assessments are 0.920, 0.922, and 0.892 respectively. Correlation between post-discharge risk heart rate and the Modified Early Warning System (MEWS) component for heart rate is 0.855. The minimal excess risk values for creatinine and heart rate roughly correspond to normal reference ranges. We also provide the risks for values outside that range, independent of expert opinion or a regression model. By summing risk functions, a first-approximation patient risk score is created, which correctly ranks 6 discharge categories by average mortality with $P < .001$ for differences in category means, and Tukey's Highly-Significant Difference Test confirmed the means were all different at the 95% confidence level.

Conclusions: Quantitative or categorical clinical variables can be transformed into risk functions that correlate well with in-hospital risk. This methodology provides an empirical way to assess inpatient risk from data available in the EHR. With just the variables in this paper, we achieve a risk score that correlates with discharge disposition. This is the first step toward creation of a universal measure of patient condition that reflects a generally applicable set of health-related risks. More importantly, we believe our approach opens the door to a way of exploring and resolving many issues in patient assessment.

ARTICLE SUMMARY

Article Focus:

- This study develops an empirical measure of all-cause mortality risk, using as examples heart rate, creatinine, and a set of 12 nursing assessments.
- It describes risk functions that enable quantitative assessment of in-patient acuity, based upon commonly available clinical measurements and 1-year mortality.

Key Messages:

- Risk functions are easily computed with the data from an EHR and the Social Security Administration Death file; these functions correlate well with in-hospital mortality, giving investigators a new tool to study the acuity of patients in the hospital.
- Excess risk functions provide a new way to view results from pathology labs beyond just considering how a measurement compares to a reference range of population norms.

Strengths and Limitations of this Study:

- Strengths: a large dataset (more than 40,000 hospital visits) was used to derive the risk functions; this is a new empirical method for evaluating univariate risk, independent of diagnosis or comorbidity, and without using population norms or expert opinion.
- Limitations: no multivariate analysis was performed on the example variables, making the associations found subject to possible unknown confounders, also the work has been done at a single site with a population skewed older than the general population.

INTRODUCTION

Clinicians regularly utilize various systems designed to quantify some aspect of patient acuity.[1] In most cases these assess risk pertaining to: a specific event such as cardiopulmonary arrest or transfer to intensive care;[2-9] or to a specific disease or procedure;[10-14] or within a specific environment, such as the ICU.[13,15,16] However, there has been no previous system created to score the over-all condition of a hospital's general ward in-patient based upon empirical evidence.

In this study, we lay the foundation necessary for an overall measure of a patient's condition. We seek to create a real-time, longitudinal index, calculated by summing empirical estimates of incremental risk. Systems to measure risk in the hospital have been based upon aggregated expert opinion,[13,16-21] or upon regression models.[15,22] For laboratory tests, risk is usually based upon the norm of a "healthy" population[23] with the notion that if a measurement is within the reference range (mean +/- 2 standard deviations), there is no risk. Unfortunately this lab method has no direct link to risk, for example: average cholesterol for the adult population is 200 mg/dL,[24] which is now understood to be "borderline high" even though at the population norm.[25]

We introduce a different method to determine a patient's risk, which does not rely or require expert opinion, nor a regression model, nor a population norm, but rather is completely empirical and evidence-based. Our hypothesis is that placing clinical variables on a linear scale of all-cause post-discharge mortality produces risk functions that are directly correlated with in-hospital mortality. Adding together risk functions of differing underlying metrics is a step toward creation of a general patient condition score of empirically-determined risks. These

functions are readily computed by combining clinical data available in a hospital's Electronic Health Record (EHR) with mortality data available from the Social Security Administration.

This is one of a series of studies whose objective is to demonstrate and validate the creation of such an index, derived empirically from regularly collected variables available in a hospital's EHR. In a previous study, it was demonstrated that for nursing assessments, pre-discharge assessments are strongly correlated with 1-year post-discharge mortality, and nursing assessments at admission are correlated with in-hospital mortality.[26]

We extend this work in three ways: first, by computing risk functions for vital signs and for laboratory blood tests; second, showing the relevance of 1-year post-discharge risk functions to the risk in the hospital, by computing the correlation between in-hospital risk and post-discharge risk; and third, showing that a sum of risk functions correlates with patient acuity at time of discharge, as represented by the patient's discharge disposition (e.g., to home or rehab or skilled nursing facility).

This common linear scale of a risk function reflects the health consequences of any value of the variable in terms of all-cause risk of mortality associated with that value, independent of diagnosis. One advantage of having various routinely available in-hospital clinical variables expressed in terms of percent risk is that they then can be linearly added in some fashion to assign a total risk index for each patient at any moment in time, given the variable values for that patient. The current study illustrates our new methodology using several basic variables as an example, including quantitative, such as heart rate or creatinine level, and categorical, such as twelve pass/fail nursing assessments. We then demonstrate the utility of a first-approximation risk score based upon this example, which we compute by simply adding the risks associated with these example variables.

The full details of construction and validation of a real-time, inpatient condition score is the subject of a forthcoming study. This new measure is currently being used and evaluated in several medical centers, and is called the Rothman Index in memory of Florence A. Rothman, whose death inspired this research. The various measures necessary to form an index in other areas of research can be determined by the methodology developed here, and we encourage application of our methods.

METHODS

General approach and data

A methodology for assessment of hospital in-patient risk should have the following properties:

1. The variables must be readily accessible in the EHR;
2. The various risks must be empirically determined;
3. The scale must be linear, allowing risks to be additive;
4. The methodology must be statistically rigorous.

To be linear and additive, the calculated risks are expressed in percent, as opposed to odds or ratios. Although in-hospital percent mortality risks can be ascertained, inpatient deaths are usually at such low rates that it may be difficult to achieve adequate statistical significance. However, the period 1-year post-discharge can more easily achieve statistical significance, since there is time to accumulate a sufficient number of deaths. The problem then becomes establishing correspondence between post-discharge risks on the one hand, and in-hospital risks, on the other.[26,27] In the following, we demonstrate that post-discharge mortalities associated

with exit values of variables have a direct relationship to in-hospital mortalities associated with entry values of these variables.

To demonstrate the methodology that can be utilized for the various types of clinical variables available in the EHR, we analyze two quantitative variables and a set of twelve categorical variables. Specifically, we provide the details for a vital sign (heart rate), a laboratory test (creatinine), and nursing assessments (*cf.* Rothman, Solinger *et al.*[26] for definition and discussion of nursing assessments). Clinical data, discharge dates, and Social Security numbers for the periods 1/2004-12/2004 and 6/2005-6/2006 were extracted from the EHR at Sarasota Memorial Hospital (SMH), an 805-bed community hospital. Our cohort for this study were patients admitted for any reason during this period, excluding obstetrics, pediatric and psychiatric patients, which determined the study size of 43,302 in-patient admissions. Demographic data and diagnostic data have not been collected for this population; however, our subject community hospital serves a population skewed older than the US average. Death records were acquired from the Social Security Administration Death Master File. Approval for the work was granted by the SMH Institutional Review Board.

Calculation of "excess risk" functions for each variable

For quantitative variables, we tabulated the numbers of living and dead patients associated with each value of the variable, and took a frequency-weighted moving average (calculated at the maximum granularity, e.g. 0.1 mg/dL for creatinine and 1 beat per minute for heart rate) over all values reported. By subtracting the minimum mortality associated with a variable from that variable's mortality results, we found the absolute mortality increase or net "excess risk" of mortality for the various values of the variable. This method was utilized to

associate deaths within a period 1-year post-discharge with variable values at discharge, and in-hospital mortality with variable values at admission.

For categorical variables (*e.g.,* nursing assessments where physiological systems are evaluated by nurses as "within normal limits" or "not within normal limits"[26]), the mortalities associated with each category were calculated, producing simple functions of category vs. mortality. The excess risk function is the difference between mortality for a category and that for the category at which mortality is a minimum.

For every variable, we calculated two excess risk functions and the Pearson correlation between them. The two excess risk functions were determined from 1) post-discharge mortality associated with the last values before discharge, and 2) in-hospital mortality associated with the first values after admission. Data analysis was performed by Systat version 13 (Systat Corp., Chicago, Illinois, USA).

Finally, to investigate our methodology's utility for constructing an empirically-based risk score of patients, we added together the risks associated with each patient's heart rate, creatinine level, and the set of nursing assessments, as recorded in the hospital's EHR, to obtain an overall "risk score" and then tested the scores by ranking of discharge dispositions. To test whether this score corresponds to the approximate condition of discharged patients, we calculated the average score among patients for each of 6 discharge categories, namely: home, home with health care, rehab center, skilled nursing facility, hospice, death. Separation of means was tested by ANOVA and by Tukey's "honestly-significant difference" test.

RESULTS

Table 1 gives the distribution statistics for admission and discharge values of heart rate and creatinine. The excess risk functions for heart rate and creatinine and nursing assessments

are given in Figures 1 - 3. The excess risk functions for creatinine and heart rate are U-shaped, with both low and high values associated with higher mortality risks, and minimal risks for intermediate values. For comparison, the Modified Early Warning System (MEWS) component for heart rate is also graphed.[21] Pearson correlation coefficients for comparing point-by-point excess in-hospital risks with excess post-discharge risks are 0.920 and 0.922 respectively, $P < .001$. Passing a nursing assessment ("within normal limits") is found to be associated with fewer deaths than failing ("not within normal limits") in all cases. The correlation of excess risk in-hospital compared to post-discharge is 0.892.

Table 1. Distribution statistics of entry and exit values of creatinine and heart rate.

	Entry Creatinine	*Exit Creatinine*	*Entry Heart*	*Exit Heart*
Number of Cases	32,232	31,336	42,202	41,173
Median	1	0.9	79	77
Arithmetic Mean	1.273	1.183	80.335	78.097
Mode	0.8	0.8	80	70
Standard Deviation	1.225	1.115	17.189	15.073

With all of these example variables on a common linear scale of risk, the risks can be added together to form an overall score for patient condition (a rather crude score, limited to our example variables). To test whether this score approximately corresponds to patient condition at discharge, we calculated the average overall score among patients just before discharge, for 6 categories listed in Table 2, and the 1-year mortality for each category. The average score properly ranked the discharge dispositions, and there was excellent separation between the averages for each of the categories. This is confirmed by an ANOVA calculation of means with

$F = 2{,}657$, and Tukey's Honestly-Significant Difference Test in Systat, with $P < .001$ for all pair-wise differences in means at the 95% confidence level.

Table 2. A sample overall risk score for patients in 6 discharge dispositions. All means are pairwise statistically significantly different with $P < .001$.

Discharge disposition	*Average Risk Score*	*+/- Error*	*% 1-year Mortality*	*N*
Home	7.5	0.1	5.5	23,791
Home with health care	12.2	0.1	9.4	6,919
Rehab center	16.7	0.2	11.2	2,157
Skilled nursing facility	24.2	0.2	25.7	5,977
Hospice	36.3	0.4	84.3	1,341
Expired	42.4	0.4	100	1,254

DISCUSSION

Characteristics of Lab Results (Creatinine)

Our function for percent absolute increase in risk of mortality, hereinafter referred to as "excess risk", has minimal values (below 4%) between 0.5 - 1.3 mg/dL, roughly corresponding to the reference range for creatinine as 0.5 - 1.2 mg/dL, which is determined by samples from a healthy population (given by SMH lab with their equipment's expected error being $\pm$0.1 mg/dL).[27] One major advantage of our methodology is to provide a function of risk for values outside that reference range, as determined by all-cause mortality statistics, unrelated to any specific disease and independent of any specific model. Although this is a one-center result, it is based on over 30,000 observations, and has a $P < .010$ for most values of post-discharge risks.

Characteristics of Vital Sign Results (Heart Rate)

Our excess risk function is a relative minimum (below 4%) for the range 47 - 74 bpm, which is rather lower than the range some studies give as normal, 60-80 bpm (*e.g.,* Reunanen et al).[28] For comparison, we also graphed the heart rate component of MEWS, scaled to fit our results, with each MEWS point set equal to 25% excess risk. MEWS assigns zero relative risk from 50 to 100 bpm, which according to our results puts patients near the high end of the zero-risk MEWS range at a mortality risk of over 15%. It is worth noting that the overall results, while differing in details, are nonetheless quite similar, allowing for the rough granularity of MEWS. Of course, the methodology behind the two results is completely different, as ours is derived from actual increase in mortality, without the need to gather expert opinion. We have also calculated excess risk functions for other vital signs (e.g., systolic and diastolic blood pressure, pulse oximetry); those functions will be published elsewhere, as our primary purpose here is to illustrate the methodology.

Characteristics of Categorical Variable Results (Nursing Assessments)

Excess risks for binary variables, such as nursing assessments that are categorized as either "within normal limits" or "not within normal limits", are computed by merely taking the differences between the all-cause mortality rates of the two possibilities. The lower risk therefore is identically zero, the higher is the difference. For categorical variables that are not binary, an excess risk function would be computed as the difference between the category having the lowest mortality, and the mortality rate for each of the other categories.

When comparing all nursing assessment in-hospital risks versus post-discharge risks, we found the "food" assessment (indicating a difficulty with chewing or swallowing or appetite) was an outlier, the post-discharge risk being proportionately much greater. This may be because in-

patients who are not able to eat can be given their nutrition intravenously or with feeding tubes; for discharged patients, this is rarely available. The eleven other nursing assessments are similar in nature to a doctor's general "review of systems"[29] (e.g., gastrointestinal, musculo-skeletal, genitourinary), while food stands alone (omitting the outlier increases the correlation from 0.892 to 0.934).

Utility and Meaning of the Excess Risk Methodology

One must address the issue of the meaning and utility of the methodology developed here, if it is to be useful in the hospital setting. First, the post-discharge risks correlate well with the in-hospital risks, showing that the former can be used as a measure of the latter. Secondly, we find that the risk score created by simply adding the in-hospital risks associated with the last values of our example variables before discharge (nursing assessments, heart rate, and creatinine) approximately corresponds to patient condition at discharge across the acuity spectrum of discharged patients. As shown in Table 2, the average risk scores among patients within each of the 6 discharge categories correspond exactly with the progression that would be expected for an increasing risk of death: home, home with health care, rehab center, skilled nursing facility, hospice and expired. Thus these risk functions are meaningful in terms of patient condition. This further suggests that a more sophisticated score could be developed to track each patient's condition within the hospital, or to predict readmission; these are subjects of our current research.

The correlation with acuity across the acuity spectrum suggests that these measurements may be applicable to those patients critically ill, possibly in the ICU, and also to those patients on a general hospital ward. Additionally, it is clear that excess risk functions may be used in many different ways. We have shown an example where our function qualitatively reproduces a univariate risk function (MEWS for heart rate) supplied by experts while providing more

quantitative detail, and examples where the minima of excess risk functions reflect population-derived reference ranges. These measures of patient risk could prove helpful in pharmaceutical or epidemiological research as an indication of outcomes.[30]

Studying all-cause mortality rates associated with clinical variables yields information on general risks associated with the variables. In forthcoming studies, we compare the risks associated with various lab tests to their standard reference ranges. This methodology provides direct estimates of the risks associated with values both within and outside the reference range, which the usual demographic studies of healthy populations do not. This is an area that warrants further investigation, and may be another way that reference ranges can be established.

Finally, since any clinical variable can be associated with a function of excess risk by the methodology utilized in the current study, a researcher can choose any combination of disparate variables to describe some specific aspect of the condition of a patient in a hospital, and transform these into risk functions; this, in turn, allows placing the values onto a common linear scale, and combining them to create an index for the specific purpose intended. This index would then be empirically determined, without reference to models or to expert opinion, and based strictly upon data from the EHR.

CONCLUSIONS

Any quantitative or categorical clinical variable in the EHR can be transformed into an excess risk function. This associates the absolute increased percent risk of dying from any cause after hospital discharge with each value of the variable. We have shown this to be directly correlated with in-hospital patient risk. Moreover, the resultant risks can be added to obtain a measure of total risk that corresponds well with discharge disposition. In a forthcoming study,

we demonstrate the building of a more complex index based upon these principles, which is expected to satisfy additional and more stringent tests of construct validity.

We believe our approach opens the door to a way of exploring and resolving many issues in patient assessment. Clearly, researchers with access to the database of a hospital's EHR can perform retrospective research to determine risks associated with clinical and physiological variables, stratified by age, gender, race or any administrative classification. This enables researchers to explore many new relationships using disparate variables, becoming a new and meaningful use of the EHR.

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Contributorship

MJR and SIR conceived this research issue, and performed the preliminary investigations. MJR performed the data extraction; SIR and ABS extended the scope of the investigation; ABS analyzed the extended dataset, searched the literature, and wrote the first draft of the manuscript. All authors contributed to the interpretation of the results and critical revision of the manuscript for important intellectual content and approved the final version of the manuscript. SIR is the guarantor.

Data Sharing

Qualified researchers may apply to the corresponding author for the study's data.

Competing Interests

None

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None. Our research was self-initiated and independent.

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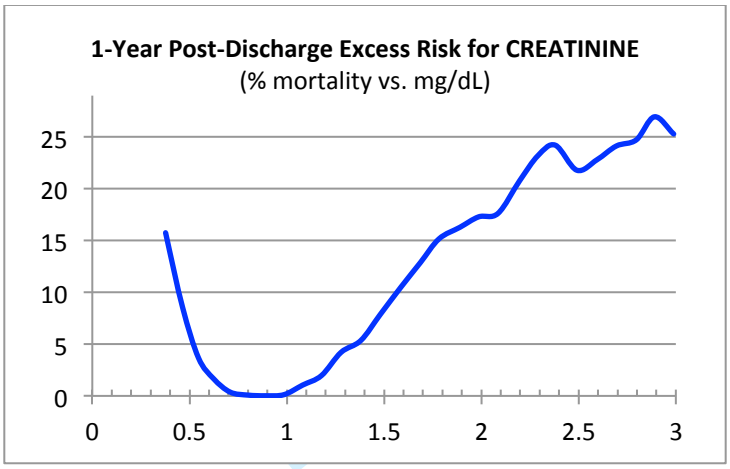

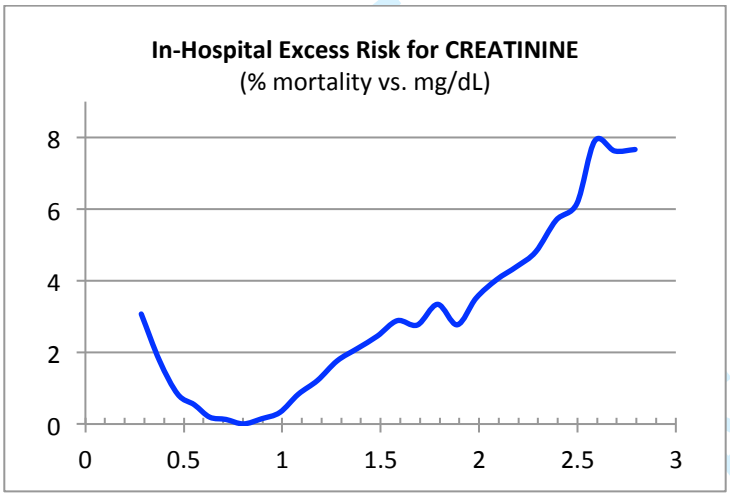

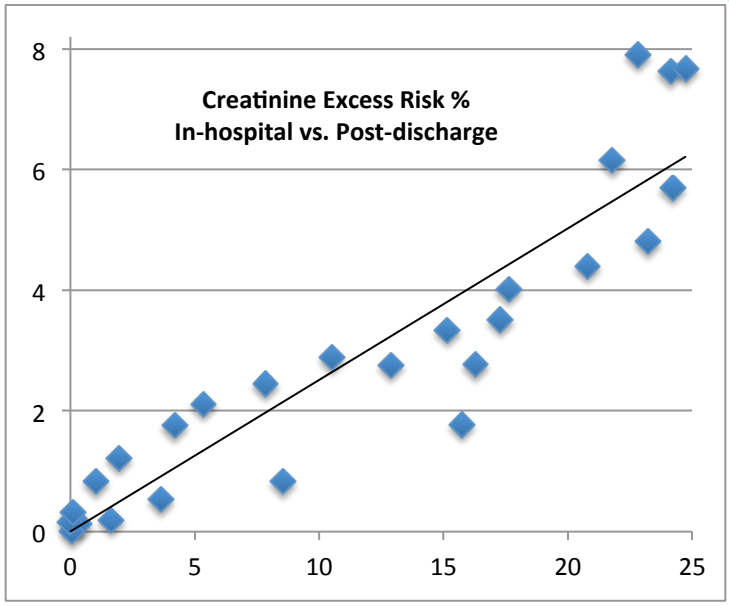

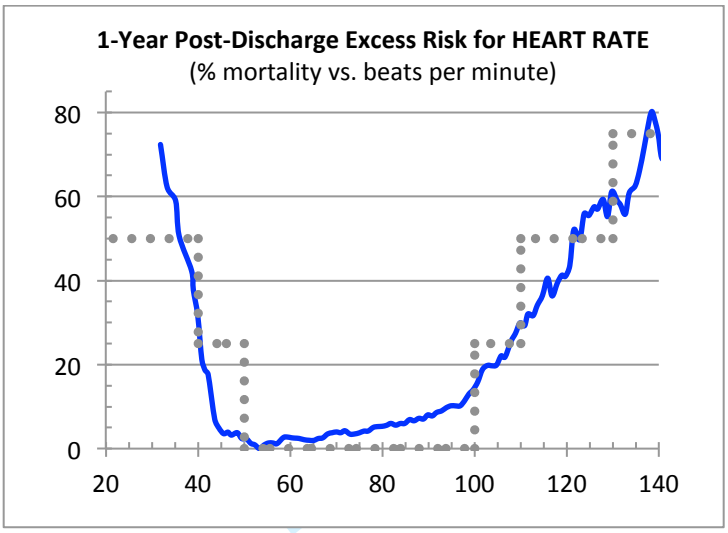

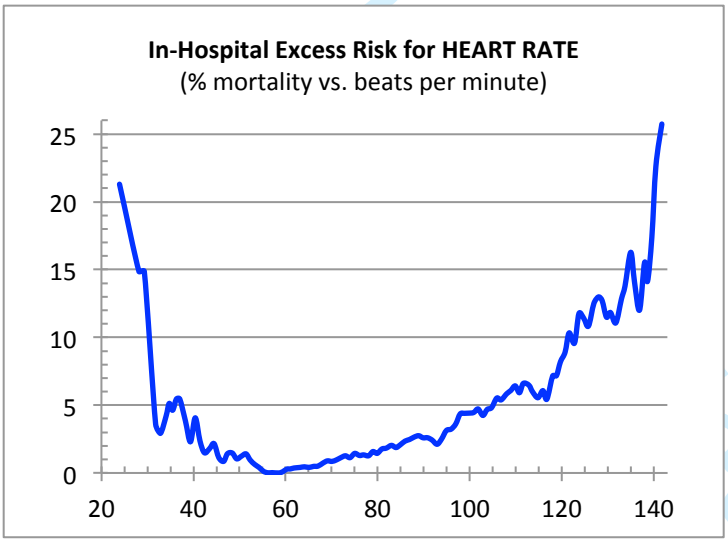

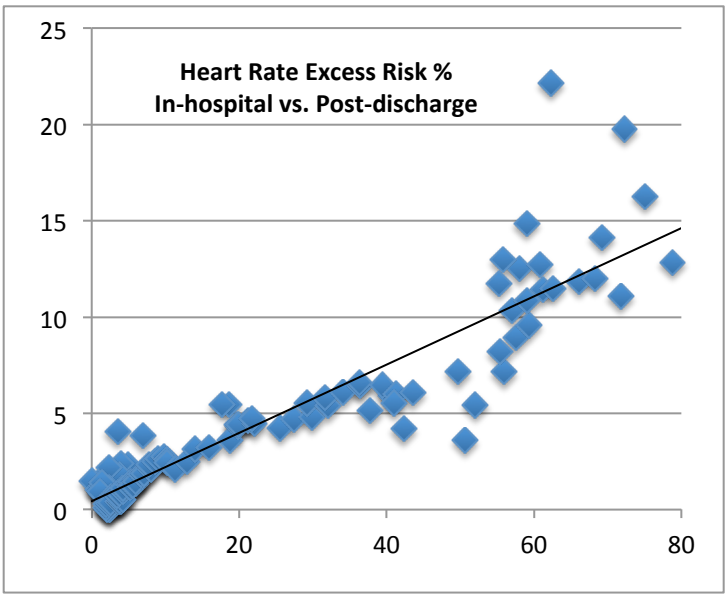

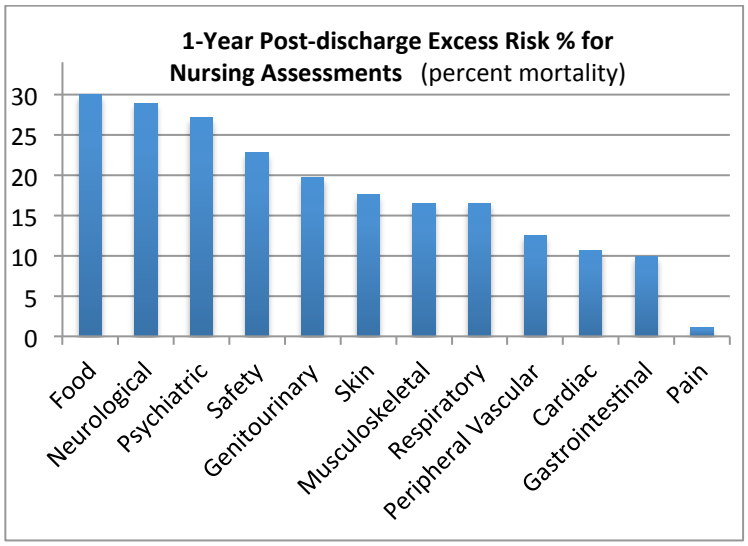

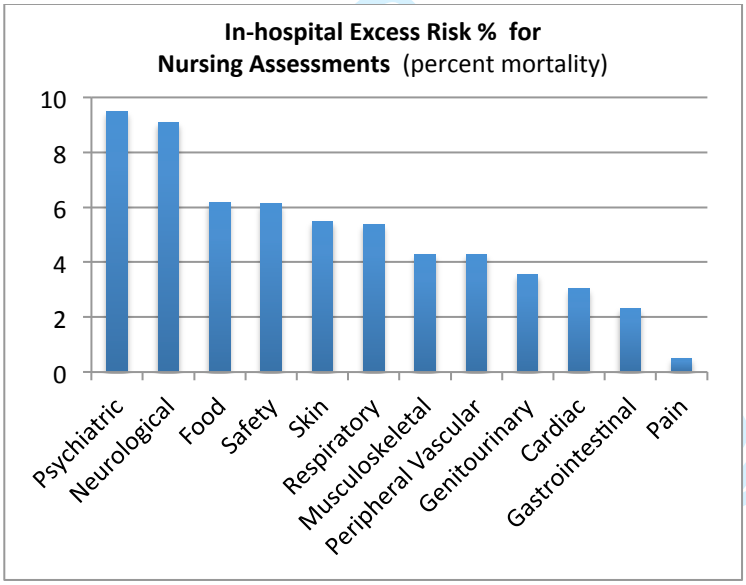

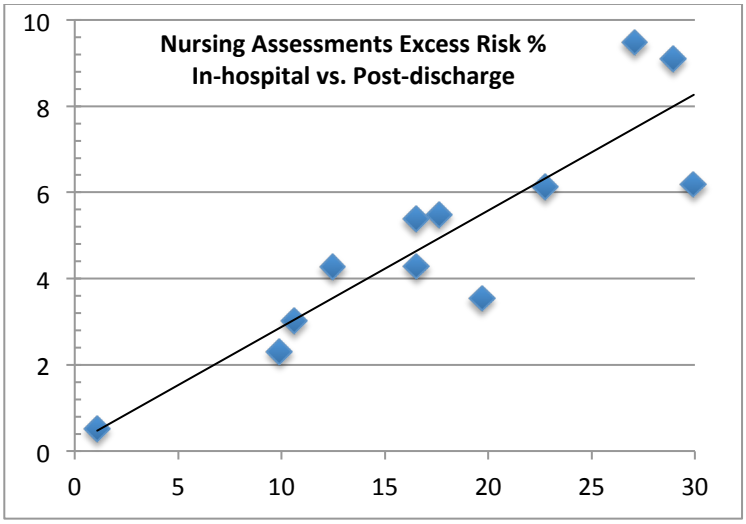

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Placing clinical variables on a common linear scale of empirically-determined risk: a step toward construction of a general patient condition score from the Electronic Health Record

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Placing clinical variables on a common linear scale of empirically-determined risk: a step toward construction of a general patient condition score from the Electronic Health Record

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ARTICLE SUMMARY

Article Focus:

- This study develops an empirical measure of all-cause mortality risk, using as examples heart rate, creatinine, and a set of 12 nursing assessments.
- It describes risk functions that enable quantitative assessment of in-patient acuity, based upon commonly available clinical measurements and 1-year mortality.

Key Messages:

- Risk functions are easily computed with the data from an EHR and the Social Security Administration Death file; these functions correlate well with in-hospital mortality, giving investigators a new tool to study the acuity of patients in the hospital.
- Excess risk functions provide a new way to view results from pathology labs beyond just considering how a measurement compares to a reference range of population norms.

Strengths and Limitations of this Study:

- Strengths: a large dataset (more than 40000 hospital visits) was used to derive the risk functions; this is a new empirical method for evaluating univariate risk, independent of diagnosis or comorbidity, and without using population norms or expert opinion.
- Limitations: no multivariate analysis was performed on the example variables, making the associations found subject to possible unknown confounders, also the work has been done at a single site with a population skewed older than the general population.

Abstract:

Objective: To explore the hypothesis that placing clinical variables of differing metrics on a common linear scale of all-cause post-discharge mortality provides risk functions that are directly correlated with in-hospital mortality risk.

Design: Cohort study of in-hospital and post-discharge mortality of patients over two 1-year periods.

Setting: An 805-bed community hospital in the southeastern United States.

Participants: 42302 inpatients admitted for any reason, excluding obstetrics, pediatric and psychiatric patients.

Outcome Measures: All-cause in-hospital and post-discharge mortalities, and associated correlations.

Results: Pearson correlation coefficients comparing in-hospital risks with post-discharge risks for creatinine, heart rate and a set of twelve nursing assessments are 0.920, 0.922, and 0.892 respectively. Correlation between post-discharge risk heart rate and the Modified Early Warning System (MEWS) component for heart rate is 0.855. The minimal excess risk values for creatinine and heart rate roughly correspond to normal reference ranges. We also provide the risks for values outside that range, independent of expert opinion or a regression model. By summing risk functions, a first-approximation patient risk score is created, which correctly ranks 6 discharge categories by average mortality with $P < .001$ for differences in category means, and

Tukey's Honestly Significant Difference Test confirmed the means were all different at the 95% confidence level.

Conclusions: Quantitative or categorical clinical variables can be transformed into risk functions that correlate well with in-hospital risk. This methodology provides an empirical way to assess inpatient risk from data available in the EHR. With just the variables in this paper, we achieve a risk score that correlates with discharge disposition. This is the first step toward creation of a universal measure of patient condition that reflects a generally applicable set of health-related risks. More importantly, we believe our approach opens the door to a way of exploring and resolving many issues in patient assessment.

INTRODUCTION

Clinicians regularly utilize various systems designed to quantify some aspect of patient acuity.[1] In most cases these assess risk pertaining to: a specific event such as cardiopulmonary arrest or transfer to intensive care;[2-11] or to a specific disease or procedure;[12-16] or within a specific environment, such as the ICU;[15,17,18] or for after-the-fact risk adjustment, such as to compare performance of medical units.[19-22] However, there has been no previous system created to score the real-time over-all condition of individual patients within a hospital's general ward, across the acuity spectrum, based upon empirical evidence from the Electronic Health Record (EHR).

In this study, we lay the foundation necessary for an overall measure of a patient's condition. We seek to create a contemporaneous longitudinal index, calculated by summing empirical estimates of incremental risk. Systems to measure risk in the hospital have been based upon aggregated expert opinion,[15,18,23-27] or upon regression models.[17,28] And, for

laboratory tests, risk as reported to physicians by pathology labs is usually based upon the norm of a "healthy" population[29] with the notion that if a measurement is within the reference range (mean +/- 2 standard deviations), there is no risk. Unfortunately this lab method has no direct link to risk; for example serum cholesterol for the adult population would have placed the norm at 200 mg/dL,[30] which in light of extensive medical evidence is now understood to be "borderline high".[31]

We introduce a different method to estimate a patient's risk, which does not rely or require expert opinion, or a regression model, or a population norm, but rather is completely empirical and evidence-based. Our hypothesis is that placing clinical variables on a linear scale of all-cause post-discharge mortality produces risk functions that are directly correlated with in-hospital mortality. Adding together risk functions of differing underlying metrics is a step toward creation of a general patient condition score of empirically-based risks. These functions are readily computed by combining clinical data available in a hospital's EHR with mortality data available from the Social Security Administration.

This is one of a series of studies whose objective is to demonstrate and validate the creation of such an index, derived empirically from regularly collected variables available in a hospital's EHR. In a previous study, we demonstrated that for nursing assessments, pre-discharge assessments are strongly correlated with 1-year post-discharge mortality, and nursing assessments at admission are correlated with in-hospital mortality.[32]

We extend this work in three ways: first, by computing risk functions for vital signs and for laboratory blood tests; second, showing the relevance of 1-year post-discharge risk functions to the risk in the hospital, by computing the correlation between in-hospital risk and post-discharge risk; and third, showing that a sum of risk functions correlates with patient acuity at time of discharge, as represented by the patient's discharge disposition (e.g., to home or rehab or skilled nursing facility).

This common linear scale of a risk function reflects the health consequences of any value of the variable in terms of all-cause risk of mortality associated with that value, independent of diagnosis. One advantage of having various routinely available in-hospital clinical variables expressed in terms of percent risk is that they then can be linearly added in some fashion to assign a total risk index for each patient at any moment in time, given the variable values for that patient. The current study illustrates our new methodology using several basic variables as an example, including quantitative, such as heart rate or creatinine level, and categorical, such as twelve pass/fail nursing assessments. We then demonstrate the utility of a first-approximation risk score based upon this example, which we compute by simply adding the risks associated with these example variables.

The full details of construction and validation of a real-time, inpatient condition score is the subject of a forthcoming study. This new measure is currently being used and evaluated in several medical centers, and is called the Rothman Index in memory of Florence A. Rothman, whose death inspired this research. The various measures necessary to form an index in other areas of research can be determined by the methodology developed here, and we encourage application of our methods.

METHODS

General approach and data

A methodology for assessment of hospital in-patient risk should have the following properties:

1. The variables must be readily accessible in the EHR;
2. The various risks must be empirically determined;
3. The scale must be linear, allowing risks to be additive;
4. The methodology must be statistically rigorous.

To be linear and additive, the calculated risks are expressed in percent, as opposed to odds or ratios. Although in-hospital percent mortality risks can be ascertained, inpatient deaths are usually at such low rates that it may be difficult to achieve adequate statistical significance. However, the period 1-year post-discharge can more easily achieve statistical significance, since there is time to accumulate a sufficient number of deaths. The problem then becomes establishing correspondence between post-discharge risks on the one hand, and in-hospital risks, on the other.[32,33] In the following, we demonstrate that post-discharge mortalities associated with exit values of variables have a direct relationship to in-hospital mortalities associated with entry values of these variables.

To demonstrate the methodology that can be utilized for the various types of clinical variables available in the EHR, we analyze two quantitative variables and a set of twelve categorical variables. Specifically, we provide the details for a vital sign (heart rate), a laboratory test (creatinine), and nursing assessments (for definition of nursing assessments see Table 2).[32] Clinical data, discharge dates, and Social Security numbers for the periods 1/2004-12/2004 and 6/2005-6/2006 were extracted from the EHR at Sarasota Memorial Hospital (SMH), an 805-bed community hospital. Our cohort for this study were patients admitted for any reason during this period, excluding obstetrics, pediatric and psychiatric patients, which determined the study size of 42302 in-patient admissions. Demographic data and diagnostic data have not been collected for this population; however, our subject community hospital serves a population skewed older than the US average. Death records were acquired from the Social Security Administration Death Master File. Ethical considerations associated with this study have been reviewed by the SMH Institutional Review Board, which approved the study.

Calculation of "excess risk" functions for each variable

For quantitative variables, we tabulated the numbers of living and dead patients associated with each value of the variable, and took a frequency-weighted moving average (calculated at the maximum granularity, e.g. 0.1 mg/dL for creatinine and 1 beat per minute for heart rate) over all values reported. The test samples for creatinine were collected routinely, analyzed by the SMH laboratory utilizing the Siemens Dimension Vista® System and its prescribed procedures, and results entered into the EHR. By subtracting the minimum mortality associated with a variable from that variable's mortality results, we found the absolute mortality increase or net "excess risk" of mortality for the various values of the variable. This method was utilized to associate deaths within a period 1-year post-discharge with variable values at discharge, and in-hospital mortality with variable values at admission.

For categorical variables (*e.g.*, nursing assessments where physiological systems are evaluated by nurses as "within normal limits" or "not within normal limits"[32]), the mortalities associated with each category were calculated, producing simple functions of category vs. mortality. The excess risk function is the difference between mortality for a category and that for the category at which mortality is a minimum.

For every variable, we calculated two excess risk functions and the Pearson correlation between them. The two excess risk functions were determined from 1) post-discharge mortality associated with the last values before discharge, and 2) in-hospital mortality associated with the first values after admission. Data analysis was performed by Systat version 13 (Systat Corp., Chicago, Illinois, USA).

Finally, to investigate our methodology's utility for constructing an empirically-based risk score of patients, we added together the risks associated with each patient's heart rate, creatinine level, and the set of nursing assessments, as recorded in the hospital's EHR, to obtain an overall "risk score" and then tested the scores by ranking of discharge dispositions. To test whether this score corresponds to the approximate condition of discharged patients, we

calculated the average score among patients for each of 6 discharge categories, namely: home, home with health care, rehab center, skilled nursing facility, hospice, death. Separation of means was tested by ANOVA and by Tukey's "honestly significant difference" test. For comparison, we performed the same ranking for age versus discharge disposition. To check on possible confounding, we ran Pearson correlation calculations on all pairs of variables.

RESULTS

Table 1 gives the distribution statistics for admission and discharge values of heart rate and Creatinine, while Table 2 summarizes the distribution of nursing assessment pass/fail at entry and exit. The excess risk functions for heart rate and creatinine and nursing assessments are given in Figures 1 - 3. The excess risk functions for creatinine and heart rate are U-shaped, with both low and high values associated with higher mortality risks, and minimal risks for intermediate values. For comparison, the Modified Early Warning System (MEWS) component for heart rate is also graphed.[27] Pearson correlation coefficients for comparing point-by-point excess in-hospital risks with excess post-discharge risks are 0.920 and 0.922 respectively ($P < .001$).

Table 1. Distribution statistics of entry and exit values of creatinine and heart rate.

	Entry Creatinine	*Exit Creatinine*	*Entry Heart*	*Exit Heart*
Number of Cases	32232	31336	42202	41173
Median	1	0.9	79	77
Arithmetic Mean	1.273	1.183	80.335	78.097
Mode	0.8	0.8	80	70
Standard Deviation	1.225	1.115	17.189	15.073

Passing a nursing assessment ("within normal limits") is found to be associated with fewer deaths than failing ("not within normal limits") in all cases. The correlation of excess risk in-hospital compared to post-discharge is 0.892. Note in Figures 1-3 that the "excess risk" curves are very similar for in-hospital and post-discharge (part "a" versus part "b"), though the actual mortality rates are lower in-hospital as one would expect for the shorter period of a hospital stay. Demonstrating that these are highly correlated implies the possibility of model construction from any hospital's EHR (matched with a death record), since the average hospital stay of 3.5 days makes achieving data significance difficult.

With all of these example variables on a common linear scale of risk, the risks can be added together to form an overall score for patient condition (a rather crude score, limited to our example variables). To test whether this score approximately corresponds to patient condition at discharge, we calculated the average overall score among patients just before discharge, for 6 categories listed in Table 3, and the 1-year mortality for each category. The average score properly ranked the discharge dispositions, and there was excellent separation between the averages for each of the categories. This is confirmed by an ANOVA calculation of means with $F = 2{,}657$, and Tukey's Honestly Significant Difference Test in Systat, with $P < .001$ for all pair-wise differences in means at the 95% confidence level.

It had been suggested that patients' age might be used to separate discharge disposition categories (we do not include age in our variables). However, none of the pairwise comparisons of average age by discharge disposition were different at the 95% confidence level, and the Pearson correlation between age and discharge group has a coefficient of 0.078 (virtually no relationship). It is not age itself, but age-related illness that we capture in each patient's clinical variables, and it is each patient's combined risk score that correlates with discharge disposition. Finally, we found very low correlation between any pair of variables; the 78 pair-wise Pearson

correlation coefficients are shown in Table 4, indicating lack of confounding, and lack of double counting, and thus remarkably little information overlap.

Table 2. Nursing Assessments: Standards at SMH with fail-rate upon admission and discharge. These assessments are generally performed at least once per shift. They consist of binary data, characterized either as having "met" or "not met" the standard. Although standards vary, basically the same data is being collected at every hospital. It is generally possible to construct similar binary variables from any hospital's nursing data.

NURSING STANDARDS	Upon Admission		Upon Discharge	
As defined at Sarasota Memorial Hospital (each standard is judged as "met" or not met")	**Number of cases**	**Percent Failed**	**Number of cases**	**Percent Failed**
Cardiac: Pulse regular, rate 60-100 BPM, skin warm and dry. Blood Pressure less than 140/90 and no symptoms of hypotension	**41657**	**26.4%**	**40597**	**18.9%**
Food: No difficulty with chewing, swallowing or manual dexterity. Patient consuming >50% of daily diet ordered as observed or stated.	**41645**	**23.4%**	**40579**	**13.4%**
Gastrointestinal: Abdomen soft and non-tender. Bowel sounds present. No nausea or vomiting. Continent. Bowel pattern normal as observed or stated	**41657**	**27.2%**	**40591**	**17.7%**
Genitourinary: Voids without difficulty. Continent. Urine clear, yellow to amber as observed or stated. Urinary catheter patent if present.	**41649**	**19.1%**	**40577**	**13.0%**
Musculoskeletal: Independently able to move all extremities and perform functional activities as observed or stated (includes assistive devices).	**41660**	**42.2%**	**40591**	**40.0%**
Pain: Without pain or VAS<4 or experiencing chronic pain that is managed effectively.	**41568**	**18.3%**	**40501**	**12.1%**
Neurological: Alert, oriented to person, place, time, and situation. Speech is coherent.	**41661**	**15.0%**	**40591**	**13.6%**
Peripheral/Vascular: Extremities are normal or pink and warm. Peripheral pulses palpable. Capillary refill <3 sec. No edema, numbness or tingling.	**41667**	**23.6%**	**40596**	**27.1%**
Psychosocial: Behavior appropriate to situation. Expressed concerns and fears being addressed. Adequate support system.	**41645**	**7.2%**	**40579**	**7.1%**
Respiratory: Resp. 12-24/min at rest quiet and regular. Bilateral breath sounds clear. Nail beds and mucous membranes pink. Sputum clear if present.	**41665**	**32.8%**	**40594**	**33.5%**
Safety/Fall-Risk: Safety/Fall risk factors not present. Patient is not a risk to self or others.	**41667**	**18.2%**	**40578**	**17.1%**
Skin/Tissue: Skin clean, dry and intact with no reddened areas. Patient is alert, cooperative and able to reposition self independently. Braden >15.	**41631**	**21.3%**	**40564**	**26.0%**

Table 3. A sample overall risk score for patients in 6 discharge dispositions. All means are pairwise statistically significantly different with $P < .001$.

Discharge disposition	*Average Risk Score*	*+/- Error*	*% 1-year Mortality*	*N*
Home	7.5	0.1	5.5	23,791
Home with health care	12.2	0.1	9.4	6,919
Rehab center	16.7	0.2	11.2	2,157
Skilled nursing facility	24.2	0.2	25.7	5,977
Hospice	36.3	0.4	84.3	1,341
Death	42.4	0.4	100	1,254

Table 4. Pearson Product-Moment Correlation Matrix: *R*, correlation coefficients among all component-pairs of the model. Abbreviations correspond to 12 Nursing Assessments of Table 2, plus Creatinine and Heart Rate. Also included is Age as a possible confounding factor. All pairs have low *R*-squared coefficients of determination, indicating that every variable could contribute to the model's goodness of fit (for ranking the categories of discharge disposition).

	Ag	Ca	Fo	Ga	Ge	Mu	Ne	Pa	Pe	Ps	Re	Sa	Sk	HR	CR
Age	1.0														
Cardiac	0.2	1.0													
Food	0.1	0.1	1.0												
Gastrointestinal	0.0	0.1	0.2	1.0											
Genitourinary	0.2	0.1	0.2	0.1	1.0										
Musculoskeletal	0.3	0.1	0.3	0.1	0.2	1.0									
Neurological	0.3	0.1	0.4	0.1	0.3	0.4	1.0								
Pain	-0.1	0.0	0.0	0.1	0.0	0.1	0.0	1.0							
Peripheral Vasc	0.2	0.1	0.1	0.1	0.1	0.3	0.1	0.0	1.0						
Psychosocial	0.1	0.1	0.3	0.1	0.2	0.2	0.4	0.0	0.1	1.0					
Respiratory	0.3	0.1	0.2	0.1	0.1	0.2	0.2	0.0	0.2	0.1	1.0				
Safety/Fall Risk	0.3	0.1	0.3	0.1	0.2	0.4	0.5	0.0	0.1	0.3	0.2	1.0			
Skin/Tissue	0.2	0.1	0.3	0.1	0.2	0.4	0.3	0.0	0.3	0.2	0.2	0.3	1.0		
Heart Rate	-0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	1.0	
Creatinine	0.1	0.0	0.0	0.0	0.2	0.1	0.0	0.0	0.1	0.0	0.0	0.0	0.1	0.0	1.0

DISCUSSION

Characteristics of Lab Results (Creatinine)

Our function for percent absolute increase in risk of mortality, hereinafter referred to as "excess risk", has minimal values (below 4%) between 0.5 - 1.3 mg/dL, roughly corresponding to the reference range for creatinine as 0.5 - 1.2 mg/dL, which is determined by samples from a

healthy population (given by SMH lab utilizing the Siemens Vista system with expected error of ±0.1 mg/dL).[33] One major advantage of our methodology is to provide a function of risk for values outside that reference range, as determined by all-cause mortality statistics, unrelated to any specific disease and independent of any specific model. We are comparing our "excess risk" function for Creatinine to the usual laboratory test results of "higher than," "lower than," or "within" the normal reference interval. To do this, we calculate mortality rates for members of the cohort with test results in a small interval about each value. Using a standard statistical method for calculating the power associated with utilizing samples to calculate a mortality rate for a population, $P < 0.01$ except at the very extremes of the data range, where the data is sparse.

Characteristics of Vital Sign Results (Heart Rate)

Our excess risk function is a relative minimum (below 4%) for the range 47 - 74 bpm, which is rather lower than the range some studies give as normal, 60-80 bpm (*e.g.,* Reunanen et al).[34] For comparison, we also graphed the heart rate component of MEWS, scaled to fit our results, with each MEWS point set equal to 25% excess risk. MEWS assigns zero relative risk from 50 to 100 bpm, which according to our results puts patients near the high end of the zero-risk MEWS range at a mortality risk of over 15%. It is worth noting that the overall results, while differing in details, are nonetheless quite similar, allowing for the rough granularity of MEWS. Of course, the methodology behind the two results is completely different, as ours is derived from readily accessible hospital and mortality data, as opposed to MEWS, which is based upon a consensus of expert opinion. We have also calculated excess risk functions for other vital signs (e.g., systolic and diastolic blood pressure, pulse oximetry); those functions will be published elsewhere, as our primary purpose here is to illustrate the methodology.

Characteristics of Categorical Variable Results (Nursing Assessments)

Excess risks for binary variables, such as nursing assessments that are categorized as either "within normal limits" or "not within normal limits", are computed by merely taking the differences between the all-cause mortality rates of the two possibilities. The lower risk therefore is identically zero, the higher is the difference. For categorical variables that are not binary, an excess risk function would be computed as the difference between the category having the lowest mortality, and the mortality rate for each of the other categories.

When comparing all nursing assessment in-hospital risks versus post-discharge risks, we found the "food" assessment (indicating a difficulty with chewing or swallowing or appetite) was an outlier, as are the "psychiatric" and "genitourinary" assessments, the post-discharge risk being proportionately much greater. For "food" this may be because in-patients who are not able to eat can be given their nutrition intravenously or with feeding tubes, while for discharged patients, this is rarely available. This is not true for the "psychiatric" and "genitourinary" assessments which also have large residuals, and for which we can make no compelling argument not to count them in the correlation calculation. They stand with the other nursing assessments as similar in nature to a doctor's general "review of systems"[35] (e.g., gastrointestinal, musculo-skeletal, genitourinary), while food stands alone (omitting the outlier increases the correlation from 0.892 to 0.934). Whether "food" is excluded or not, the correlation is excellent.

Utility and Meaning of the Excess Risk Methodology

One must address the issue of the meaning and utility of the methodology developed here, if it is to be useful in the hospital setting. First, the post-discharge risks correlate well with the in-hospital risks, showing that the former can be used as a measure of the latter. Secondly, we

find that the risk score created by simply adding the in-hospital risks associated with the last values of our example variables before discharge (nursing assessments, heart rate, and creatinine) approximately corresponds to patient condition at discharge across the acuity spectrum of discharged patients. As shown in Table 3, the average risk scores among patients within each of the 6 discharge categories correspond exactly with the progression that would be expected for an increasing risk of death: home, home with health care, rehab center, skilled nursing facility, hospice and death. Thus these risk functions are meaningful in terms of patient condition. This further suggests that a more sophisticated score could be developed to track each patient's condition within the hospital, or to predict readmission; these are subjects of our current research.

The correlation with acuity across the acuity spectrum suggests that these measurements may be applicable to those patients critically ill, possibly in the ICU, and also to those patients on a general hospital ward. Additionally, it is clear that excess risk functions may be used in many different ways. We have shown an example where our function qualitatively reproduces a univariate risk function (MEWS for heart rate) supplied by experts while providing more quantitative detail, and examples where the minima of excess risk functions confirm population-derived reference intervals. These measures of patient risk could prove helpful in pharmaceutical or epidemiological research as an indication of outcomes.[36] And since we use an institutional approach, which avoids collapsing data to specific categories – such as a disease – our methodology may have a future use in the measurement of hospital performance.

Limitations of this study are that no multivariate analysis was performed on the example variables, making the associations found subject to possible unknown confounders. Also the work has been done at a single site with a population skewed older than the general population.

Studying all-cause mortality rates associated with clinical variables yields information on general risks associated with the variables. In forthcoming studies, we compare the risks associated with various lab tests to their standard reference intervals. This methodology provides direct estimates of the risks associated with values both within and outside the reference interval, which the usual demographic studies of healthy populations do not. This is an area that warrants further investigation, and may be a way that decision limits can be established for lab tests.

Finally, since any clinical variable can be associated with a function of excess risk by the methodology utilized in the current study, a researcher can choose any combination of disparate variables to describe some specific aspect of the condition of a patient in a hospital, and transform these into risk functions; this, in turn, allows placing the values onto a common linear scale, and combining them to create an index for the specific purpose intended. This index would then be empirically based, without reference to models or to expert opinion, and dependent strictly and only upon data from the EHR.

CONCLUSIONS

Any quantitative or categorical clinical variable in the EHR can be transformed into an excess risk function. This associates the absolute increased percent risk of dying from any cause after hospital discharge with each value of the variable. We have shown this to be directly correlated with in-hospital patient risk. Moreover, the resultant risks can be added to obtain a measure of total risk that corresponds well with discharge disposition. In a forthcoming study, we demonstrate the building of a more complex index based upon these principles, which is expected to satisfy additional and more stringent tests of construct validity.

We believe our approach opens the door to a way of exploring and resolving many issues in patient assessment. Clearly, researchers with access to the database of a hospital's EHR can perform retrospective research to determine risks associated with clinical and physiological variables, stratified by age, gender, race or any administrative classification. This enables researchers to explore many new relationships using disparate variables, becoming a new and meaningful use of the EHR.

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Competing Interests: None

Contributorship: MJR and SIR conceived this research issue, and performed the preliminary investigations. MJR performed the data extraction; SIR and ABS extended the scope of the investigation; ABS analyzed the extended dataset, searched the literature, and wrote the first draft of the manuscript. All authors contributed to the interpretation of the results and critical revision of the manuscript for important intellectual content and approved the final version of the manuscript. SIR is the guarantor.

Data sharing: Qualified researchers may apply to the corresponding author for the study's data.

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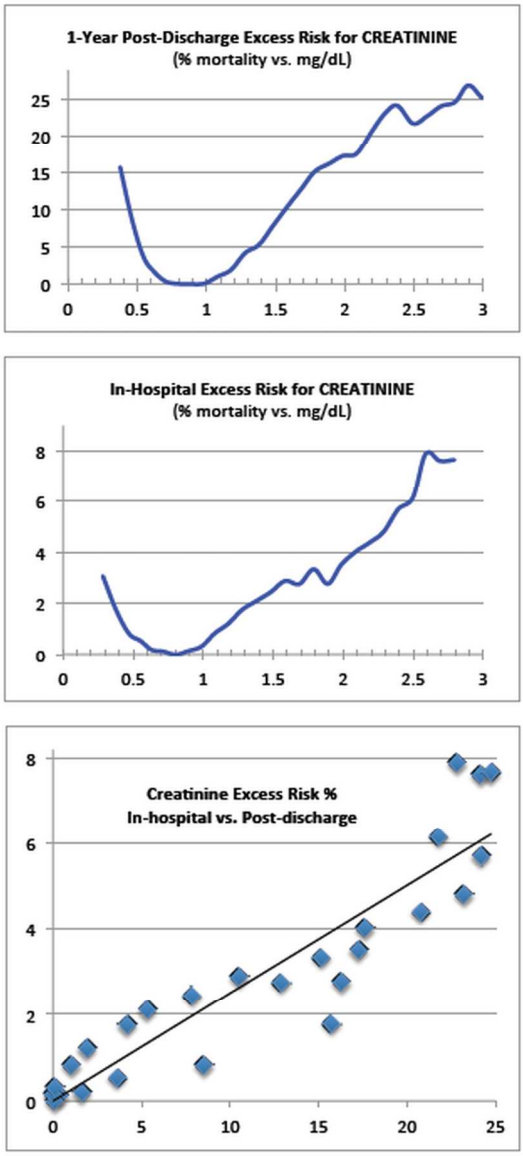

Figure 1. Creatinine Level vs. Excess Risk: a) 1-Year Post-Discharge; b) In-Hospital; c) Correlation = 0.920 The reference range for creatinine at Sarasota Memorial Hospital is 0.5 to 1.2 mg/dL.
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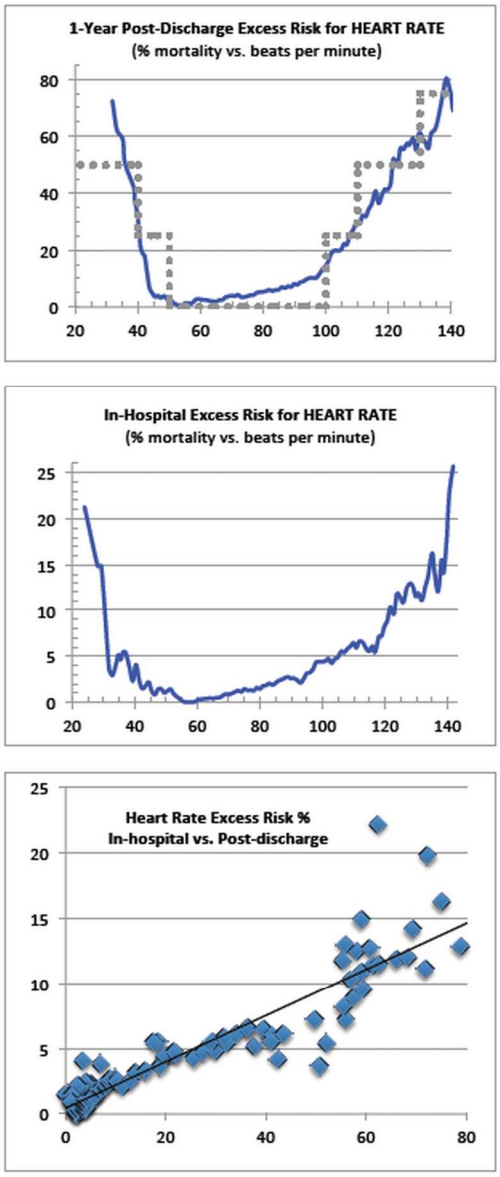

Figure 2. Heart Rate vs. Excess Risk: a) 1-Year Post-Discharge; b) In-Hospital; c) Correlation = 0.922
Displayed for comparison is the MEWS heart risk score (in gray dots), scaled to correspond roughly with our results (MEWS correlation = 0.855).
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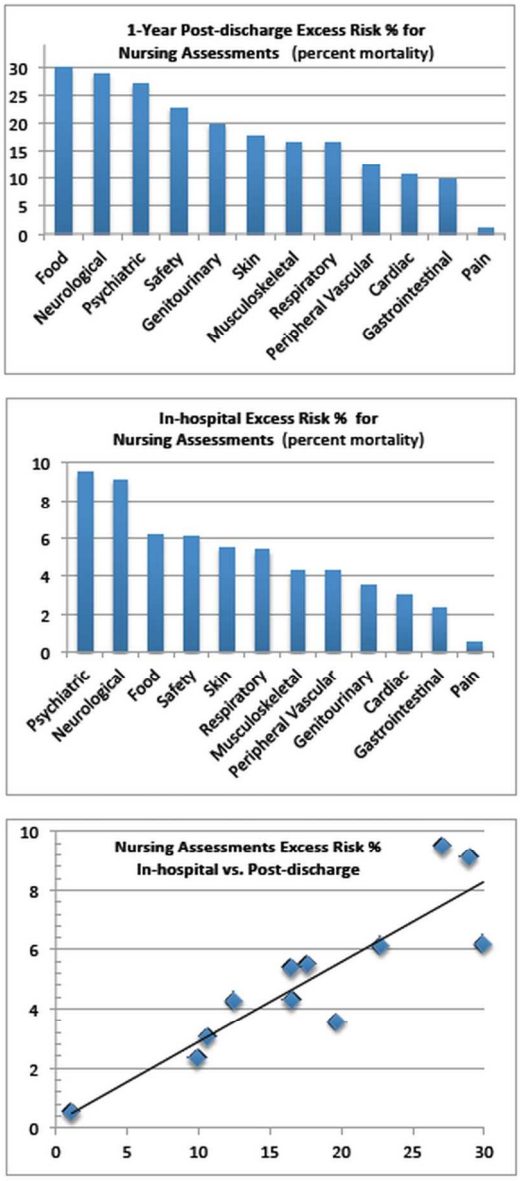

Figure 3. Nursing Assessments vs. Excess Risk: a) 1-Year Post-Discharge; b) In-Hospital; c) Correlation = 0.892 for the Set of Twelve Nursing Assessments – In-hospital vs. Post-discharge.
90x197mm (300 x 300 DPI)

This is a mark-up document, showing changes from the originally submitted manuscript.

Placing clinical variables on a common linear scale of empirically-determined risk: a step toward construction of a general patient condition score from the Electronic Health Record

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Keywords: Health Status Indicators, Risk Assessment, Risk Factors, Hospitalization /statistics & numerical data, Electronic Health Records

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ABSTRACT

Objective: To explore the hypothesis that placing clinical variables of differing metrics on a common linear scale of all-cause post-discharge mortality provides risk functions that are directly correlated with in-hospital mortality risk.

Design: Cohort study of in-hospital and post-discharge mortality of patients over two 1-year periods.

Setting: An 805-bed community hospital in the southeastern United States.

Participants: 42302 inpatients admitted for any reason, excluding obstetrics, pediatric and psychiatric patients.

Outcome Measures: All-cause in-hospital and post-discharge mortalities, and associated correlations.

Results: Pearson correlation coefficients comparing in-hospital risks with post-discharge risks for creatinine, heart rate and a set of twelve nursing assessments are 0.920, 0.922, and 0.892 respectively. Correlation between post-discharge risk heart rate and the Modified Early Warning System (MEWS) component for heart rate is 0.855. The minimal excess risk values for creatinine and heart rate roughly correspond to normal reference ranges. We also provide the risks for values outside that range, independent of expert opinion or a regression model. By summing risk functions, a first-approximation patient risk score is created, which correctly ranks 6 discharge categories by average mortality with $P < .001$ for differences in category means, and Tukey's ~~Highly~~ Honestly Significant Difference Test confirmed the means were all different at the 95% confidence level.

Conclusions: Quantitative or categorical clinical variables can be transformed into risk functions that correlate well with in-hospital risk. This methodology provides an empirical way to assess inpatient risk from data available in the EHR. With just the variables in this paper, we achieve a risk score that correlates with discharge disposition. This is the first step toward creation of a universal measure of patient condition that reflects a generally applicable set of health-related risks. More importantly, we believe our approach opens the door to a way of exploring and resolving many issues in patient assessment.

ARTICLE SUMMARY

Article Focus:

- This study develops an empirical measure of all-cause mortality risk, using as examples heart rate, creatinine, and a set of 12 nursing assessments.
- It describes risk functions that enable quantitative assessment of in-patient acuity, based upon commonly available clinical measurements and 1-year mortality.

Key Messages:

- Risk functions are easily computed with the data from an EHR and the Social Security Administration Death file; these functions correlate well with in-hospital mortality, giving investigators a new tool to study the acuity of patients in the hospital.
- Excess risk functions provide a new way to view results from pathology labs beyond just considering how a measurement compares to a reference range of population norms.

Strengths and Limitations of this Study:

- Strengths: a large dataset (more than 40000 hospital visits) was used to derive the risk functions; this is a new empirical method for evaluating univariate risk, independent of diagnosis or comorbidity, and without using population norms or expert opinion.
- Limitations: no multivariate analysis was performed on the example variables, making the associations found subject to possible unknown confounders, also the work has been done at a single site with a population skewed older than the general population.

INTRODUCTION

Clinicians regularly utilize various systems designed to quantify some aspect of patient acuity.[1] In most cases these assess risk pertaining to: a specific event such as cardiopulmonary arrest or transfer to intensive care;[2-11] or to a specific disease or procedure;[12-16] or within a specific environment, such as the ICU;[15,17,18] or for after-the-fact risk adjustment, such as to compare performance of medical units.[19-22] However, there has been no previous system created to score the real-time over-all condition of individual patients within a hospital's general ward ~~in-patient~~, across the acuity spectrum, based upon empirical evidence from the Electronic Health Record (EHR).

In this study, we lay the foundation necessary for an overall measure of a patient's condition. We seek to create a ~~real-time,~~contemporaneous longitudinal index, calculated by summing empirical estimates of incremental risk. Systems to measure risk in the hospital have been based upon aggregated expert opinion,[15,18,23-27] or upon regression models.[17,28] And, for laboratory tests, risk as reported to physicians by pathology labs is usually based upon the norm of a "healthy" population[29] with the notion that if a measurement is within the reference range (mean +/- 2 standard deviations), there is no risk. Unfortunately this lab method has no direct link to risk; for example~~: average~~ serum cholesterol for the adult population ~~is~~ would have placed the norm at 200 mg/dL,[30] which in light of extensive medical evidence is now understood to be "borderline high~~" even though at the population norm.[25~~".[31]

We introduce a different method to ~~determine~~estimate a patient's risk, which does not rely or require expert opinion, ~~nor~~or a regression model, ~~nor~~or a population norm, but rather is completely empirical and evidence-based. Our hypothesis is that placing clinical variables on a linear scale of all-cause post-discharge mortality produces risk functions that are directly correlated with in-hospital mortality. Adding together risk functions of differing underlying metrics is a step toward creation of a general patient condition score of empirically-

~~determined~~based risks. These functions are readily computed by combining clinical data available in a hospital's ~~Electronic Health Record (EHR)~~EHR with mortality data available from the Social Security Administration.

This is one of a series of studies whose objective is to demonstrate and validate the creation of such an index, derived empirically from regularly collected variables available in a hospital's EHR. In a previous study, ~~it was~~we demonstrated that for nursing assessments, pre-discharge assessments are strongly correlated with 1-year post-discharge mortality, and nursing assessments at admission are correlated with in-hospital mortality.[32]

We extend this work in three ways: first, by computing risk functions for vital signs and for laboratory blood tests; second, showing the relevance of 1-year post-discharge risk functions to the risk in the hospital, by computing the correlation between in-hospital risk and post-discharge risk; and third, showing that a sum of risk functions correlates with patient acuity at time of discharge, as represented by the patient's discharge disposition (e.g., to home or rehab or skilled nursing facility).

This common linear scale of a risk function reflects the health consequences of any value of the variable in terms of all-cause risk of mortality associated with that value, independent of diagnosis. One advantage of having various routinely available in-hospital clinical variables expressed in terms of percent risk is that they then can be linearly added in some fashion to assign a total risk index for each patient at any moment in time, given the variable values for that patient. The current study illustrates our new methodology using several basic variables as an example, including quantitative, such as heart rate or creatinine level, and categorical, such as twelve pass/fail nursing assessments. We then demonstrate the utility of a first-approximation risk score based upon this example, which we compute by simply adding the risks associated with these example variables.

The full details of construction and validation of a real-time, inpatient condition score is the subject of a forthcoming study. This new measure is currently being used and evaluated in several medical centers, and is called the Rothman Index in memory of Florence A. Rothman, whose death inspired this research. The various measures necessary to form an index in other areas of research can be determined by the methodology developed here, and we encourage application of our methods.

METHODS

General approach and data

A methodology for assessment of hospital in-patient risk should have the following properties:

1. The variables must be readily accessible in the EHR;
2. The various risks must be empirically determined;
3. The scale must be linear, allowing risks to be additive;
4. The methodology must be statistically rigorous.

To be linear and additive, the calculated risks are expressed in percent, as opposed to odds or ratios. Although in-hospital percent mortality risks can be ascertained, inpatient deaths are usually at such low rates that it may be difficult to achieve adequate statistical significance. However, the period 1-year post-discharge can more easily achieve statistical significance, since there is time to accumulate a sufficient number of deaths. The problem then becomes establishing correspondence between post-discharge risks on the one hand, and in-hospital risks, on the other.[32,33] In the following, we demonstrate that post-discharge mortalities associated with exit values of variables have a direct relationship to in-hospital mortalities associated with entry values of these variables.

To demonstrate the methodology that can be utilized for the various types of clinical variables available in the EHR, we analyze two quantitative variables and a set of twelve categorical variables. Specifically, we provide the details for a vital sign (heart rate), a laboratory test (creatinine), and nursing assessments (~~*cf.* Rothman, Solinger *et al.*[26]~~ for definition ~~and discussion~~ of nursing assessments see Table 2).[32] Clinical data, discharge dates, and Social Security numbers for the periods 1/2004-12/2004 and 6/2005-6/2006 were extracted from the EHR at Sarasota Memorial Hospital (SMH), an 805-bed community hospital. Our cohort for this study were patients admitted for any reason during this period, excluding obstetrics, pediatric and psychiatric patients, which determined the study size of ~~43,302~~42302 in-patient admissions. Demographic data and diagnostic data have not been collected for this population; however, our subject community hospital serves a population skewed older than the US average. Death records were acquired from the Social Security Administration Death Master File. ~~Approval for the work was granted~~Ethical considerations associated with this study have been reviewed by the SMH Institutional Review Board, which approved the study.

Calculation of "excess risk" functions for each variable

For quantitative variables, we tabulated the numbers of living and dead patients associated with each value of the variable, and took a frequency-weighted moving average (calculated at the maximum granularity, e.g. 0.1 mg/dL for creatinine and 1 beat per minute for heart rate) over all values reported. The test samples for creatinine were collected routinely, analyzed by the SMH laboratory utilizing the Siemens Dimension Vista® System and its prescribed procedures, and results entered into the EHR. By subtracting the minimum mortality associated with a variable from that variable's mortality results, we found the absolute mortality increase or net "excess risk" of mortality for the various values of the variable. This method was

utilized to associate deaths within a period 1-year post-discharge with variable values at discharge, and in-hospital mortality with variable values at admission.

For categorical variables (*e.g.,* nursing assessments where physiological systems are evaluated by nurses as "within normal limits" or "not within normal limits"[32]), the mortalities associated with each category were calculated, producing simple functions of category vs. mortality. The excess risk function is the difference between mortality for a category and that for the category at which mortality is a minimum.

For every variable, we calculated two excess risk functions and the Pearson correlation between them. The two excess risk functions were determined from 1) post-discharge mortality associated with the last values before discharge, and 2) in-hospital mortality associated with the first values after admission. Data analysis was performed by Systat version 13 (Systat Corp., Chicago, Illinois, USA).

Finally, to investigate our methodology's utility for constructing an empirically-based risk score of patients, we added together the risks associated with each patient's heart rate, creatinine level, and the set of nursing assessments, as recorded in the hospital's EHR, to obtain an overall "risk score" and then tested the scores by ranking of discharge dispositions. To test whether this score corresponds to the approximate condition of discharged patients, we calculated the average score among patients for each of 6 discharge categories, namely: home, home with health care, rehab center, skilled nursing facility, hospice, death. Separation of means was tested by ANOVA and by Tukey's "honestly ~~significant difference" test.~~ significant difference" test. For comparison, we performed the same ranking for age versus discharge disposition. To check on possible confounding, we ran Pearson correlation calculations on all pairs of variables.

RESULTS

Table 1 gives the distribution statistics for admission and discharge values of heart rate and Creatinine, while Table 2 summarizes the distribution of nursing assessment pass/fail at entry and exit. The excess risk functions for heart rate and creatinine and nursing assessments are given in Figures 1 - 3. The excess risk functions for creatinine and heart rate are U-shaped, with both low and high values associated with higher mortality risks, and minimal risks for intermediate values. For comparison, the Modified Early Warning System (MEWS) component for heart rate is also graphed.[27] Pearson correlation coefficients for comparing point-by-point excess in-hospital risks with excess post-discharge risks are 0.920 and 0.922 respectively ($P < .001$).

Table 1. Distribution statistics of entry and exit values of creatinine and heart rate.

	Entry Creatinine	*Exit Creatinine*	*Entry Heart*	*Exit Heart*
Number of Cases	32232	31336	42202	41173
Median	1	0.9	79	77
Arithmetic Mean	1.273	1.183	80.335	78.097
Mode	0.8	0.8	80	70
Standard Deviation	1.225	1.115	17.189	15.073

Passing a nursing assessment ("within normal limits") is found to be associated with fewer deaths than failing ("not within normal limits") in all cases. The correlation of excess risk in-hospital compared to post-discharge is 0.892. Note in Figures 1-3 that the "excess risk" curves are very similar for in-hospital and post-discharge (part "a" versus part "b"), though the actual mortality rates are lower in-hospital as one would expect for the shorter period of a hospital stay. Demonstrating that these are highly correlated implies the possibility of model

construction from any hospital's EHR (matched with a death record), since the average hospital stay of 3.5 days makes achieving data significance difficult.

With all of these example variables on a common linear scale of risk, the risks can be added together to form an overall score for patient condition (a rather crude score, limited to our example variables). To test whether this score approximately corresponds to patient condition at discharge, we calculated the average overall score among patients just before discharge, for 6 categories listed in Table ~~2~~3, and the 1-year mortality for each category. The average score properly ranked the discharge dispositions, and there was excellent separation between the averages for each of the categories. This is confirmed by an ANOVA calculation of means with $F = 2{,}657$, and Tukey's Honestly Significant Difference Test in Systat, with $P < .001$ for all pair-wise differences in means at the 95% confidence level.

It had been suggested that patients' age might be used to separate discharge disposition categories (we do not include age in our variables). However, none of the pairwise comparisons of average age by discharge disposition were different at the 95% confidence level, and the Pearson correlation between age and discharge group has a coefficient of 0.078 (virtually no relationship). It is not age itself, but age-related illness that we capture in each patient's clinical variables, and it is each patient's combined risk score that correlates with discharge disposition. Finally, we found very low correlation between any pair of variables; the 78 pair-wise Pearson correlation coefficients are shown in Table 4, indicating lack of confounding, and lack of double counting, and thus remarkably little information overlap.

Table 2. Nursing Assessments: Standards at SMH with fail-rate upon admission and discharge. These assessments are generally performed at least once per shift. They consist of binary data, characterized either as having "met" or "not met" the standard. Although standards vary, basically the same data is being collected at every hospital. It is generally possible to construct similar binary variables from any hospital's nursing data.

NURSING STANDARDS	Upon Admission		Upon Discharge	
As defined at Sarasota Memorial Hospital (each standard is judged as "met" or not met")	Number of cases	Percent Failed	Number of cases	Percent Failed
Cardiac: Pulse regular, rate 60-100 BPM, skin warm and dry. Blood Pressure less than 140/90 and no symptoms of hypotension	41657	26.4%	40597	18.9%
Food: No difficulty with chewing, swallowing or manual dexterity. Patient consuming >50% of daily diet ordered as observed or stated.	41645	23.4%	40579	13.4%
Gastrointestinal: Abdomen soft and non-tender. Bowel sounds present. No nausea or vomiting. Continent. Bowel pattern normal as observed or stated	41657	27.2%	40591	17.7%
Genitourinary: Voids without difficulty. Continent. Urine clear, yellow to amber as observed or stated. Urinary catheter patent if present.	41649	19.1%	40577	13.0%
Musculoskeletal: Independently able to move all extremities and perform functional activities as observed or stated (includes assistive devices).	41660	42.2%	40591	40.0%
Pain: Without pain or VAS<4 or experiencing chronic pain that is managed effectively.	41568	18.3%	40501	12.1%
Neurological: Alert, oriented to person, place, time, and situation. Speech is coherent.	41661	15.0%	40591	13.6%
Peripheral/Vascular: Extremities are normal or pink and warm. Peripheral pulses palpable. Capillary refill <3 sec. No edema, numbness or tingling.	41667	23.6%	40596	27.1%
Psychosocial: Behavior appropriate to situation. Expressed concerns and fears being addressed. Adequate support system.	41645	7.2%	40579	7.1%
Respiratory: Resp. 12-24/min at rest quiet and regular. Bilateral breath sounds clear. Nail beds and mucous membranes pink. Sputum clear if present.	41665	32.8%	40594	33.5%
Safety/Fall-Risk: Safety/Fall risk factors not present. Patient is not a risk to self or others.	41667	18.2%	40578	17.1%
Skin/Tissue: Skin clean, dry and intact with no reddened areas. Patient is alert, cooperative and able to reposition self independently. Braden >15.	41631	21.3%	40564	26.0%

Table 3. A sample overall risk score for patients in 6 discharge dispositions. All means are pairwise statistically significantly different with $P < .001$.

Discharge disposition	*Average Risk Score*	*+/- Error*	*% 1-year Mortality*	*N*
Home	7.5	0.1	5.5	23,791
Home with health care	12.2	0.1	9.4	6,919
Rehab center	16.7	0.2	11.2	2,157
Skilled nursing facility	24.2	0.2	25.7	5,977
Hospice	36.3	0.4	84.3	1,341
~~*Expired*~~*Death*	42.4	0.4	100	1,254

Table 4. Pearson Product-Moment Correlation Matrix: *R*, correlation coefficients among all component-pairs of the model. Abbreviations correspond to 12 Nursing Assessments of Table 2, plus Creatinine and Heart Rate. Also included is Age as a possible confounding factor. All pairs have low *R*-squared coefficients of determination, indicating that every variable could contribute to the model's goodness of fit (for ranking the categories of discharge disposition).

	Ag	Ca	Fo	Ga	Ge	Mu	Ne	Pa	Pe	Ps	Re	Sa	Sk	HR	CR
Age	1.0														
Cardiac	0.2	1.0													
Food	0.1	0.1	1.0												
Gastrointestinal	0.0	0.1	0.2	1.0											
Genitourinary	0.2	0.1	0.2	0.1	1.0										
Musculoskeletal	0.3	0.1	0.3	0.1	0.2	1.0									
Neurological	0.3	0.1	0.4	0.1	0.3	0.4	1.0								
Pain	-0.1	0.0	0.0	0.1	0.0	0.1	0.0	1.0							
Peripheral Vasc	0.2	0.1	0.1	0.1	0.1	0.3	0.1	0.0	1.0						
Psychosocial	0.1	0.1	0.3	0.1	0.2	0.2	0.4	0.0	0.1	1.0					
Respiratory	0.3	0.1	0.2	0.1	0.1	0.2	0.2	0.0	0.2	0.1	1.0				
Safety/Fall Risk	0.3	0.1	0.3	0.1	0.2	0.4	0.5	0.0	0.1	0.3	0.2	1.0			
Skin/Tissue	0.2	0.1	0.3	0.1	0.2	0.4	0.3	0.0	0.3	0.2	0.2	0.3	1.0		
Heart Rate	-0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	1.0	
Creatinine	0.1	0.0	0.0	0.0	0.2	0.1	0.0	0.0	0.1	0.0	0.0	0.0	0.1	0.0	1.0

DISCUSSION

Characteristics of Lab Results (Creatinine)

Our function for percent absolute increase in risk of mortality, hereinafter referred to as "excess risk", has minimal values (below 4%) between 0.5 - 1.3 mg/dL, roughly corresponding to the reference range for creatinine as 0.5 - 1.2 mg/dL, which is determined by samples from a

healthy population (given by SMH lab utilizing the Siemens Vista system with ~~their equipment's~~ expected error ~~being~~of ±0.1 mg/dL).[33] One major advantage of our methodology is to provide a function of risk for values outside that reference range, as determined by all-cause mortality statistics, unrelated to any specific disease and independent of any specific model. ~~Although this is a one-center result, it is based on over 30,000 observations, and has a $P < .010$ for most values of post-discharge risks.~~We are comparing our "excess risk" function for Creatinine to the usual laboratory test results of "higher than," "lower than," or "within" the normal reference interval. To do this, we calculate mortality rates for members of the cohort with test results in a small interval about each value. Using a standard statistical method for calculating the power associated with utilizing samples to calculate a mortality rate for a population, $P < 0.01$ except at the very extremes of the data range, where the data is sparse.

Characteristics of Vital Sign Results (Heart Rate)

Our excess risk function is a relative minimum (below 4%) for the range 47 - 74 bpm, which is rather lower than the range some studies give as normal, 60-80 bpm (*e.g.,* Reunanen et al).[34] For comparison, we also graphed the heart rate component of MEWS, scaled to fit our results, with each MEWS point set equal to 25% excess risk. MEWS assigns zero relative risk from 50 to 100 bpm, which according to our results puts patients near the high end of the zero-risk MEWS range at a mortality risk of over 15%. It is worth noting that the overall results, while differing in details, are nonetheless quite similar, allowing for the rough granularity of MEWS. Of course, the methodology behind the two results is completely different, as ours is derived from ~~actual increase in~~readily accessible hospital and mortality~~, without the need~~ data, as opposed to ~~gather~~MEWS, which is based upon a consensus of expert opinion. We have also calculated excess risk functions for other vital signs (e.g., systolic and diastolic blood pressure,

pulse oximetry); those functions will be published elsewhere, as our primary purpose here is to illustrate the methodology.

Characteristics of Categorical Variable Results (Nursing Assessments)

Excess risks for binary variables, such as nursing assessments that are categorized as either "within normal limits" or "not within normal limits", are computed by merely taking the differences between the all-cause mortality rates of the two possibilities. The lower risk therefore is identically zero, the higher is the difference. For categorical variables that are not binary, an excess risk function would be computed as the difference between the category having the lowest mortality, and the mortality rate for each of the other categories.

When comparing all nursing assessment in-hospital risks versus post-discharge risks, we found the "food" assessment (indicating a difficulty with chewing or swallowing or appetite) was an outlier, as are the "psychiatric" and "genitourinary" assessments, the post-discharge risk being proportionately much greater. ~~This~~For "food" this may be because in-patients who are not able to eat can be given their nutrition intravenously or with feeding tubes, while for discharged patients, this is rarely available. ~~The eleven~~This is not true for the "psychiatric" and "genitourinary" assessments which also have large residuals, and for which we can make no compelling argument not to count them in the correlation calculation. They stand with the other nursing assessments ~~are~~as similar in nature to a doctor's general "review of systems"[35] (e.g., gastrointestinal, musculo-skeletal, genitourinary), while food stands alone (omitting the outlier increases the correlation from 0.892 to 0.934). Whether "food" is excluded or not, the correlation is excellent.

Utility and Meaning of the Excess Risk Methodology

One must address the issue of the meaning and utility of the methodology developed here, if it is to be useful in the hospital setting. First, the post-discharge risks correlate well with the in-hospital risks, showing that the former can be used as a measure of the latter. Secondly, we find that the risk score created by simply adding the in-hospital risks associated with the last values of our example variables before discharge (nursing assessments, heart rate, and creatinine) approximately corresponds to patient condition at discharge across the acuity spectrum of discharged patients. As shown in Table ~~2~~3, the average risk scores among patients within each of the 6 discharge categories correspond exactly with the progression that would be expected for an increasing risk of death: home, home with health care, rehab center, skilled nursing facility, hospice and ~~expired~~death. Thus these risk functions are meaningful in terms of patient condition. This further suggests that a more sophisticated score could be developed to track each patient's condition within the hospital, or to predict readmission; these are subjects of our current research.

The correlation with acuity across the acuity spectrum suggests that these measurements may be applicable to those patients critically ill, possibly in the ICU, and also to those patients on a general hospital ward. Additionally, it is clear that excess risk functions may be used in many different ways. We have shown an example where our function qualitatively reproduces a univariate risk function (MEWS for heart rate) supplied by experts while providing more quantitative detail, and examples where the minima of excess risk functions ~~reflect~~confirm population-derived reference ~~ranges~~intervals. These measures of patient risk could prove helpful in pharmaceutical or epidemiological research as an indication of outcomes.[36] And since we use an institutional approach, which avoids collapsing data to specific categories – such as a disease – our methodology may have a future use in the measurement of hospital performance.

Limitations of this study are that no multivariate analysis was performed on the example variables, making the associations found subject to possible unknown confounders. Also the work has been done at a single site with a population skewed older than the general population.

Studying all-cause mortality rates associated with clinical variables yields information on general risks associated with the variables. In forthcoming studies, we compare the risks associated with various lab tests to their standard reference ~~ranges~~intervals. This methodology provides direct estimates of the risks associated with values both within and outside the reference ~~range~~interval, which the usual demographic studies of healthy populations do not. This is an area that warrants further investigation, and may be ~~another~~a way that ~~reference ranges~~decision limits can be established for lab tests.

Finally, since any clinical variable can be associated with a function of excess risk by the methodology utilized in the current study, a researcher can choose any combination of disparate variables to describe some specific aspect of the condition of a patient in a hospital, and transform these into risk functions; this, in turn, allows placing the values onto a common linear scale, and combining them to create an index for the specific purpose intended. This index would then be empirically ~~determined~~based, without reference to models or to expert opinion, and ~~based~~dependent strictly and only upon data from the EHR.

CONCLUSIONS

Any quantitative or categorical clinical variable in the EHR can be transformed into an excess risk function. This associates the absolute increased percent risk of dying from any cause after hospital discharge with each value of the variable. We have shown this to be directly correlated with in-hospital patient risk. Moreover, the resultant risks can be added to obtain a

measure of total risk that corresponds well with discharge disposition. In a forthcoming study, we demonstrate the building of a more complex index based upon these principles, which is expected to satisfy additional and more stringent tests of construct validity.

We believe our approach opens the door to a way of exploring and resolving many issues in patient assessment. Clearly, researchers with access to the database of a hospital's EHR can perform retrospective research to determine risks associated with clinical and physiological variables, stratified by age, gender, race or any administrative classification. This enables researchers to explore many new relationships using disparate variables, becoming a new and meaningful use of the EHR.

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FIGURES (LEGENDS)

Figure 1. Creatinine Level vs. Excess Risk: a) 1-Year Post-Discharge; b) In-Hospital; c) Correlation = 0.920 The reference range for creatinine at Sarasota Memorial Hospital is 0.5 to 1.2 mg/dL.

Figure 2. Heart Rate vs. Excess Risk: a) 1-Year Post-Discharge; b) In-Hospital; c) Correlation = 0.922 Displayed for comparison is the MEWS heart risk score (in gray dots), scaled to correspond roughly with our results (MEWS correlation = 0.855).

Figure 3. Nursing Assessments vs. Excess Risk: a) 1-Year Post-Discharge; b) In-Hospital; c) Correlation = 0.892 for the Set of Twelve Nursing Assessments – In-hospital vs. Post-discharge**.**