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Development and validation of a continuously age-adjusted measure of patient condition for hospitalized children using the electronic medical record

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ABSTRACT

Awareness of a patient's clinical status during hospitalization is a primary responsibility for hospital providers. One tool to assess status is the Rothman Index (RI), a validated measure of patient condition for adults, based on empirically derived relationships between 1-year post-discharge mortality and each of 26 clinical measurements available in the electronic medical record. However, such an approach cannot be used for pediatrics, where the relationships between risk and clinical variables are distinct functions of patient age, and sufficient 1-year mortality data for each age group simply do not exist. We report the development and validation of a new methodology to use adult mortality data to generate continuously age-adjusted acuity scores for pediatrics.

Clinical data were extracted from EMRs at three pediatric hospitals covering 105,470 inpatient visits over a 3-year period.

The RI input variable set was used as a starting point for the development of the pediatric Rothman Index (pRI). Age-dependence of continuous variables was determined by plotting mean values versus age. For variables determined to be age-dependent, polynomial functions of mean value and mean standard deviation versus age were constructed. Mean values and standard deviations for adult RI excess risk curves were separately estimated. Based on the "find the center of the channel" hypothesis, univariate pediatric risk was then computed by applying a z-score transform to adult mean and standard deviation values based on polynomial pediatric mean and standard deviation functions. Multivariate pediatric risk is estimated as the sum of univariate risk. Other age adjustments for categorical variables were also employed.

Age-specific pediatric excess risk functions were compared to age-specific expert-derived functions and to in-hospital mortality. AUC for 24-h mortality and pRI scores prior to unplanned ICU transfers were computed. Age-adjusted risk functions correlated well with similar functions in Bedside PEWS and PAWS. Pediatric nursing data correlated well with risk as measured by mortality odds ratios. AUC for pRI for 24-h mortality was 0.93 (0.92, 0.94), 0.93 (0.93, 0.93) and 0.95 (0.95, 0.95) at the three pediatric hospitals. Unplanned ICU transfers correlated with lower pRI scores. Moreover, pRI scores declined prior to such events.

A new methodology to continuously age-adjust patient acuity provides a tool to facilitate timely identification of physiologic deterioration in hospitalized children.

Abbreviations: AUC, area under the curve for a receiver operating characteristic computation; CHP, Children's Hospital of Pittsburgh; CI, confidence interval; ECMO, extracorporeal membrane oxygenation; EMR, electronic medical record; ICU, intensive care unit; LOS, length of stay; MEWS, Modified Early Warning System; OR, odds ratio; PAWS, Pediatric Advanced Warning Score; PEWS, Pediatric Early Warning Score; pRI, Pediatric Rothman Index; PRISM, Pediatric Risk of Mortality; PIM, Pediatric Index of Mortality; RI, Rothman Index; ROC, Receiver Operating Characteristic; YNHH, Yale-New Haven Hospital; LR+, positive likelihood ratio; LR−, negative likelihood ratio.

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1. Introduction

Timely identification of children at risk of clinical deterioration, especially young children, has been the motivation for the creation of various pediatric "early warning systems" which signal early physiologic decline that may lead to deleterious clinical outcomes (e.g., heightened morbidity and mortality) and related economic consequences (e.g., extended hospital length of stay and additional resource utilization) [1–5]. These systems are designed for use on the hospital ward and employ risk-assessment rules that are usually derived from the consensus opinions of expert clinicians. Despite a lack of demonstrated clinical effectiveness, such systems have become commonplace in the hospital setting and are even gaining consideration as a standard of care [6].

In practice, to obtain a score from these systems, nurses must typically enter data or information into the electronic medical record (EMR), consult a reference for age-dependent norms, and sometimes even compute the composite score to obtain a result. This process is error–prone and adds to nursing workload; moreover, entries tend to be made at irregular intervals. With the proliferation of EMR systems, hospitals now have a platform well-suited to a significantly improved approach that can harness a frequently updated and automated calculation of risk that draws upon a wider range of data available within the EMR. The Rothman Index (RI) represents such an improvement. The RI addresses many of the above stated issues for adult inpatients [7], realizes the cited benefit and promise of a comprehensive EMR, and offers an approach that outperforms other adult early warning systems such as MEWS (Modified Early Warning System) in identifying patients at risk of deterioration [8]. Developing a methodology to adapt this important adult model (highly viewed paper, honored at 2013 AMIA) to the pediatric domain, which is often overlooked with regard to modeling, would therefore be both clinically and methodologically valuable.

Previously, the identification of at-risk pediatric patients (patients ranging in age from newborn to age 18) focused on three principal types of data, specifically: diagnoses (e.g., transplant, epilepsy, congenital defects) [5], treatments (e.g., intubation, vasopressor infusion, number of medications administered) [3], and vital signs [2–5,9]. The adult RI and the newly derived pediatric version are focused instead on reflecting the physiologic impact of diseases and/or treatments without direct reference to either the proximate or ultimate cause of the patient's condition. Thus, neither diagnosis nor treatment is included. Rather, vital signs and other types of physiological data available in the EMR, specifically clinical laboratory and nursing assessment data, are used. These inputs are continually gathered throughout a patient's stay and allow the model to closely track evolving patient status.

Experts have estimated the risk of deterioration associated with specific ranges of each vital sign and have done so for defined age ranges [2,9]. We have automated and refined this process by constructing risk curves from empirical mortality data [10]. We have also included as an input nursing assessments that are generally accepted as meaningful reflections of the patient's state. In fact, some early warning systems explicitly incorporate nursing concerns into their scores [4]. We use a systematic comprehensive extract of nursing data which are recorded in the EMR during each nursing shift. Prior work has shown that such nursing data have significant clinical implications [11]. Each nursing assessment is categorized as "met" or "not met" based on whether or not the patient meets a certain minimum standard for 11 physiologic systems. The Braden Scale, a nursing tool for assessing pressure ulcer risk and which is comprised of 6 subscales (activity, mobility, sensory perception, friction and sheer, nutrition and moisture) is also included.

Most previously developed early warning systems have additional limitations. Some, by design, are for use with patients on the general hospital ward. Others address risk of mortality in the ICU (e.g., PRISM III [Pediatric Risk of Mortality III] and PIM 2 [Pediatric Index of Mortality 2]) [12–16]. In contrast, we sought to design a single automated system for both general acute care and critical care patients. Creation of a tool that follows the patient from the ward to the ICU and back allows for the visualization of trends in the patient's condition throughout the hospital stay, enhancing the clinician's ability to monitor and track physiologic status, as well as offering an opportunity for earlier detection of declining condition, perhaps in time to avoid a medical crisis. The objective of the present study and modeling effort was to create such a tool for pediatric patients – the pediatric Rothman Index (pRI).

2. Materials and methods

The pRI represents a novel assessment to gauge and track the evolving physiologic status of hospitalized pediatric patients and represents a new methodology to extend the adult RI. Since the development of the pediatric version is founded in the creation and validation of the adult version, an understanding of the adult methodology is appropriate to this discussion. Although the materials and methods used to create and validate the adult RI have been described elsewhere [7,8], an abbreviated review and schematic is provided herein for clarity (Fig. 1).

2.1. Summary of the adult Rothman Index methodological approach

The following steps were taken in the development of the adult RI:

(1) A survey of EMR data was conducted to identify easily collectable, non-static, candidate variables to construct a general, continuously updated, patient-condition score for adults.
(2) To estimate the in-hospital risk associated with each variable, individual risk functions were computed by comparing the final pre-discharge measurements with 1-year post-discharge mortality.
(3) A step-wise logistic regression of all candidate variables against 1-year mortality established the importance of each variable to facilitate variable selection for the model. The coefficients of the regression were not needed or employed in the model, itself, however. The regression was only used for variable selection. Table 1 lists the final variable set that was identified through the regression. Fig. 2 presents the Excess Risk Curves. In each plot, the final value of the variable prior to discharge is shown vs. 1-year all-cause mortality. Data are from 22,265 in-patients at Sarasota Memorial Hospital in 2004. Raw data are bucketed and a function is fitted to interpolate between bucket averages. Risk values are set to a constant above and below data extrema.

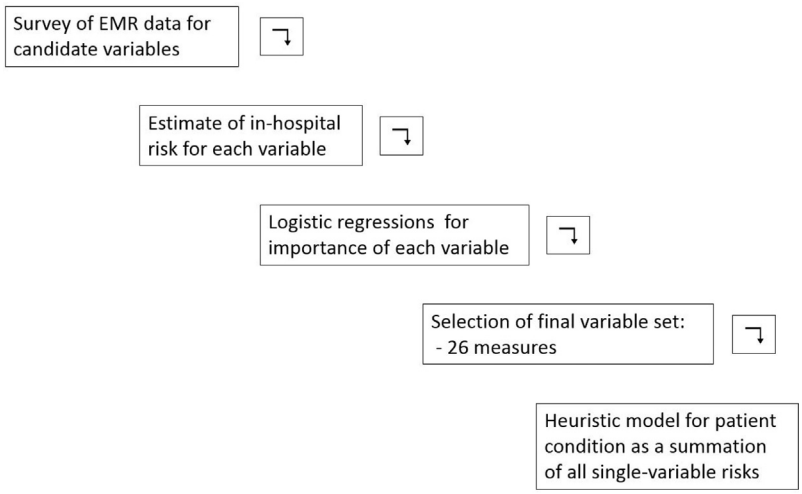

Fig. 1. Development of the Rothman Index (RI).

Table 1
Twenty-six variables chosen as inputs to the RI.

Vital signs	Nursing assessments (head-to-toe)	Nursing assessments (other)	Laboratory tests (blood)	Cardiac rhythm
Temperature	Cardiac	Braden score	Creatinine	Asystole
Diastolic blood pressure	Respiratory		Sodium	Sinus rhythm
Systolic blood pressure	Gastrointestinal		Chloride	Sinus bradycardia
Oxygen saturation	Genitourinary		Potassium	Sinus tachycardia
Respiration rate	Neurological		BUN	Atrial fibrillation
Heart rate	Skin		WBC	Atrial flutter
	Safety		Hemoglobin	Heart block
	Peripheral vascular			Junctional rhythm
	Food/nutrition			Paced
	Psychosocial			Ventricular fibrillation
	Musculoskeletal			Ventricular tachycardia

Rothman, MJ; Rothman, SI; Beals, J. JBI. 2013; 46; 5; 837–848.

(4) A heuristic model quantifying patient condition (overall risk) was constructed by summing the single-variable risks.
(5) To extend the adult data for use with a pediatric population of hospitalized patients, accommodation had to be made for the variation in normal physiologic values as a function of age. Hence a new methodology was developed, as described in Sections 2.3.2 and 2.3.3.

The score is indexed from 100 and reduced as a function of increasing risk. Risk is calculated as the sum of the excess risk represented by each individual variable at a given time, as shown in Eq. (1):

$$Rothman\ Index = 100 - (Scale\ Factor) \sum_{Input=1}^{\#Varaibles} Excess\ Risk_{Input} \quad (1)$$

A score of 100 is achieved only when all input variables are at a minimum (zero excess risk) value. A scaling factor ensures the majority of patients on a general medical-surgical unit fall within a dynamic range from 0 to 100, rendering subtle deterioration easily detectable as a falling RI score. Critically ill patients may have negative RI values (the minimum possible RI score is −91). As it is rare all 26 variables are measured at the same time, the model must allow for missing data. We address this by using the most recent value of each variable when computing the RI, limiting the acceptable time that a measurement can be carried forward (e.g. to 15 h in order to span nursing shifts). If a variable is completely missing for a particular patient, zero excess risk is assigned.

Laboratory tests are generally collected less frequently than vital signs and nursing assessments. To take advantage of the information from laboratory tests without sacrificing accuracy over time, the RI model is composed of 2 sub-models (RI_{noLab} and $RI_{withLab}$). Both sub-models are computed as in Eq. (1); RI_{noLab} uses only nursing assessments and vital signs; $RI_{withLab}$ uses nursing assessments, vital signs and laboratory tests. As the laboratory data age, their relevance to the patient's current condition diminishes; therefore, $RI_{withLab}$ is blended by a linear decay with RI_{noLab}; after 48 h, RI_{noLab} is used solely, until new laboratory data become available. At a minimum, computing a patient's RI requires a set of vital signs and nursing assessments.

The model is thus a simple linear combination of the two sub-models as a function of time, based on the most recent available laboratory data, as shown in Eq. (2):

$$Rothman\ Index = \left[RI_{noLab}\left(\frac{TimeSinceLabs}{48}\right)\right] + Smoothing\ Function\left[RI_{withLab}\left(1 - \frac{TimeSinceLabs}{48}\right)\right] \quad (2)$$

where "TimeSinceLabs" has a maximum value = 48 h.

This approach allows the lab results to smoothly and gradually "age-out" as they became too far removed in time to be relevant. When new lab data arrives again, then the $RI_{withLab}$ sub-model is selected. A "Smoothing Function", shown in Eq. (2), and described in Appendix B of Ref. [7], was added to enhance continuity when RI switches from RI_{noLab} to $RI_{withLab}$.

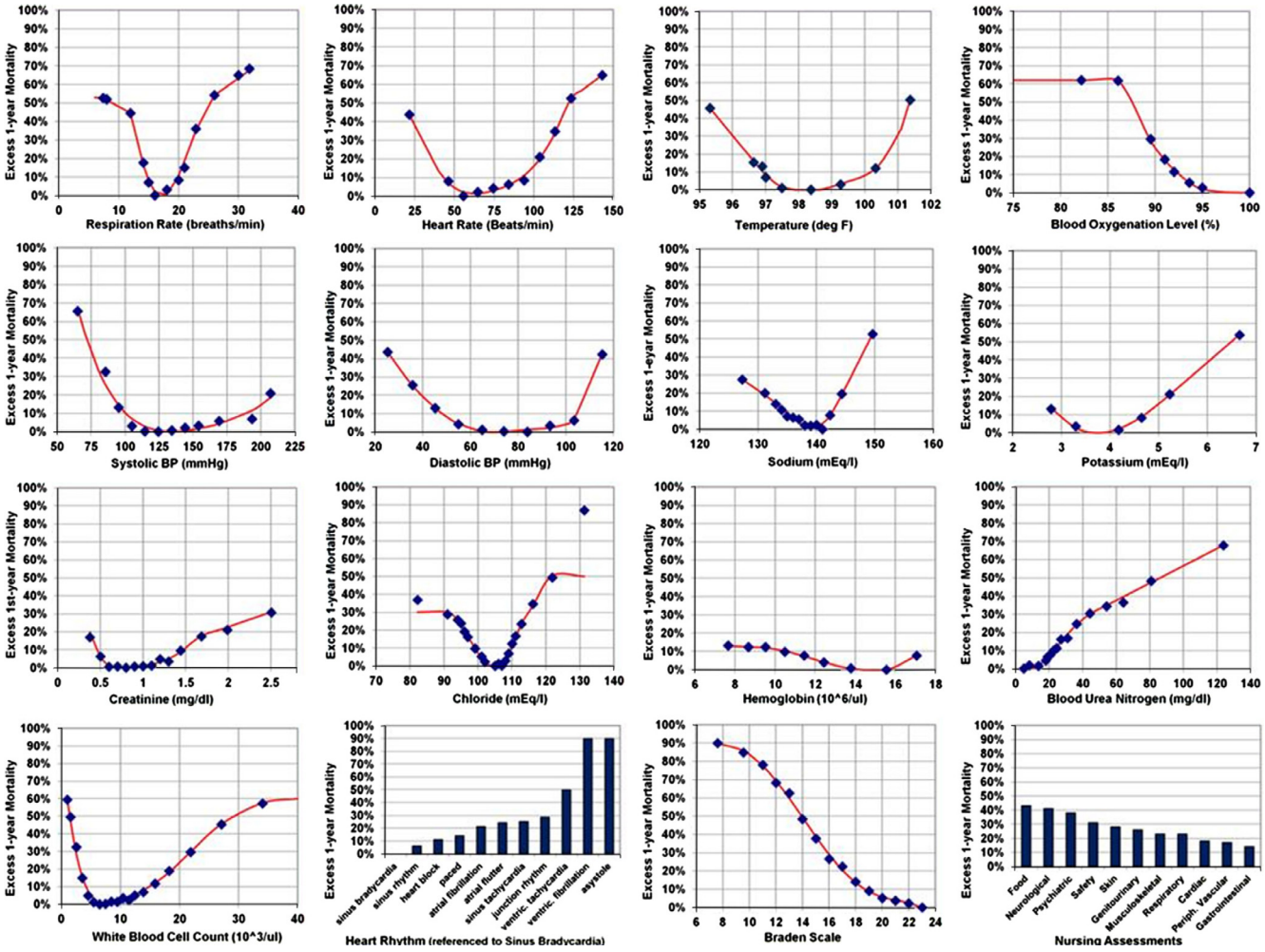

Fig. 2. Excess risk curves from the Rothman Index. Rothman, MJ; Rothman, SI; Beals, J. JBI. 2013; 46; 5; 837–848.

2.2. Setting and data for the Pediatric Rothman Index (pRI)

Institutional Review Board approval was obtained from two children's hospitals to conduct a retrospective cohort study utilizing EMR data from inpatients less than 18 years of age. Data was obtained from a third children's hospital under a Business Associates Agreement and they have agreed to publication of some results from that work. Yale-New Haven Hospital (YNHH) has an obstetrics unit and their extract included well-baby data. Children's Hospital of Pittsburgh (CHP) does not have an obstetrics unit; consequently, data were provided from infants and children referred for the management of significant illness. Data from YNHH covered 19,431 visits, i.e., all inpatient discharges from 1/1/2010 through 12/31/2011. Data from CHP covered 64,303 visits, which represented all inpatient discharges from 5/1/2009 through 5/31/2012. Data from the third children's hospital covered 21,736 visits, which represented all inpatient discharges from 1/1/2013 to 12/31/2013. Data were extracted from three EMR systems – the Allscripts Sunrise Clinical Manager (Chicago, IL) at YNHH, the Cerner Millennium EMR (Kansas City, MO) at CHP, and the Epic EMR at the third hospital.

2.3. Study variables

Candidate variables for the pRI were limited to those that are widely collected and entered into the EMR on a frequent basis, including full body system ("head-to-toe") nursing assessments and the Braden Scale, vital signs, and clinical laboratory test results. Date of birth was captured as part of the automated registration system, a component of both EMRs.

2.3.1. Nursing assessments

Nursing assessments by physiological system and their minimum standards are listed in Table 2. The interpretation and relevance of these assessments are a function of age. For example, the psychosocial assessment for a 17-year old would interpret "crying" as an indication of an abnormal condition, whereas the same assessment for a 2-year old would not.

If charting by exception, the nurse answers a master question for each physiological system, such as: "Is the patient's behavior appropriate to the situation?" Answers to master questions are designated "met" or "not met." In hospitals that do not use charting by exception, a series of questions related to the physiological system may be raised; in this case, the entire category is marked "not met" if the answer to any one of the questions reflects a deviation from normal. Although assessment questions may vary between hospitals, each hospital collects the essentially same data. A safety assessment is derived from either the Morse fall risk scale or the Humpty-Dumpty fall risk scale, also as appropriate for age. The Pediatric Braden Scale (Braden Q) was utilized in place of the Braden Scale as appropriate by age [17].

Table 2
Nursing assessments of patients upon admission, with corresponding standards and mortality odds ratios (OR).

Assessment	Mortality OR (C. I. 95%)	Commonly-used standards
Peripheral-vascular	27.8 (22.4, 34.5)	Extremities are normal or pink and warm. Peripheral pulses palpable. Capillary refill <3 s. No edema, numbness or tingling
Neurological	25.9 (20.2, 33.1)	Alert, oriented to person, place, time, and situation. Speech is coherent. Alternate version for younger patients
Musculoskeletal	12.5 (9.4, 16.6)	Independently able to move all extremities and perform functional activities as observed or stated (includes assistive devices)
Food-nutrition	7.3 (5.6, 9.5)	No difficulty with chewing, swallowing or manual dexterity. Patient consuming >50% of daily diet ordered as observed or stated
Respiratory	7.1 (5.8, 8.8)	Resp. rate at rest appropriate for age, quiet and regular. Bilateral breath sounds clear. Nail beds and mucous membranes pink. Sputum clear, if present
Cardiac	7.1 (5.3, 9.6)	Pulse regular, age-appropriate heart rate, skin warm and dry. No symptoms of hypertension or hypotension
Gastrointestinal	6.3 (5.0, 7.9)	Abdomen soft and non-tender. Bowel sounds present. No nausea or vomiting. Continent. Bowel pattern normal as observed or stated
Genitourinary	6.1 (4.8, 7.9)	Voids without difficulty. Continent as age appropriate. Urine clear, yellow to amber as observed or stated. Urinary catheter patent if present
Safety	4.2 (2.8, 6.5)	Verbalizes/demonstrates the ability/willingness to follow instructions/activity/orders. Uses call light appropriately. Total fall risk score is 2 or less. Patient is not a risk to self or others. Alternate version for younger patients, e.g. Humpty Dumpty Fall Risk Screening Tool
Skin	2.4 (1.9, 2.9)	Skin clean, dry and intact with no reddened areas. Patient is alert, cooperative and able to reposition self independently
Psychosocial	1.4 (0.8, 2.4)	Behavior appropriate to age and situation. Expressed concerns and fears being addressed. Adequate support system

The ORs are univariate and therefore not multiplicative. They are computed by taking the in-hospital death rate of the patients who failed to meet the standards of a given nursing assessment at admission divided by the in-hospital death rate of the patients who did meet that nursing assessment standard at admission. The ORs are not used in computing the pRI. They demonstrate the clinical significance of each pediatric nursing assessment.

2.3.2. Vital signs and laboratory test results

For each vital sign and laboratory test variable, we plotted the value of the variable versus age to determine if the variable was a significant function of age. To construct these graphs each variable value-age pair was sorted by age, bucketed into equal-sized groups, and the means computed for each group. For example, 4,110,793 values of heart rate and age were sorted by age and divided into 186 equal buckets, each containing approximately 20,000 values. The means were fitted to a set of polynomials, generating a piecewise continuous function for mean value versus age. These polynomial functions were developed solely for the purpose of interpolating between empirically determined points so that we would be able to estimate, for example, a mean heart rate, for any age less than 18 years old. An example of the piecewise continuous construction is shown below (Fig. 3) for mean heart rate as a function of age in weeks. In this manner we produced continuous functions for each age-dependent mean and standard deviation. These allow us to make age adjustments to capture the changing physiology. The choice as to the number of polynomials to use to describe the function was solely based on the shape of that function and the ability of an "up to 6th order" polynomial to effectively interpolate between the points.

Visual inspection of the graphs was used as an initial screen for age dependence. Some variables were clearly age-dependent (e.g. heart rate), others clearly not (e.g. temperature). The next step required review of the candidate graphs by the domain experts (pediatricians) on the project. Some variable means had only a minor variation with age, or a localized variation (such as in the first week of life). For simplicity, those variables with minor variation were not selected for age adjustment in this initial model. Others had a distinct variation, but were judged not to be representative of a general trend. An example was serum glucose. Glucose means did increase with age (birth to age 18) from about 90 to 160 mg/dL, however this was the result of selective measurement (the diabetic sub-population) rather than a change in normal physiology, and so was not selected for age-adjustment in the model.

The final set of variables chosen for age-adjustment was: heart rate, diastolic blood pressure, systolic blood pressure, respiration rate and serum creatinine. The first four are natural choices considering the underlying biophysics of heat transfer and surface area. The last, creatinine, increases with age as muscle mass increases.

Similarly, a piecewise continuous function was constructed for the standard deviation of the mean versus age. Means and standard deviations were estimated for each adult RI excess risk curve.

The computation of pediatric excess risk requires determining the age of the child at each new data element's timestamp, and then for each age-adjusted continuous variable using the piecewise continuous mean and standard deviation functions to estimate a Z-score (Eq. (3)). To compute the transformed variable, which would then be applied to an adult Excess Risk Curve (Fig. 2), adult mean and standard deviations were used with the derived Z-score (Eq. (4)).

$$\text{Z-score}_{\text{pediatric}} = (\text{Value}_{\text{age}} - \text{Mean}_{\text{age function}})/\text{Standard Deviation}_{\text{age function}} \quad (3)$$

$$\text{Transformed variable} = (\text{Z-score}_{\text{pediatric}})(\text{Standard Deviation}_{\text{adult}}) + \text{Mean}_{\text{adult}} \quad (4)$$

This process transforms previously established adult predictors into continuously age-adjusted pediatric predictors. In practice, a pRI score reflects a child's total physiologic condition and is computed as 100 minus the scaled sum of the risks from each of the 26 model variables. Variables are: 11 nursing assessments (Table 2), Braden Scale [17], 6 vital sign inputs (systolic blood pressure, diastolic blood pressure, heart rate, respiration rate, temperature, oxygen saturation), 7 laboratory tests (chloride, potassium, sodium, BUN, creatinine, white blood count, hemoglobin), and cardiac pattern (e.g., sinus rhythm, heart block). Details related to the handling of missing data, special considerations for laboratory results (i.e., potential time-sensitive decay), and scaling are described briefly above and in prior published work [7].

2.3.3. Summary

The RI input variable set was used as a starting point for pRI development. Age-dependence of continuous variables was determined by plotting mean values versus age. For variables determined to be age-dependent, piecewise continuous polynomial functions of mean value and mean standard deviation versus age were constructed. From RI excess risk curves, adult mean and

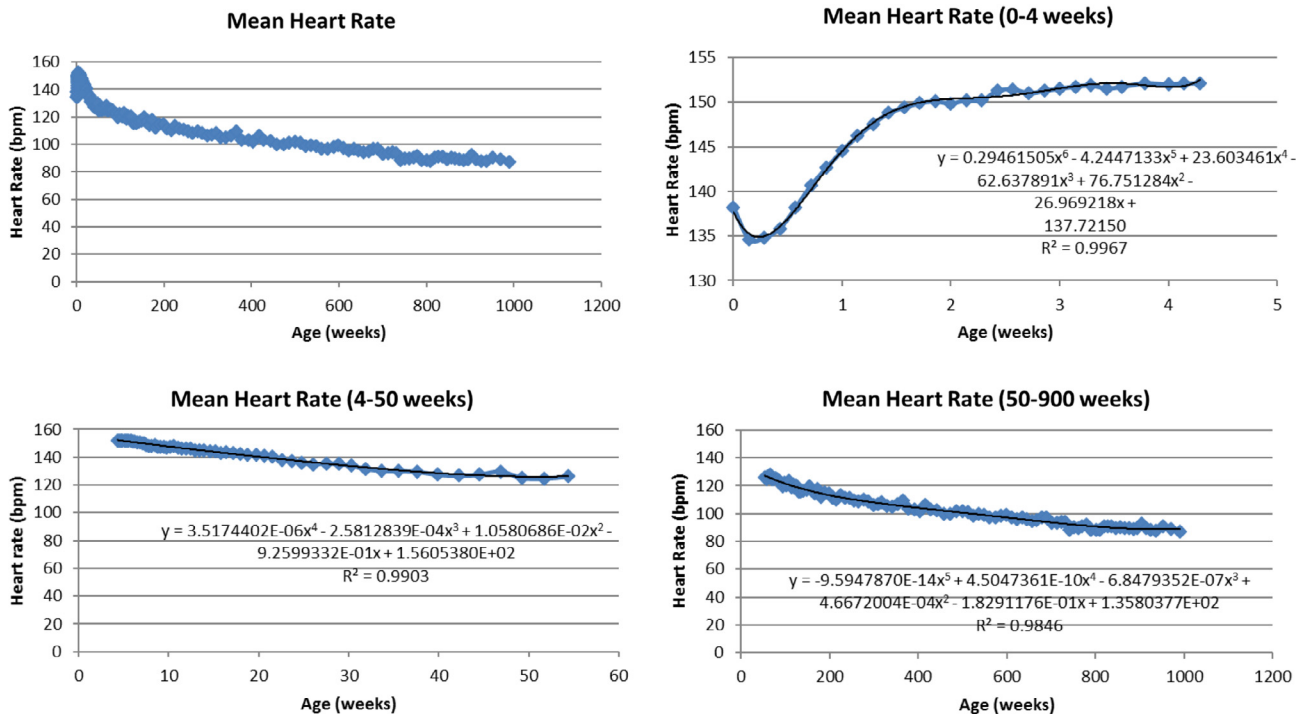

Fig. 3. A graph showing mean heart rate versus age in weeks for the dataset followed by three graphs showing the set of polynomials used to construct a piecewise continuous function of mean heart rate (beats/minute) vs. age (weeks). Note age ranges (x-axes) used for each function: in the first graph 0–4 weeks, in the second 4–50 weeks, and in the third 50–900 weeks. The y-axis for the 0–4 week curve has been changed to highlight the shape of the curve.

standard deviations were estimated. Univariate pediatric risk was then computed by applying a z-score transform with adult mean and standard deviation values and pediatric mean and standard deviation functions. Thereafter, in a heuristic model, multivariate pediatric risk is estimated as the sum of univariate risks (Fig. 4).

2.4. Validation

2.4.1. Validation of components

The continuously age-adjusted risk functions described above were compared to published scaled risk functions for Bedside PEWS and PAWS scores though a range of ages [2,9]. Bedside PEWS was developed for use with pediatric inpatients to provide early warning of need for urgent non-code admission to the ICU, while PAWS was validated in emergency department patients to predict the need for ICU admission. Both Bedside PEWS and PAWS incorporate age-group risk functions which are "step functions." To overlay these age-group step functions with pRI risk functions, we set the maximum point deviation to 50% excess risk. Bedside PEWS risk functions are on a 4-point scale, so 1 point is deemed to equate to 12.5% excess risk. PAWS is on a 3-point scale, so 1 point is deemed to equate to 16.7% excess risk. We chose an age to compute the pRI function in the middle of the Bedside PEWS age group. We tested the relevance of pediatric nursing assessments by computing in-hospital mortality odds ratios.

2.4.2. Validation of pRI

The pRI score is calculated every time a component of the model's input is updated in the EMR. For each hospital data set, the pRI was used to compute Receiver Operator Characteristics (ROC) curves for 24-h mortality [18]. Area Under the Curve (AUC) and 95% CI were calculated to quantify sensitivity and specificity. Also, sensitivity and specificity, false positive and false negative rates, positive and negative predictive values, and positive and negative likelihood ratios were computed for in-hospital mortality. To assess the behavior of the pRI as a continually updated measure capable of indicating changes or trends in the patient's clinical condition, the average decline before and after an unplanned transfer to the ICU was calculated. Unplanned transfer to the ICU was defined as movement to an ICU of a patient who was hospitalized at least 24 h before transfer, had a stay in the ICU of at least 24 h, and had no operating room utilization in the 2 h prior to an ICU admission. Mortality, length of stay, plus the minimum and final pRI outputs for patients with an unplanned ICU transfer were then compared to patients without an unplanned transfer.

3. Results

3.1. Nursing assessments versus in-hospital mortality

Table 2 illustrates the relationship between the initial pediatric nursing assessment (whether the assessment's minimum standard was "met" or "not met" by the patient) and the likelihood of dying in the hospital. Not meeting a minimum standard for the assessment was strongly associated with a significantly higher risk of dying, except for the psychosocial assessment which had a weak relationship with mortality. Peripheral-vascular (e.g., capillary refill and edema) and neurological assessments were most effective in identifying patients at high risk.

3.2. Continuous age-adjustment

All continuous variables in the model were examined for age dependence in pediatric patients; five variables with significant age dependencies were identified: heart rate, respiration rate, systolic blood pressure, diastolic blood pressure, and serum creatinine (see Fig. 5 for age dependence of heart rate). Modeling of vital sign data demonstrated strong association between deviation from mean values and excess mortality in the pediatric patient population.

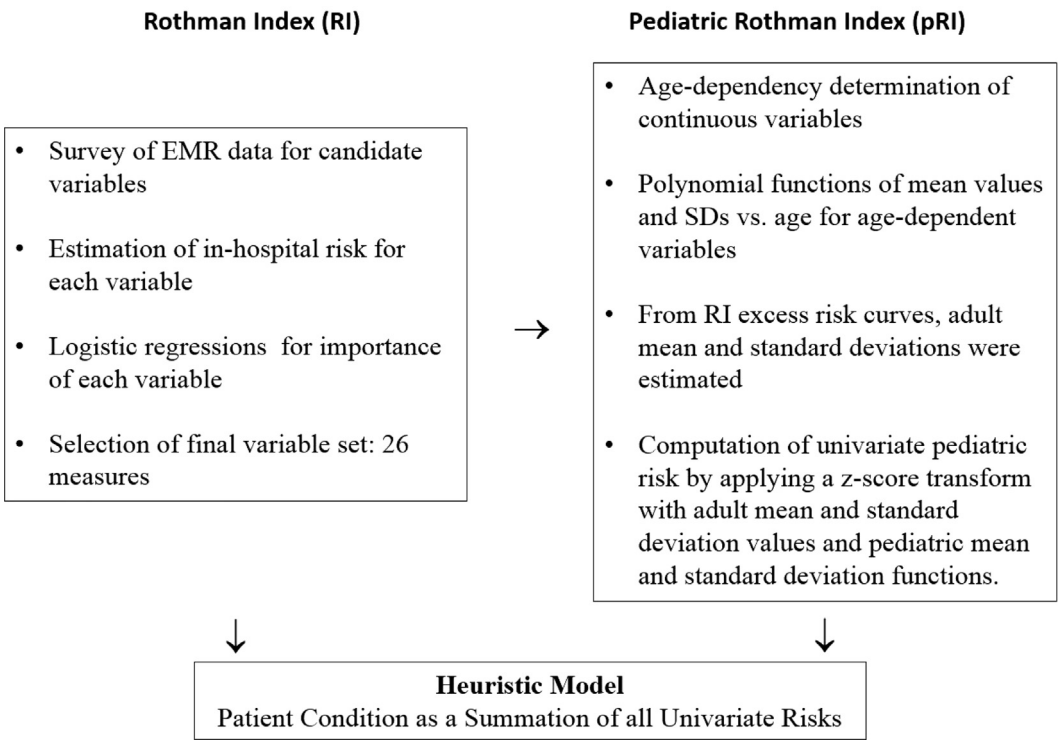

Fig. 4. RI methodology and modifications for pRI development.

Utilization in our model of the large data set from participating study sites resulted in risk functions which agree well with expert-derived Bedside PEWS and PAWS overlays. Age-adjusted excess risk curves for heart rate, respiration, and systolic blood pressure are shown in Figs. 6–8.

3.3. 24-Hour and in-hospital mortality

The pRI performed equally well at both study sites in predicting 24-h mortality despite differences in patient populations and practitioners. The AUC for CHP was 0.95 (0.95, 0.95) and the AUC for YNHH was 0.93 (0.92, 0.94). See Fig. 9.

At a pRI value of 30, the sensitivity and specificity, positive and negative predictive values, and the positive and negative likelihood ratios were computed for in-hospital mortality. Sensitivity and specificity at a pRI of 30 were respectively 88% (84, 92) and 97% (97, 97) for CHP and 51% (40, 63) and 99% (99, 100) for YNHH. Complete results are shown in Table 3. Additional characteristics are shown in Table 4.

3.4. Discriminating patient visits with an unplanned transfer to the ICU

The association of pRI scores with unplanned ICU transfers was analyzed using data from CHP. Of 64,213 hospital visits, 63,535 occurred without an unplanned transfer and 678 occurred with at least one unplanned transfer. As expected, clear differentiation in the profile of these cohorts as defined by mortality and length of stay (LOS) was noted. Mortality rate and LOS were 0.42% and 4.0 days versus 4.95% and 35.6 days, respectively, for patients without and with unplanned transfers. Sharp differences were seen, as defined by the averages of both the minimum and final pRI scores, 71.1 and 87.4 for patients without an unplanned transfer versus 33.4 and 71.1 for patients with an unplanned transfer. Additionally, the pRI detected changes in patient condition *prior* to unplanned transfers to the ICU, yielding an opportunity to identify at-risk individuals for earlier treatment to prevent further deterioration. Temporal variation of the pRI scores in patients who underwent unplanned transfer was further studied. On average, the pRI score declined prior to unplanned entry into the ICU as

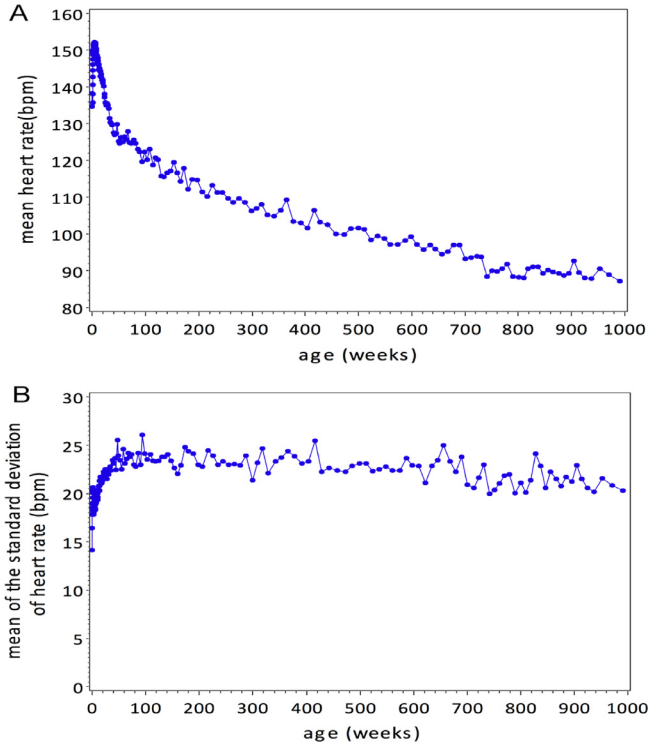

Fig. 5. Analysis of heart rate based on data from 83,734 patient visits from two pediatric hospitals shows: (A) variation of mean heart rate (beats per minute) versus age (weeks) and (B) variation of the standard deviation of heart rate (beats per minute) versus age (weeks).

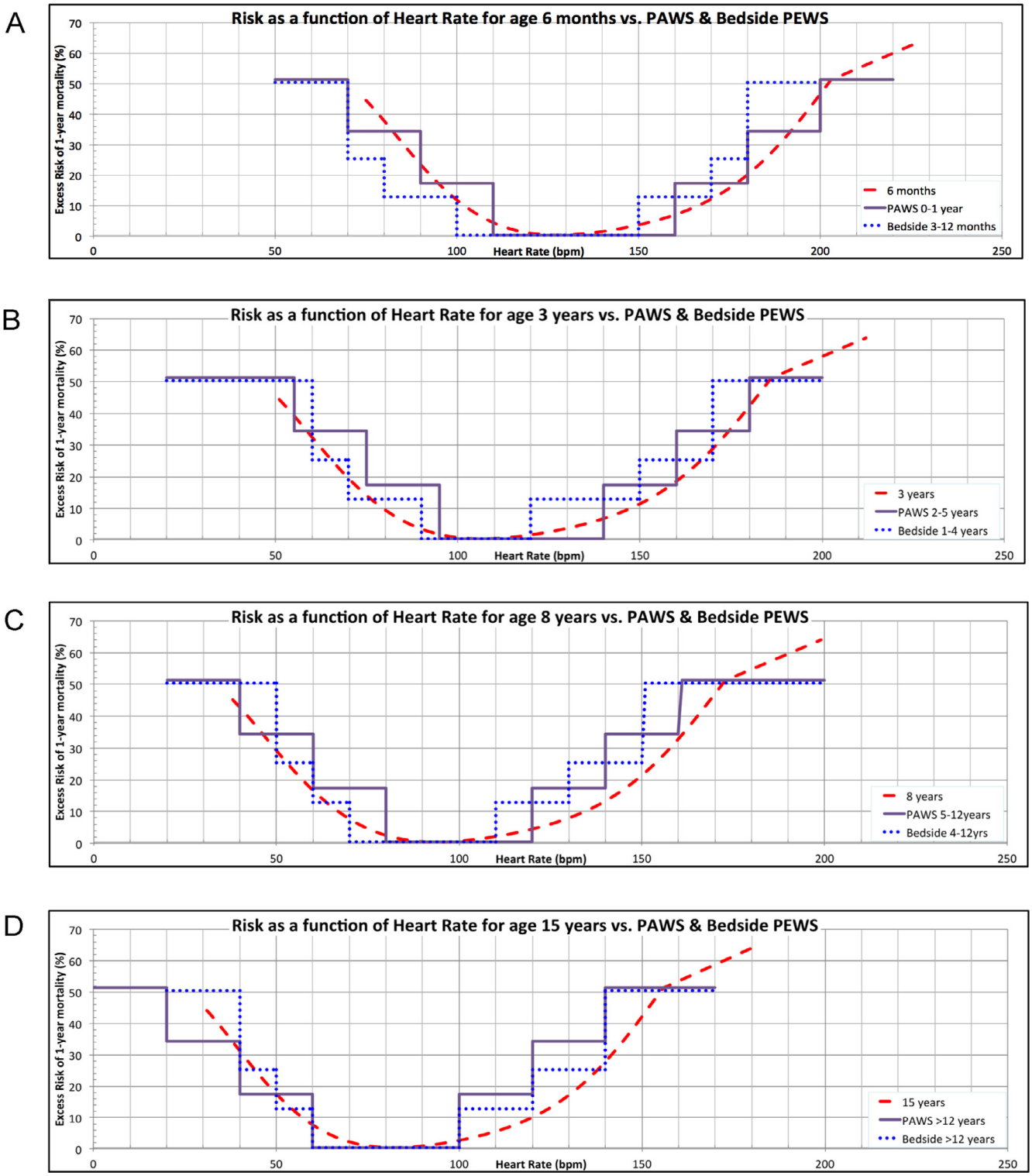

Fig. 6. Comparison of age-adjusted excess risk curves for heart rate with risk functions from bedside PEWS and PAWS for ages: (A) 6 months, (B) 3 years, (C) 8 years, and (D) 15 years of age.

shown in Fig. 10. The decline began more than 12 h prior to transfer, suggesting opportunities to intervene in advance with this patient group.

4. Discussion

The pRI is the first continuously age-adjusted, automatically updated measure of patient acuity spanning the full age range of pediatric inpatients. It improves upon previous scoring systems, such as Bedside PEWS and PAWS developed for manual computation, by leveraging the hospital's EMR investment and analyzing multiple elements in an evolving clinical data set to provide a robust and continuous reflection of a patient's physiologic state and risk of death. A computation of risk is performed every time a new measurement enters the EMR and, hence, can expose both rapid and subtle changes in patient status. The pRI also relies upon

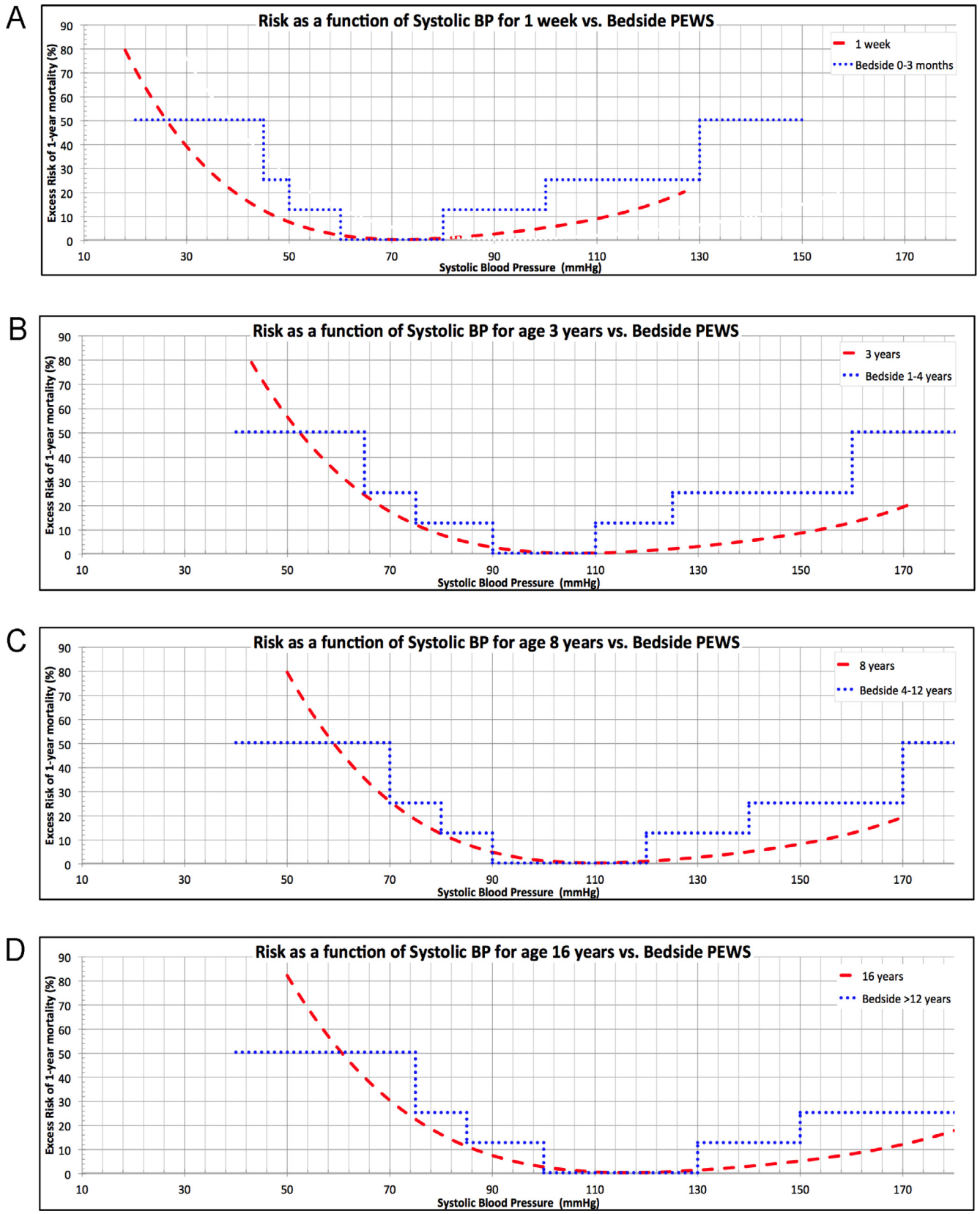

Fig. 7. Comparison of age-adjusted excess risk curves for systolic blood pressure with risk functions from bedside PEWS for ages: (A) 1 week, (B) 3 years, (C) 8 years, and (D) 16 years of age.

nursing assessments which are already a major component of the EMR. With its ability for continual reassessment of patient status and suitability for graphical display, the pRI can make trends in a patient's clinical state more clearly visible.

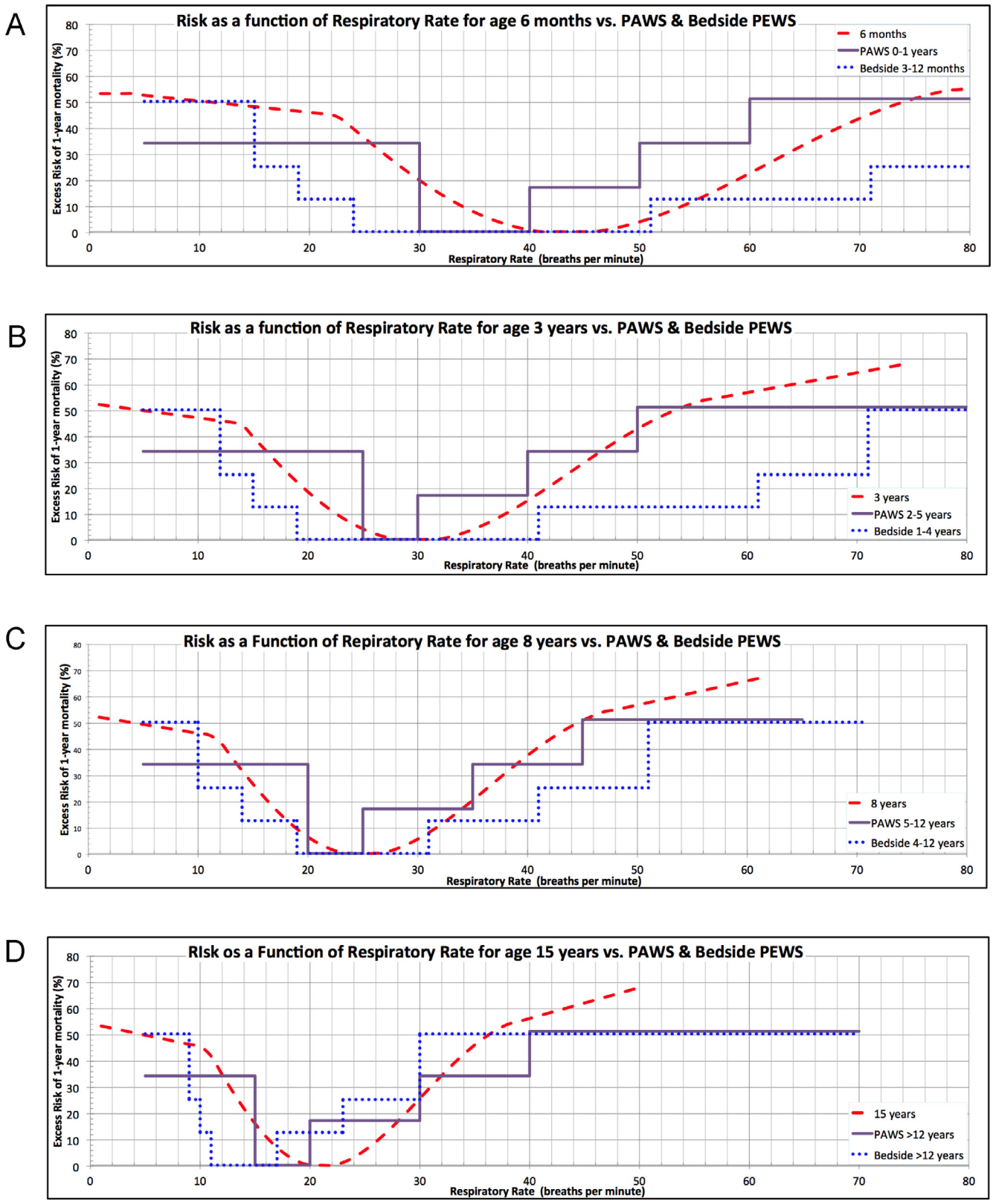

Fig. 8. Comparison of age-adjusted excess risk curves for respiratory rate with risk functions from bedside PEWS and PAWS for ages: (A) 6 months, (B) 3 years, (C) 8 years, and (D) 15 years of age.

The age adjustment for the model rests on the "find the center of the channel" hypothesis, which holds that the mean of the distribution is likely to be the optimal value. We created mean and standard deviation curves for our five age-adjusted parameters. Other investigators have created similar age-adjusted median curves for heart rate, systolic blood pressure, and respiration [19–21]. Our curves, while not identical, are similar despite different methodologies and data sets from two different EMRs. Compar-

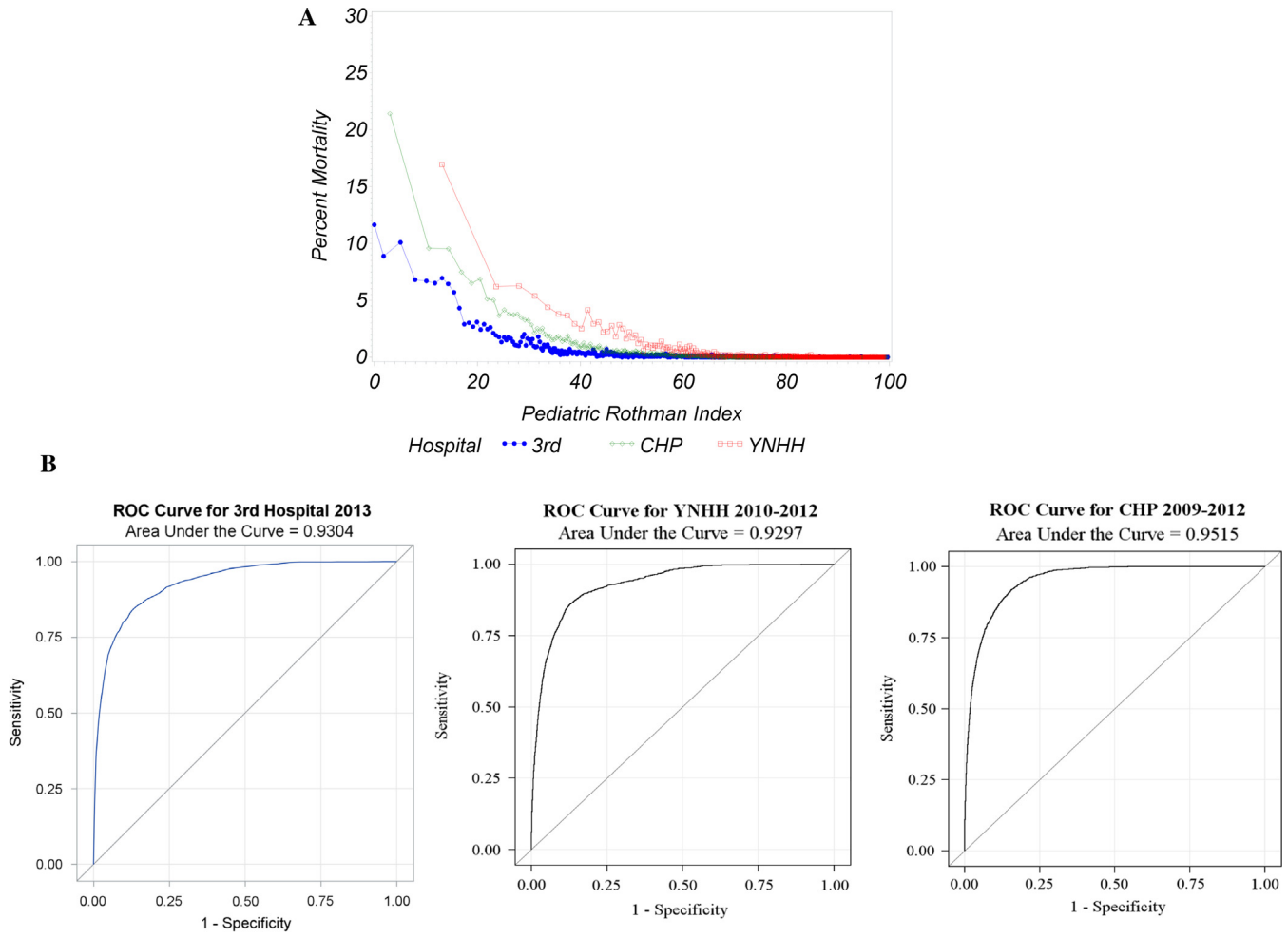

Fig. 9. 24-h mortality versus pRI for a 3rd children's hospital, CHP, and YNHH (part A) and the associated ROC curves (part B). In the 24-h mortality plot for CHP, there are 5,990,813 pRI points which are divided into 800 equal-sized buckets and averaged. In the plot for YNHH there are 919,779 pRI points which are divided into 400 equal buckets and averaged. In the plot for the 3rd hospital, there are 2,718,130 pRI points which are divided into 1000 buckets. The 3rd hospital is similar to CHP in serving acutely ill children.

Table 3
Statistical measures for in-hospital mortality at CHP and YNHH, 95% CI in parentheses.

Measure	CHP pRI = 30	YNHH pRI = 30	YNHH pRI = 35	Definition
PPV	12.40% (11.04, 13.87)	27.40% (20.35, 35.39)	22.07% (16.69, 28.24)	Percentage of correct positive predictions
NPV	99.94% (99.92, 99.96)	99.80% (99.73, 99.86)	99.84% (99.77, 99.89)	Percentage of correct negative predictions
Sensitivity	88.12% (83.93, 91.54)	51.28% (39.69, 62.77)	60.26% (48.54, 71.17)	Likelihood of mortality for patients who fall below the cut point
Specificity	97.05% (96.92, 97.18)	99.45% (99.34, 99.55)	99.14% (99.00, 99.27)	Likelihood of survival for patients who do not fall below the cut point
LR+	29.87 (28.14, 31.77)	93.24 (70.21, 124.85)	70.07 (55.51, 88.90)	Probability of non-survivors falling below the cut point/ probability of survivors falling below the cut point
LR−	0.12 (0.09, 0.17)	0.49 (0.39, 0.62)	0.40 (0.31, 0.53)	Probability of non-survivors not falling below the cut point/ probability of survivors not falling below the cut point

PPV – positive predictive value.
NPV – negative predictive value.
LR+ – positive likelihood ratio.
LR− – negative likelihood ratio.
LOS – length of stay.

ison of our excess risk curves with risk functions developed by experts in other acuity models demonstrates a generally excellent fit across a full set of typical pediatric age groups (Figs. 6–8), thus validating the comparable components of the pRI model and at the same time eliminating arbitrary age brackets. However, we do note one exception to the agreement with these expert-derived curves was found regarding respiratory rate, especially for older children. There, the reported Excess Risk Curve has a minimum at about 21 breaths per minute (bpm), while Bedside PEWS has a minimum at 14 and PAWS at 17. These other systems seem to reflect MEWS

Table 4
Comparative characteristics of three children's hospitals.

	CHP	YNHH	3rd Children's hospital
AUC for 24 h mortality	0.95 (0.95, 0.95)	0.93 (0.92, 0.94)	0.93 (0.93, 0.93)
Mean mortality	0.35%	0.30%	0.70%
Mean LOS (days)	5.2	3.7	6.5

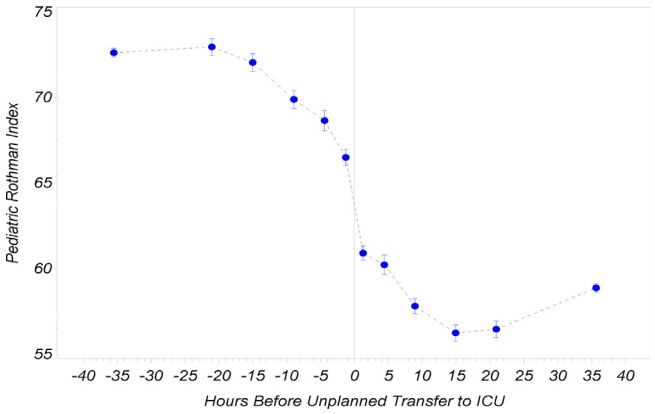

Fig. 10. Pediatric Rothman Index, mean and ±2 standard errors, versus time before and after unplanned transfers to ICU. The time of the unplanned transfer to the ICU is denoted as "0". Negative numbers represent hours prior to transfer, positive numbers hours after transfer. There were 678 patient visits in which an unplanned ICU transfer occurred.

which for adults sets the minimum at 11 bpm. Examination of data from more than 25 adult hospitals demonstrates that the vast majority of adult respiratory rates recorded are 18 or 20 bpm. Therefore, our derived minimum of 21 bpm for a 15-year-old, a somewhat higher value than is normal for an adult as expected, agrees with observation, if not with these experts.

Laboratory data are added using the same excess risk curve approach. Moreover, systematic data extracts from pediatric nursing assessments, the components of which are new to acuity modeling, correlate well with in-hospital mortality. These assessments are an important new source of clinical information for a pediatric early warning system because patients tend to not meet nursing assessment standards before abnormal vital signs herald decompensation. Therefore, they add to the model's ability to detect deterioration at an earlier point in time.

As noted earlier, the pRI adds a new methodology to our previous work on the RI, whose development has been previously described in detail elsewhere [7]. The adult RI model validation demonstrated that the relationship between the final pre-discharge value of a variable and 1-year post-discharge mortality could effectively estimate the immediate risk associated with a particular value of that variable.

In the current work, we have established the validity of the new pediatric methodology, both in terms of each model component (single variable risk curves and simplified nursing assessments) and in the excellent overall performance of pRI against standard metrics.

Twenty-four hour mortality is the standard measure of performance for acuity systems, as well as the *only* unambiguous measure; however, mortality is a rare outcome in pediatric patients. Given the relative infrequency of pediatric mortality, using the original RI development methodology, i.e., deriving excess risk curves for each input variable (a relationship between the value of a variable just prior to discharge and 1-year post-discharge mortality), would not have been possible. It would necessitate access to large 1-year post-discharge mortality datasets for each specific age. These data are simply not available. Our approach, which leverages relationships derived from adult data, through the derivation of an age-adjustment methodology, has the benefit of obviating the need for what is essentially unobtainable data and has the added benefit of providing continuous age-adjustment of risk.

The pRI model has an excellent ability to identify children likely to die within 24 h as measured by the AUC. Although mortality rates in pediatric populations are low, we note that the AUC results (0.95, 0.93) are similar to those reported for adult populations (0.93, 0.95, 0.93) where mortality rates are much higher [7]. With appropriately chosen pRI cut points, patients at risk of in-hospital mortality can be identified. Note the positive likelihood ratios in Table 3. Further, a cut point of 30 at CHP captures 88% of those patients who will expire in the hospital, while a similar cut point at YNHH captures 51%. (This difference may reflect the high acuity patient population at CHP, which lacks the obstetric and normal newborn population present at YNHH.) If the pRI were to be used for an alert system, a higher value at YNHH would be more appropriate (35 is shown as an example), thus increasing the sensitivity while lowering the positive predictive value.

Although the meaning of labs and vital signs is invariant across hospitals, that of nursing assessments is not. There are variations in style of assessment, so that at one hospital certain nursing assessments will be monitored regularly and at other irregularly. Also, we've seen instances where a given condition will generally be rated a "met" at one hospital and "not met" at another. This leads to (small) variation in meaning of pRI across hospitals. This is readily apparent in observing the 24-h mortality curve shown in Fig. 9A.

For example, 5% 24-h mortality at YNHH occurs at about pRI = 32 and for CHP at 20.

At the third children's hospital, 5% mortality occurs at about pRI = 17, very close to CHP's number. CHP and the third hospital are similar hospitals in that they serve sick children rather than a combination of obstetrics and sick children, which is the case at YNHH.

Far more common than death, are unplanned transfers from medical-surgical units to an ICU. Patients with an unplanned transfer to the ICU tend to have, as expected, higher acuity and consequently markedly lower pRI scores (mean minimums of 33.4 vs. 71.1). The lower the pRI score, the more likely the measurement is associated with an "unplanned transfer visit". On average, the pRI declines about 10 points in the 24 h prior to ICU transfer, followed by an additional decline of about 10 points in the 12 h after ICU admission, which is significant in a scale where medical-surgical patients typically fall in a range from 100 to 0. The trend in physiologic deterioration prior to and after unplanned transfer to the ICU further validates the pRI.

The pRI model is incorporated into software which has been integrated into the EMR systems at study sites and produces a continually updated line graph for clinicians to use in the care of pediatric patients. The model has also been introduced at several other hospitals. The available software for computing pRI integrates with most EMRs. Although nursing assessments are universally used within hospital settings, documentation is different at each hospital. To accommodate these differences a table is generated to map existing nursing forms to the binary inputs needed to compute pRI.

Additionally, due to the differing nature of populations served by diverse providers, cut points for generating pRI alerts may also vary among institutions. Consequently, location-specific cut-off values are tested and related recommendations for acceptable standards are offered to hospital staff. Decisions made by individual hospitals are partly a function of their protocols.

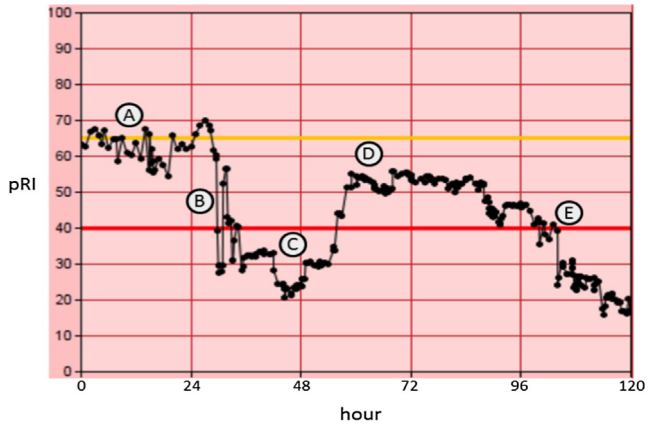

Fig. 11. Graph of pRI scores of a 2-week-old infant with congenital heart disease showing: (A) infant observed to be stable, although physiologically compromised, (B) acute deterioration and arrest leading to ECMO (extracorporeal membrane oxygenation) cannulation, (C) stabilization on ECMO, (D) improved status 24 h after ECMO started, and (E) new deterioration with an episode of line-related, staphylococcal septic shock. Each data point is a recomputed pRI score as new input data became available. Each vertical line represents midnight.

Further on this point, our goal is to provide information in a manner which is conducive to improving patient care. We work with hospitals, analyzing historical data to provide a graduated series of alerts. The cut-points discussed above represent "Very High Acuity Alerts". We also provide lesser alerts sensitive to changes in state: a "High Acuity Alert" might be triggered when pRI falls 50% within 12 h and a "Medium Acuity Alert" might be triggered when pRI falls 40% in 24 h. Graduated alerts are matched with protocols for graduated levels of attention.

Multiple articles about the parent measure of pRI – the original Rothman Index – have been published and it is currently in use at a number of major academic medical centers and community hospitals in the United States [22–24]; outcome studies which show reduction in mortality with use of the RI are ongoing [25]. The pRI is also in use, and in early tests has been effective in providing early warning of critical instability and deterioration.

A pRI graph showing the clinical course for a 2-week old infant with congenital heart disease is shown in Fig. 11.

5. Limitations

The pediatric model assumes that the shape of the excess risk functions computed using data from an adult population applies to a pediatric population. While this is predominately true and supported by appropriate comparisons of the performance of the pRI with that of Bedside Pews and PAWS across a variety of components, we expect to make further modifications to the pRI model to account for some differences in the shapes of these curves. Additionally, the completeness of the data sets used to build and validate the model was sometimes limited by the delayed entry or omission of nursing assessment information for specific patients, particularly well-babies. Finally, this study was conducted retrospectively, which is suitable for initial modeling efforts. However, we realize that the true impact of this novel, continuously age-adjusted, automatically computed, pediatric acuity score would best be quantified in a controlled, prospective comparative study.

6. Conclusion

A new methodology for creating age-adjusted excess risk curves was developed, allowing the data from the original Rothman Index model for evaluating the evolving clinical status of adult patients to be applied to pediatric patients. A completely empirical approach has been shown to reproduce the risk assessments generated by expert clinicians. The new Pediatric Rothman Index (pRI) provides a continuously age-adjusted assessment of a child's risk of physiologic deterioration during hospitalization. Integrated with the hospital's EMR, the pRI accesses a broader range of clinical information compared with predecessor systems while reducing nursing workload as compared with other acuity tools. When tested against the standard performance metrics for acuity, 24-h mortality, and sensitivity to patterns which may lead to unplanned transfers, the pRI performs well. This performance, coupled with its suitability for frequent automatic computation, may provide clinicians with the means to more easily monitor subtle and sometimes rapid changes in the physiologic status of hospitalized children, providing increased opportunities for earlier intervention.

7. Statement for journal publication

7.1. Conflict of interest

Authors (Drs. Joseph Tepas, Andrew Nowalk, Allen Hsiao, James Levin and Dr. Joan Rimar) declare no conflict of interest. Two authors received salary support from the nonprofit Yale-New Haven Hospital (Dr. Allen Hsiao, partial, and Dr. Joan Rimar, full) which has a strategic and financial partnership with PeraHealth Inc. Dr. Michael Rothman is an employee and shareholder in PeraHealth, Inc. of Charlotte NC, a company that uses the Rothman Index within its products. Dr. Albert Marchetti was compensated by PeraHealth for consultation and editorial support. Dr. James Levin passed away during the course of the project.

7.2. Access to the Pediatric Rothman Index

The authors will provide access to the pRI score to qualified researchers, without cost.

Acknowledgements

We would like to thank the staff at Children's Hospital of Pittsburgh and the Children's Hospital at Yale New Haven Hospital for assistance in obtaining the data. Also we would like to thank Steven I. Rothman, MS, of the F.A.R. Institute for assistance with figures and a careful review of the manuscript. Finally, we would also like to acknowledge Joseph Beals IV, PhD, for a careful reading of the manuscript.

Appendix A. Selection of age-dependent variables

Selection was a function of careful consultation with the pediatricians on the team. We found a significant age dependence for glucose (see figure below) with the mean rising from less than 100 to 160 as age increased from zero to 18 years (see Fig. A1).

However, there is no physiological basis for presuming such an age-related increase. Rather what we are seeing is selective measurement. The glucose measurements were dominated by measurements specifically on diabetics, and are not producing age-related norms for a general population. This is a case where any statistical test would have suggested inclusion of serum glucose as an age-adjusted parameter, but domain expertise indicates that it would not be suitable (see Fig. A2).

White Blood Count is an example of a continuous variable which does not require age adjustment.

In summary, although we used statistical tests when appropriate, the selection of variables for age adjustment was a manual

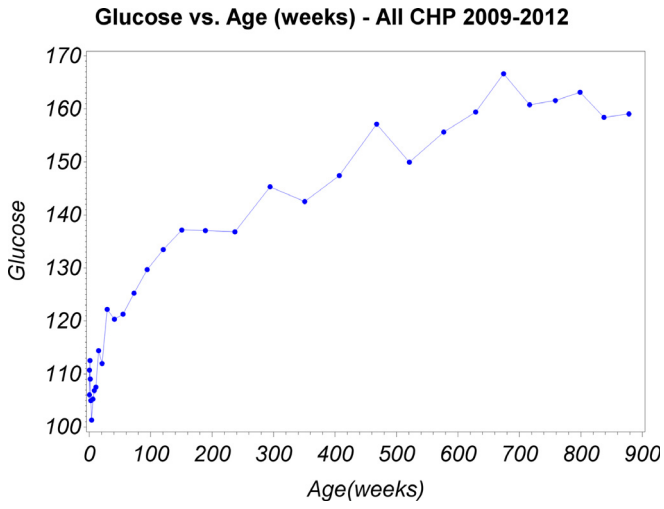

Fig. A1. Mean serum glucose (mg/dL) versus age in weeks. Each dot is the average of about 12,800 data points.

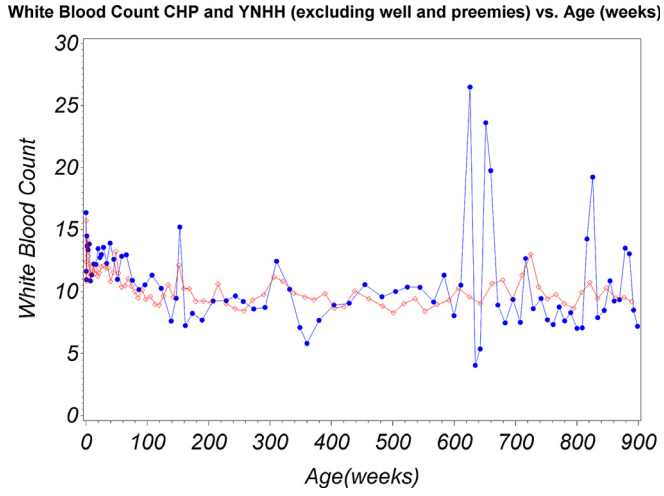

Fig. A2. Mean white blood cell count (×1000/μL) versus age in weeks. Dots represent CHP, 1280 data points in each mean. Triangles represent YNHH, 280 data points in each mean.

process, consisting of plotting and reviewing graphs and consulting with domain experts.

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