Prognosis and Real Time Analytics

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“I think you’ll find our clinic has the finest baby doctors in the country.”
Neonatal Intensive Care Unit

- Infant deaths <28 days of age 4 per 1000 live births in the USA.
- 13% of admitted babies die with birth weight between 501-1500 g die.
- Death or major morbidity affects 49-60% of babies in the NICU of developed countries.
- Early identification of clinical problems in the NICU has the most beneficial impact on patient outcome, much more so than in older children, adults, and the elderly.
Newborn Baby Peculiarities

- Unable to communicate
- Little physiological reserve
- Feels pain
- Sensory modalities not developed
- Monitoring of key systems imperfect
- Hidden State
Low Hanging Fruit

- Electronic medical record
- ICD-10 codes
- Heuristic bias on what is put in
- Qualitative endpoints
- Many results are dumbed down: imaging, electrographic, electroencephalographic, endoscopic, invasive tests, histopathological studies
OF COURSE, IT'S STILL A COMPLETE MYSTERY AS TO HOW THE ANCIENTS EVEN MANAGED TO MOVE THESE MASSIVE STONES....

What if we were able to see the stones being put in place?
Real Time Data

- Lot of real time data collected
- Unable to comprehend the relationships
- Thresholds set as alarms
- Episodic points of attention
- Most data wasted
Prognosis

• “I don’t know what it is, but something is wrong”

• Years of experience on the limits of normality and the beginning clinical course of clinical occurrences.

• Understanding of data in a dynamic fashion. Instinctual understanding of progression. Is the patient getting better or worse?
Heart Rate Variability

- Obstetric use of fetal heart rate variability.
- 3 minute EKG of healthy and sick preterm and term infants showed that newborn HR and RR variability at term equivalent gestation was somewhat prognostic of mental scale of the Bayley MDI at 8 months of age but not at 12 months of age.
- 2 hour EKG found a correlation with high frequency heart rate variability with pain scores after a surgical procedure.
- 60-minute recording revealed that extubation failure in premature infants was associated with decreased heart rate variability.
- 25-min HR recordings found reduced HR variability linked to sepsis, newborn mortality and necrotizing enterocolitis. This led to the development of the commercial HeRO system.
Real Time Monitoring of Heart Rate - HeRO System

- Electrocardiographic QRS and RR intervals.
- Derivation of HeRO score from three coefficients (S.D., asymmetry, entropy)
- Important to look at multiple derivatives.
HeRO System

• HRC index is a score from 1 to 5, 1 being normal and 5 indicating a five-fold increased risk of sepsis in the next 24 hours.

• An increase in index of more than 1-2 points over the infant’s baseline without another explanation is used to raise the suspicion of sepsis.

• Clinical utility is in Late Onset Sepsis.
Mortality Reduction Using HeRO

• 3,003 premature infants <1500 gram monitoring with HeRO reduced relative mortality by 22% and absolute mortality by 2%.

• NOT SIGNIFICANT
  – Sepsis not different (358/1500 vs. 379/1489)
  – Blood cultures drawn for the suspicion of sepsis (1.8 vs 1.6 per month)
  – Days on antibiotics (15.7 vs 15.0)

Moorman et al, J Pediatr 2011; 159:900-6
Lessons from HeRO

• Real time data is the way to go.
• Combination of different mathematical endpoints are probably better than looking at only traditional descriptive statistics.
• Individual mathematical endpoints may have different weightage in different clinical occurrences.
• Allows caretaker to take into context of the disease course.
• Locked in to one proprietary algorithm.
• Looks only at one physiological variable. Heart rate goes up and down to many stimuli.
• Non-specificity for many clinical occurrences.
What If?

Why use limited inputs in clinical scenarios, when much more data was available?

What if we only monitored the gas tank in a Formula 1 race car?
Combinatorial Analysis

- 138 preterm ≤34 weeks or <2000 g in weight
- Scoring algorithm: heart rate, respiratory rate and oxygen saturation characteristics in the first 3 hours after delivery.
- This score predicted high morbidity defined by moderate or severe bronchopulmonary dysplasia, >stage 2 retinopathy of prematurity, >grade 3 intraventricular hemorrhage, NEC or death with 86% sensitivity and 96% specificity.

Necrotizing Enterocolitis
Predicting Necrotizing Enterocolitis - HeRO

- HRC index shows a modest rise before surgical NEC and smaller rise before medical NEC

Example

- Baby M, case of necrotizing enterocolitis (NEC)
- NEC was found at 1400 hr. Nursing found abdomen full, tense, no BS. X-ray 1405 hr.
- Fellow’s note at 0919: Tolerating feeds and stooling, will continue to advance. Does not breathe over the vent very often.
- 21 hr before, at 1700: Abdomen is slightly full but he is voiding and stooling. ‘Personal communication: felt queasy, not enough to call doctors’.
- 42 hr before, at 2000: ‘noted small area of duskeness (~1cm circle) near umbilicus. MD notified and at bedside to assess, no changes.’
Physiological Variables

Information in four variables, sampled at approximately one-hour intervals, was analyzed using Temporal Data Mining (TDM) algorithms.
Before NEC

8 channels of information during 5.5 days before NEC. An episode of necrotizing enterocolitis (NEC) is indicated by arrow. Temperature (Temp), respiratory rate (RR), oxygen saturation (O2Sat) and Heart rate (HR), are marked “Lo” when 1 standard deviation below and “Hi” when 1 standard deviation above mean.

Human mind cannot comprehend the patterns or pick out important periods as it is happening or even afterwards.
Temporal Proximity

- Sequences of 6 events are about 100 times unlikely to occur randomly, with 99.5% confidence.
Five Event Sequences

- sequences of 5 events are 87 times unlikely to occur randomly with 99.5% confidence.
Control Patient

- 133 days’ worth of data from another premature baby that had only one episode of urinary tract infection (diagnosed by only positive urine culture of E. coli without urinalysis findings), showed that the entire hospital course contained no significant 5-event, 6-event, or 7-event long sequences.
- Generating a random data set with thousand days’ worth of data also did not generate 3-, 4- or higher event sequences.
Conclusions

• Temporal Data Mining in the NICU could in future provide smart and quantitative tools to augment clinical acumen.
• Combinatorial Analysis using Big Data Analytics is the future.
• The more the variables the better.
Predictive Health Analytics

1. **4D Healthware**
Online subscription service collects data from EMRs and from wearable medical devices to one location, streamlining it into an interface readable for patients, and operable across multiple platforms.

2. **Jvion**
An On-demand software-as-a-service does not run out of a data warehouse, thus less expensive. Uses pre-seeded solutions, taking the variables of a patient's situation and categorizing it into the most likely predicted outcome, targets individual illnesses and diseases.

3. **Revolution Analytics**
Microsoft purchased company for its "R" programming language.

4. **RightCare**
Analyzes patient data and produces a score indicating how likely a patient is to be readmitted. It then connects patients with post-acute care providers based on their preferences. Added to any EMR.

5. **VitreosHealth**
Takes a financial approach, offers a risk profile for populations based on data aggregated from EMRs, claims and non-clinical data and provides recommendations to improve outcomes and reduce costs. It is connected to ACO priorities and organizes the data into a chart interface, readable for physicians as well as analysts.
Prescriptive Health Analytics

- Includes evidence, recommendations and actions for each predicted category or outcome
- In order to be successful, the clinical event prediction and subsequent intervention should be both content driven and clinician driven.
Data from Multiple Systems

- Time-stamping and time-synchronization at Data Collection Appliance (DCA). Data Aggregation Gateway (DAG) at laptop. EDW - Electronic Data Warehouse.
Connectivity Option 2

- Delay is in order of 1 second
- Real time data

Heart rate, EKG
Respiratory rate
Oxygen saturation
Blood pressure

Spacelabs

Laptop

DAG

NICU Server

DMC Server

Cerner

Delay is in order of 1 second
Real time data
Connectivity Architecture - 2 Options

- Monitor Loader (Traditional HL7)
- ICS G2 Database
- Clinical Event Interface
- Device Interface Engine
- Launch Clinical Access
- Spacelabs ICS G2

(Simplified Workflows)

Cerner

XPRESSNET
Data Mining

Real time Data Collection

Identification

Consecutive 8/12 hr shifts preceding discovery

Trends

Advanced Analytics

Optimal Display

Biomarkers

Pneumothorax
Sepsis
Necrotizing enterocolitis
Intraventricular hemorrhage
Real Time Analytics

- Biomarkers should be user-friendly:
- Unni-Tan boxes at bedside

Baby X - Bed No.
“There was no umbilical cord. These days, babies are connected by Bluetooth.”