Risk Stratification for Health-Care Associated *C. diff*

Learning Evolving Patient Risk Processes for *C. diff* Colonization

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Clostridium difficile (*C. diff*)

- Bacteria takes over the gut when normal flora gets wiped out
- Transmitted through the mouth
- Causes severe diarrhea, intestinal diseases
- Treatment: metronidazole, oral vancomycin
- 20% of cases relapse within 60-days (Pepin J et al., 2005)

Source: http://www.helladelicious.com/wp-content/uploads/2012/05/Gut-Flora-Bacteria.jpg
http://newsimg.bbc.co.uk/media/images/41223000/jpg/_41223637_clostridium203spl.jpg

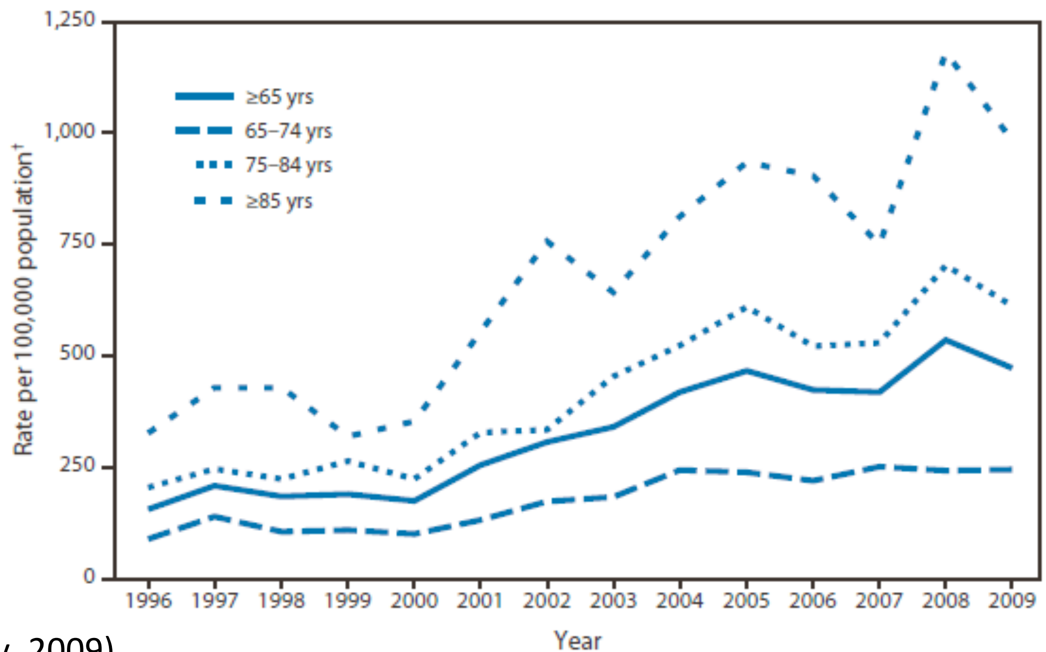
Prevalence

- Hospital-acquired: 178,000/year

  (McDonald et al., 2006)

- On par with number of new cases of invasive breast cancer in the US each year

  (American Cancer Society, 2009)



(CDC, 2011)

Risk Factors

Time Invariant

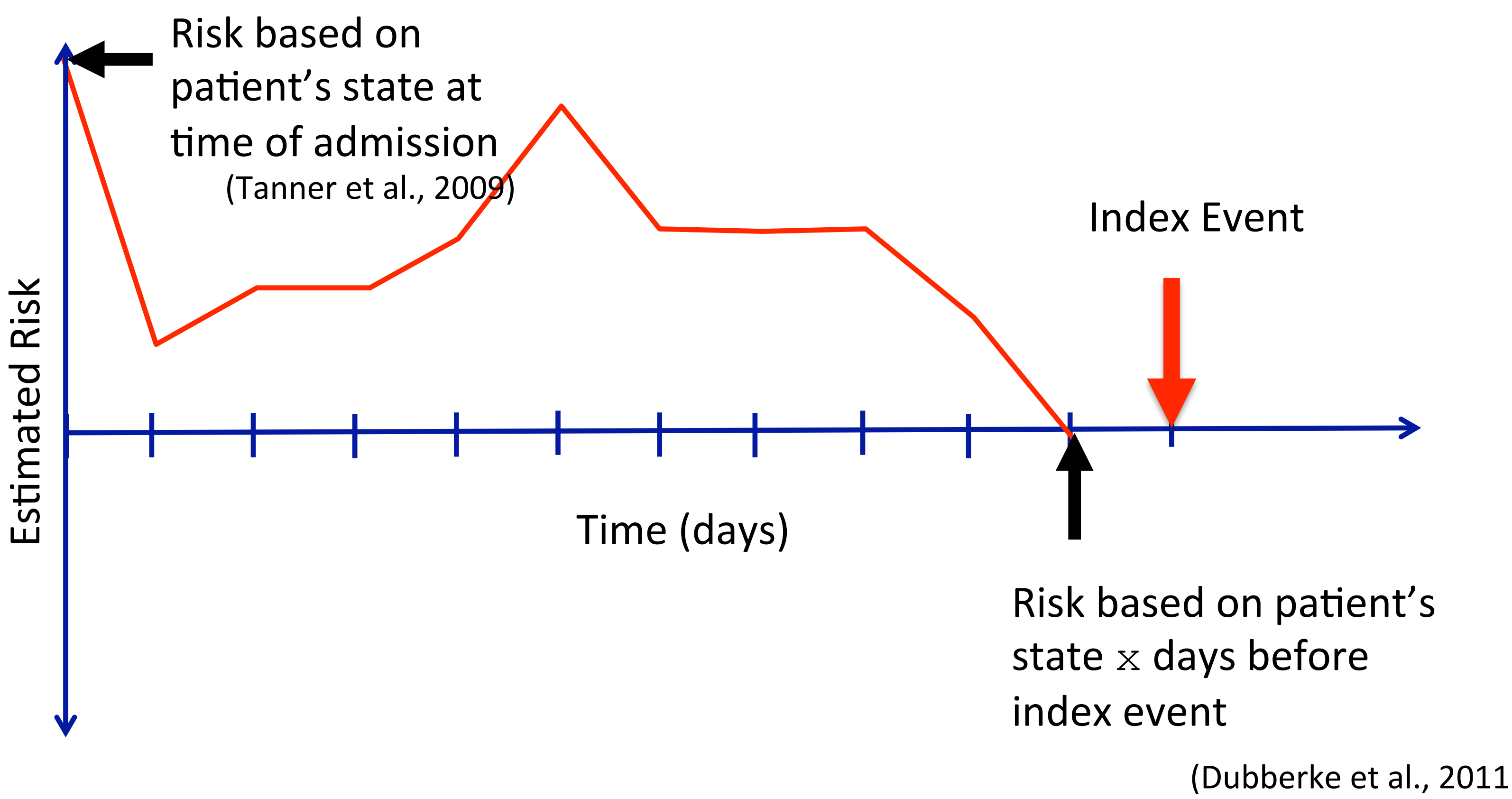
- Collected at the time of admission
- *e.g., admission complaint, previous admissions, home meds*

Time Varying

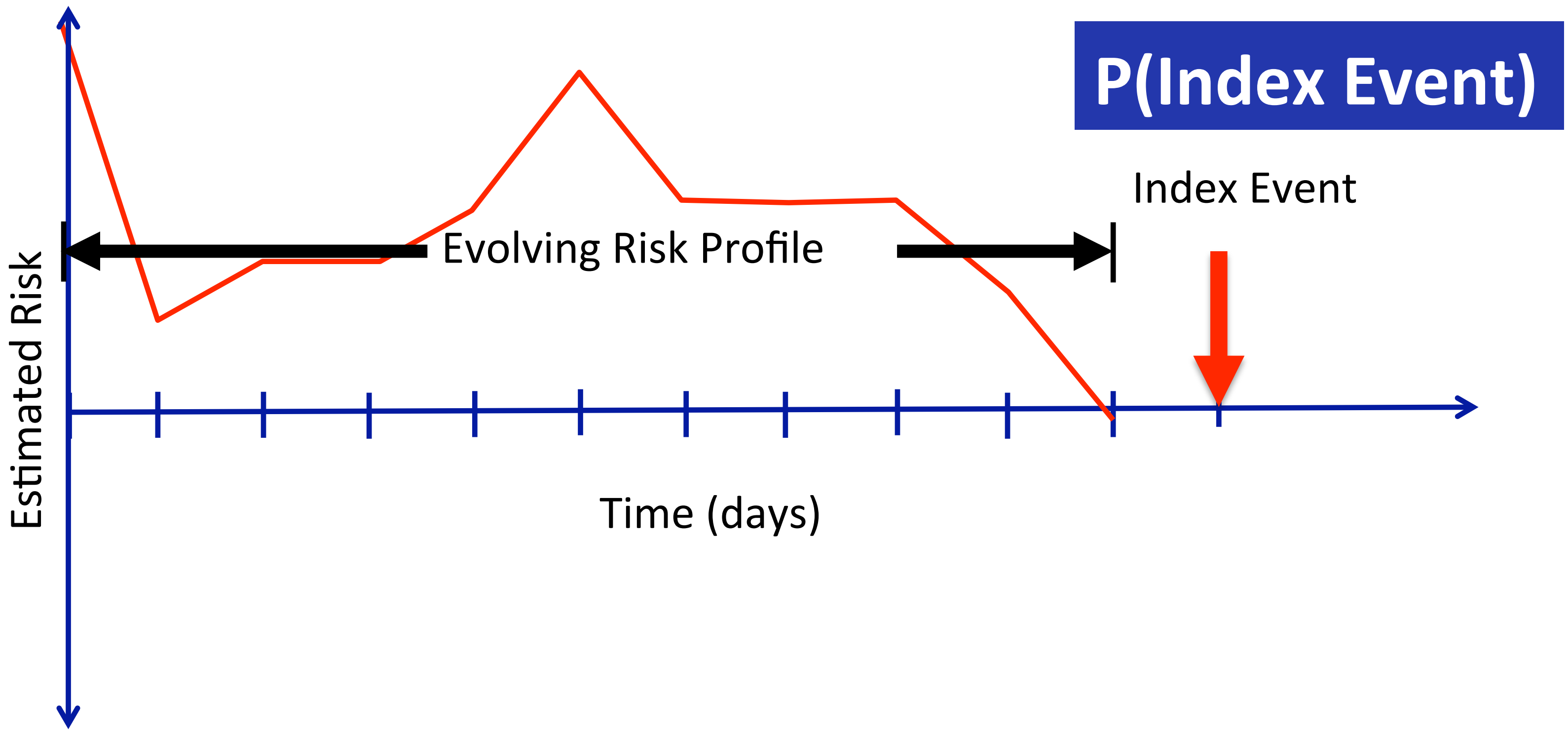
- Changes during the hospitalization
- *e.g., current meds, current procedures, current location, hospital conditions*

Representing and reasoning about temporal processes promises to enhance the accuracy of inferences about risk.

Typical Approach in Clinical Literature



Our Approach

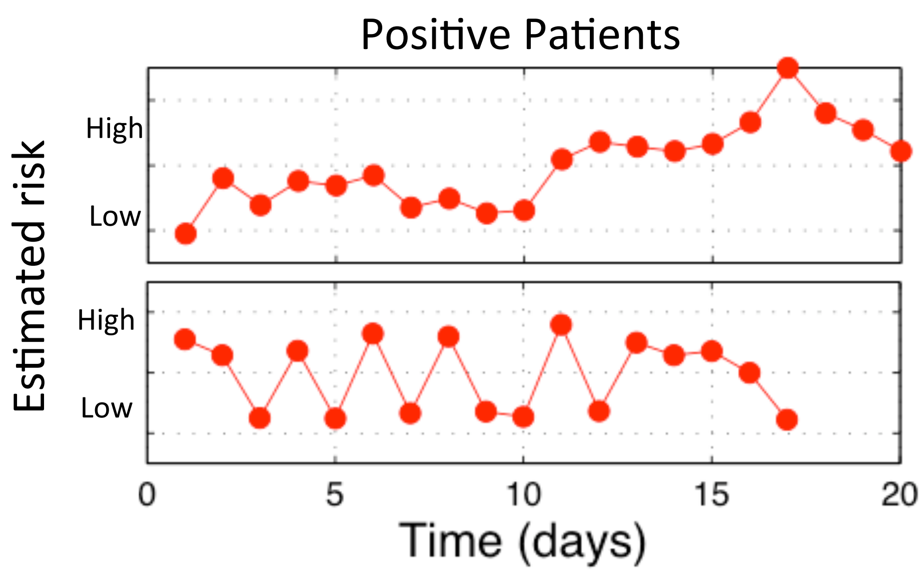


Risk Processes

Hypothesis: extracting and analyzing evolving patient risk can lead to a more accurate model for predicting infections

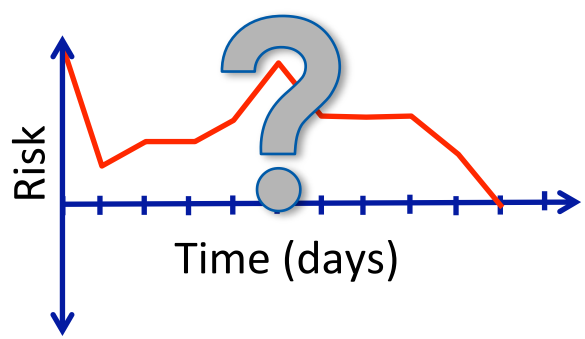
Risk Process:

describes the evolution of risk over the course of a hospital admission



Inferring Risk Processes

- Challenges:
  - No ground truth about risk
    - Retrospective data → not all patients get tested
    - Actual risk on any day is unknowable
  - Thousands of correlated variables

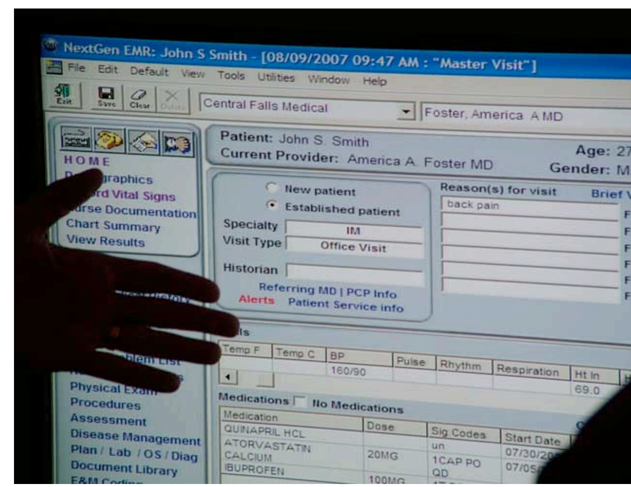


The Data

- Database from a large urban hospital in the US
- In-patient stays from a single year
- Inclusion criteria (see paper for details)
  - Eliminate easily identifiable cases

Population:

- ~10,000 hospital admissions
- ~200 Positive *C. diff* cases



Experimental Setup

- Training & Testing
  - Randomly subsampled the negative class
  - Split data into stratified training and test sets 70/30.
  - Training set 1,251 admissions (127 positive)
  - Testing set 532 admissions (50 positive)

Features

Time Invariant		Time Varying
• prev. ICD 9 codes	• patient's age	• lab results
• home medications	• patient's marital status	• procedures
• prev. admission medications	• patient's sex	• location room
• patient's city	• expected surgery	• location unit
• attending MD	• ER admission	• medications
• Hospital service	• dialysis	• vitals
• admission source	• diabetic	• day of admission
• financial class code	• history of C. diff	• unit CP
• admission complaint	• num. hospital visits (90 days)	• hospital wide CP
• admission procedure	• avg., max., total los (90 days)	
• patient's race		

Features: >10,000 variables for each day of every hospital admission

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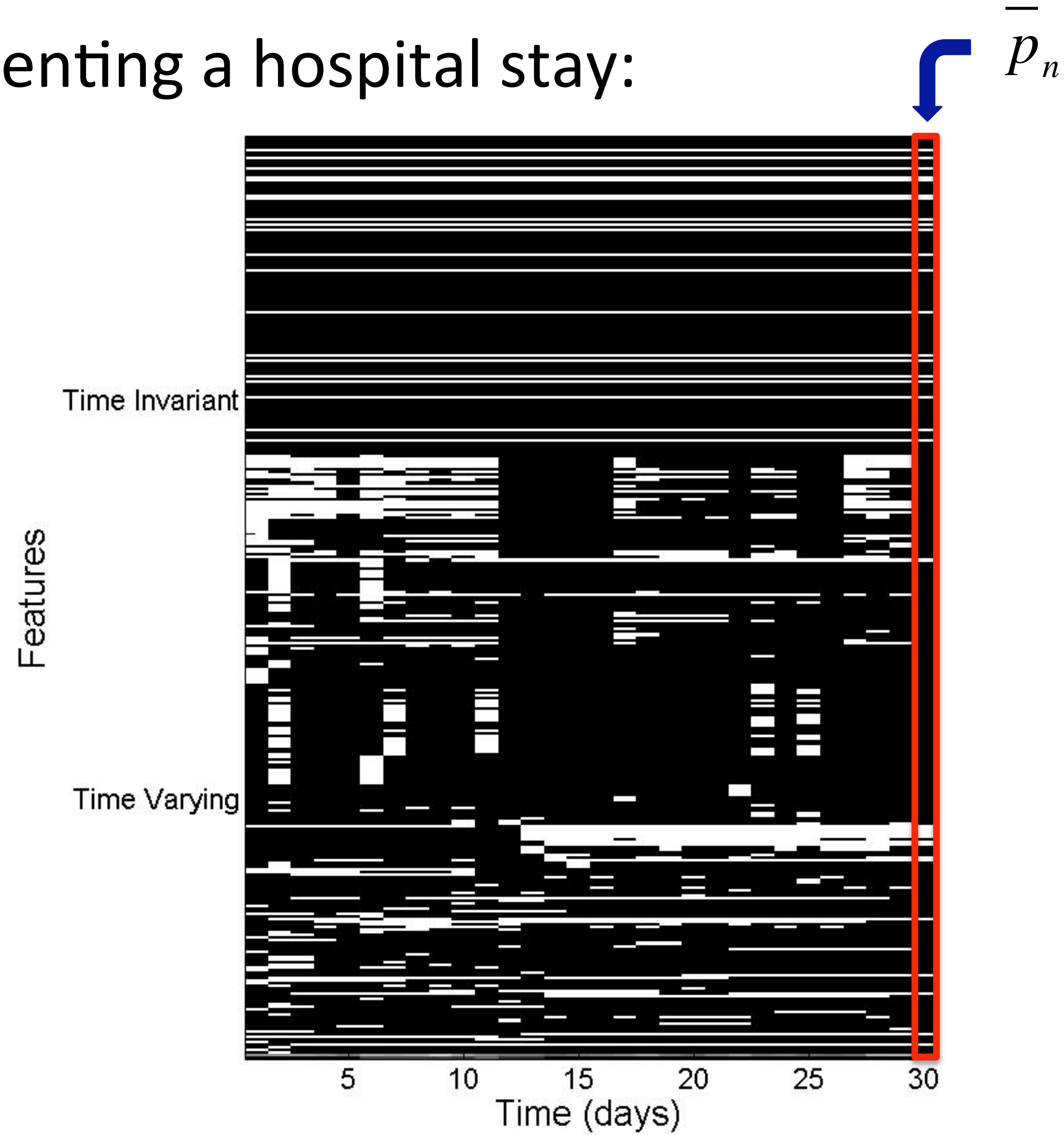
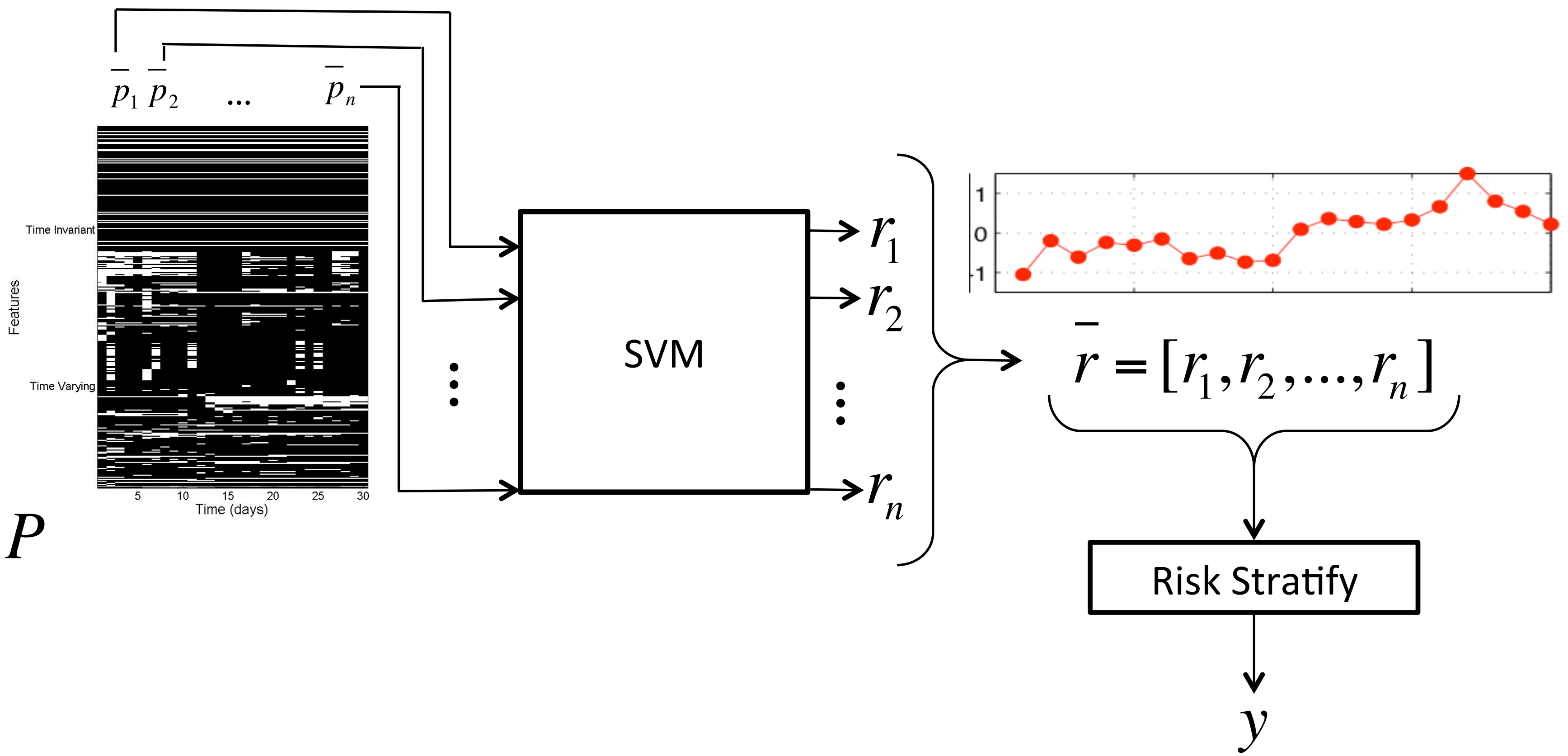
Representing a hospital stay:



Our Approach to Risk Stratification



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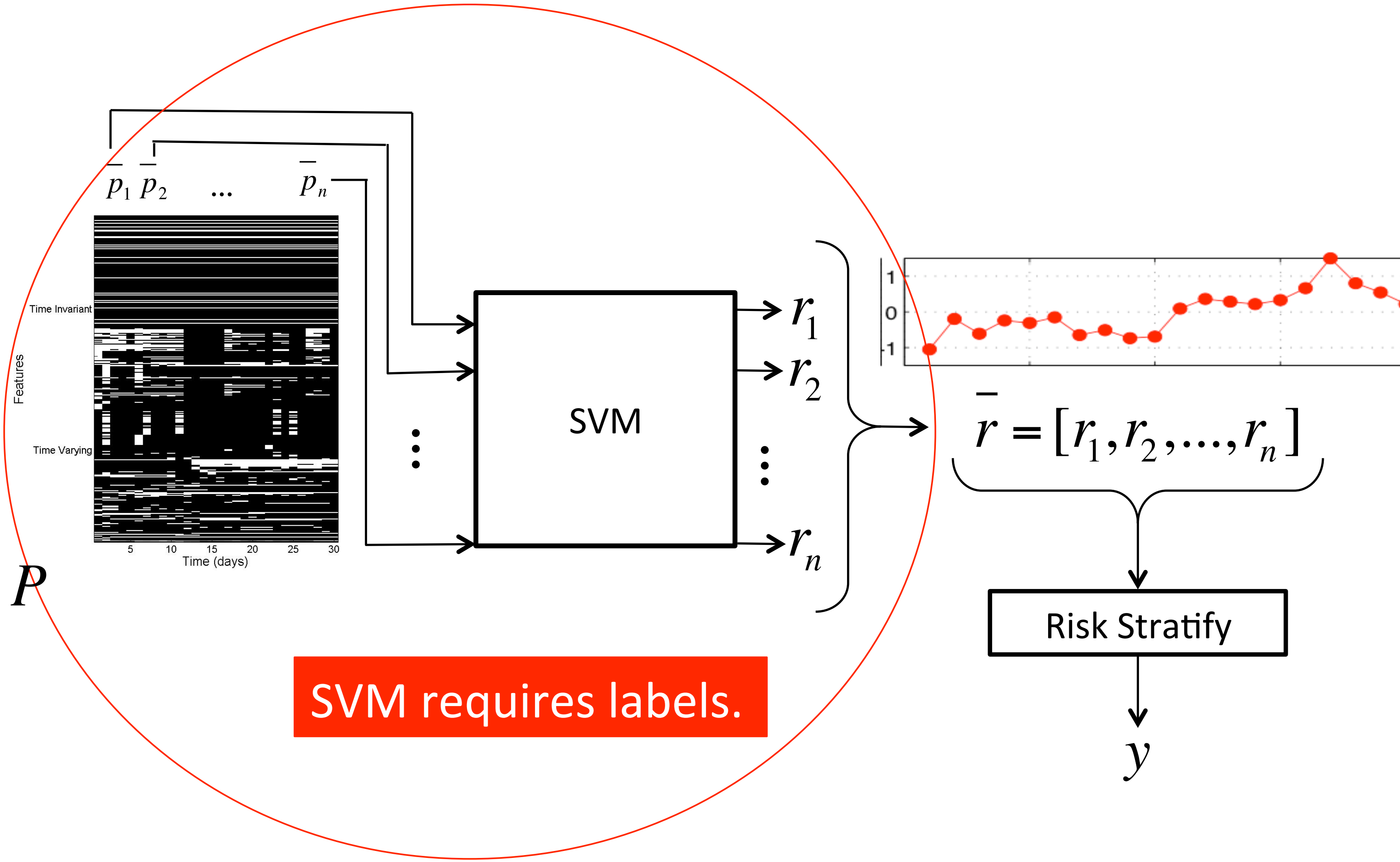
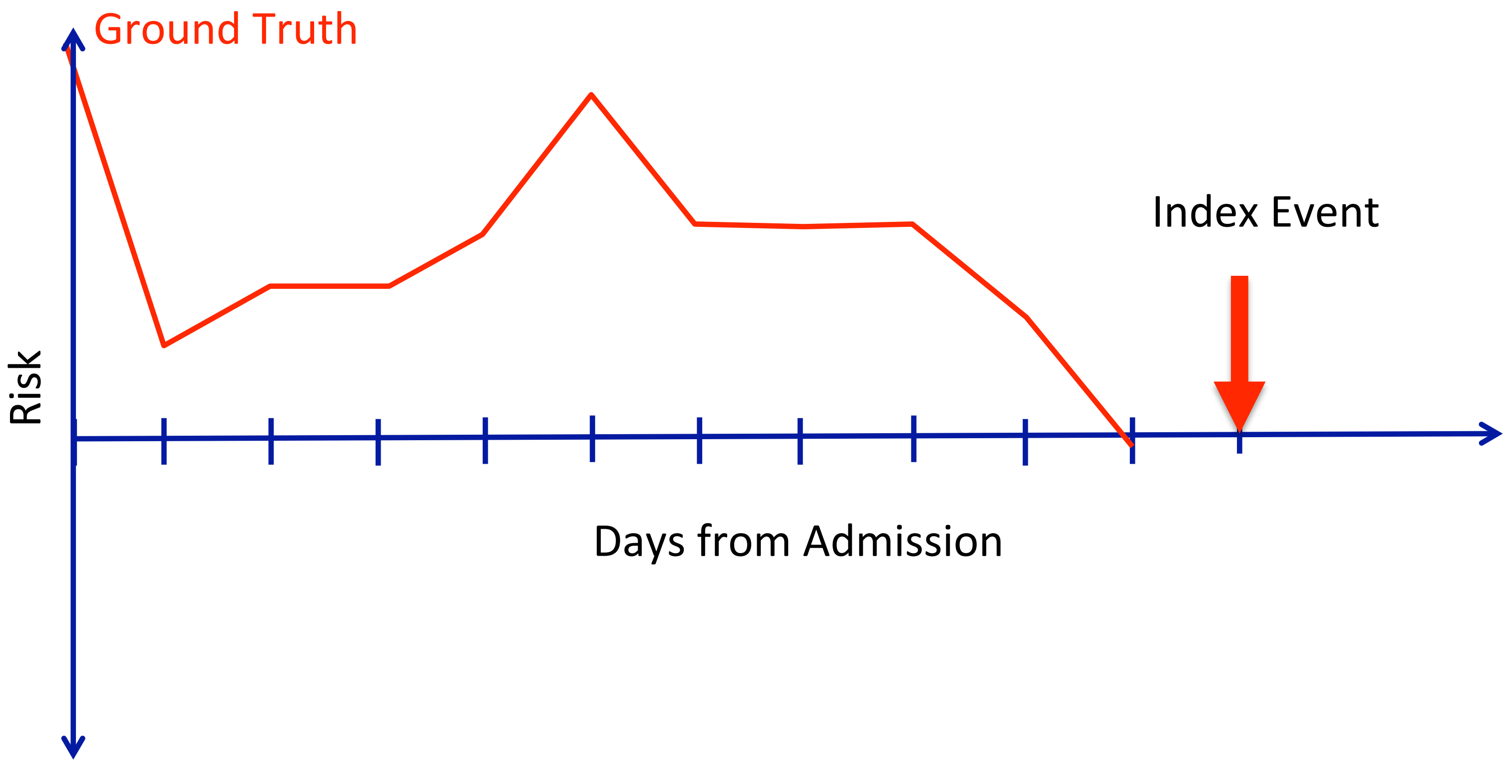


Labeling the Data



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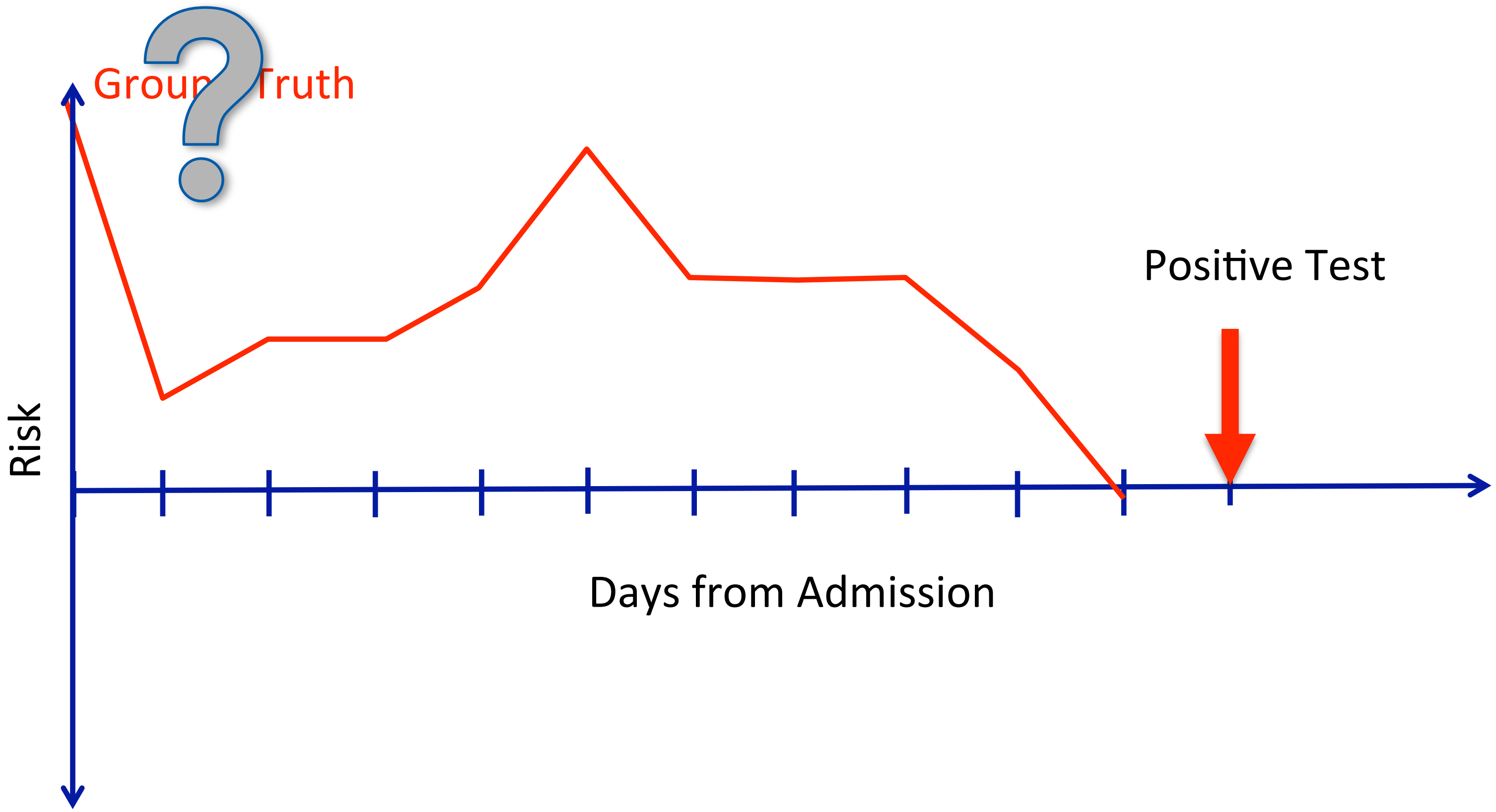

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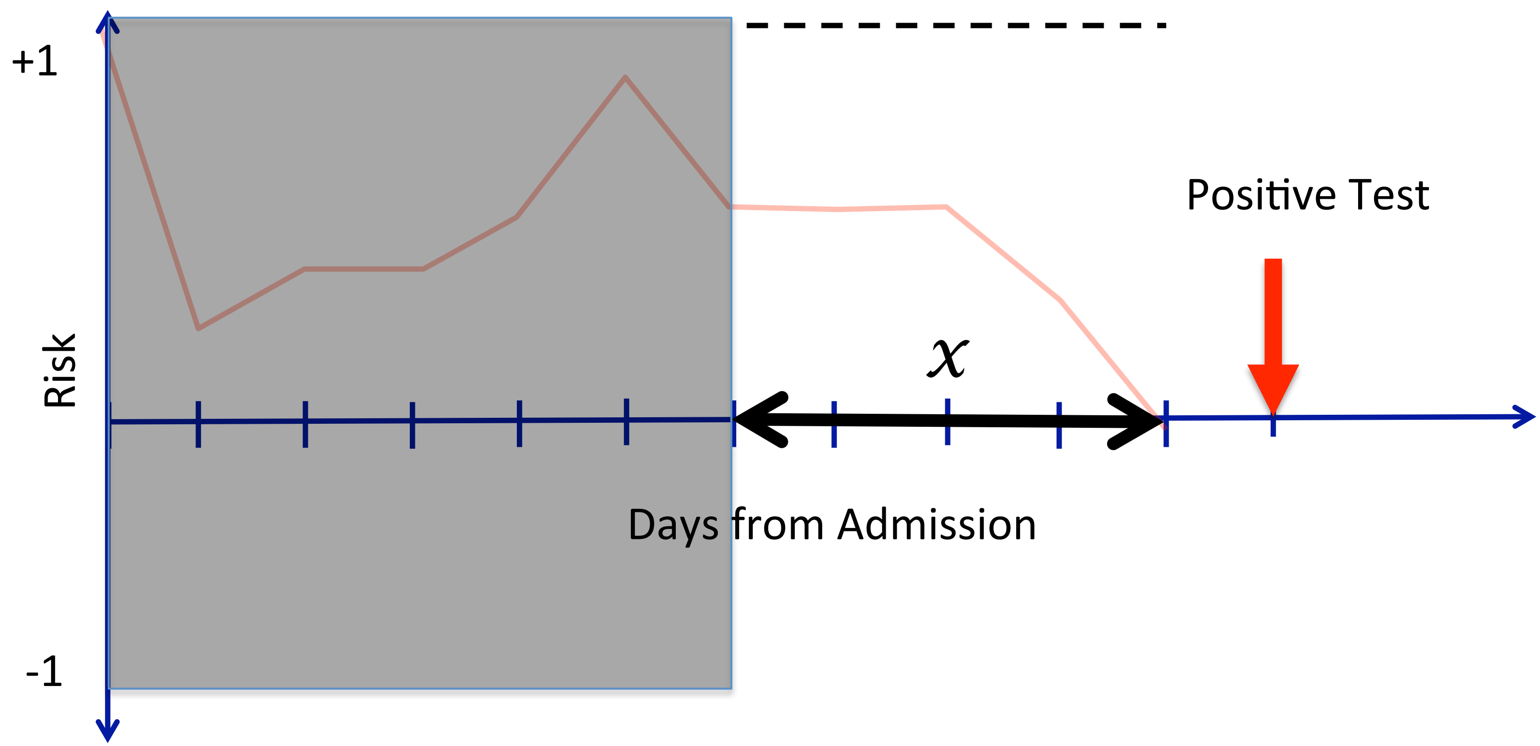

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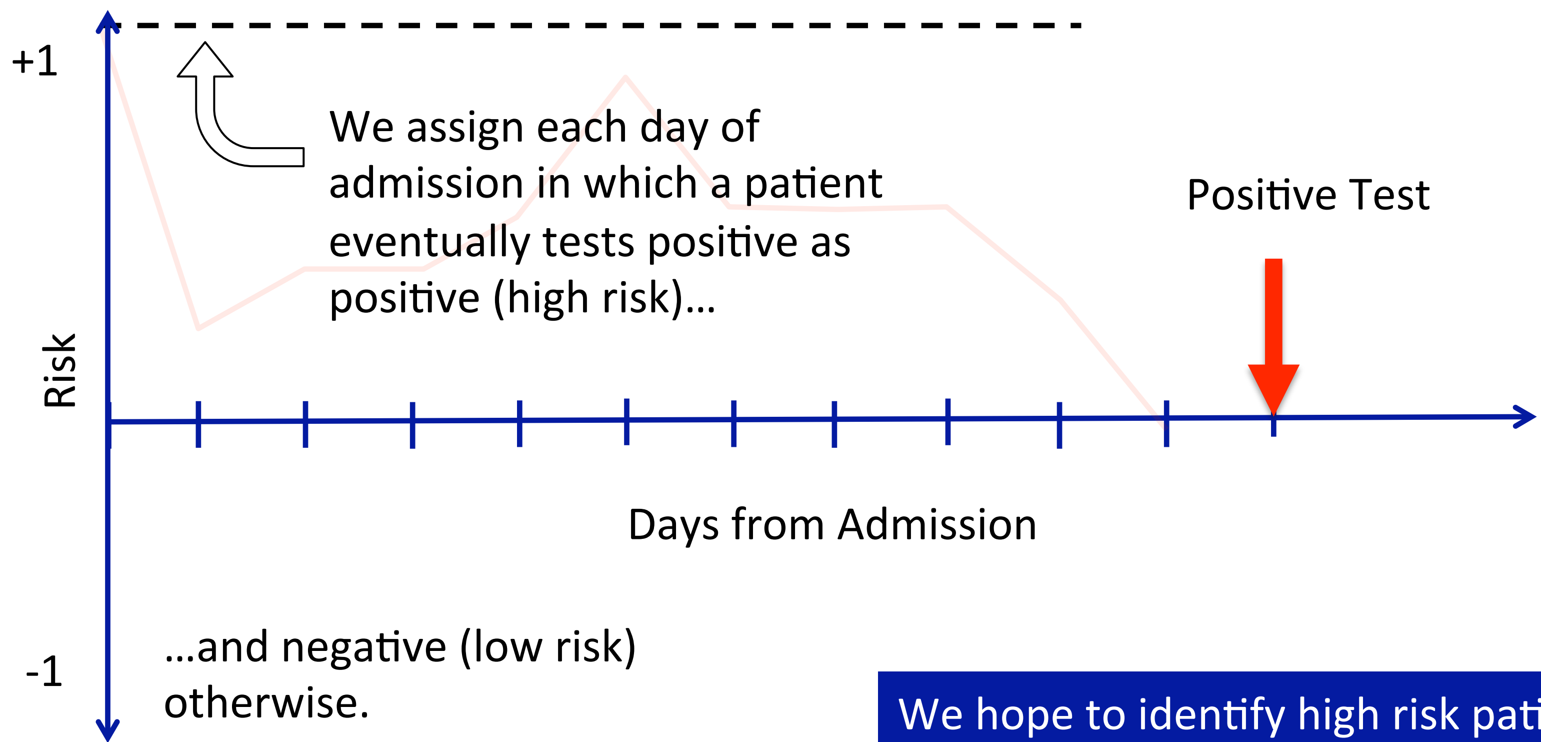
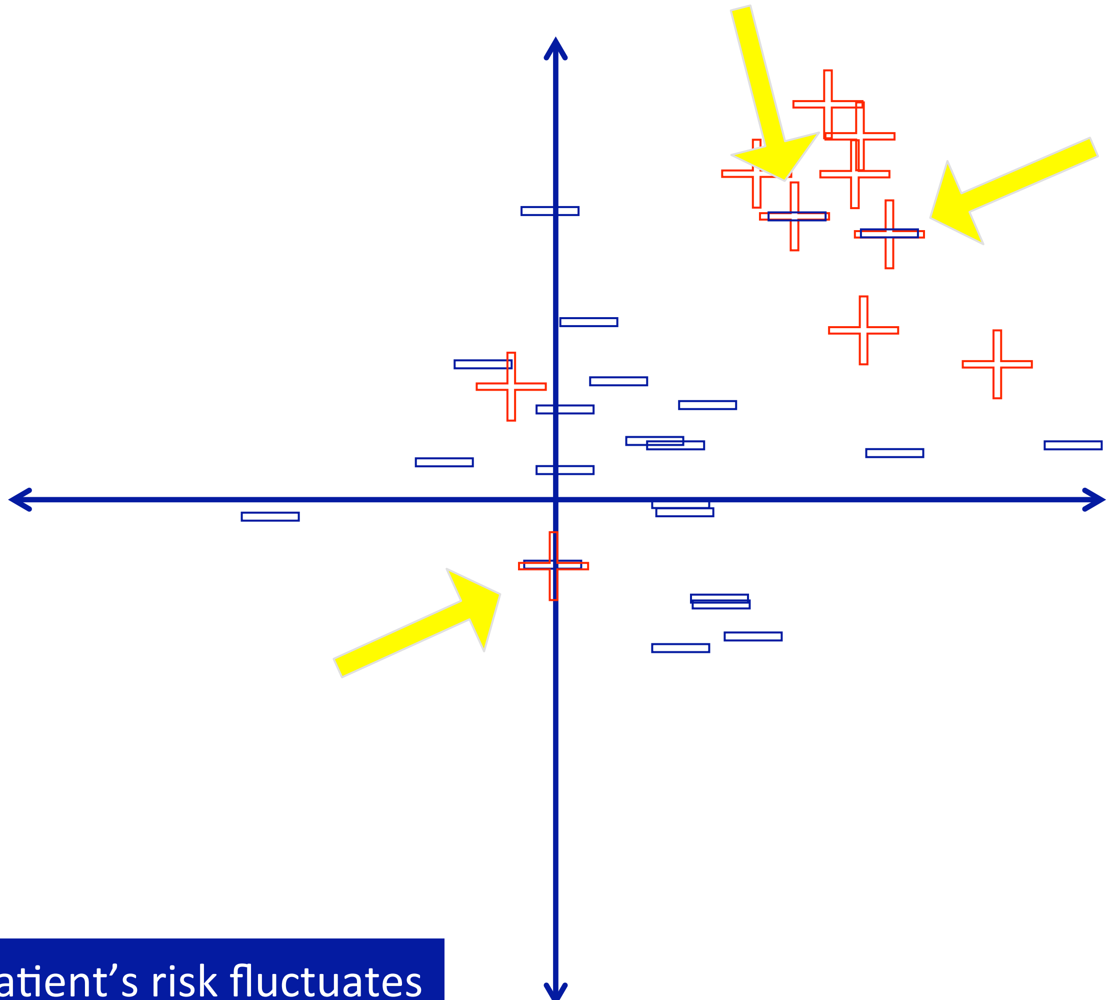


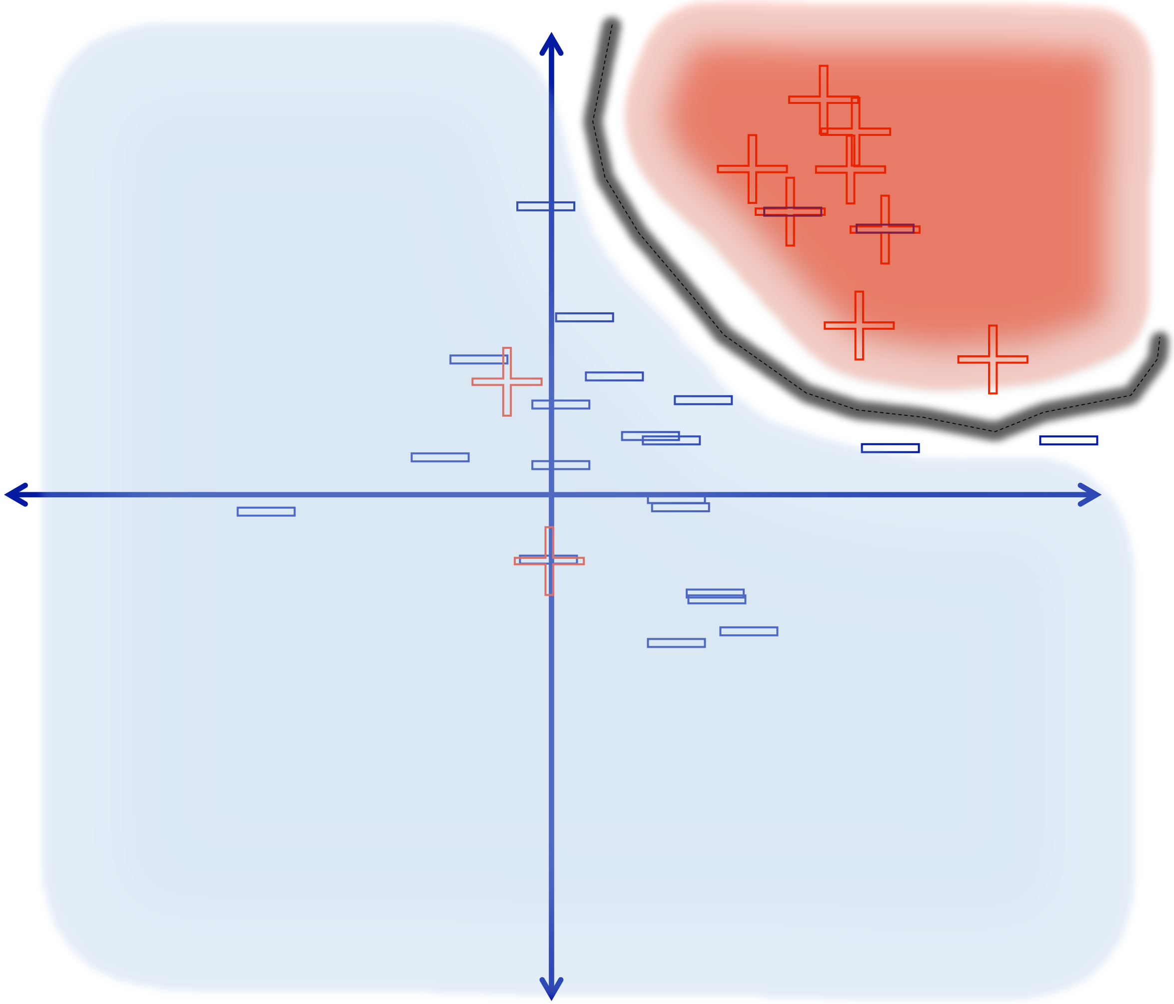
We hope to identify high risk patients as early as possible.

Learning the Decision Boundary



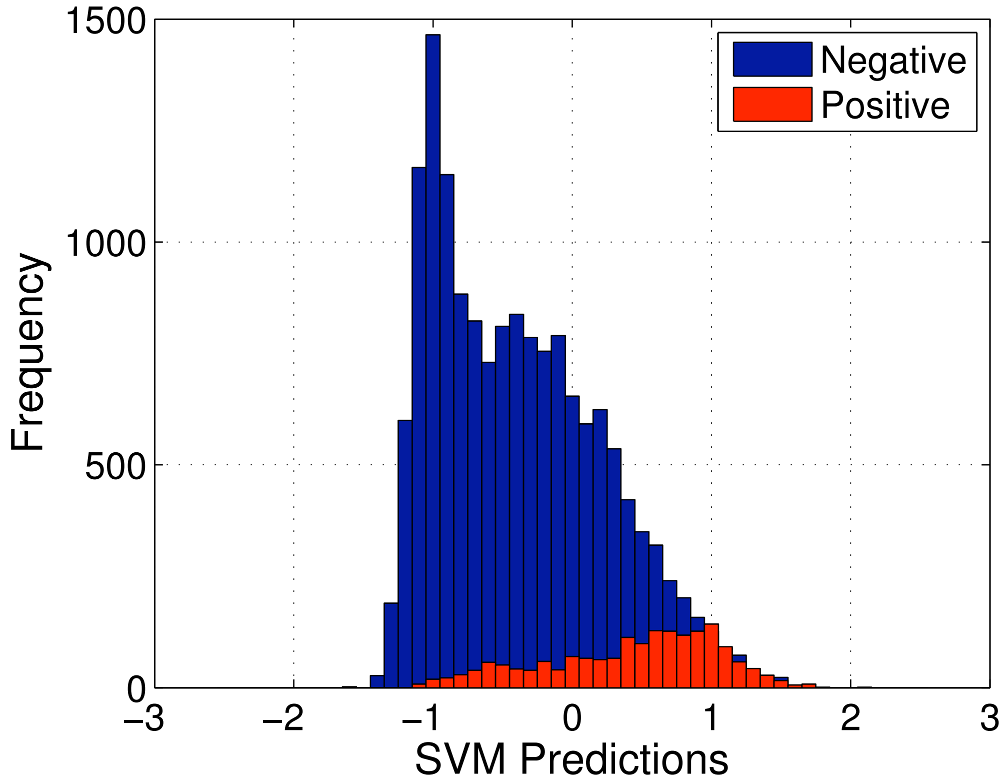
We expect a patient's risk fluctuates
→ noise in the training labels

Learning the Decision Boundary



Note: Simplified illustration. We learn a linear hyperplane in the high dimensional feature space.

Daily Risk -> SVM Continuous Predictions

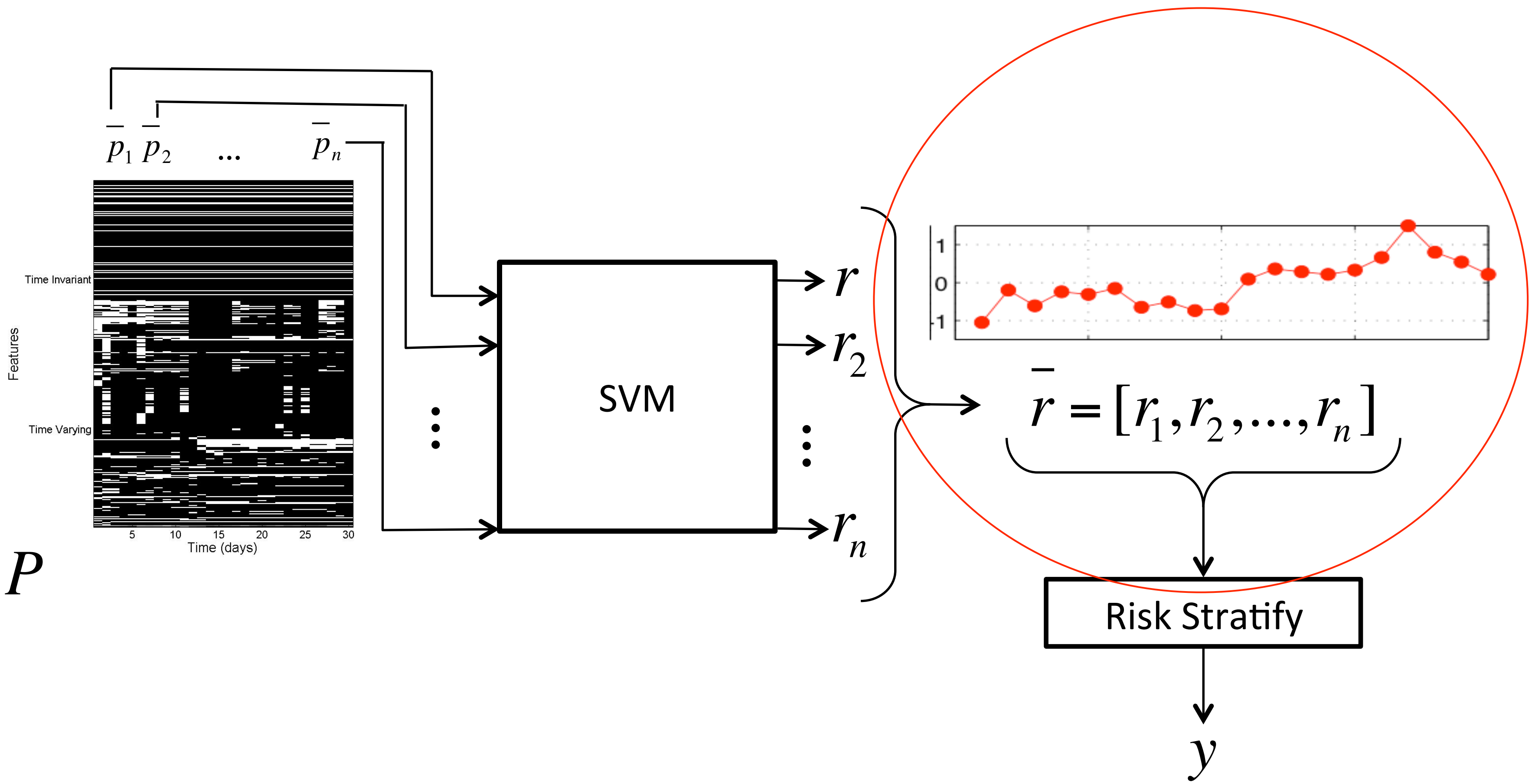


(Training data)

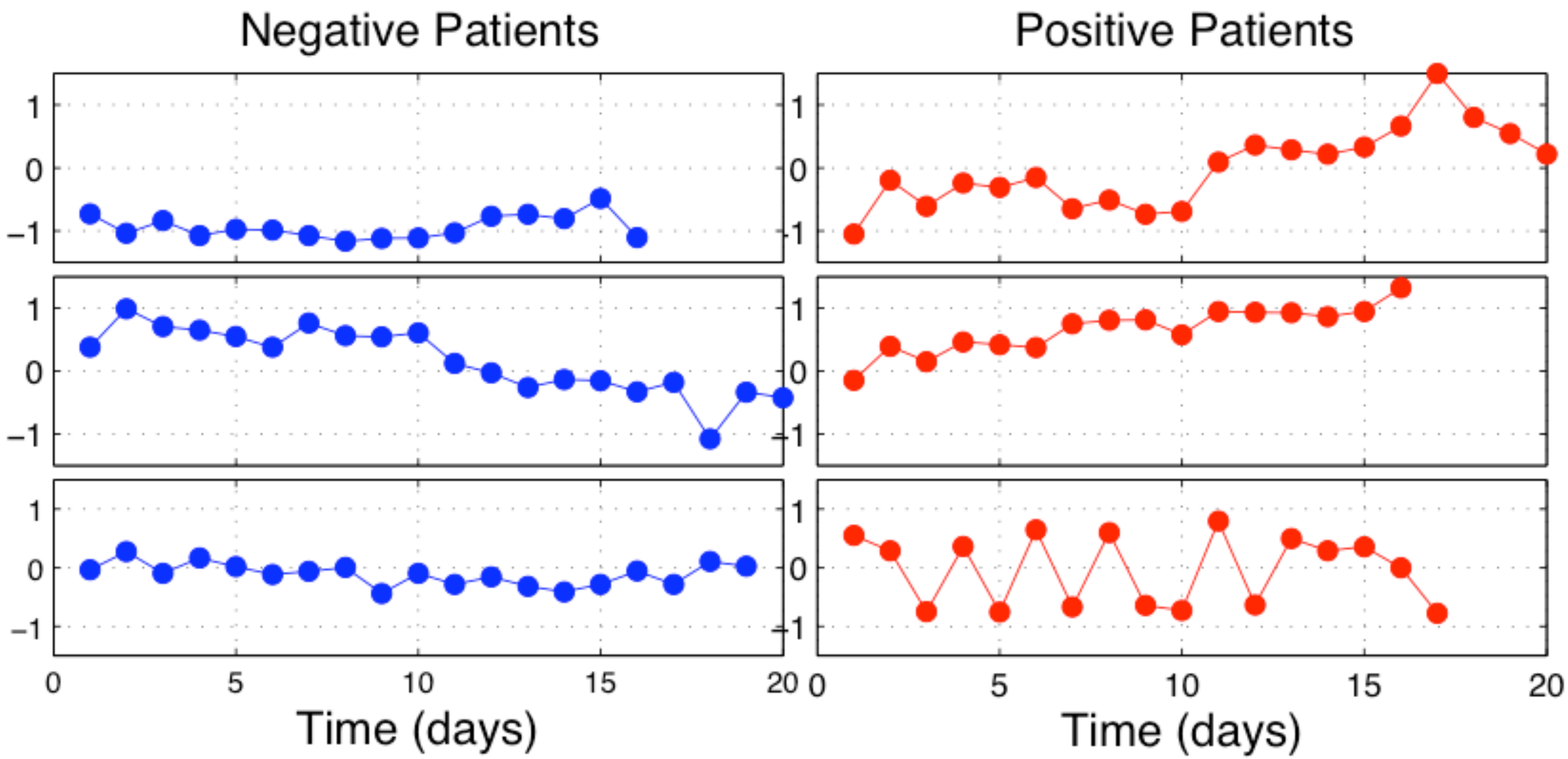
We consider the distance each feature vector lies from the SVM decision boundary this results in a **continuous** prediction for each day.

$$r_d = \overline{w} \bullet \overline{p_d} - b$$

Our Approach to Risk Stratification



Example Risk Processes



Using Risk Processes for Risk Stratification

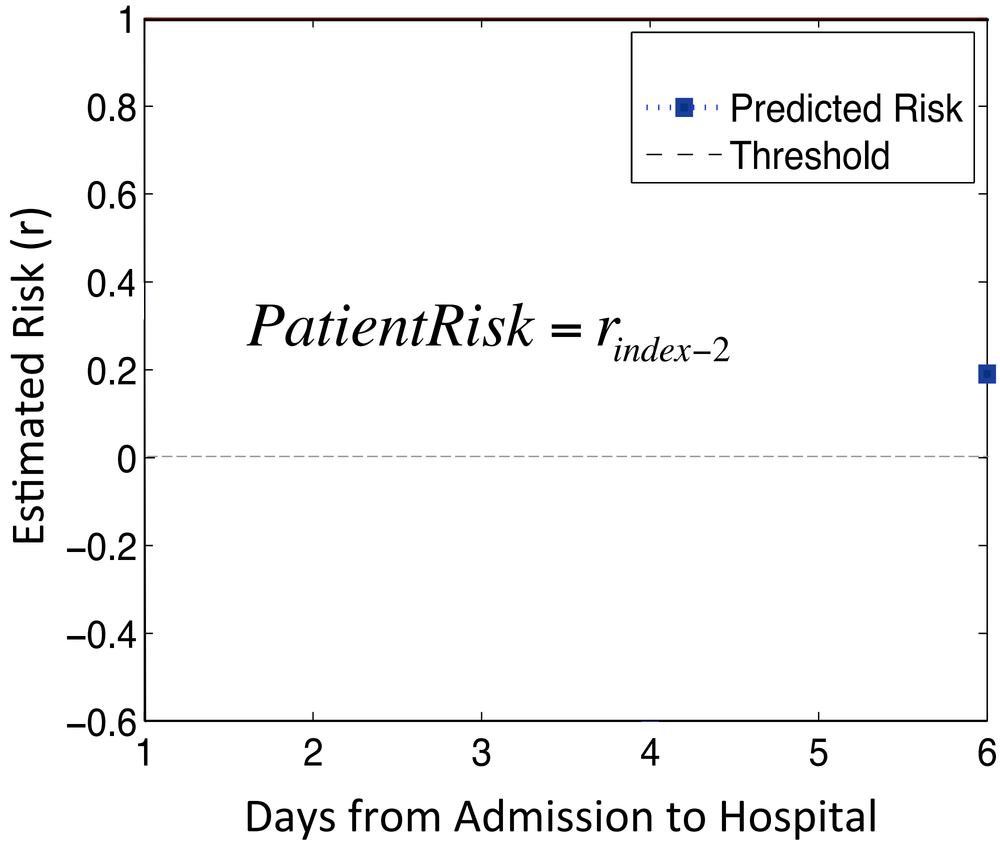
- Instantaneous approach:
  - Analogous to typical risk stratification approaches (Dubberke et al., 2011)
  - Considers value of risk process only on day of prediction
- Cumulative approach:
  - Combine estimates from all previous days

    E.g., constant, linear, and quadratic weighted averages

Evaluating Instantaneous Approach

Patient tests positive for *C. diff* on day 8

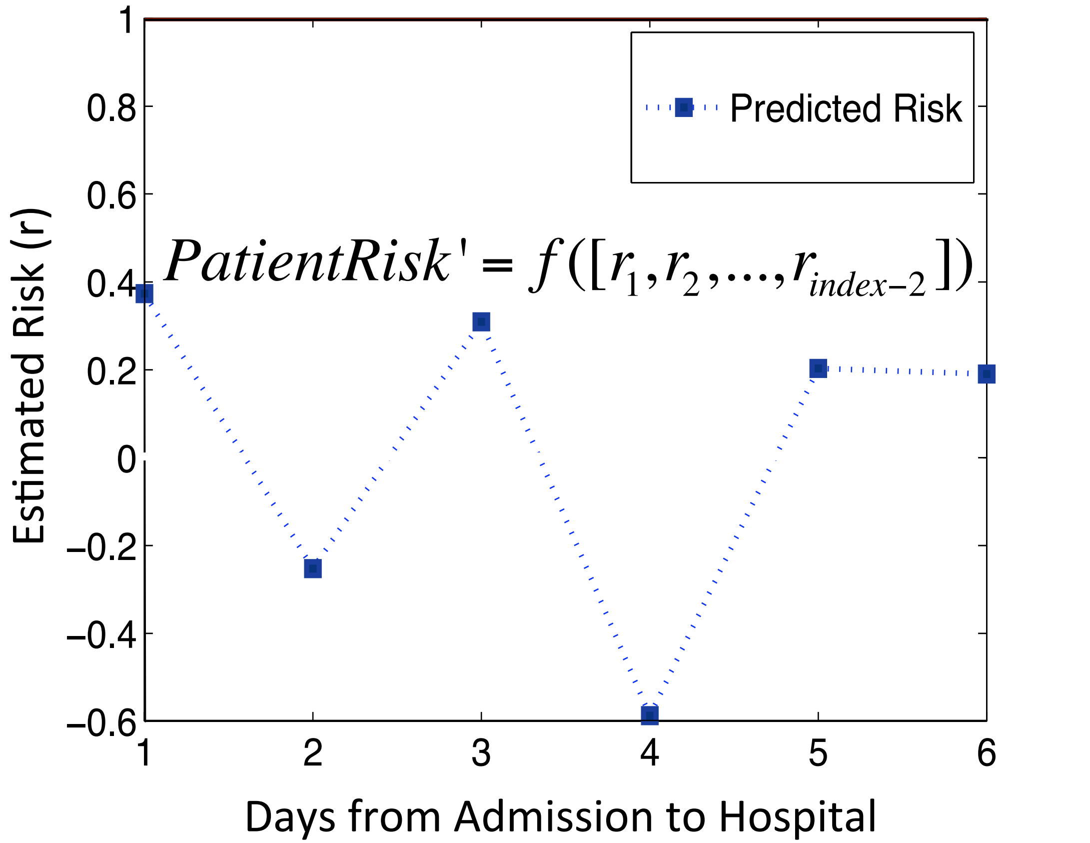
- Consider **instantaneous** estimate for patient risk at a constant distance before the index event e.g., 2 days



Compute classifier performance by sweeping the decision threshold from min to max.

Evaluating Cumulative Approach

Patient tests positive for *C. diff* on day 8



- **Combine** estimates for patient risk from the time of admission up to a constant distance from the index event e.g., 2 days

Compute classifier performance by sweeping the decision threshold from min to max.

Defining the Index Event

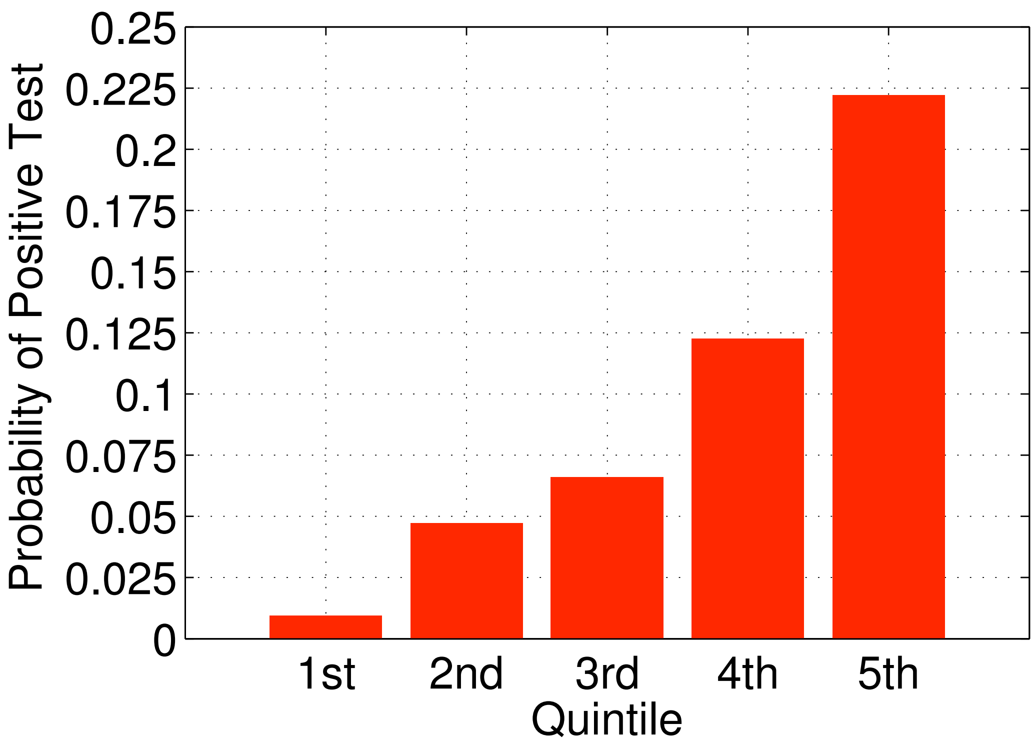
- Positive Examples → day of positive test result
  - We consider only data collected up to two days before a positive test result
- Negative Examples → midpoint of admission
  - Considering discharge as the index event can lead to deceptively good results

Results

Cumulative

Approach	Testing AUROC (95% CI)
Constant weighted avg.	0.7518 (0.69-0.81)
Linear weighted avg.	0.7444 (0.67-0.80)
Quadratic weighted avg.	0.7360 (0.67-0.80)
Instantaneous	0.6870 (0.61-0.77)

Results



Patients in the 5th quintile are at >20-fold greater risk than those in the 1st quintile!

Conclusion

- First step in analyzing how patient risk for acquiring *C. diff* may evolve during a hospitalization
  - Improvement over existing methods
- Next steps:
  - Find patterns of risk that lead to worse/better outcomes
  - Investigate application in other contexts (e.g., other HAIs, in-hospital mortality, LOS)

Acknowledgements

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