Data-driven diagnosis of serious bacterial infection: what are we predicting, when and why?

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Outline

No data – Sorry!

Background

Current applications of data-driven diagnosis for sepsis/serious bacterial infection (SBI)

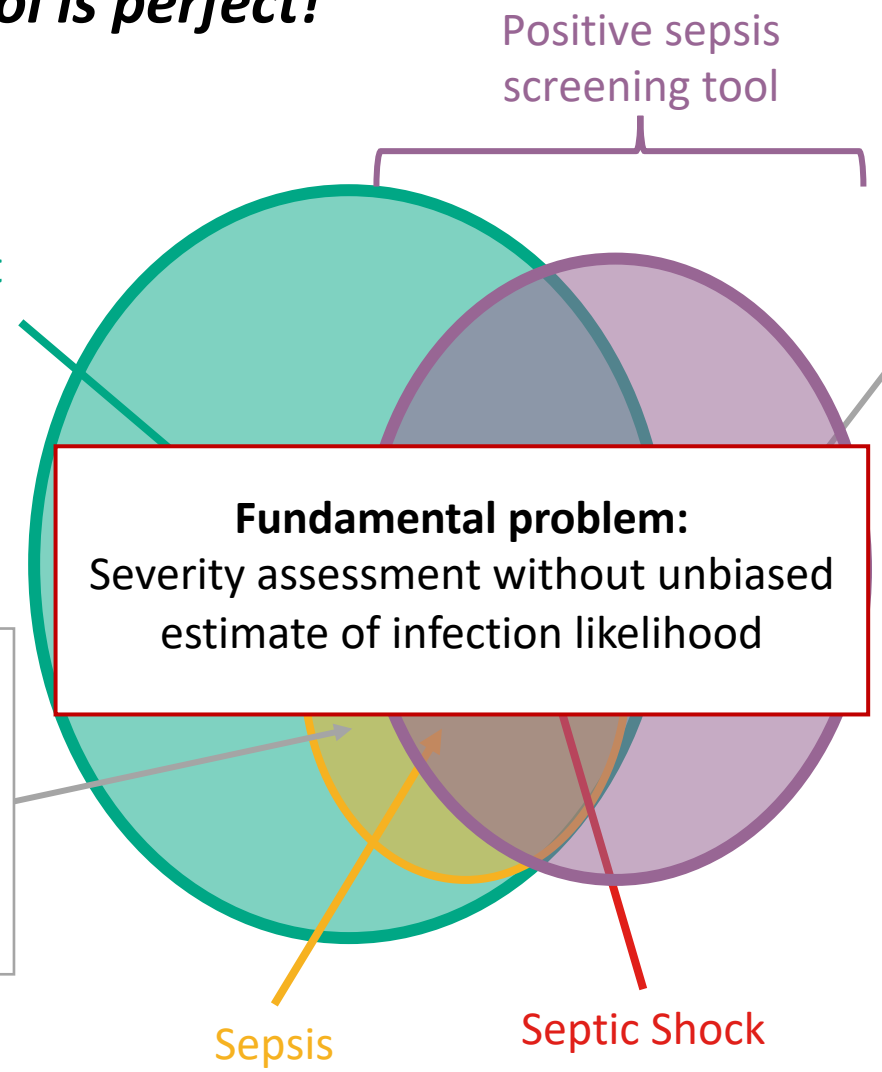
Defining SBI for ML model development

Planned study

Discussion

Current approach to sepsis assessment

No screening tool is perfect!



Positive sepsis screen (NEWS2 ≥5 and/or Red Flag) but no infection.

At least 20% of patients with positive sepsis screen do not have infection.

No benefit and potential harms from antibiotics

Fundamental problem:
Severity assessment without unbiased estimate of infection likelihood

Negative sepsis screen (NEWS2 <5 and no Red Flag) but sepsis present

Need to be mindful that screening tools are not 100% sensitive

'Sticky diagnoses'

- Prescribing etiquette
- 'Culture-negative' sepsis

Can we move beyond standardized 'one-size-fits-all' risk scores and single biomarkers in sepsis assessment and leverage the richness of structured data within electronic health records to estimate likelihood of severe bacterial infection to guide initial management decisions?

Sepsis prediction

INFECTIOUS DISEASE/ORIGINAL RESEARCH

Development and Evaluation of a Machine Learning Model for the Early Identification of Patients at Risk for Sepsis

Ryan J. Delahanty, PhD; JoAnn Alvarez, MS; Lisa M. Fl

JAMIA Open, 3(2), 2020, 252–260
doi: 10.1093/jamiaopen/ooaa006
Advance Access Publication Date: 11 April 2020
Research and Applications

Research and Applications

Machine learning for early detection of sepsis: an internal and temporal validation study

Corey,[5,6]

Contents lists available at ScienceDirect

Computers in Biology and Medicine

journal homepage: www.elsevier.com/locate/cbm

putational approach to early sepsis detection

Calvert[a], Daniel A. Price[a], Uli K. Chettipally[b,c], Christopher W. Barton[c],

Burdick *et al. BMC Med Inform Decis Mak* (2020) 20:276
https://doi.org/10.1186/s12911-020-01284-x

RESEARCH

Validati
algorith
a retros
up to 4
from 46

Hoyt Burdick[1,2],

Intensive Care Med (2020) 46:383–400
https://doi.org/10.1007/s00134-019-05872-y

SYSTEMATIC REVIEW

Machine learning for the prediction of sepsis: a systematic review and meta-analysis of diagnostic test accuracy

Lucas M. Fleuren[1,2*], Thomas L. T. Klausch[3], Charlotte L. Zwager[1], Linda J. Schoonmade[4], Tingjie Guo[1],

DICAL INFORMATICS Desautels et al

Journal of the American Medical Informatics Association, 30(7), 2023, 1349–1361
https://doi.org/10.1093/jamia/ocad075
Advance Access Publication Date: 12 May 2023
Review

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ID; Lisa

BMJ Open Respiratory Research

Effect of a machine lea
severe sepsis predictio
patient survival and h
stay: a randomised cli

David W Shimabukuro,[1] Christopher W Barto

Check for updates

Review

Deployment of machine learning algorithms to predict sepsis: systematic review and application of the SALIENT clinical AI implementation framework

Anton H. van der Vegt[1], Ian A. Scott[2], Krishna Dermawan[3], Rudolf J. Schnetler[4],

nature medicine

Prospective, multi-site study of patient outcomes after implementation of the TREWS machine learning-based early warning system for sepsis

Roy Adams[1,2], Katharine E. Henry[2,3], Anirudh Sridharan[4], Hossein Soleimani[5], Andong Zhan[2,3],

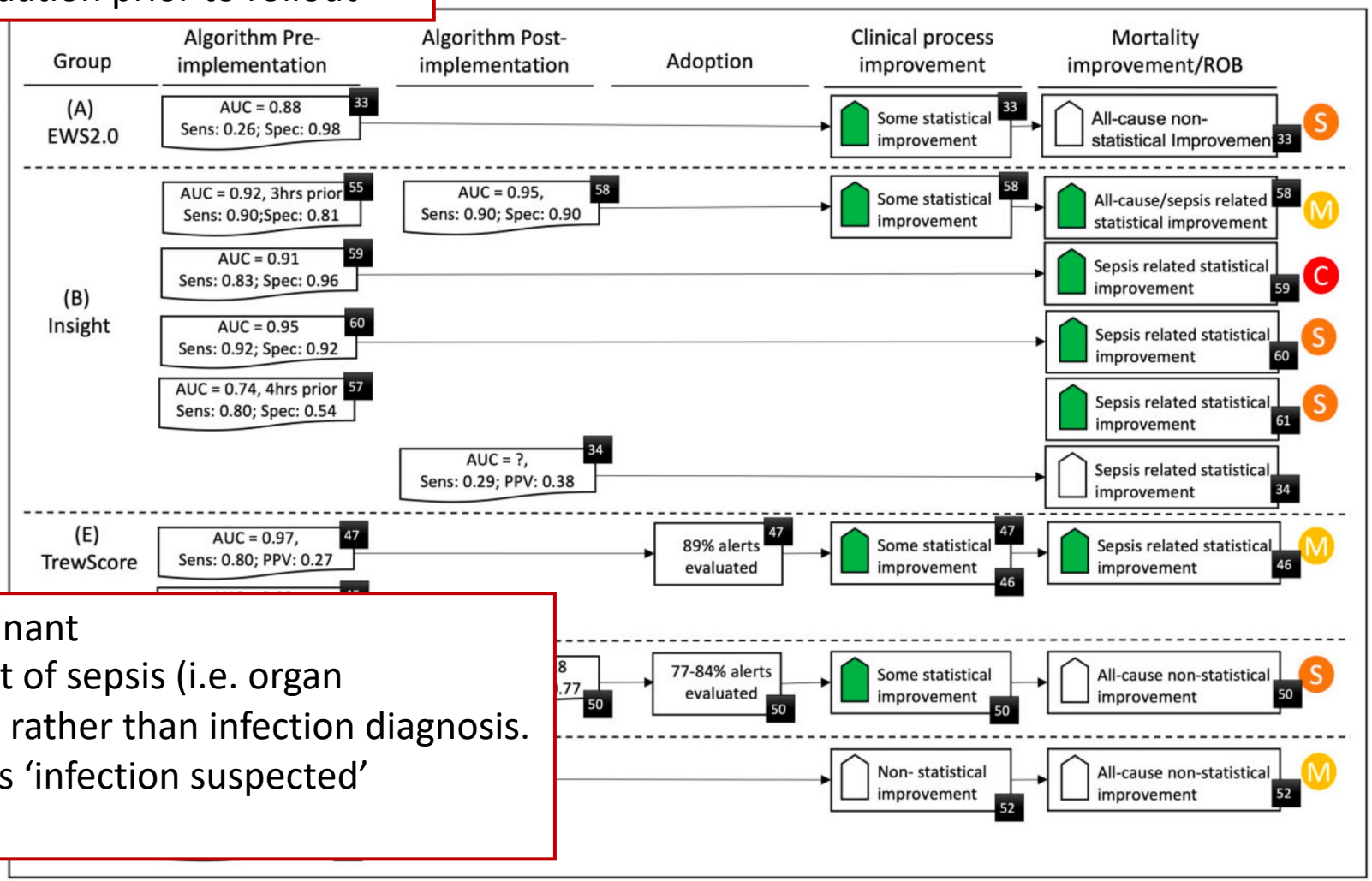
method to identify patients with severe sepsis or septic shock in the emergency department

Samuel M. Brown[1,2,7*†], Jason Jones[3†], Kathryn Gibb Kuttler[1,4], Roger K. Keddington[5], Todd L. Allen[6] and

Sepsis prediction

- Limited evaluation prior to rollout

Paper	Target Condition	No. Models	Models	No. Patients	No. Features	Hrs bef. Onset
Emergency Department						
Horng, 2017	Sepsis	13	SVM, GLM, NB, EM	230936	10-12	-
Haug, 20					24	-
Delahanty					12	-
Brown, 2						
In-Hospital						
Khojandi, 2018						
Futoma, 2017						
McCoy, 2017	Severe sepsi					
Lin, 2018	Sept					
Khoshnevisan, 2018	Sept					
Thiel, 2010	Sept					
Giannini, 2019	Severe sepsis and Sept					
Intensive Care Unit						
Wang, 2018						
Shashikumar II, 2017						
Shashikumar I, 2017						
Scherpf, 2019						
Desautels, 2016						
Nemati, 2018						
Calvert II, 2016						
Kim, 2017						
Van Wyk, 2018						
Van Wyk, 2019						
Moss, 2016	Seve					
Guillen, 2015	Seve					
Shimabukuro, 2017	Seve					
Henry, 2015	Sept					
Calvert I, 2016	Sept					
ED/In-Hospital/ICU						
Barton, 2019						
Mao, 2017	Sepsis, Severe sepsis, Sept					



- ICU predominant
- Predict onset of sepsis (i.e. organ dysfunction) rather than infection diagnosis.
- ‘All comer’ vs ‘infection suspected’ population.

Fleuren *et al., ICM* 2020; van der Vegt *et al., JAMIA* 2023

Sepsis prediction

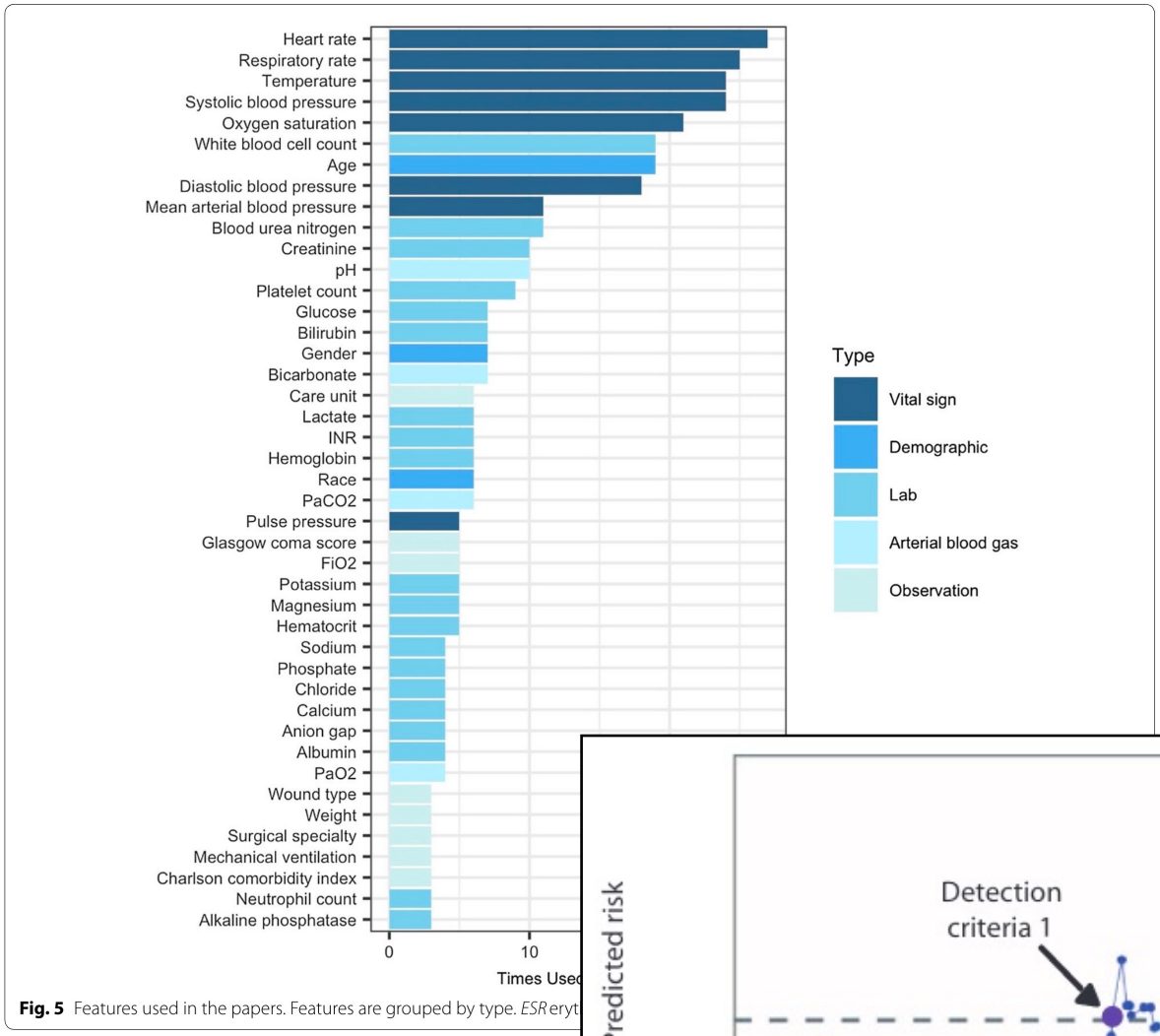
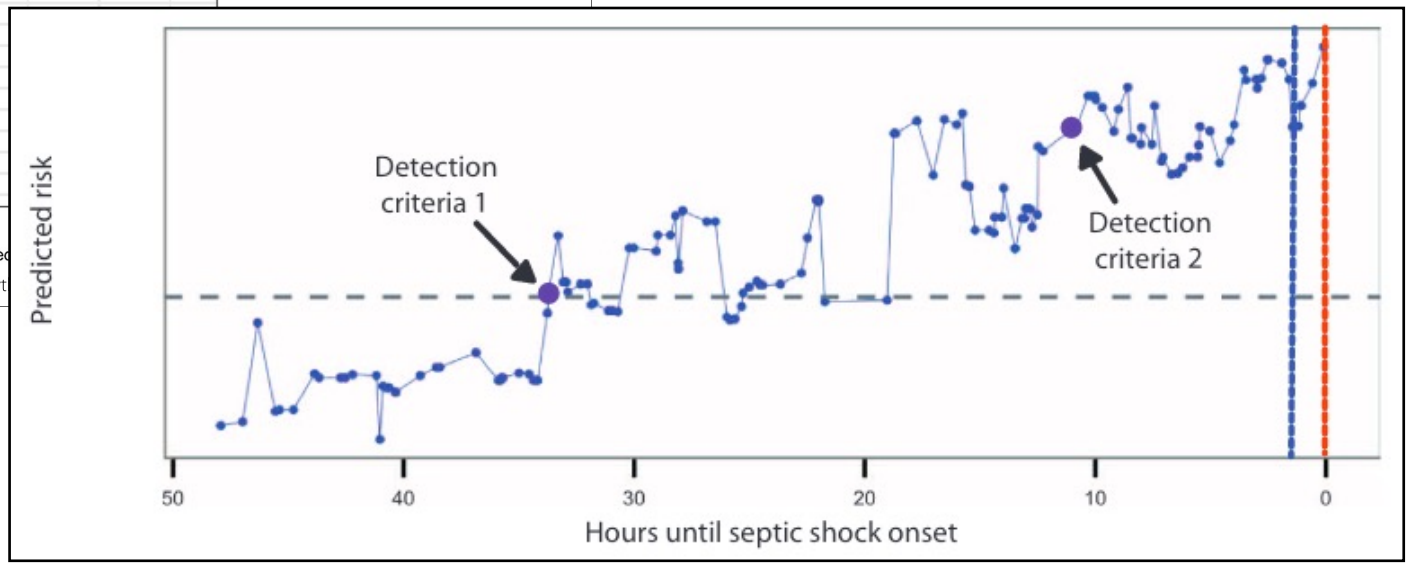


Fig. 5 Features used in the papers. Features are grouped by type. *ESR* eryt

Feature set / parameters typically limited to acute physiology and lab parameters.

Focus – early detection and treatment initiation; Prediction time frame up to onset of septic shock.



Henry *et al. Sci Trans Med* 2015; Fleuren *et al., ICM* 2020

RESEARCH ARTICLE

Development and validation of machine learning-driven prediction model for serious bacterial infection among febrile children in emergency departments

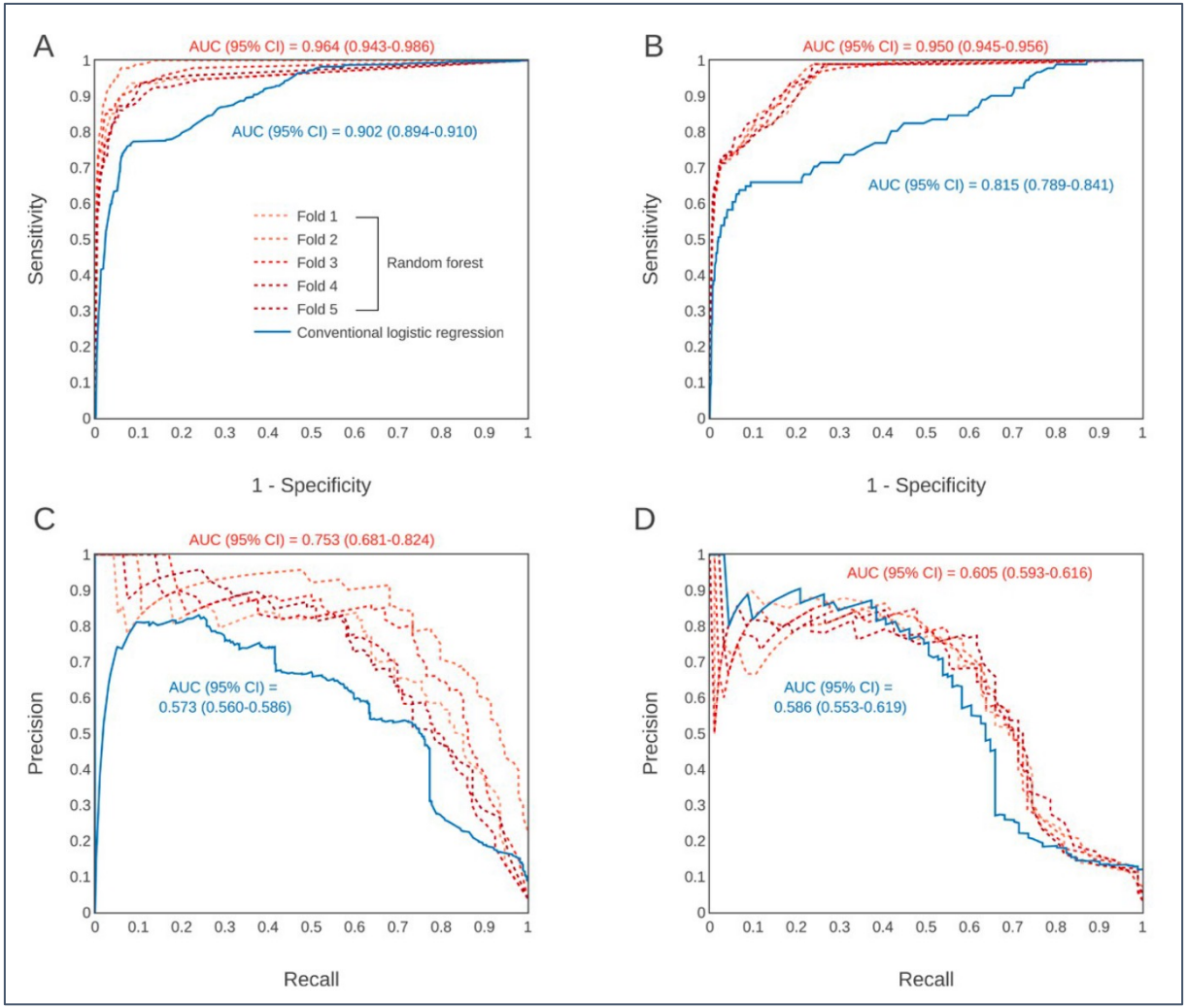
Bongjin Lee[1☯], Hyun Jung Chung[2☯], Hyun Mi Kang[3], Do Kyun Kim[4], Young Ho Kwak[4]*

Serious bacterial infection diagnosis

Serious Bacterial Infection

(1) Bacteremia defined by growth of a single bacterial pathogen;
(2) Acute pyelonephritis defined by growth of a single bacterial urinary tract pathogen at ≥ 10^5 cfu/mL and presence of a renal involvement on DMSA scan, or by any bacterial growth on urine obtained by suprapubic aspiration or ≥ 10^4 colony-forming units/mL of a single pathogen on urine obtained by bladder catheterization;
(3) Lobar pneumonia diagnosed on chest radiography;
(4) Bacterial meningitis with a positive cerebrospinal fluid culture;
(5) Bone or joint infections defined as local isolation or isolation in blood culture of a microorganism with concomitant arthritis;
(6) Sepsis defined according to Levy et al.

Bacteremia	26 (5.6[a])
Urinary tract infection	434 (93.1[a])
Lobar pneumonia	4 (0.9[a])
Bacterial CNS infection	1 (0.2[a])
Septic arthritis	1 (0.2[a])



Predicting urinary tract infections in the emergency department with machine learning

R. Andrew Taylor, Christopher L. Moore, Kei-Hoi Cheung, Cynthia Brandt

Syndrome-specific diagnosis

Retrospective cohort of ED visits with symptoms potentially attributable to a UTI and urine culture results.

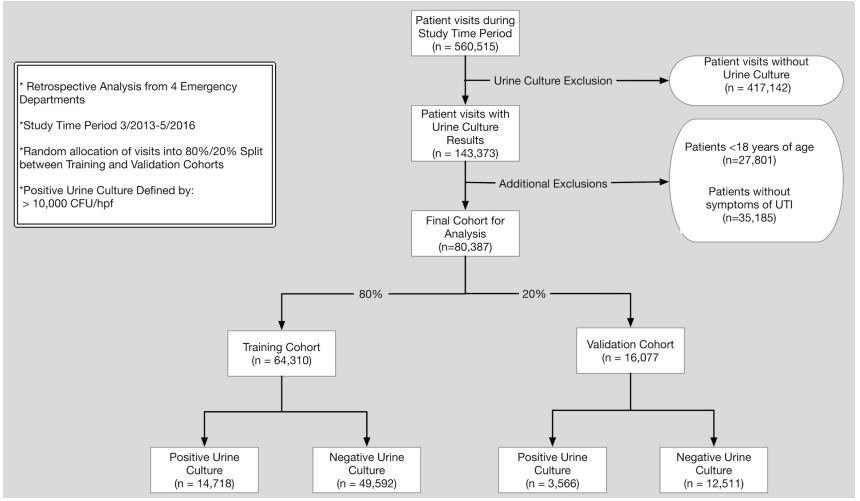
Primary outcome: positive urine culture with >10^4 CFU/HPF

Secondary: (1) provider documentation of UTI diagnosis; (2) provider gave antibiotics OR documented a diagnosis of UTI.

Predictor variables: demographics, vitals, lab results, urinalysis results, **outpatient medications, past medical history**, chief complaint, and structured historical and physical exam findings

Models developed using full (211 variables) and reduced (10 variables) variable sets. Reduced selected a priori

Machine learning approach: Several different models; 10-fold cross validation; trained and validated on a random 80%/20% split.



Models	AUC (95%CI)	Sensitivity (95% CI)	Specificity (95% CI)	+LR (95% CI)	-LR (95% CI)	Accuracy (95% CI)	P–value
XGBoost	**.904(.898-.910)**	61.7(60.0–63.3)	94.9 (94.5–95.3)	12.0(11.1–13.0)	.404(.387-.421)	87.5 (87.0–88.0)	NA
Random Forest	.902(.896-.908)	57.3(55.6–58.9)	96.0 (95.6–96.3)	14.3(13.0–15.6)	.445(.428-.462)	87.4 (86.9–87.9)	0.58
Adaboost	.880(.874-.887)	62.2(60.6–63.8)	92.3(91.8–92.7)	8.06(7.54–8.61)	.409(.392-.427)	85.6(85.1–86.2)	< .001
Support Vector Machine	.878(.871-.884)	49.6(47.9–51.2)	96.8(96.4–97.1)	15.3(13.8–16.9)	.521(.504-.538)	86.3(85.7–86.8)	< .001
ElasticNet	.892(.885-.898)	56.8(55.2–58.4)	94.9(94.5–95.2)	11.1(10.2–12.0)	.455(.438-.473)	86.4(85.9–87.0)	< .001
Logistic Regression	.891 (.884-.897)	57.5(55.8–59.1)	94.7(94.3–95.1)	10.9(10.0–11.8)	.449(.432-.466)	86.4(85.9–87.0)	< .001
Neural Network	.884 (.878-.890)	54.6(52.9–56.2)	95.3(95.0–95.7)	11.7(10.8–12.8)	.476(.460-.494)	86.3(85.8–86.8)	<001

	Model	TP	FN	TN	FP	Sens (95%CI)	Spec (95%CI	Acc (95%CI)	Diff Sens (95%)
Overall									
	UTI diagnosis	1447	2077	10432	1881	41.3 (39.7–42.9)	84.7 (84.1–85.4)	75.1 (74.4–75.8)	NA
	XGBoost	2819	705	10432	1881	80.0 (78.6–81.3)	84.7 (84.1–85.4)	83.7 (83.1–84.2)	38.7 (38.1–39.4)
	Reduced XGBoost	2626	898	10432	1881	74.5 (73.0–75.9)	84.7 (84.1–85.4)	82.5 (81.9–83.0)	33.2 (32.5–33.9)

Taylor *et al., PLoS ONE* 2018

Development and validation of models for detection of postoperative infections using structured electronic health records data and machine learning

Monitoring and Surveillance

Kathryn L. Colborn, PhD[a,b,c,d,*], Yaxu Zhuang, MS[c], Adam R. Dyas, MD[a,b],

Retrospective study to develop and validate parsimonious, interpretable models for conducting surveillance of postoperative infections using structured electronic health records data.

Primary outcome: Comparison to curated dataset of postoperative outcomes data from the American College of Surgeons National Surgical Quality Improvement Program.

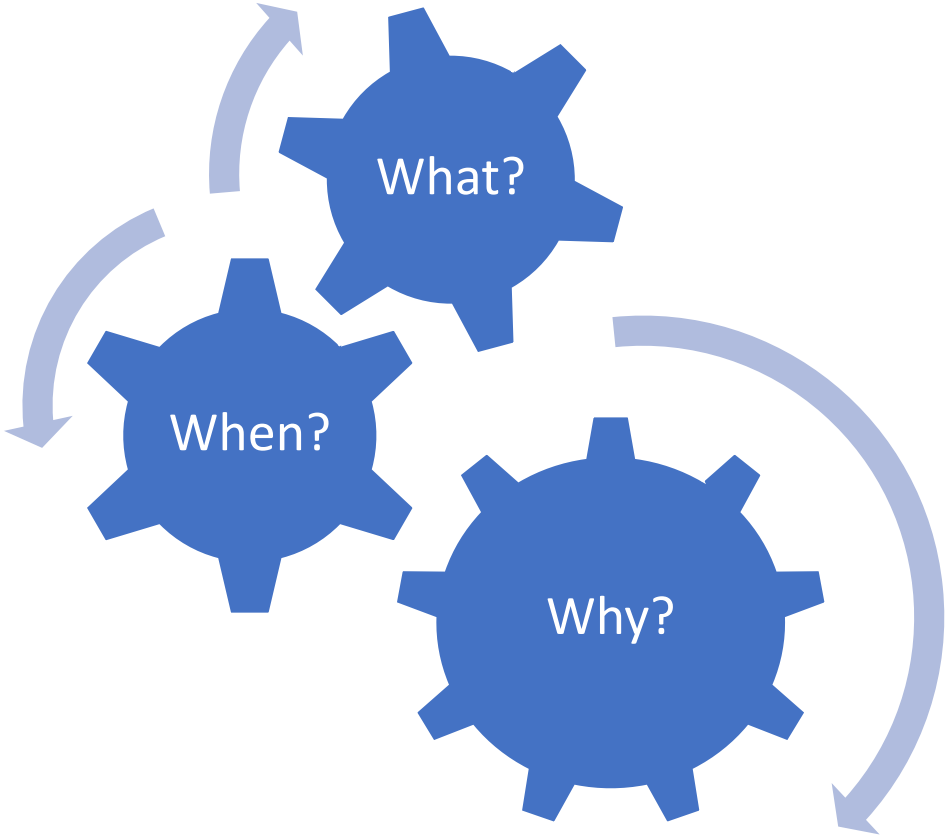
Predictor variables included **coding diagnoses and procedures, inpatient medications**, demographics, lab results.

Analytic approach: penalised regression with knockoffs framework.

Model	Estimates				
	Beta	OR	LCL	UCL	*P* value
Surgical site infections					
(Intercept)	−5.1187				
Phecode 080: "Postoperative infection"	2.7245	15.25	11.82	19.67	< .001
Phecode 1011: "Complications of surgical and medical procedures"	0.886	2.43	1.85	3.18	< .001
At least 1 antibiotic prescribed between 2–30 d after surgery	2.0891	8.08	6.51	10.02	< .001
Laboratory procedure: Blood culture	2.041	7.7	6.38	9.29	< .001
Urinary tract infections					
(Intercept)	−6.1696				
Phecode 590: "Pyelonephritis"	2.3597	10.59	4.44	25.23	< .001
Phecode 591: "Urinary tract infection"	1.9223	6.84	5.16	9.05	< .001
Phecode 592.X: "Cystitis," "Urethritis," "Urethral stricture due to infection"	1.7764	5.91	3.6	9.7	< .001
Phecode 599.X: Various symptoms involving the urinary system	1.1322	3.1	2.36	4.09	< .001
At least 1 antibiotic prescribed between 2–30 d after surgery	1.2781	3.59	2.58	5	< .001
Laboratory procedure: Urine culture	1.6599	5.26	3.78	7.32	< .001
Laboratory procedure: *Clostridioides difficile* PCR	0.4246	1.53	0.92	2.55	0.1
Sepsis					
(Intercept)	−7.2263				< .001
Phecode 540.X: "Acute appendicitis," "Appendicitis," "Appendiceal conditions"	2.0447	7.73	5.53	10.79	< .001
Phecode 994.X: "Sepsis," "SIRS"	2.4980	12.16	9.23	16.02	< .001
At least 1 antibiotic prescribed between 2–30 d after surgery	1.6909	5.42	4.14	7.11	< .001
Laboratory procedure: CBC auto diff	1.3637	3.91	2.07	7.38	< .001
Laboratory procedure: Blood culture	1.9005	6.69	5.36	8.34	< .001
Laboratory procedure: Magnesium serum	1.2173	3.38	2.65	4.30	< .001
Laboratory procedure: Peripheral blood smear	1.4547	4.28	3.00	6.12	< .001
Pneumonia					
(Intercept)	−7.3366				
Phecode 480.X: Bacterial, viral, and fungal pneumonias	2.5952	13.4	9.17	19.57	< .001
Phecode 501: "Pneumonitis due to inhalation of food or vomitus"	1.7072	5.51	3.03	10.03	< .001
Phecode 1013: "Asphyxia and hypoxemia"	0.9214	2.51	1.67	3.78	< .001
At least 1 antibiotic prescribed between 2–30 d after surgery	1.812	6.12	3.59	10.44	< .001
Laboratory procedure: Magnesium serum	0.7905	2.2	1.37	3.56	.001
Laboratory procedure: Vancomycin trough	0.9937	2.7	1.84	3.96	< .001
Laboratory procedure: Respiratory culture	1.4024	4.06	2.52	6.55	< .001
Laboratory procedure: Blood gasses	1.511	4.53	3.02	6.79	< .001

CBC, complete blood count; *LCL*, lower confidence limit; *OR*, odds ratio; *PCR*, polymerase chain reaction; *SIRS*, systemic inflammatory response syndrome; *UCL*, upper confidence limit.

Data-driven infection diagnosis



Applications of data-driven infection diagnosis

Prediction of serious bacterial infection

Early detection of septic shock

Early detection of serious bacterial infection

Highlight for specialist input

Learning health system

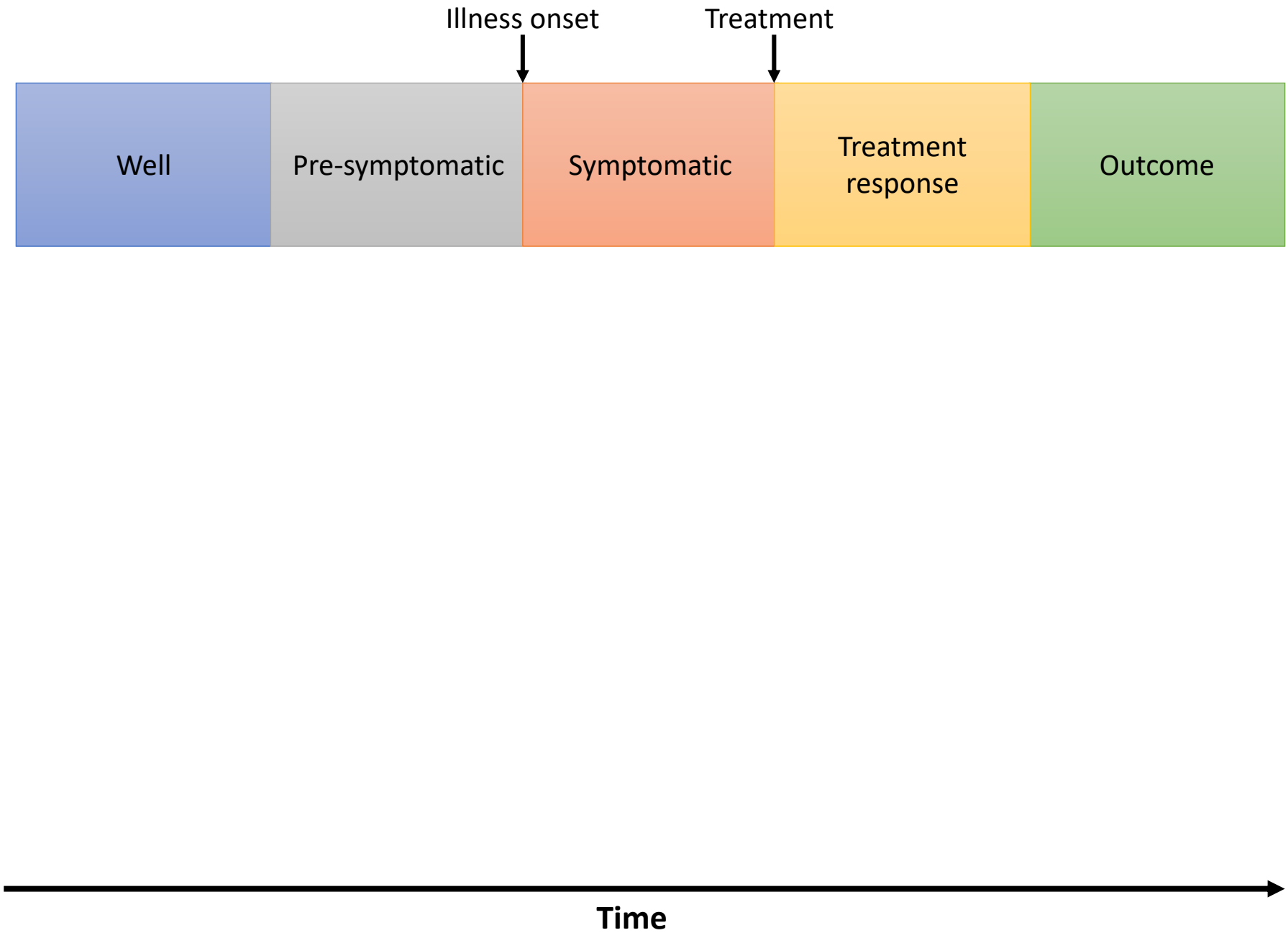
Prediction of sepsis

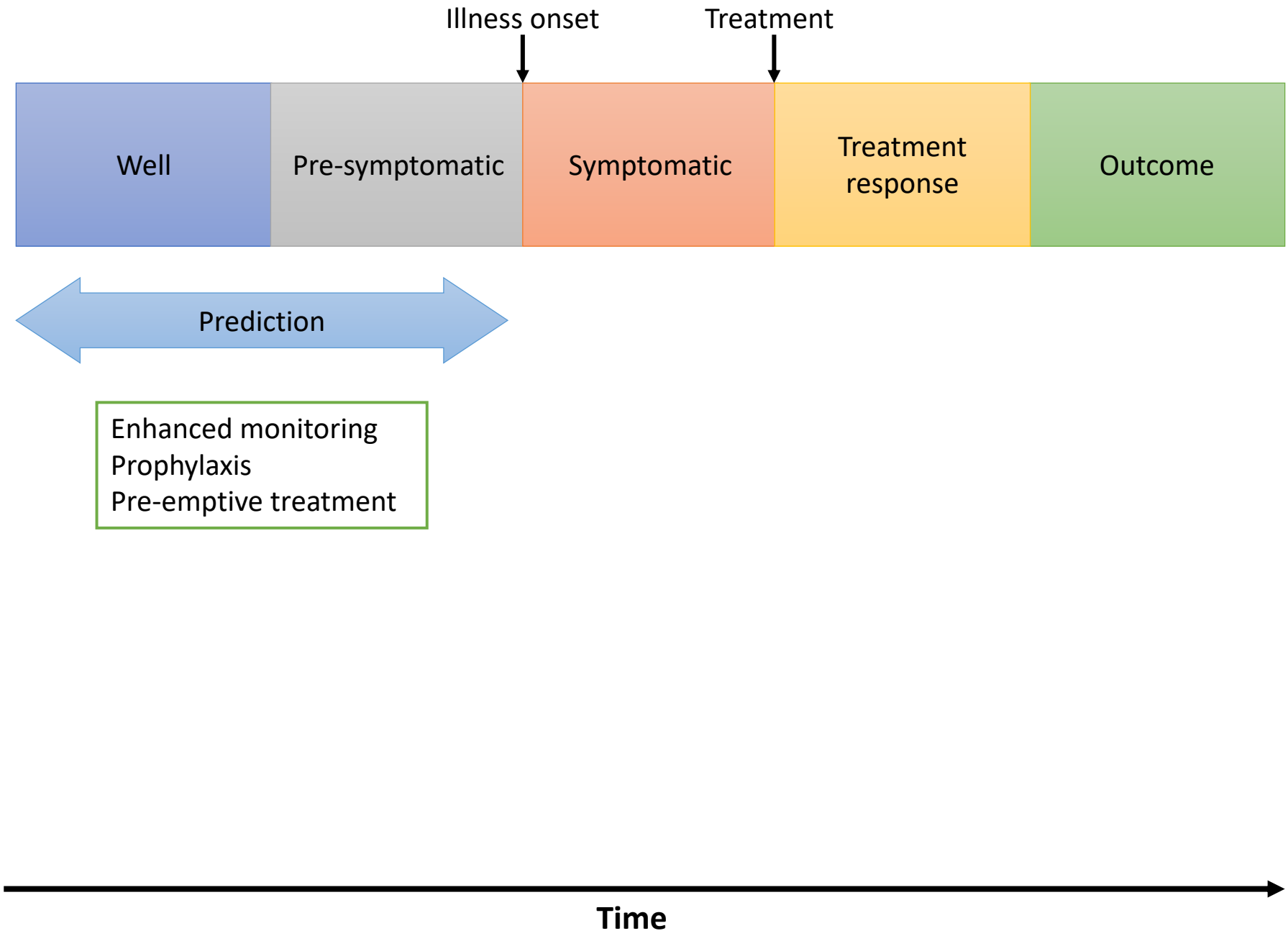
Early rationalisation of antibiotics

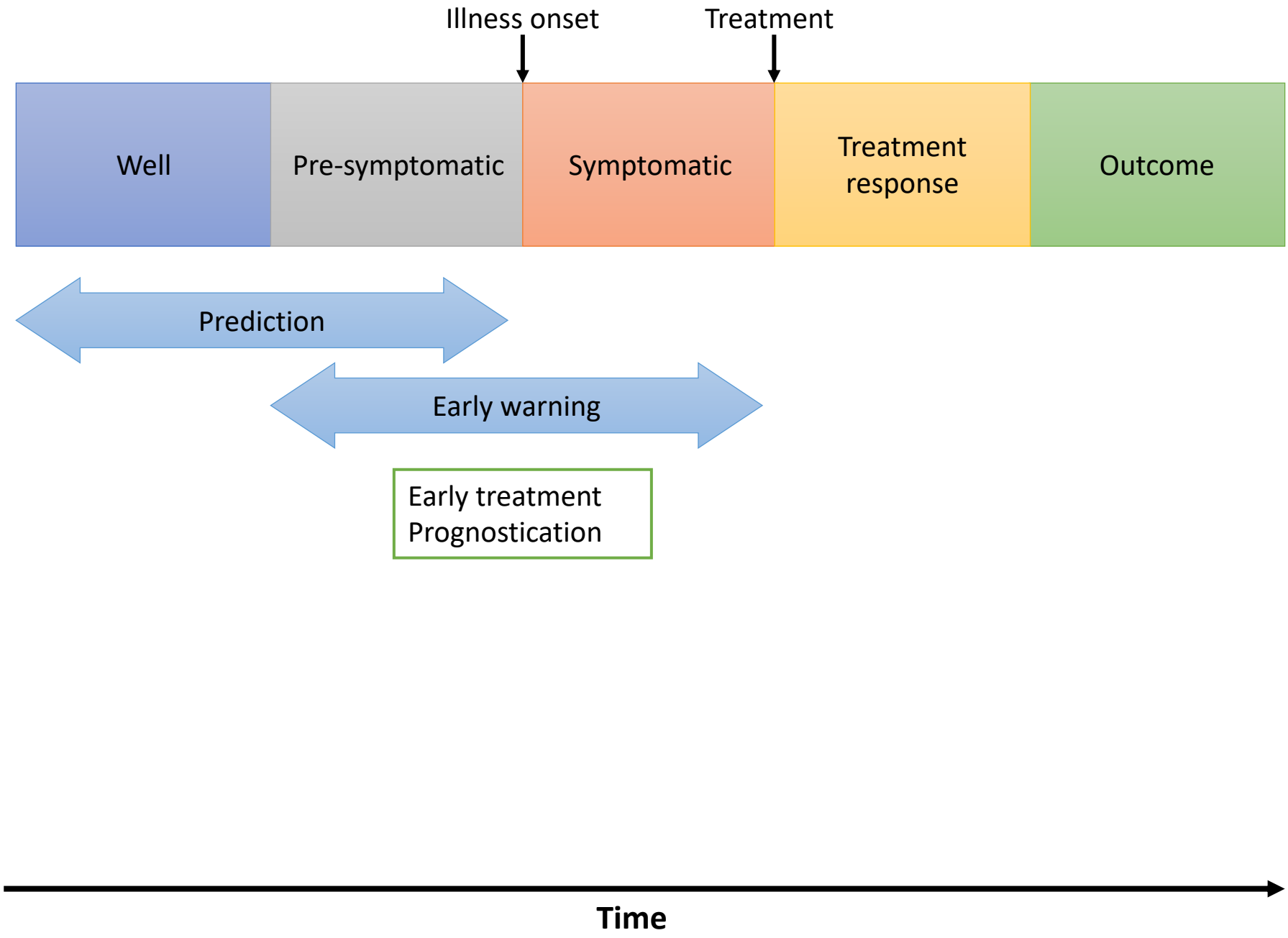
Outbreak detection

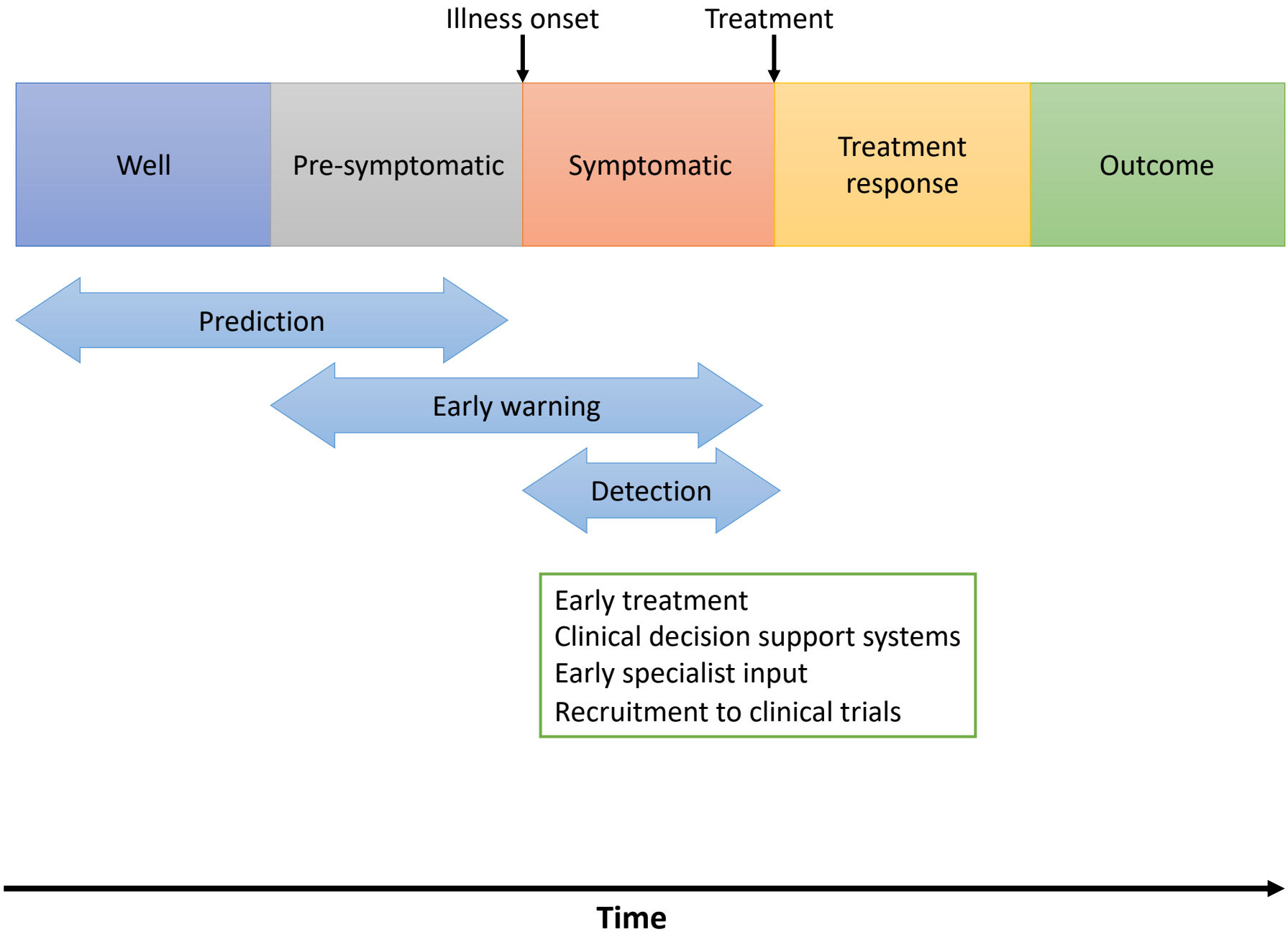
Early recruitment to clinical trials

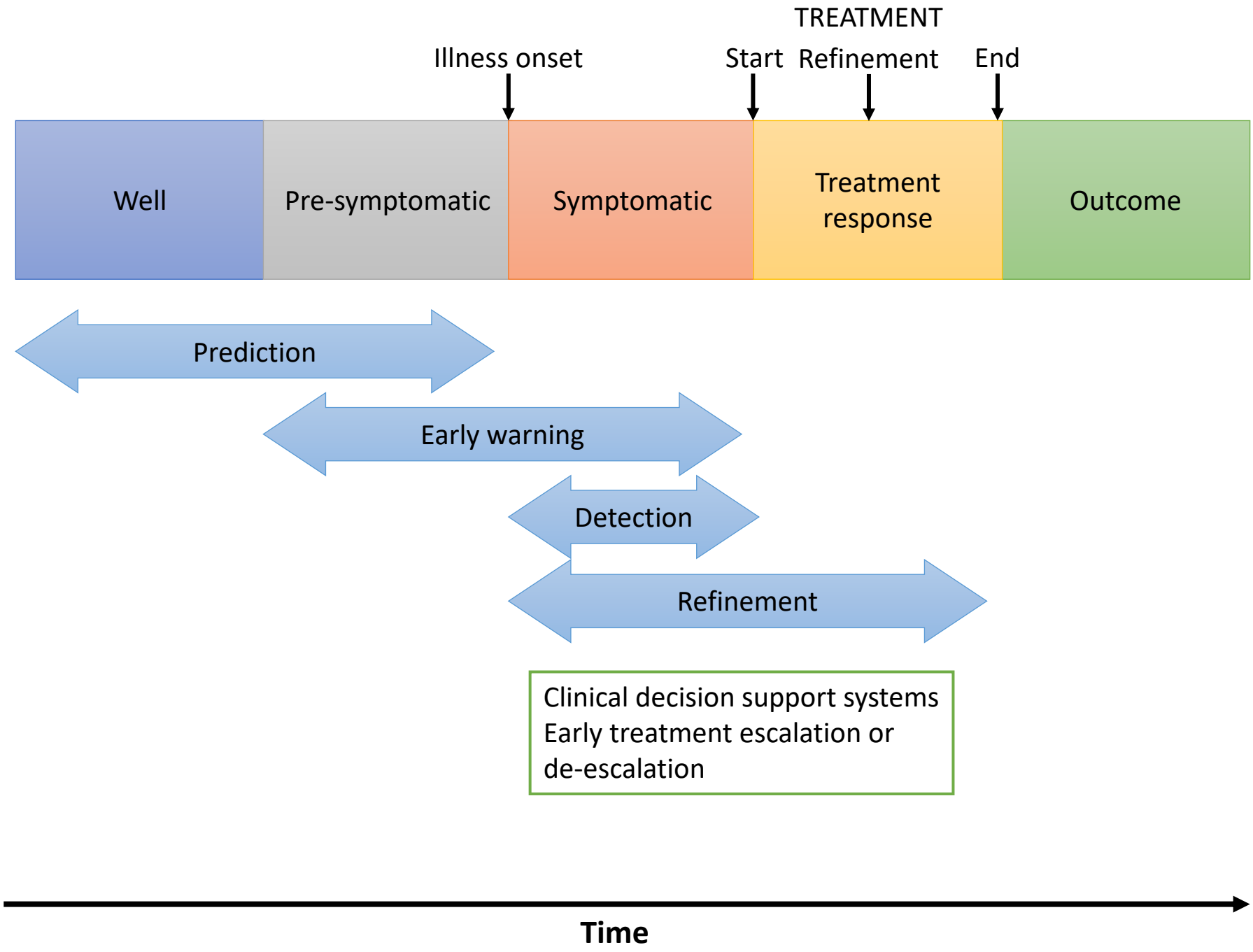
Service monitoring and evaluation

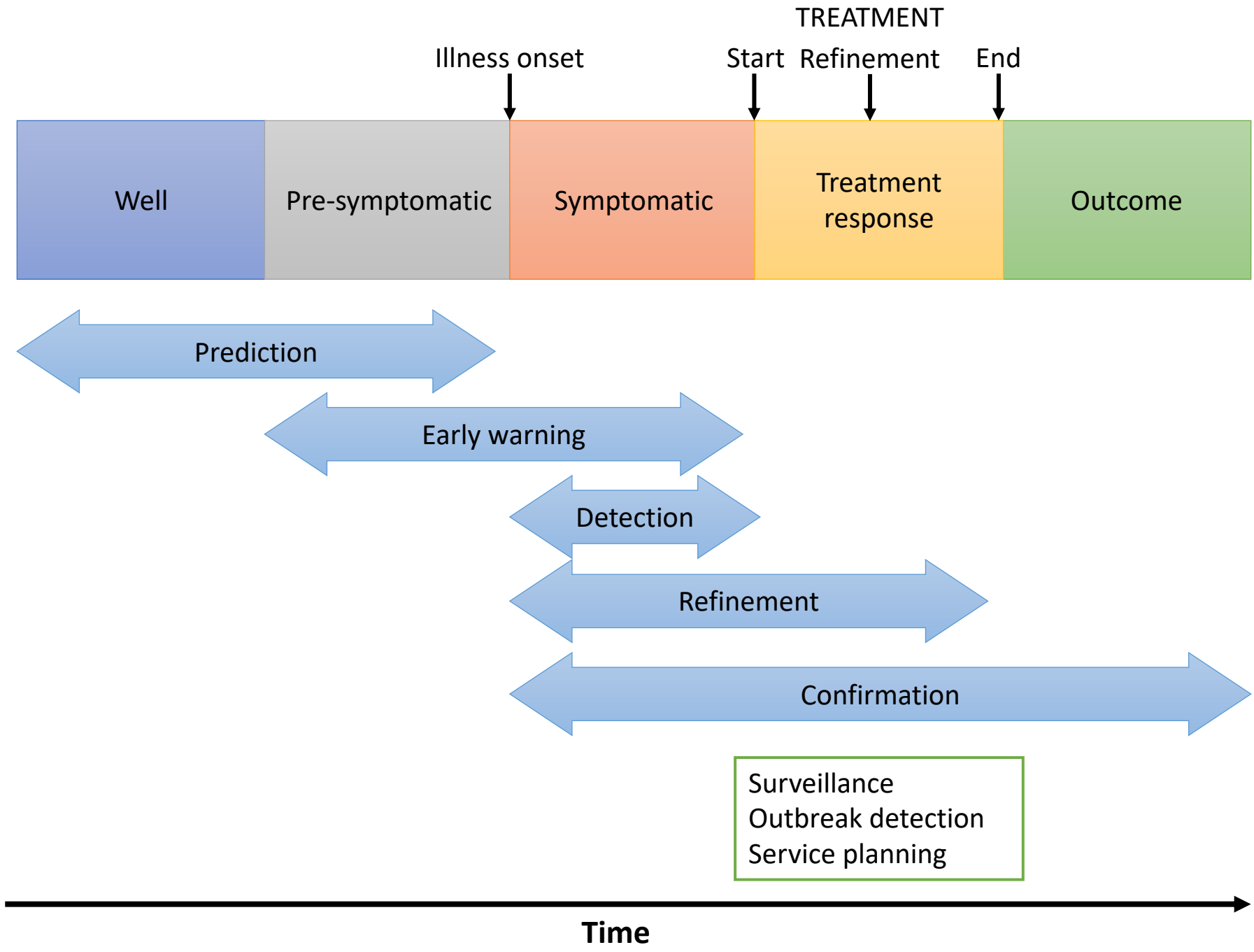

Illness onset
Treatment
Well
Pre-symptomatic
Symptomatic
Treatment response
Outcome
Time


Illness onset
Treatment
Well
Pre-symptomatic
Symptomatic
Treatment response
Outcome
Prediction
Enhanced monitoring
Prophylaxis
Pre-emptive treatment
Time


Illness onset
Treatment
Well
Pre-symptomatic
Symptomatic
Treatment response
Outcome
Prediction
Early warning
Early treatment
Prognostication
Time


Illness onset
Treatment
Well
Pre-symptomatic
Symptomatic
Treatment response
Outcome
Prediction
Early warning
Detection
Early treatment
Clinical decision support systems
Early specialist input
Recruitment to clinical trials
Time


TREATMENT
Illness onset
Start
Refinement
End
Well
Pre-symptomatic
Symptomatic
Treatment response
Outcome
Prediction
Early warning
Detection
Refinement
Clinical decision support systems
Early treatment escalation or de-escalation
Time


TREATMENT
Illness onset
Start
Refinement
End
Well
Pre-symptomatic
Symptomatic
Treatment response
Outcome
Prediction
Early warning
Detection
Refinement
Confirmation
Surveillance
Outbreak detection
Service planning
Time

Applications of data-driven infection diagnosis

Pre-treatment initiation applications

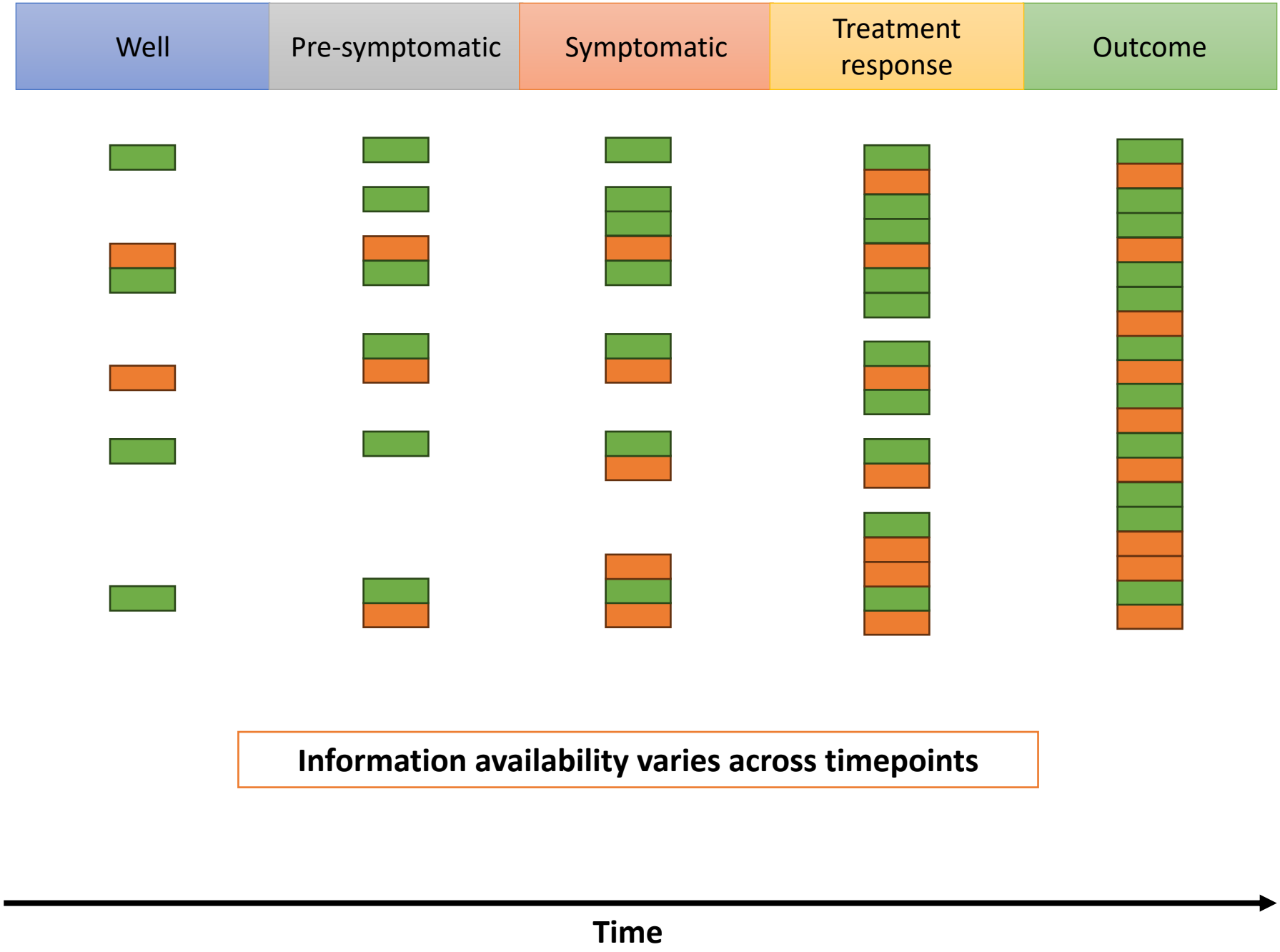
- Prediction of serious bacterial infection
- Prediction/Early detection of deterioration e.g. sepsis or septic shock
- Early detection of serious bacterial infection

Post-treatment initiation applications

- Early rationalisation of antibiotics
- Early specialist input
- Recruitment to clinical trials

Delayed applications

- Surveillance and cluster detection
- Service monitoring and evaluation
- Learning health system


Well
Pre-symptomatic
Symptomatic
Treatment response
Outcome
Information availability varies across timepoints
Time

Prediction time frames

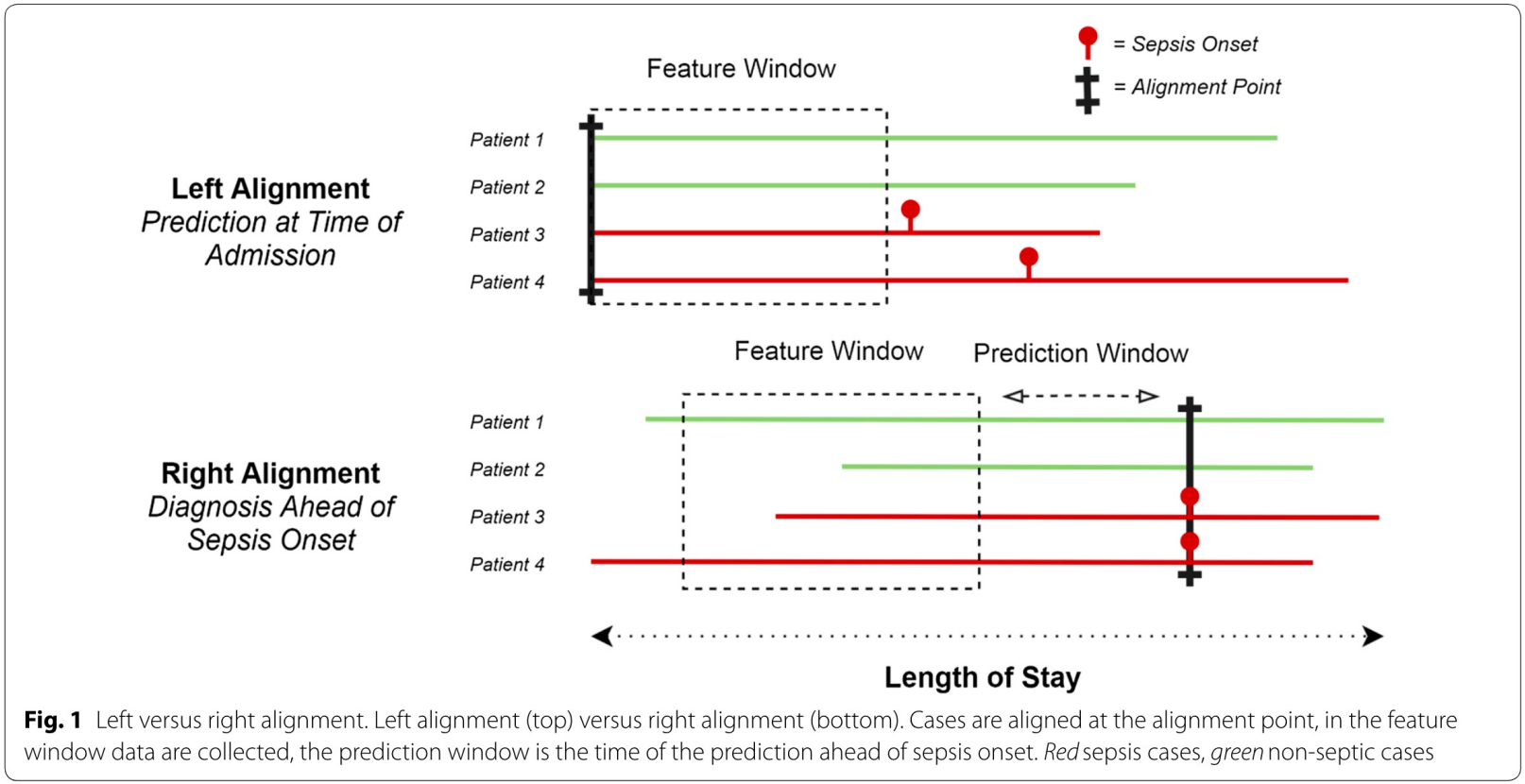
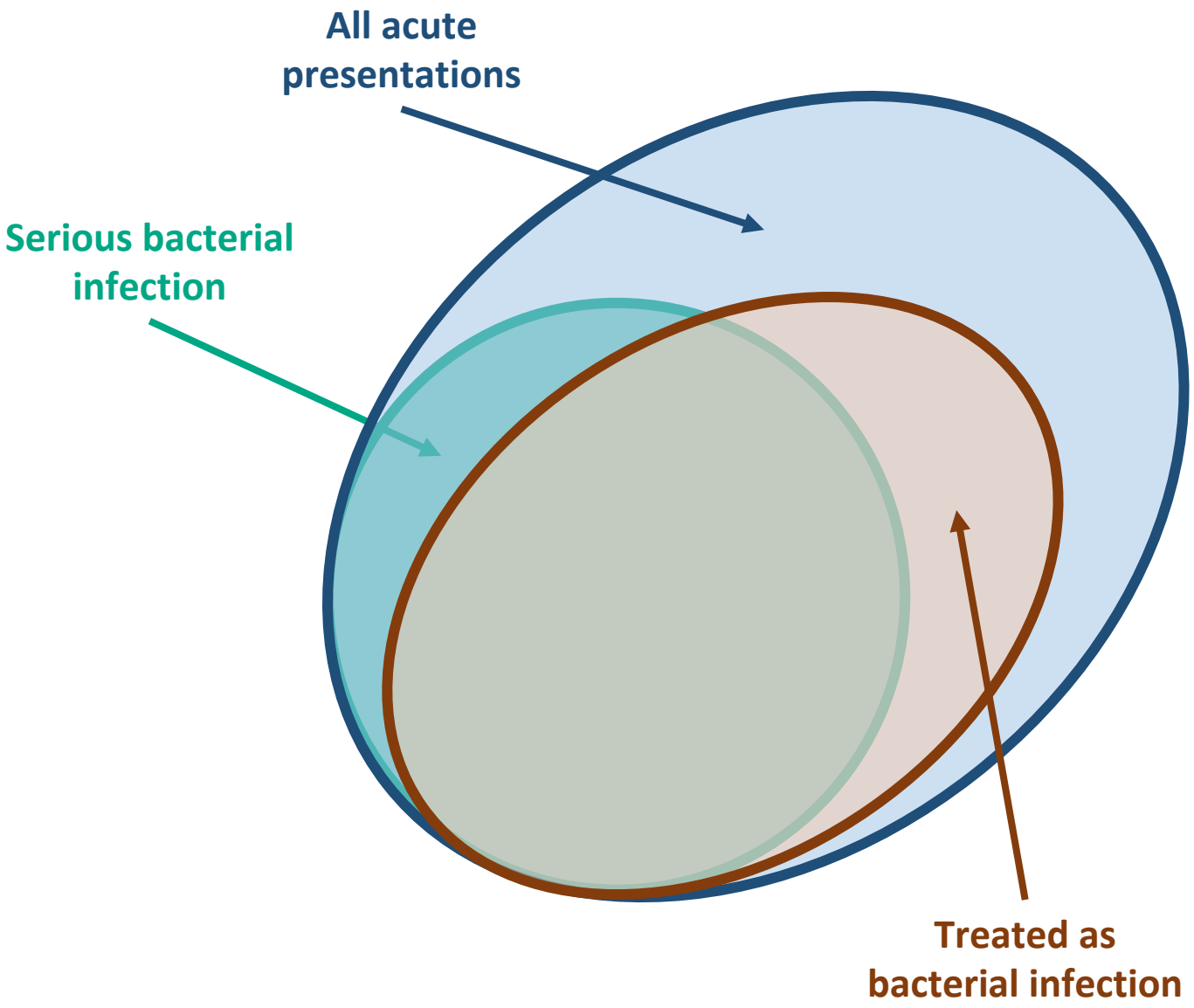


Fig. 1 Left versus right alignment. Left alignment (top) versus right alignment (bottom). Cases are aligned at the alignment point, in the feature window data are collected, the prediction window is the time of the prediction ahead of sepsis onset. *Red* sepsis cases, *green* non-septic cases

Fleuren *et al., ICM* 2020

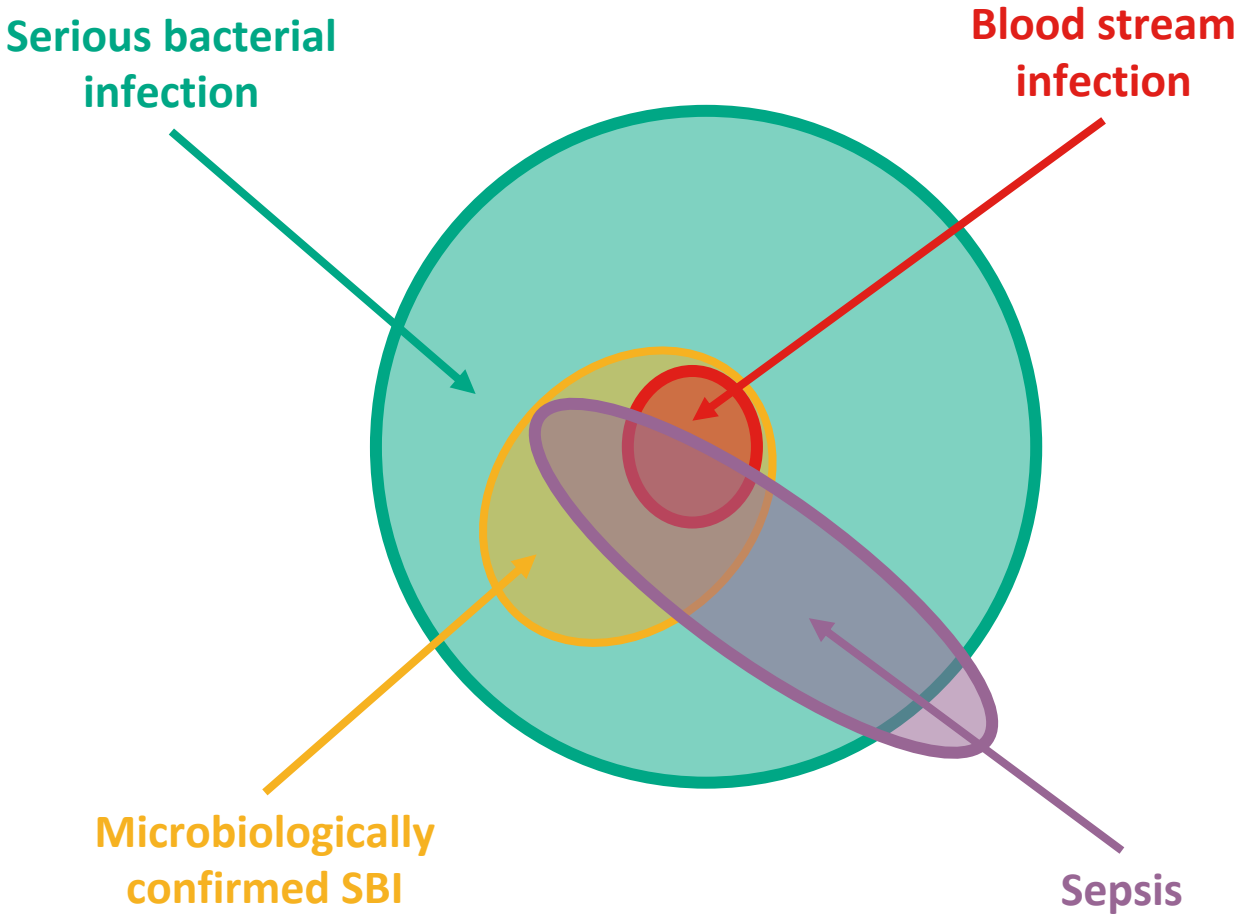
Defining serious bacterial infections



All acute presentations & **treated as bacterial infection** define relevant sampling frames (i.e. derivation populations) for model development.

Need to define **extractable EHR proxies** of **serious bacterial infection** to define reference standard.

Defining serious bacterial infections



Possible extractable EHR proxies:

Serious bacterial infection?

Microbiologically confirmed?

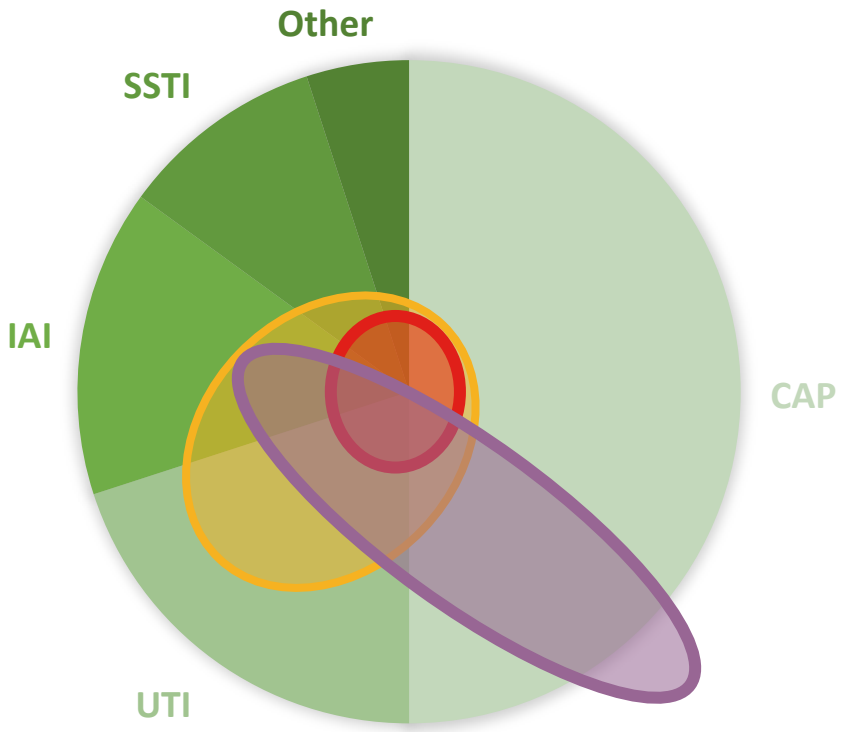
Blood stream infection?

Sepsis?

Linder *et al., Lancet Digital Health* 2023

Defining serious bacterial infections

Common infection syndromes



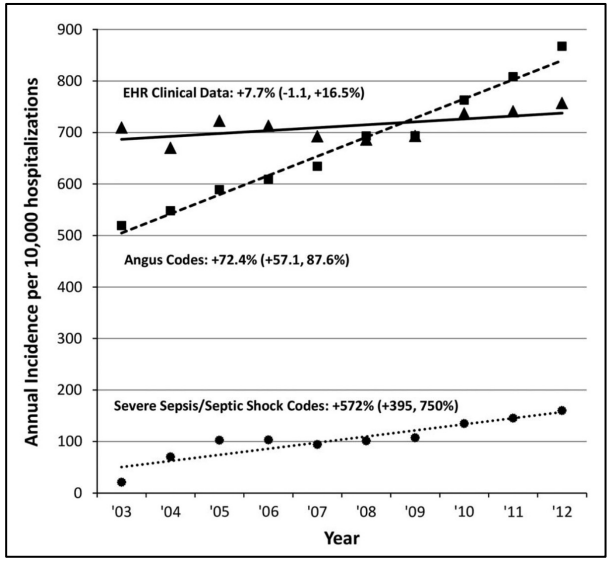
Defining serious bacterial infections

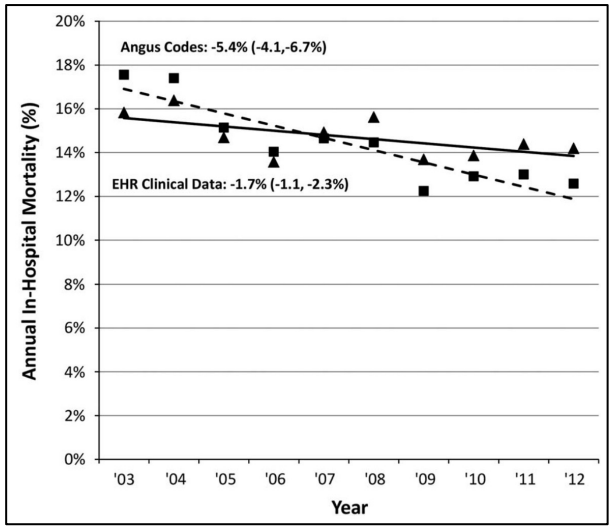
Table 2 Target condition definitions per paper per setting

			Components of sepsis definition					
	Paper	**Target condition definition as reported**	**ICD**	**SIRS**	**SOFA**	**AB**	**Cult**	***Grouped***
ED	*Sepsis*							
	Delahanty et al	- ≥1 sign of acute organ dysfunction[a] - Antibiotic day and organ dysfunction within ±2 calendar days of a blood culture draw						*None*
	Haug et al	- ICD-9 codes						*None*
	Horng et al	- ICD-9 codes						*None*
In-hospital	*Sepsis*							
	Futoma et al	- ≥2 abnormal vital signs[b] - Blood culture drawn for a suspected infection - ≥1 abnormal laboratory value indicating early signs of organ failure						*None*
	Khojandi et al	- ≥2 SIRS criteria - Retrospective manual examination						*None*
	McCoy et al	- ≥2 point change in SOFA criteria - Abnormal white blood cell count alongside an order of antibiotics within a 24-hour period						*None*
	Severe Sepsis							
	McCoy et al	- ≥2 SIRS criteria - ≥2 organ dysfunction lab results[b]						*None*
	Septic Shock							
	Khoshnevisan et al	- ICD-9 codes - Systolic blood pressure < 90 mmHg for at least 1 hour - Mean arterial pressure < 65 mmHg for at least 1 hour - Any vasopressor administration						*None*
	Lin et al	- ICD-9 codes - Systolic blood pressure < 90 mmHg for at least 30 minutes - Mean arterial pressure < 65 mmHg for at least 30 minutes - A decrease in systolic blood pressure >= 40mmHg within an 8-hour period - Any vasopressor administration						*None*
	Thiel et al	- ICD-9 code - Need for vasopressors within 24 hours of ICU transfer						*None*
ICU	*Sepsis*							
	Calvert II et al	- ICD-9 codes - ≥2 SIRS criteria for sepsis for a 5 hour period of time Sepsis onset: beginning of 5 hour period						*Calvert*
	Desautels et al	- ≥2 point change in SOFA criteria - Time of infection: antibiotics between 24 hours prior to and 72 hours after blood culture acquisition Sepsis onset: earliest point of SOFA change						*Seymour (Sepsis-3)*
	Kam et al	- ICD-9 codes - ≥2 SIRS criteria for sepsis for a 5 hour period of time Sepsis onset: beginning of 5 hour period						*Calvert*
	Nemati et al	- ≥2 point change in SOFA criteria 24 hours before and 12 hours after time of infection - Time of infection: antibiotics between 24 hours prior to and 72 hours after blood culture acquisition Sepsis onset: earliest point of SOFA change or time of infection						*Seymour (Sepsis-3)*

Fleuren *et al., ICM* 2020

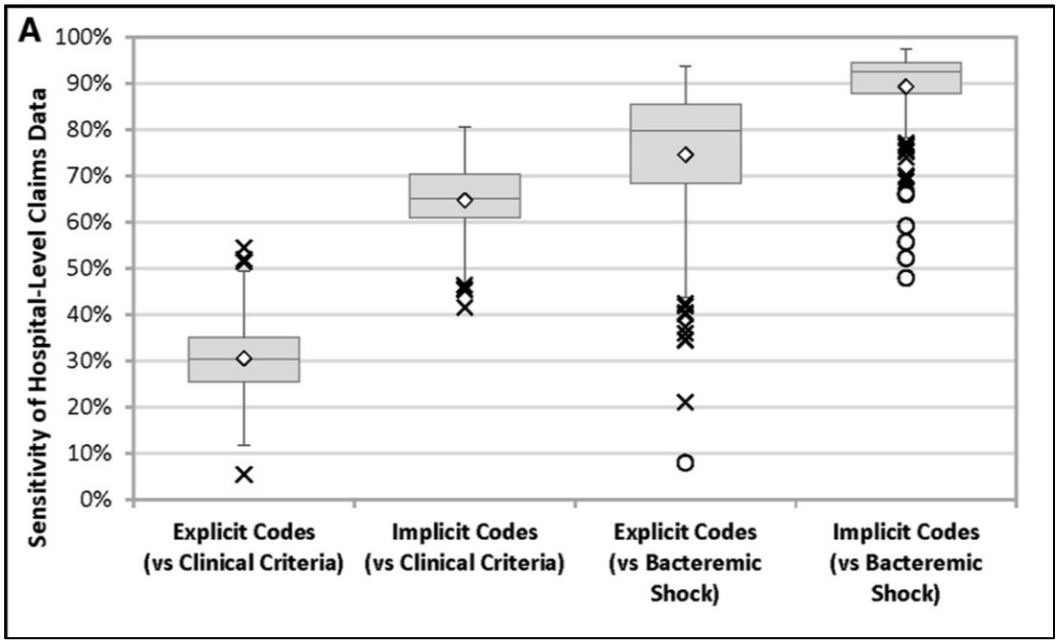
Defining serious bacterial infections





Claims based (or clinical-coding based) diagnoses of sepsis have poor sensitivity verses objective clinical criteria extracted from EHR based on suspicion of infection (cultures and/or (V Abx) and organ dysfunction.

Automatically extracted criteria may 'over call' sepsis if organ dysfunction not attributable to sepsis or 'miss' sepsis if less than defined minimum duration of Abx given.



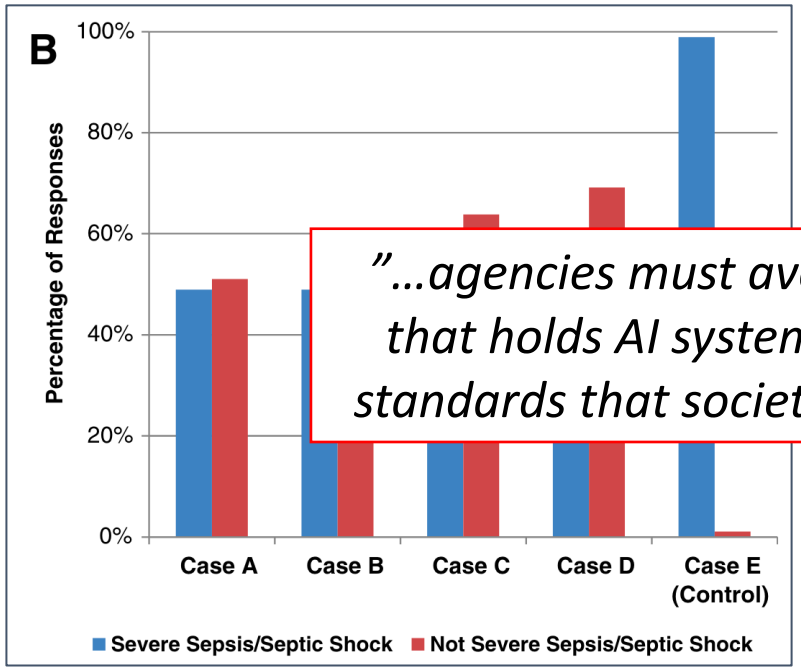
Rhee *et al., Infect Control Hosp Epidemiol* 2016; Rhee *et al., Crit Care Med* 2019

Defining serious bacterial infections

Improving reproducibility of 'ground-truthing' processes

- Increase expertise of graders
- Increase number of graders for each case
- Ensure unbiased disagreement resolution process

Diagnosing sepsis is subjective and highly variable: a survey of intensivists using case vignettes



"…agencies must avoid a precautionary approach that holds AI systems to such an impossibly high standards that society cannot enjoy their benefits."

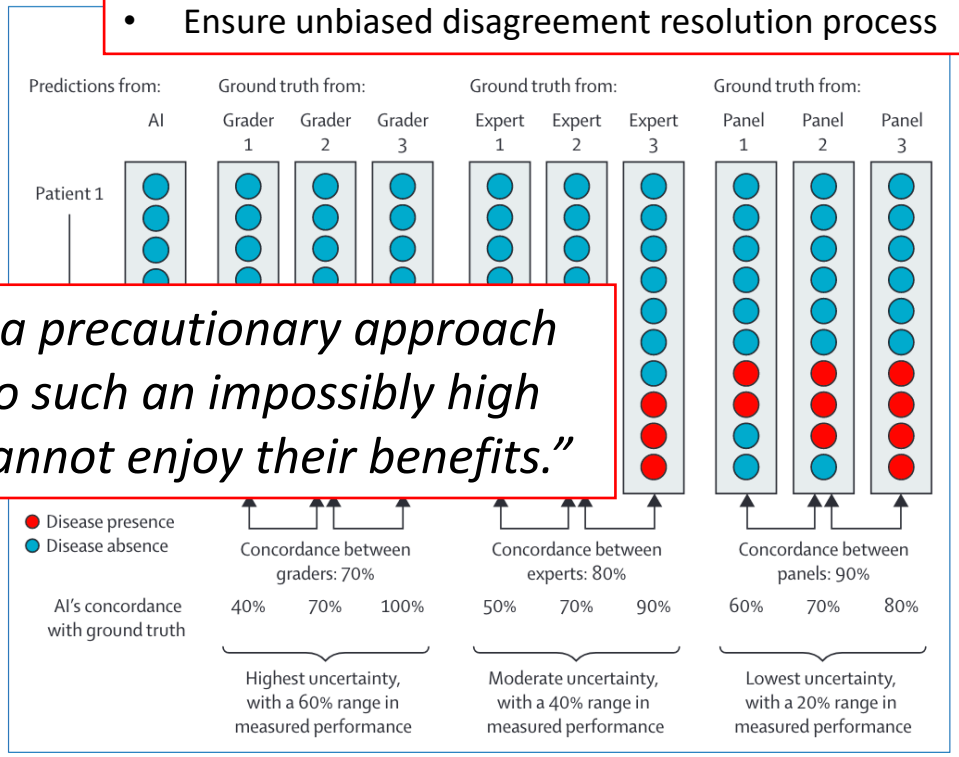


Figure: **AI model evaluation against ground truth from different ground-truthing processes**

Rhee *et al., Crit Care* 2016; Chen *et al., Lancet Digital Health* 2021

Data-driven diagnosis of serious bacterial infection

OVERALL AIM:

Use machine learning approaches to derive and validate data-driven diagnostic signatures of *serious bacterial infection* in patients assessed in emergency departments with clinically-suspected infection.

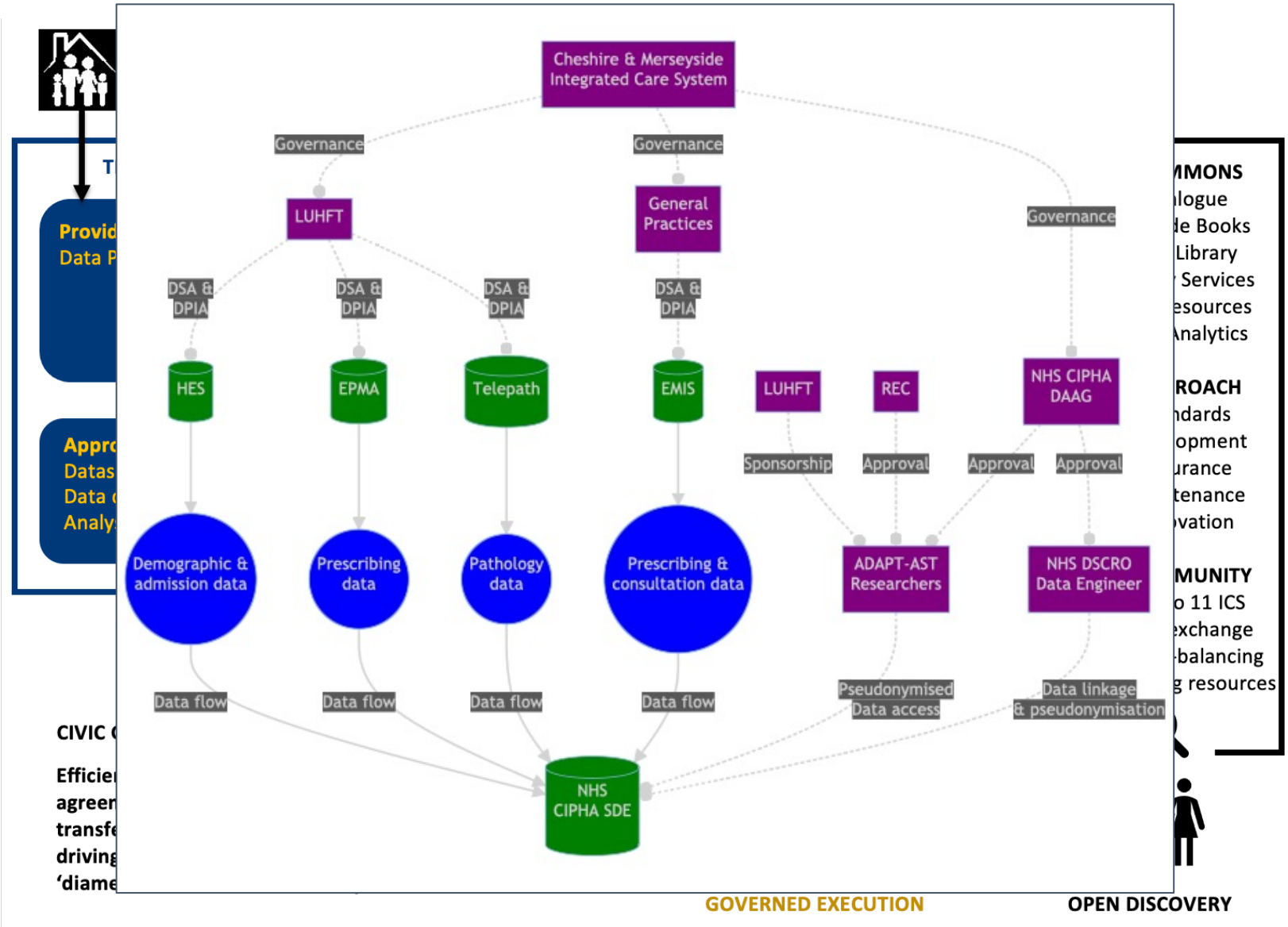
SPECIFIC OBJECTIVES:

- Investigate the impact on model accuracy of utilising different approaches to data labelling of varying resource requirements: clinical coding, microbiological, composite +/- manually curated.
- Investigate the impact on model accuracy of systematically incorporating proxies of existing comorbidities and past medical history.
- Update outcome prediction at key clinical nodes: treatment initiation and treatment review.

EXPLORATORY OBJECTIVES:

- *Explore syndrome specific vs overall SBI models*
- *Derive syndrome specific models for surveillance purposes based on data available at treatment completion*

Liverpool Secure Data Environment – Current configuration



Ainsworth J, Buchan I. Combining Health Data Uses to Ignite Health System Learning. Methods Inf Med. 2015;54(6):479-87

Potential datasets

Dataset	Primary Care	Hospital Care
Demographics	Age, Sex, Residence	Age, Sex, Residence
Administrative	Consultations, Other appointments	Admission, transfer, discharge dates
Clinical coding	Acute and chronic illnesses (READ –> SNOMED-CT)	SUS/HES - Primary and secondary diagnoses (ICD10); Procedural codes (OPCS-4)
Laboratory	Microbiology Other laboratory (infrequent)	Microbiology Other laboratory (monitoring)
Observations	?	Triage and routine monitoring
Prescribing	Acute and recurrent	Inpatient and TTOs
Standard Forms	N/A	Standard assessments (e.g., VTE, MUST)
Free text	Consultation notes	Clinical notes ?exceptions e.g. triage assessment, radiology requests

Sampling frame

General criteria for data use

Inclusion criteria

Adult aged >=18 years **AND**

Admission to LUHFT acute hospital site between 1st April 2017 and 31st October 2023 **AND**

Complete consultant episodes registered on patient administration system.

Exclusion criteria

Registered 'opt out' from use of medical records for population health and research purposes

Analysis specific criteria: *Identify any serious bacterial infection in those with clinically suspected / possible infection*

At least ONE of the following must be present to identify record as possible infection:

At least one antibiotic prescription (excluding prophylatic antibiotics) **OR**

A blood culture request **OR**

Clinical coding diagnosis for infection syndrome **AND** Inpatient death

Analysis specific criteria: *Identify serious bacterial infection in all acute attendees*

Use general criteria

Considerations

Clinician pre-existing biases in preselected suspected infection population.

Class imbalance and less clinically-applicable in all-comer group.

Reference Standard: Any serious bacterial infection

Reference standard	Proposal	Advantages	Disadvantages
Bloodstream infection	Significant pathogen, excluding contaminants	Objective Straightforward	Insensitive Restricts sampling frame to patients with cultures
Microbiology	As per Lee paper minus sepsis criteria	EHR extractable	Insensitive Restricts sampling frame to patients with cultures
Clinical coding	Explicit codes for sepsis plus major infection codes (SOS bundle)	EHR extractable	Uncertain and variable accuracy
Composite	As per Lee including sepsis criteria +/- physiology & biomarker response	Potentially EHR extractable	Circularity bias
Clinician adjudicated	Manual notes review with bespoke extraction tool with interrater agreement in sample vs. all	Robust, clinically credible	Hugely laborious for ?limited gain; inconsistency; information governance – re-identification loops

Performance Evaluation Measures

Diagnostic accuracy at baseline – Pre-treatment initiation
Sensitivity, Specificity, AUROC, PPV, NPV, Precision-Recall
Diagnostic accuracy at treatment review – 48-72 hour node
Sensitivity, Specificity, AUROC, PPV, NPV, Precision-Recall Optimise calibration for low risk strata
Model diagnostics
Feature importance assessment – Added value of comorbidity data?

Data parameters - Feature set

	Variables
Demographics	Age, Sex, LSOA, Ethnicity
Administrative	Admit date, time, location
Clinical coding	See next
Microbiology	Prior urine, blood, sputum, sterile site samples last 6 months: specimen date, type, culture, organism code; specimen specific details
Other laboratory	Hb, Plt, WCC, Neut, Lymph, Mono, Na, K, Urea, Creat, eGFR, ALP, ALT, Bil, GGT, INR, PT, APTT, Lactate, pH, HCO3, paO2, PaCO2, Glucose, Albumin, Ca, PO4, Mg (First, Min, Max, Mean, Median)
Observations	Temp, HR, RR, FiO2, SBP, DBP, Sat, AVPU (First, Min, Max, Mean, Median)
Prescribing	Acute & Recurrent prescriptions last 6 months

Considerations

Assess full and limited feature sets -> ease of implementation

Data cleaning, scaling and imputation approach?

Categorising past medical history

- **Pre-defined and selected comorbidities**
  - Literature review and expert consensus
- **Data-driven approach**
  - All codes
- **Composite measures**
  - Charlson comorbidity index
  - Elixhauser Method
  - Comorbidity count – Weighting?

Primary care - Pre-existing code (e.g. OPEN Safely) mapping SNOMED-CT to broad diagnoses e.g. chronic liver disease.

Secondary care – Analogous packages for HES?

Machine learning approach

- Preferred Supervised ML approaches – to be determined
  - Multiple data types
  - High dimensionality
  - Repeated measures - Infection risk calculated at baseline and 48-72 hours.
    - Dynamic vs static windows/nodes
- Chief considerations
  - Interpretability
  - Non-linear associations
  - Implementation
    - Assess limited models – based on reduced parameters
    - Assess added values of comorbidity data – requires more complex data integration.

Discussion points

- What is the optimal sampling frame?
  - All comers or suspected infection?
- Tackling the reference standard problem
  - Data driven approaches to dealing with labelling uncertainty
  - Semi-supervised approaches
- How to best utilise prior comorbidity and infection treatment information
- Any value in tackling syndrome specific diagnostic models
  - Relevant to stewardship
  - Important for surveillance - > learning health systems
- Approach to incorporating information accrued after initial treatment initiation node?
  - Dynamic vs static nodes