OHIO HOSPITAL ASSOCIATION

EARLY WARNING SYSTEM FOR TIMELY ANTIBIOTIC ADMINISTRATION

November 17, 2021

CONTINUING EDUCATION

- The link for the evaluation of today's program is: https://www.surveymonkey.com/r/Sepsis-Nov21

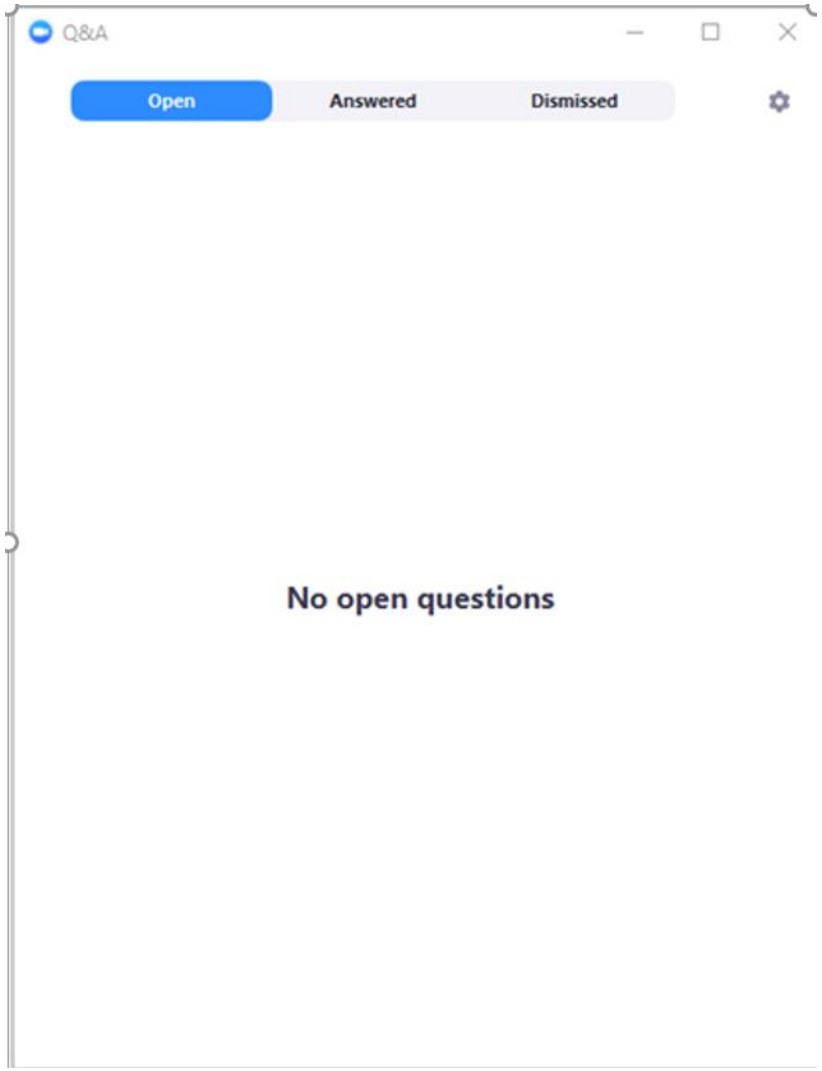
- Please be sure to access the link, complete the evaluation form, and request your certificate. The evaluation process will remain open **two weeks** following the webcast. Your certificate will be emailed to you when the evaluation process closes after the 2-week process.

- If you have any questions, please contact Dorothy Aldridge (Dorothy.Aldridge@ohiohospitals.org)

SEPSIS WEBSITE

ohiohospitals.org/sepsis

SUBMITTING QUESTIONS



PRESENTER

Division of Pulmonary and Critical Care Medicine
Director of Clinical Informatics for Research Support
The MetroHealth System

Assistant Professor of Medicine, School of Medicine
Case Western Reserve University

Surviving sepsis, with help from an EHR-integrated early warning system: A randomized controlled quality improvement initiative

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Director of Clinical Informatics for Research Support
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Disclosures / Conflicts of Interest

- Research funding and consulting fees from Danaher.

- The study was designed and implemented *after* the introduction of the sepsis EWS in our EHR. The vendor had no role in this study beyond the provision of supporting information on the EWS.

MetroHealth

HIMSS Analytics STAGE 7

HIMSS Davies Award
NICHOLAS E. DAVIES

HealthCare's most wired
WINNER 2017

MAGNET RECOGNIZED
AMERICAN NURSES CREDENTIALING CENTER

Better Health Partnership
Collaborating for a healthy community

1
Tertiary Care, Academic, Trauma Center

2
Community Hospitals

4
Emergency Departments

19
Years of data in Epic

25,000
Inpatient Stays per year

140,000
ED Visits per year

1,250,000
Outpatient visits per year

Academic Safety-Net Healthcare System

1st public health care system in US to

- **Install the Epic EHR** (1999)
- **Achieve HIMSS Stage 7 EMRAM using Epic** (2014, 2017)
- **Receive the HIMSS Enterprise Davies award** (2015)

Topics to cover

- Sepsis - how can we do better?
- Can informatics and predictive analytics help?
- Our approach to implementing Epic’s solution.
- The outcome of our randomized controlled quality improvement initiative.

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The tension

Early antibiotics - always good in hindsight

Kumar, Anand, et al. "Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock." *Critical care medicine* 34.6 (2006): 1589-1596.

Liu, Vincent X., et al. "The timing of early antibiotics and hospital mortality in sepsis." *American journal of respiratory and critical care medicine* 196.7 (2017): 856-863.

However…

- Sepsis is ill defined
- Forcing physicians to act faster can have unanticipated consequences
  - => Rushing ED providers raises the risks of misdiagnoses and antibiotic overuse

    (complications that were documented when reducing door to antibiotic time was proposed as a quality measure for community acquired pneumonia in 2007).

Our pre-implementation state – we can *always* do better

- We were not achieving 1 hour response times (controversial).
- We did not have a standardized team-based response to sepsis
- Stakeholders were not always aware of which patients to prioritize
- Sepsis order set utilization was very low (but is that wrong?)

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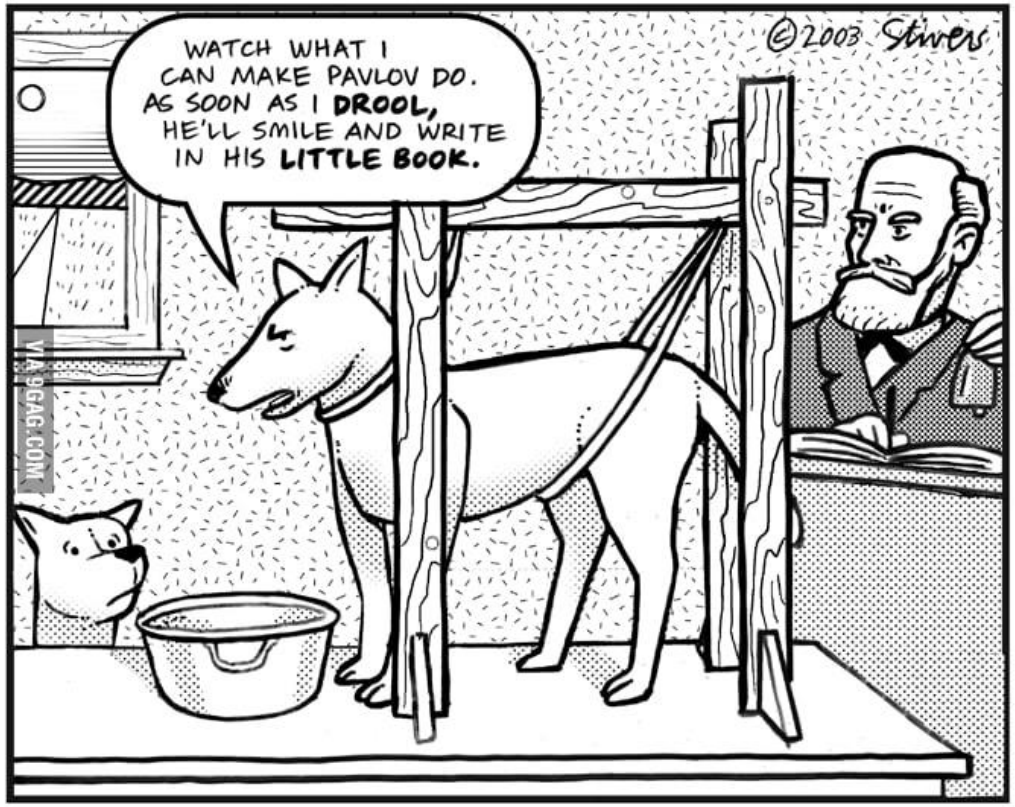
Clinical informatics and predictive analytics to the rescue?

- The complexity of the data involved lends itself to more sophisticated data science approaches
- The drive for **earlier**, **automated detection** of sepsis has prompted the development of
    - rule-based sepsis screening tools and
    - prediction-based early warning systems (EWS)

- **Most** data supporting the use of such systems is in the form of **pre-post intervention** studies associated with improvements in:
    - mortality
    - time to antibiotics
    - and rates of sepsis bundle compliance

Prior data limitations



- Vast majority are retrospective / observational
- Pre-post suffer from Hawthorne effect (e.g. hand hygiene under surveillance)
- Lack of high-quality reference / control group
- Sepsis mortality always goes down historically… ?new processes / standards and overdiagnoses.

Our EHR vendor's solution

- Derived and externally validated, based on penalized logistic regression incorporating several structured EHR variables (demos, vitals, labs, diagnoses and procedures)
    - Gold standard of sepsis: diagnosis + sepsis specific order or a flowsheet completion
    - Model "trigger" was 6 hours before that
    - 405,000 encounters in the derivation / validation set (80/20)
        - AUC = 0.76 - 0.83
        - PPV 16%, NPV 97%
    - Now leveraged by over **100 institutions – but where was the data?**

However….
CDS: Limits and misgivings

- Alert fatigue, workflow disruptions are common

- Clinical improvement with CDS is small to modest at best (Meta-analysis of controlled studies by Kwan et al in 2020).
- Clinicians accept complex solutions, so long as they are perceived to be useful (e.g. Jansen-Kosterink et al, 2021)

CDS + Predictive Analytics = It's complicated

Complicates CDS by combining CDS misgivings with the vagueness of more advanced statistical methodology and opacity of black box solutions (Duran 2021).

End users are:

- Generally interested in prediction-based CDS (Takamine 2021).
- Naturally Bayesian in their thinking (Gill 2005).

However, they:

- Prefer processing "mechanistic" risk factors.
- Struggle with statistical concepts such as sensitivity, discrimination or calibration (Whiting 2015).
- Are worried about exacerbating disparities with more complex models, even when older constructs have the same biases.
    - E.g. Poor pooled cohort equation calibration in more socioeconomically deprived neighborhoods (Dalton 2017).

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What's an institution to do?

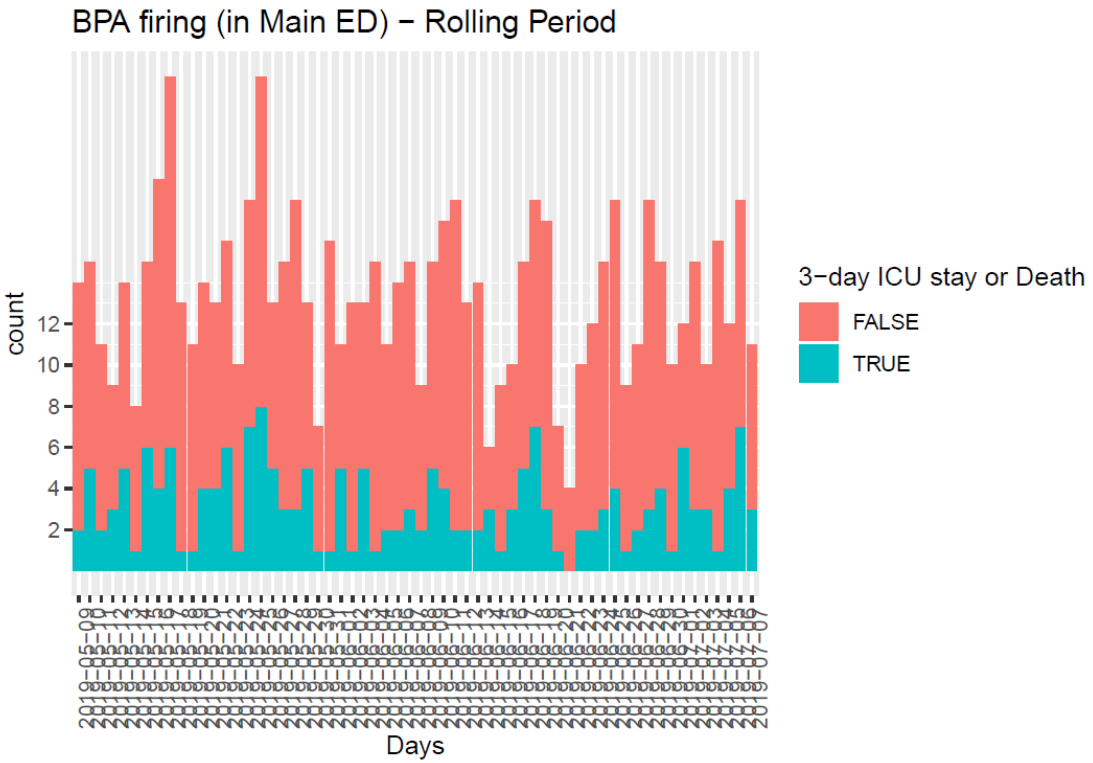
Form a committee!

- Quality
  - Brook Watts (CQO)
- Infectious Disease / Pharmacy
  - Michelle Hecker (Director of Antibiotic Stewardship)
  - Brain McCrate (PharmD)
  - Lewis Hunter (PharmD)
- Emergency Medicine
  - Chuck Emerman (ED Division Chief)
  - Aurelia Cheng (ED sepsis champion)
  - Jonathan Siff (Associate CMIO)
- Clinical Informatics
  - Yasir Tarabichi (Pulm + Director of Research Informatics)
  - David Kaelber (CMIO)
  - David Bar-Shain (Director of Informatics for CDS)

Step 1: Internal Validation

Internal validations elicit confidence for buy-in

- Turn it on in the background (score is calculated whenever chart is touched) – **for 9 months.**
- Silent alert at **<u>proposed threshold (5)</u>** = **1,644 ED encounters**, on average less than 12 times per day.
- Sensitivity of 89.5% and a specificity of 68.4% for the **<u>outcomes of death and/or 3-day ICU stay in patients with suspected infection</u>**.*
- PPV of 27%, NPV of 98%.
- The alert fired before antibiotics were administered 53.6% of the time = **<u>LEAD-TIME OPPORTUNITY</u>**



*Sepsis-3 definition of infection = culture sampling followed by antibiotic administration within 72 hours, or antibiotic administration followed by culture sampling within 24 hours.

Step 2: Design implementation

Deciding to take the plunge

	Sensitivity	Specificity
SIRS >= 2*	91.0	13.0
qSOFA >= 2*	53.6	66.7
MEWS >=5*	59.1	70.1
NEWS >= 7*	76.5	52.7
Epic EWS >= 5	89.5	68.4

*Against same outcomes, as reported in a different study by Churpek et al.

=>

Relatively favorable (and relatable) performance

+

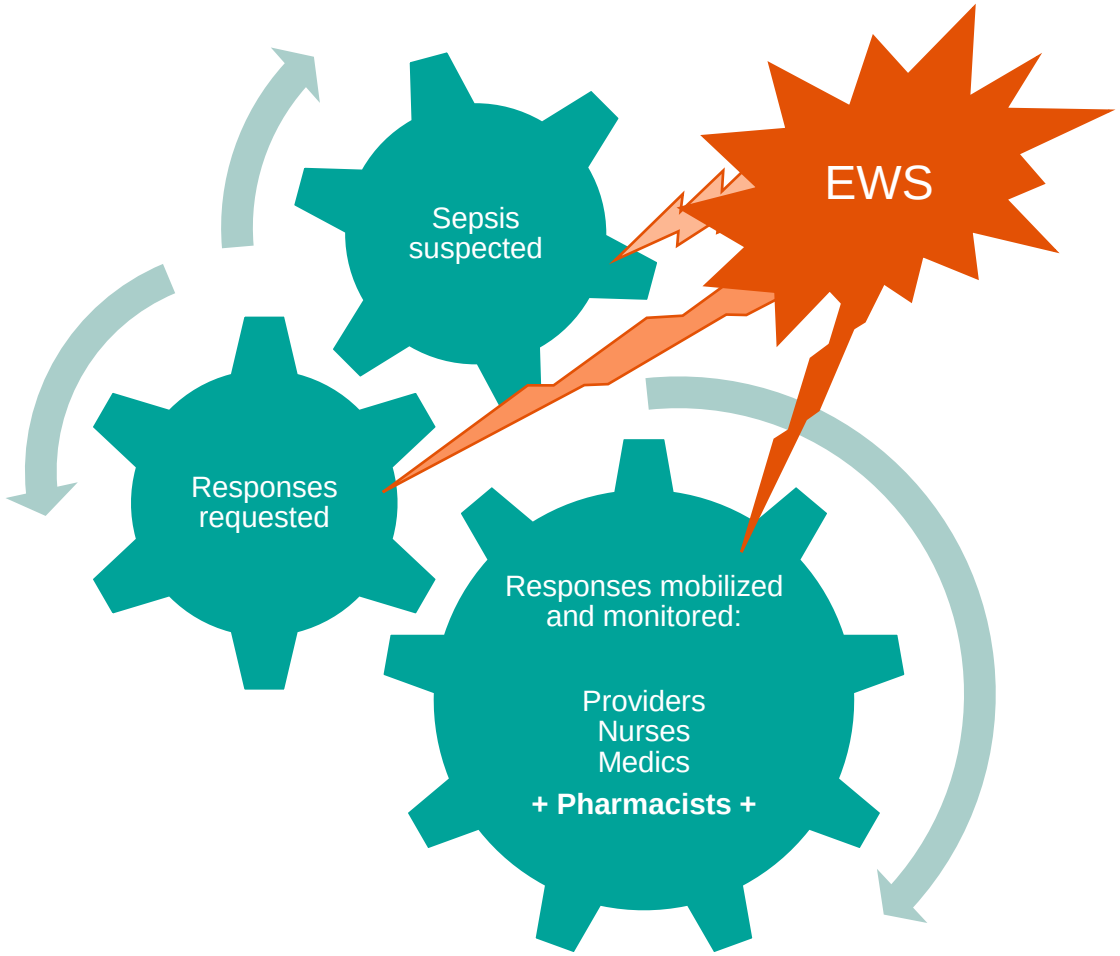
LEAD-TIME OPPORTUNITY

- Based on these favorable characteristics, we are interested in implementation.
- We don't know if this will work in our setting, and fear unanticipated consequences, provider agitation or burnout.
- Implementation resources are limited and the local impact unknown… we want a robust comparison group.
  - Roll out in half the ED?
  - Alternating days?
  - Randomize?

Step 2: Design implementation

Where does the model-based CDS fit?

- Based on available data - time to antibiotics was the agreed upon **process** measure to target.
- We were intent on leveraging **pharmacists** in the process as a result.
- (Figure) The EWS *could* hasten each cog's input as shown, but more importantly provides a common rallying point / trigger for multidisciplinary interaction.
- Alerting mechanism deliberated with stakeholders.

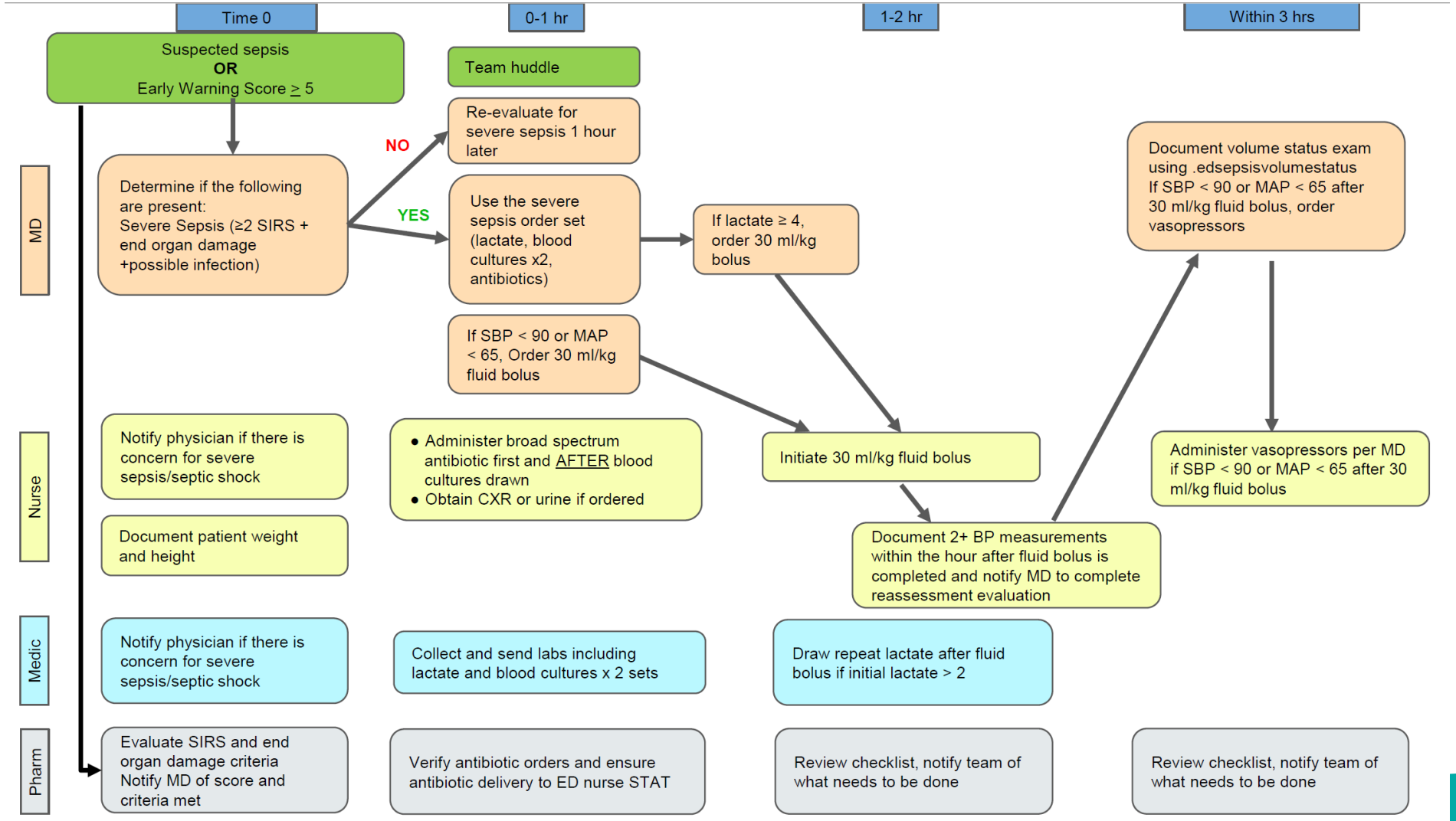


Step 2: Design implementation (continued)

Pre-work:

In conjunction with stakeholders

Integrate pharmacist, standardize responses for all septic patients and educate providers

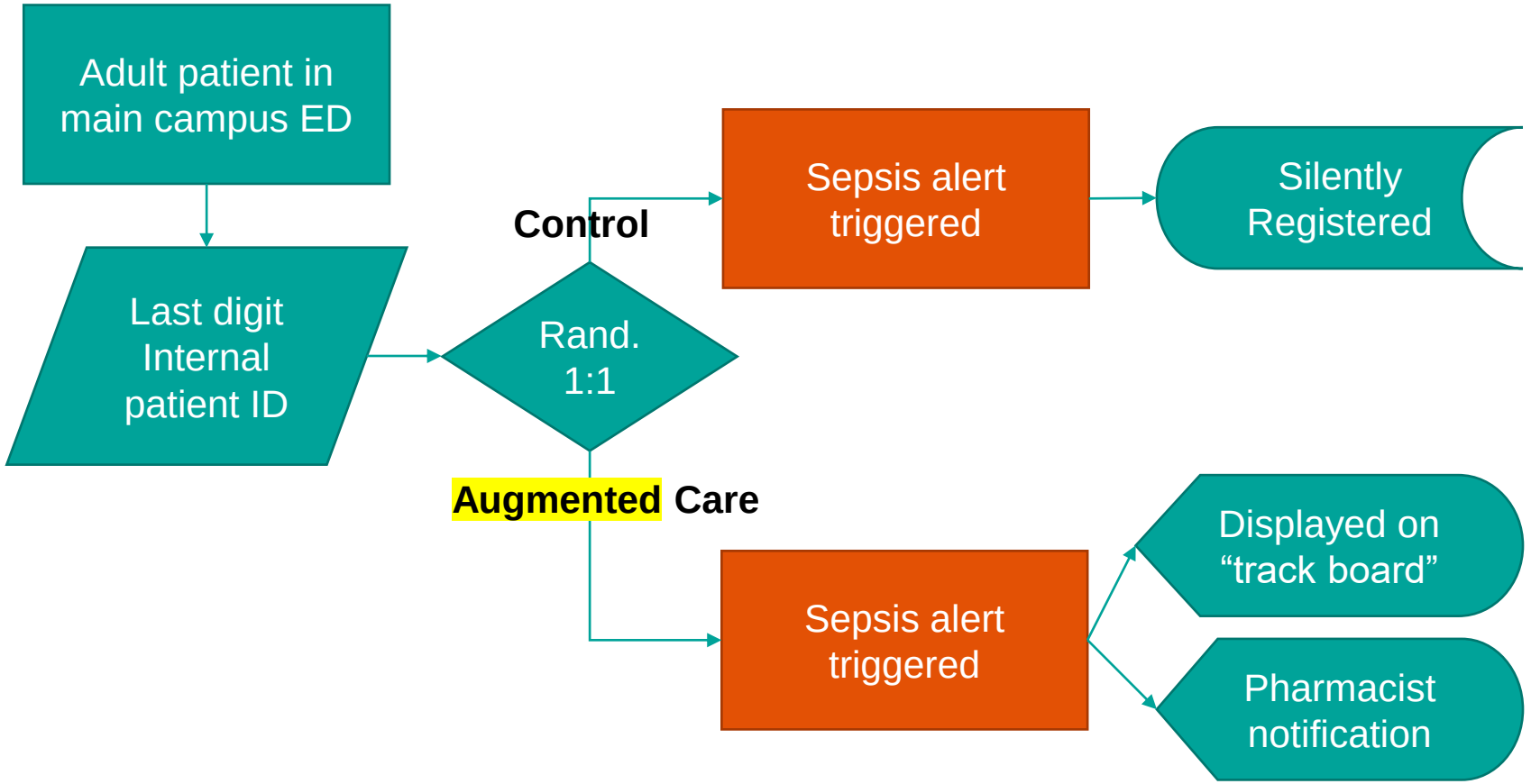


Question:

Will an EHR-integrated, provider and pharmacist facing sepsis early warning system improve sepsis-associated **process measures** (time to antibiotics) and sepsis-associated **outcomes** (days alive and out of hospital) in our ED setting?

Step 2: Design implementation (continued)

EHR pieces / proposed intervention overview



	Private	CC	Sepsis
33 year old Female)	No	Wound Check	—
62 year old Female)	No	Leg/thigh symptoms	—
(33 year old Male)	No	Leg/thigh symptoms; Localized r...	—
(60 year old Female)	No	Shortness of breath	
year old Female)	No	Shortness of breath	—

&

> **Best Practice** 0 unread, 13 total

Status	Subject	Msg Date	Msg Time
? Pend	Early Sepsis Early Warning ...	10/13/2020	12:06 AM
? Pend	Early Sepsis Early Warning ...	10/13/2020	3:11 AM

MetroHealth

Notice Not Human Subject Research

Date: August 12, 2019

To: Yasir Tarabichi

From: Ann Avery, M.D.

RE: IRB19-00558 ED sepsis early warning system: A randomized controlled prospective study

Dear Dr. Tarabichi:

On August 12, 2019, the IRB reviewed the following protocol:

IRB19-00558 ED sepsis early warning system: A randomized controlled prospective study

The IRB determined that the proposed activity is not research involving human subjects as defined by DHHS and FDA regulations.

Please describe the project as "quality improvement" in public presentations, academic curriculum vitae, publications, and any other representations to any third-party audience with a planned statement similar to: "This project was undertaken as a Quality Improvement Initiative at The MetroHealth System."

IRB review and approval by this organization is not required. This determination applies only to the activities described in the IRB submission and does not apply should any changes be made. If changes are made and there are questions about whether these activities are research involving human in which the organization is engaged, please submit a new request to the IRB for a determination.

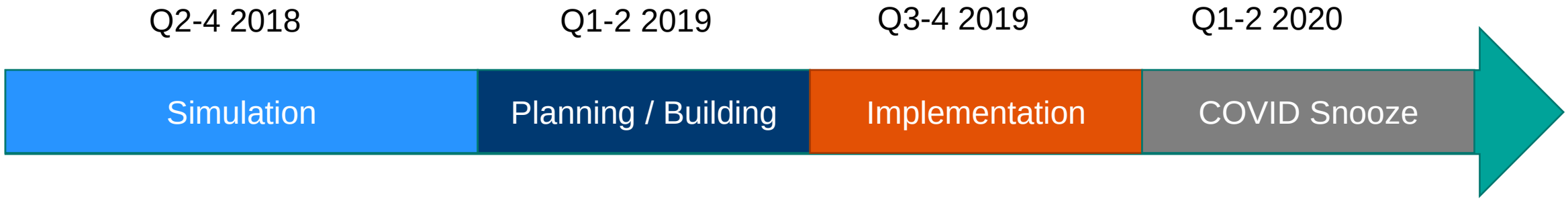
Sincerely,

Ann Avery, M.D.

Step 3: Activate

2 years in the making

- Automated reports that captured data of interest
- Biweekly meetings of data review with multispecialty representation
- Blinded chart review when appropriate



Topics to cover

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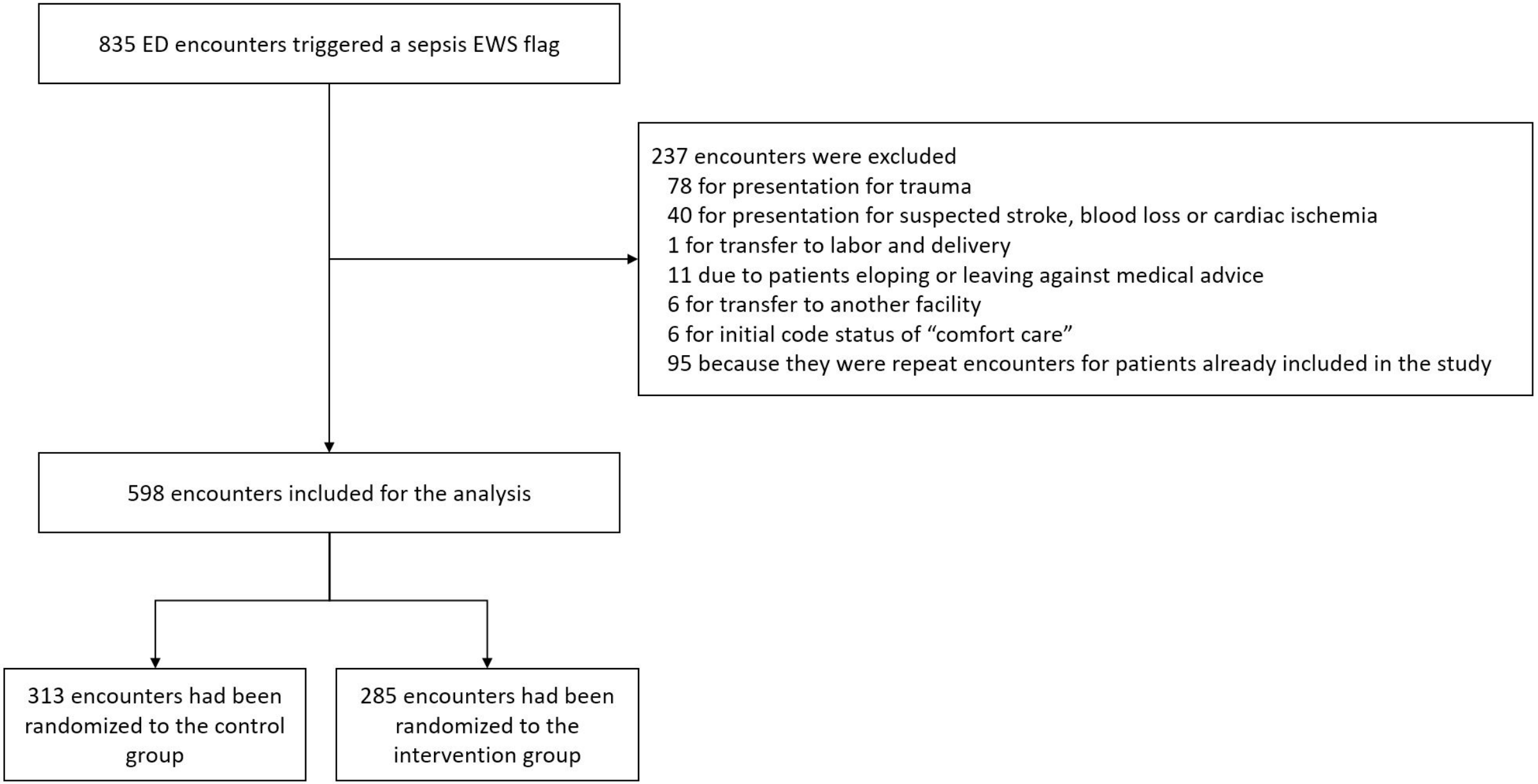
From 8/16/2019- 12/16/2019

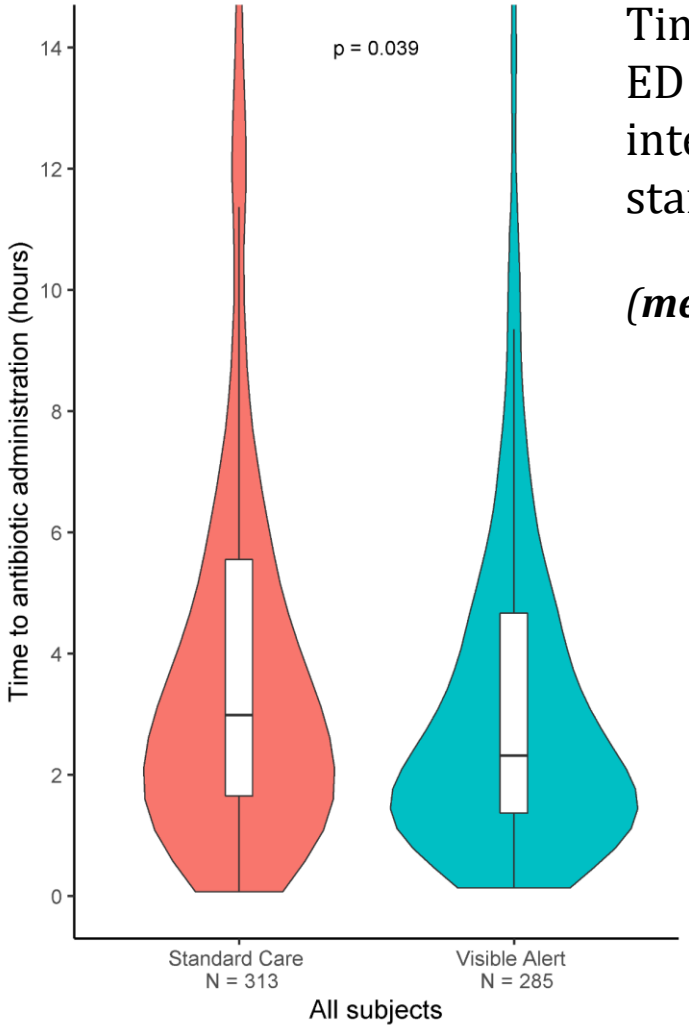
Results: Subjects



Results: Demographics

	Standard Care (N=313)	Augmented Care with Sepsis EWS Alert (N=285)
Age (years)		
Median (IQR)	62.2 (51.3 - 71.8)	61.5 (52.6 - 70.1)
Sex		
Female	144 (46.0%)	146 (51.2%)
Male	169 (54.0%)	139 (48.8%)
Race		
White	183 (58.5%)	150 (52.6%)
Black	108 (34.5%)	107 (37.5%)
Ethnicity		
Non-Hispanic	279 (89.1%)	240 (84.2%)
Hispanic	26 (8.3%)	37 (13.0%)
Weight (kg)		
Median (IQR)	79.9 (63.4 - 99.1)	81.6 (64.2 - 105.6)
Time from admission to alert (hours)		
Median (IQR)	1.2 (0.5 - 2.2)	1.0 (0.4 - 2.1)

Results

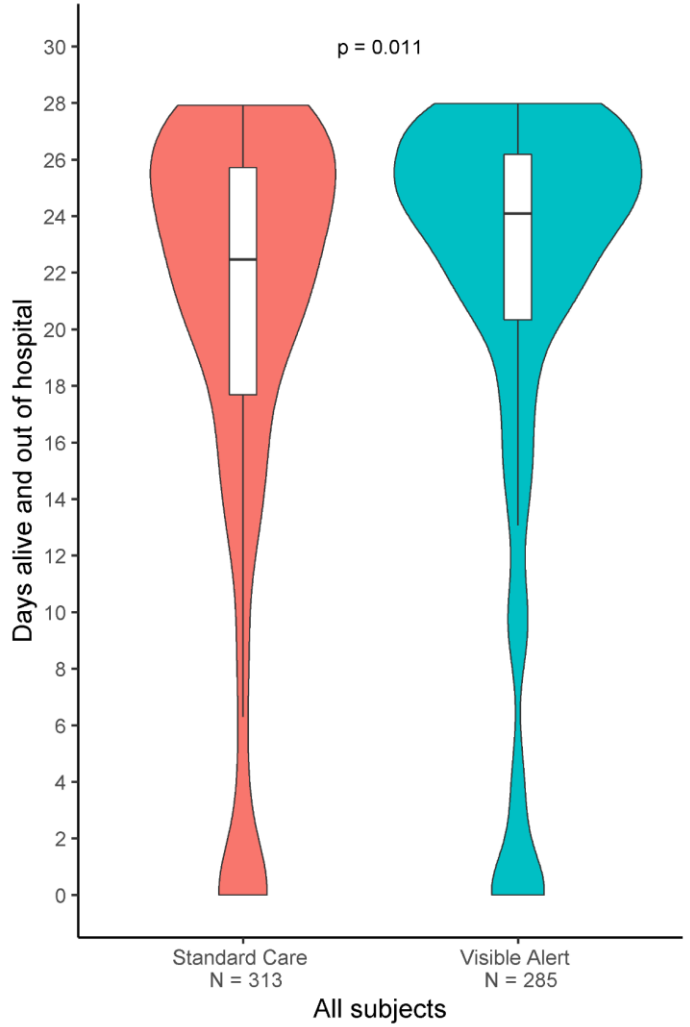


Time to antibiotic administration from ED arrival was shorter in the intervention group compared to the standard care group.

*(**median 2.3 hours vs 3.0 hours**, p = 0.039).*

Days alive and out of hospital was greater in the intervention group compared to the standard care group

*(**median 24.1 days vs 22.5 days**, p = 0.011)*



Results: Main outcome components

	Standard Care (N=313)	Augmented Care with Sepsis EWS Alert Alert (N=285)	p- value
Length of stay (days) Median (IQR)	4.0 (1.4 - 7.0)	3.2 (1.1 - 6.2)	0.12
Hospital mortality	25 (8.0%)	13 (4.6%)	0.086
28-day mortality	31 (9.9%)	17 (6.0%)	0.077
28-day re-presentation to ED or hospital	96 (30.7%)	70 (24.6%)	0.096

Results: Primary outcomes in sub-group analysis

	Standard Care (N=180)	Augmented Care with Sepsis EWS Alert (N=161)	p- value
Days alive and out of hospital (DAOH) in score first subgroup Median (IQR)	21.2 (15.9 - 24.5)	23.0 (17.9 - 25.3)	0.013
Time to antibiotic administration from arrival in score first subgroup (hours) Median (IQR)	3.6 (2.2 - 6.8)	2.7 (1.5 - 4.9)	0.001

Results: Supporting analyses

- **DAOH and time to antibiotics** were **negatively correlated**, with a Pearson correlation coefficient of -0.18 (95% confidence interval [CI], -0.085 to -0.27).

- The intervention group had a **shorter time from alert to antibiotic ordering** (median 0.6 hours [IQR, 0.0 – 2.6] vs 1.4 hours [IQR, 0.2 – 3.9], p = 0.043)
- The intervention group **had less time from order placement to administration** (median 0.4 hours [IQR, 0.2 - 0.9] vs 0.7 [IQR, 0.3 – 1.4] hours, p = 0.001)

Additional Findings

- No differences in comorbidity scores or day 1 SOFA scores
- Approximately 40% were admitted to the ICU (35% vs 40%, NS)
- No differences in rates of antibiotic usage (67.7% vs 70%, NS), rates of fluid resuscitation or relative volumes of fluid resuscitation
- No differences in C. diff diagnoses

- No unanticipated events or missed opportunities noted on blinded chart review

Study Conclusions

- Patients presenting to the ED who were randomized to a sepsis early warning system notification visible to both pharmacist and clinical staff had a reduction in time to antibiotics and a modestly greater number of days alive and out of hospital compared to those who had the alert hidden from view.

- There were no significant differences in rates of antibiotic use, fluid resuscitation volume or *C. difficile* diagnosis.

Why do we think our approach was the right one?

- **Internal validation** bred confidence, local PPV and NPV were contrasted to established screening mechanisms (like qSOFA).
- Involving **stakeholders** early in the discussion and allowing them to mold the intervention was crucial.
- The alert was simple, unobtrusive and **integrated into an obvious workflow** location (no extra apps, sites or clicking).
- We fought the urge to show numbers, electing for an **all or none alert** (think D-dimer or lactate).
- **Pharmacists were well poised to be the sepsis response champions** – post-hoc analyses show that both time from presentation to antibiotic order and time from order to administration were significantly hastened.

Why do our results differ from others'?

- We **limited the scope** of the model to the ED (which enriched the PPV).
- We validated to a **different definition of sepsis** – but one that is generally **more widely accepted** (infection + 3 day ICU stay or death, the *same* outcome leveraged by qSOFA).
- Most importantly, the study did not assess the value of the model in isolation (i.e. validated in vacuum => ignoring physician judgement), rather how it **augmented** provider care.
- Our study is the **first prospective randomized controlled** study of such sepsis early warning system in the ED setting.

CDS: Bates' Ten Commandments (2003)

1. Speed is everything
2. Anticipate needs, deliver in real time
3. Fit into workflow
4. Little things matter (usability)
5. Physicians resist stopping
6. Changing direction is easier
7. Simple interventions work best
8. Ask for info only when really needed
9. Monitor impact, get feedback and respond
10. Manage and maintain

Meta-analysis of CDS studies generally support these:

Most effective CDSS used (Kawomoto et al (2005):

1. Automated alerts
2. Provision of recommendations rather than assessments
3. Provision of decision support at time and location of decision making
4. Computer-based alerts

CDSS also successful when (Roshanov 2013):

1. CDS during Charting/CPOE avoided
2. Providers forced to supply reason for override
3. Patients advised as well

Critical Care Medicine
Society of Critical Care Medicine

Improving Timeliness of Antibiotic Administration Using a Provider and Pharmacist Facing Sepsis Early Warning System in the Emergency Department Setting: A Randomized Controlled Quality Improvement Initiative

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Christine Wang, BS[3]
David C. Kaelber, MD, PhD, MPH[3,6,7]
Brook Watts, MD, MS[3,8]
Michelle T. Hecker, MD[3,9]

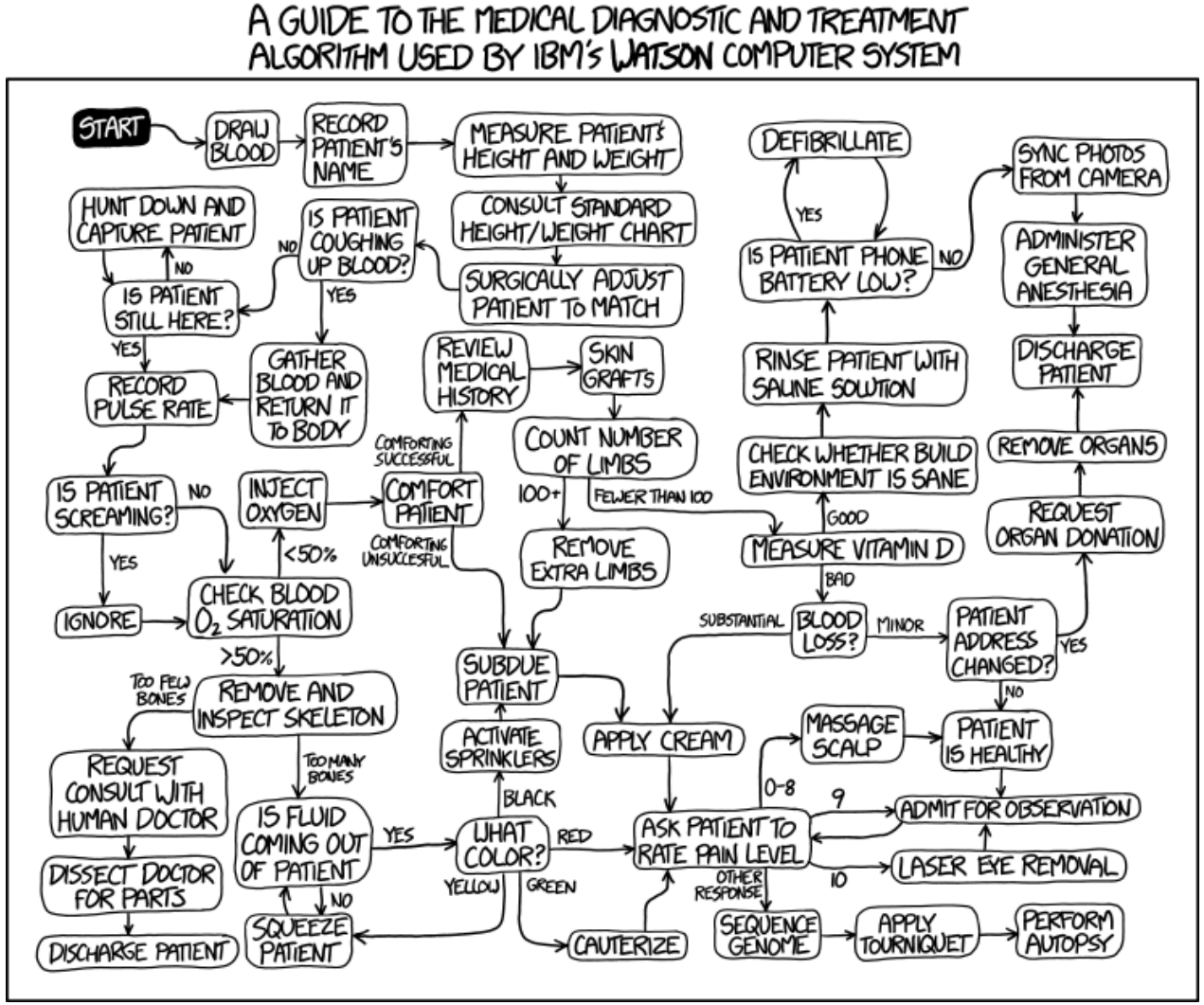
OBJECTIVES: Results of pre-post intervention studies of sepsis early warning systems have been mixed, and randomized clinical trials showing efficacy in the emergency department setting are lacking. Additionally, early warning systems can be resource-intensive and may cause unintended consequences such as antibiotic or IV fluid overuse. We assessed the impact of a pharmacist and provider facing sepsis early warning systems on timeliness of antibiotic administration and sepsis-related clinical outcomes in our setting.

DESIGN: A randomized, controlled quality improvement initiative.

SETTING: The main emergency department of an academic, safety-net healthcare system from August to December 2019.

PATIENTS: Adults presenting to the emergency department.

INTERVENTION: Patients were randomized to standard sepsis care or standard care augmented by the display of a sepsis early warning system–triggered flag in the electronic health record combined with electronic health record–based emergency department pharmacist notification.



https://xkcd.com/1619/

Questions?

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OHA collaborates with member hospitals and health systems to ensure a healthy Ohio

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