Early Onset Sepsis in Neonates: It's All About the Exam, Baby!

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Talk Overview

- What is a clinical exam based approach for EOS?
- How is clinical exam useful?
- Is it safe?
- Why clinical exam is fundamental to any EOS approach?

check up by Gan Khoon Lay from the Noun Project

Clinical Exam 'Official' AAP Approach for EOS Risk Assessment

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

CLINICAL REPORT Guidance for the Clinician in Rendering Pediatric Care

Management of Neonates Born at ≥35 0/7 Weeks' Gestation With Suspected or Proven Early-Onset Bacterial Sepsis

Karen M. Puopolo, MD, PhD, FAAP,[a,b] William E. Benitz, MD, FAAP,[c] Theoklis E. Zaoutis, MD, MSCE, FAAP,[a,d]
COMMITTEE ON FETUS AND NEWBORN, COMMITTEE ON INFECTIOUS DISEASES

Old School Empiric | Sepsis Calculator | Clinical Exam

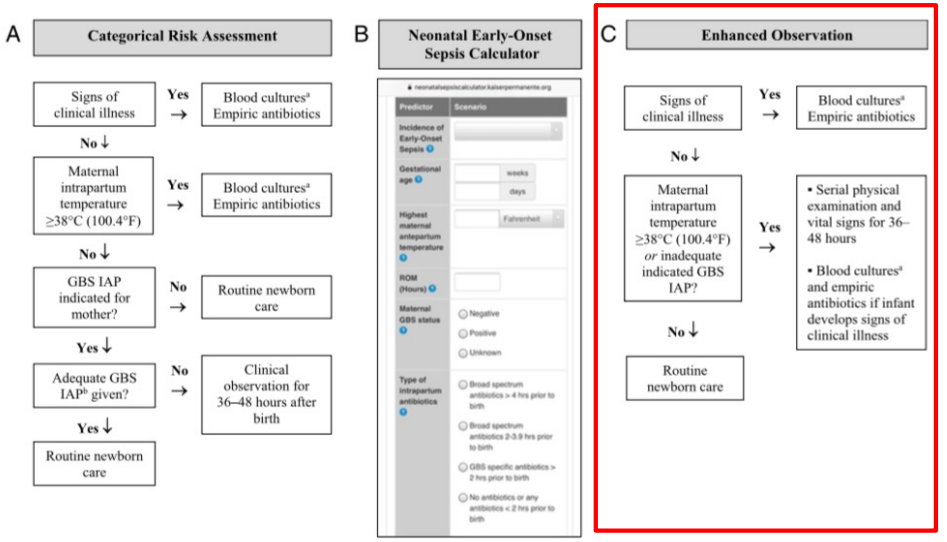

FIGURE 1
Options for EOS risk assessment among infants born ≥35 weeks' gestation. A, Categorical risk assessment. B, Neonatal Early-Onset Sepsis Calculator. The screenshot of the Neonatal Early-Onset Sepsis Calculator (https://neonatalsepsiscalculator.kaiserpermanente.org/) was used with permission from Kaiser-Permanente Division of Research. C, Enhanced observation. [a] Consider lumbar puncture and CSF culture before initiation of empiric antibiotics for infants who are at the highest risk of infection, especially those with critical illness. Lumbar puncture should not be performed if the infant's clinical condition would be compromised, and antibiotics should be administered promptly and not deferred because of procedure delays. [b] Adequate GBS IAP is defined as the administration of penicillin G, ampicillin, or cefazolin ≥4 hours before delivery.

Puopolo KM, AAP COFN. Pediatrics. 2018;142(6):e20182894.
Puopolo KM, AAP COFN. Pediatrics. 2019; 144(2):e20182894.

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Clinical Exam: Not that Novel!

Sensitivity of Perinatal Risk Factors in Identifying Infected Infants

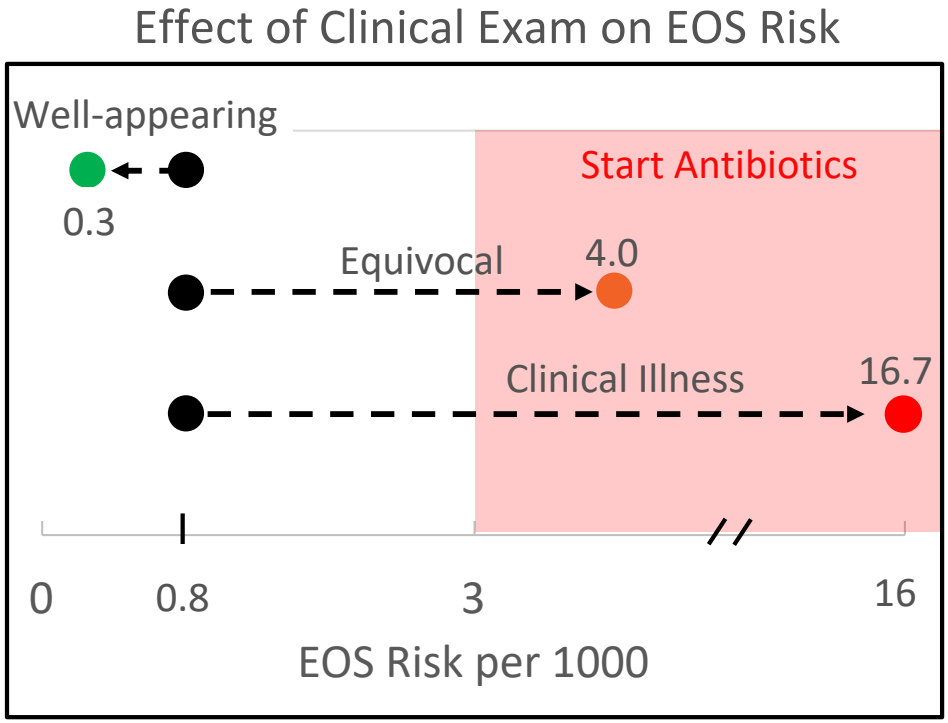
	Perinatal Risk Factor(s)	% Infants Needed to Treat	% EOS Cases Identified
CDC Yes/No Risks →	1) Maternal Fever or Broad-spectrum antibiotics and/or 2) ROM ≥ 18 h and/or 3) GBS colonized but no IAP	16.6%	47%
Kaiser Calculator →	Risk ≥ 0.5 per 1000 at birth	6.1%	45%

>50% of EOS cases are in 'low risk' infants
Only identified using Clinical Exam!

Kaiser 1995-2007 -> N=608,014 late preterm and term infants
Puopolo KM, et al. Pediatrics. 2011;128(5):e1155-63.

Kaiser Sepsis Calculator 2.0
- Clinical Exam Drives Treatment -

- Risk at birth adjusted based on <u>Clinical Exam</u> over first 24 h
- 'Large' weight to exam
  - Well-appearing: LR -> 0.41
  - Equivocal:* LR -> 5
  - Clinical Illness: LR -> 21.1

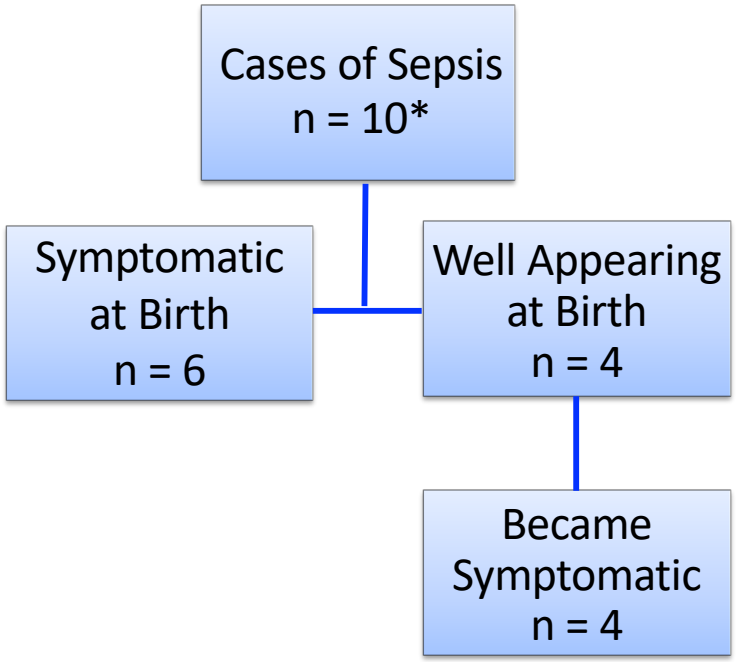


*Equivocal = 2 findings for >2h of tachycardia, tachypnea, temperature instability, or mild respiratory distress

Escobar G, Puopolo K et al. *Pediatrics* Jan 2014. 30-36.
Kuzniewicz M, Walsh E et al. *Joint Commission Journal on Quality and Patient Safety*. May 2016. 42 (5): 232-239.

All Roads Lead to…..Clinical Exam
Kaiser Experience with Calculator (n=56,261)

- 6 ‘symptomatic’ at birth
- 4 ‘well-appearing’ at birth
  - All ‘low’ risk based on perinatal risk factors (Risk <0.3 per 1000)
  - Developed signs of illness at 5 to 20 hours of life
  - Identified based on clinical exam



Kuzniewicz MW, et al. *JAMA Pediatr.* 2017;171(4):365-371

*excluding 2 cases of apparent asymptomatic transient bacteremia

All Roads Lead to…..Clinical Exam
Systematic review 2017-2020 → N=234 EOS Cases

- Applied Kaiser EOS calculator to all EOS cases
- At birth, EOS calculator recommended:
  - 44% 'Routine vitals'
  - 15% 'More frequent vitals'
- "Clinical vigilance remains essential for all newborns"
  - Even when using the EOS calculator

Achten NB ….Benitz WE. *J Pediatr*. 2021 Jul;234:77-84.e8.

All Roads Lead to…..Clinical Exam
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- At birth, EOS calculator recommended:
  - 44% 'Routine vitals'
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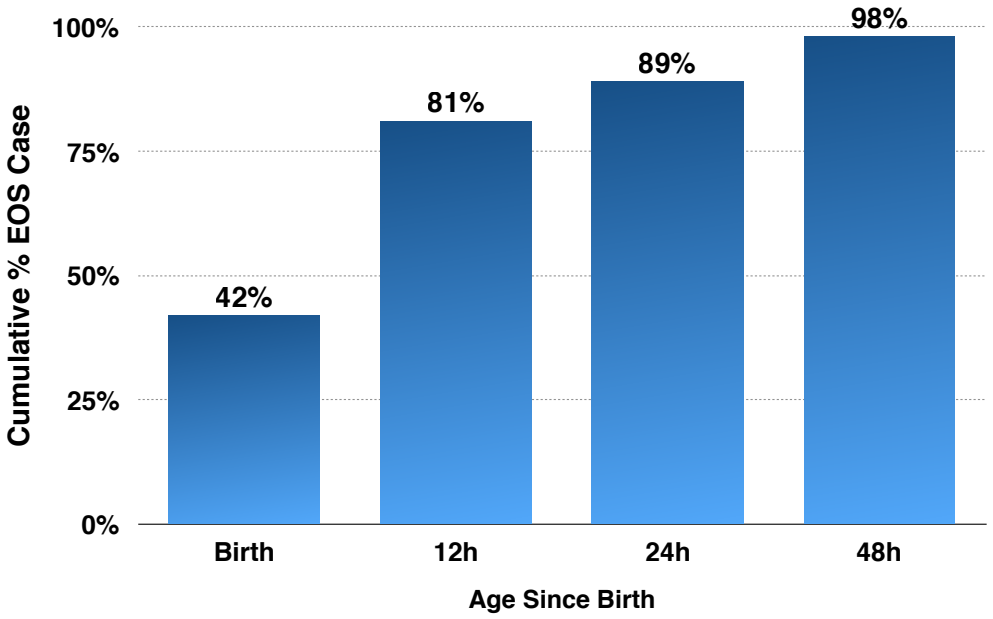
- "Clinical vigilance remains essential for all newborns"
  - Even when using the EOS calculator
- A system of care to support repeated clinical assessments/exams will be essential for all EOS approaches!

Achten NB ….Benitz WE. *J Pediatr*. 2021 Jul;234:77-84.e8.

Clinical Signs of EOS: When and What to Focus On?

- When do neonates present?
  - About half at birth (40-50%)
  - Most within first 24 hours of age
    - Time period for increased vigilance?

Time of Onset of Clinical Signs of EOS



Subset with available data N=149 Cases EOS

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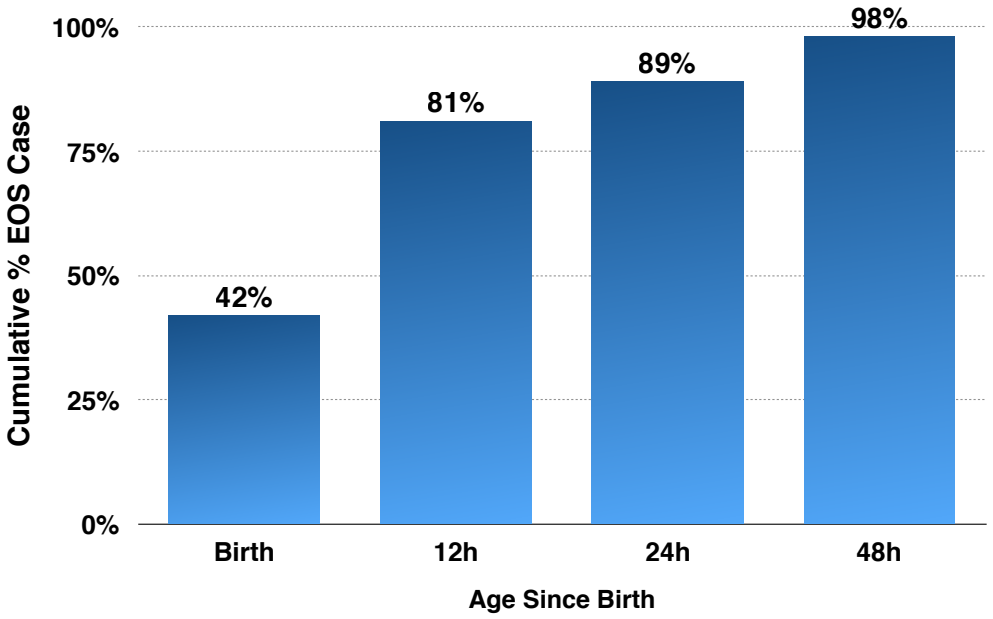
Clinical Signs of EOS: When and What to Focus On?

- When do neonates present?
  - About half at birth (40-50%)
  - Most within first 24 hours of age
    - Time period for increased vigilance?
- How do neonates present?
  - Apnea, Tachypnea
  - Respiratory distress: G/F/R
  - Pallor or poor perfusion
  - Lethargy / Change in activity
  - Vital sign instability
  - Hypoglycemia
  - Jaundice
  - Etc.

Most Common

Time of Onset of Clinical Signs of EOS



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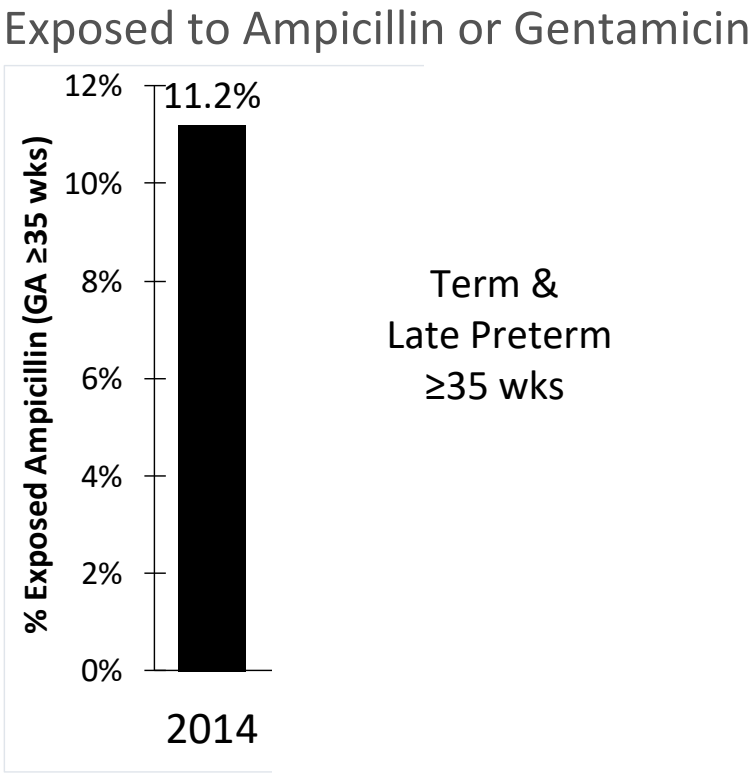
What dose a clinical exam approach look like?

Lucile Packard Children's Hospital Experience

- Previous approach based on CDC/AAP guidelines
  - Chorioamnionitis → Antibiotics
  - Other risk factors → CBC and serial CRPs
- High Antibiotic Utilization Rate
- Choriophobia
  - 'These babies are sick'
  - 'Always treated these babies'
- Formal QI initiative needed



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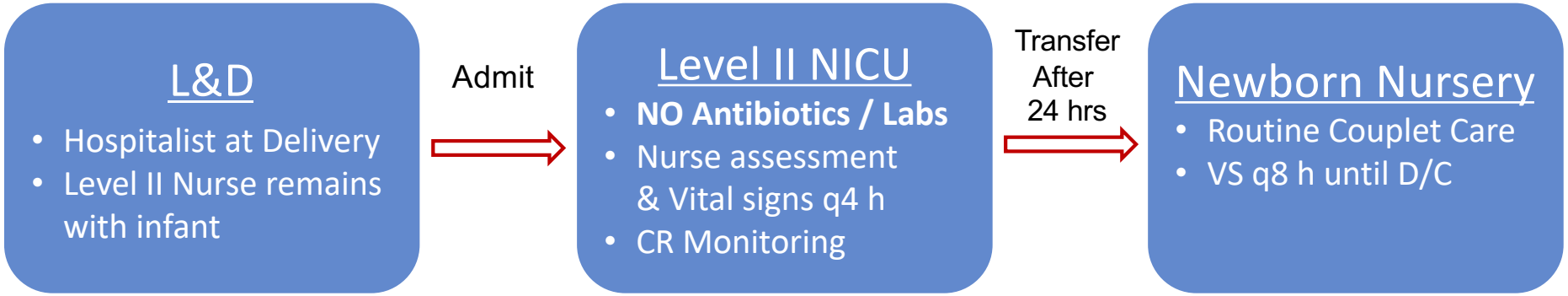
LPCH: Clinical Exam Based Approach
- Phase 1: Admit to Level II NICU -

Chorioamnionitis Exposed Infants: Well Appearing



Started March 2015

LPCH: Clinical Exam Based Approach
- Phase 1: Admit to Level II NICU -

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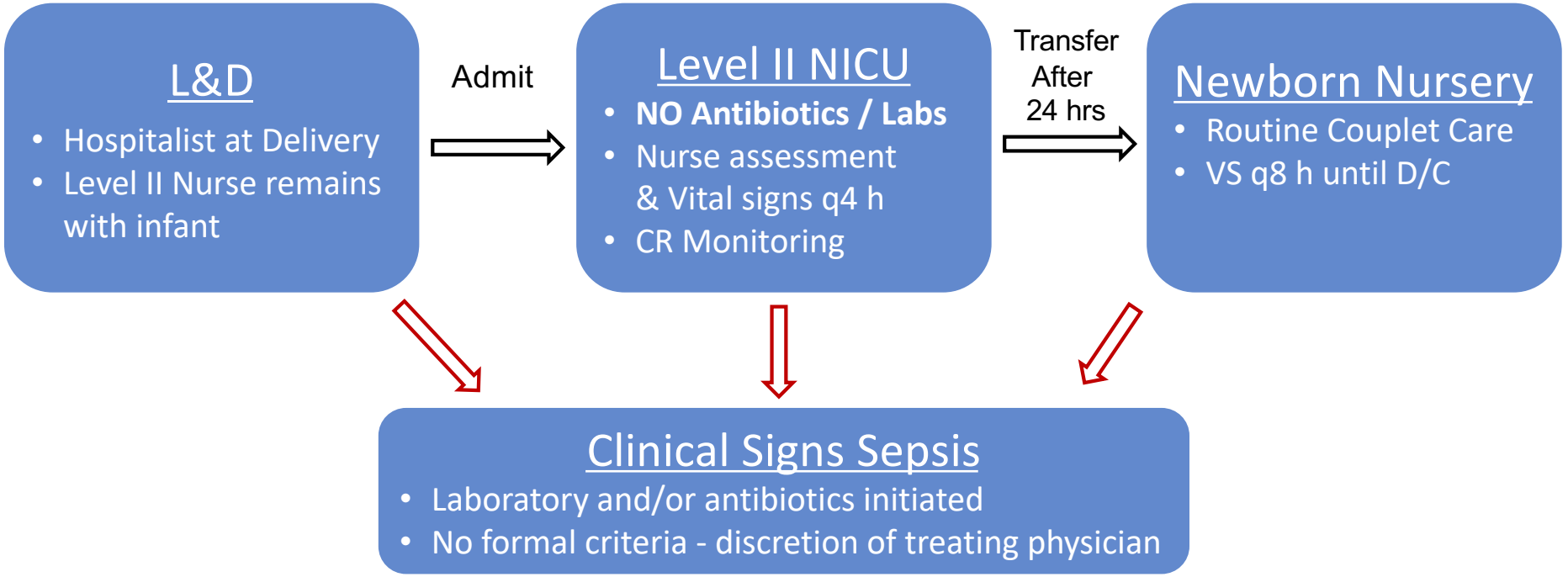
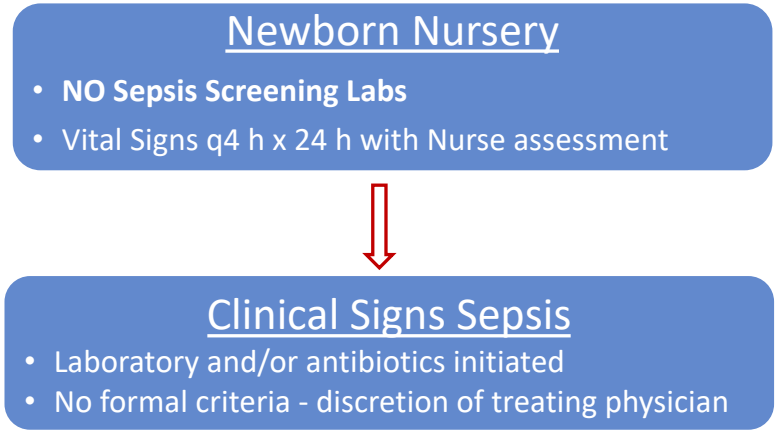


Started March 2015

LPCH: Concurrent Change in Newborn Nursery

- No routine use of sepsis screening labs
  - Regardless of risk factors
- Vitals signs q4 hr x 24 hours
  - All infants!

Well Appearing Infants:
Regardless of Risk Factors

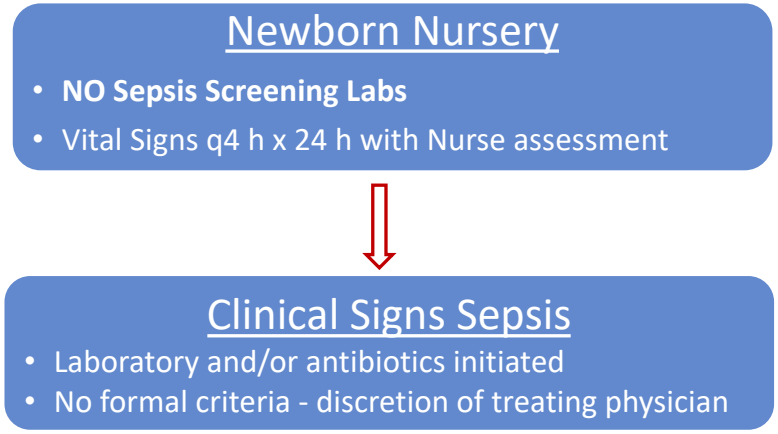


Started 2015

LPCH: Concurrent Change in Newborn Nursery

- No routine use of sepsis screening labs
  - Regardless of risk factors
- Vitals signs q4 hr x 24 hours
  - All infants!
- Lay down building blocks for future
  - Infrastructure & resources
  - Workflow & processes of care
  - Nursing education and skills
  - ‘Breakdown’ old ways → Gain trust → Cultivate new culture

Well Appearing Infants:
Regardless of Risk Factors



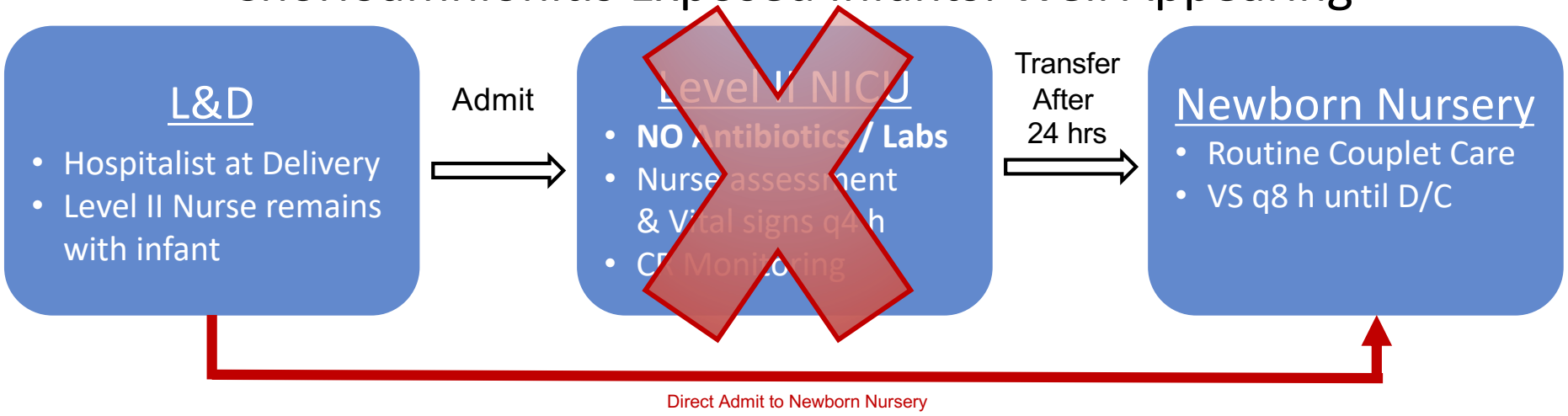
Started 2015

Ongoing Education to Health Care Team = Key

- #ALL BABIES at RISK for sepsis
- Focus on Targeted Signs of sepsis
  - Respiratory (apnea, tachypnea, F/G/R)
  - Vital sign instability
  - Poor perfusion or pallor
  - Lethargy / Change in activity
- If concerned about baby
  - More frequent assessments / physical exams
  - Monitor in newborn nursery triage area
- Finding symptomatic babies is a CATCH, not a miss!
- Empower nurses -> advocates for baby-mother dyad

LPCH: Clinical Exam Based Approach
- Phase 2: Admit to Newborn Nursery -

Chorioamnionitis Exposed Infants: Well Appearing

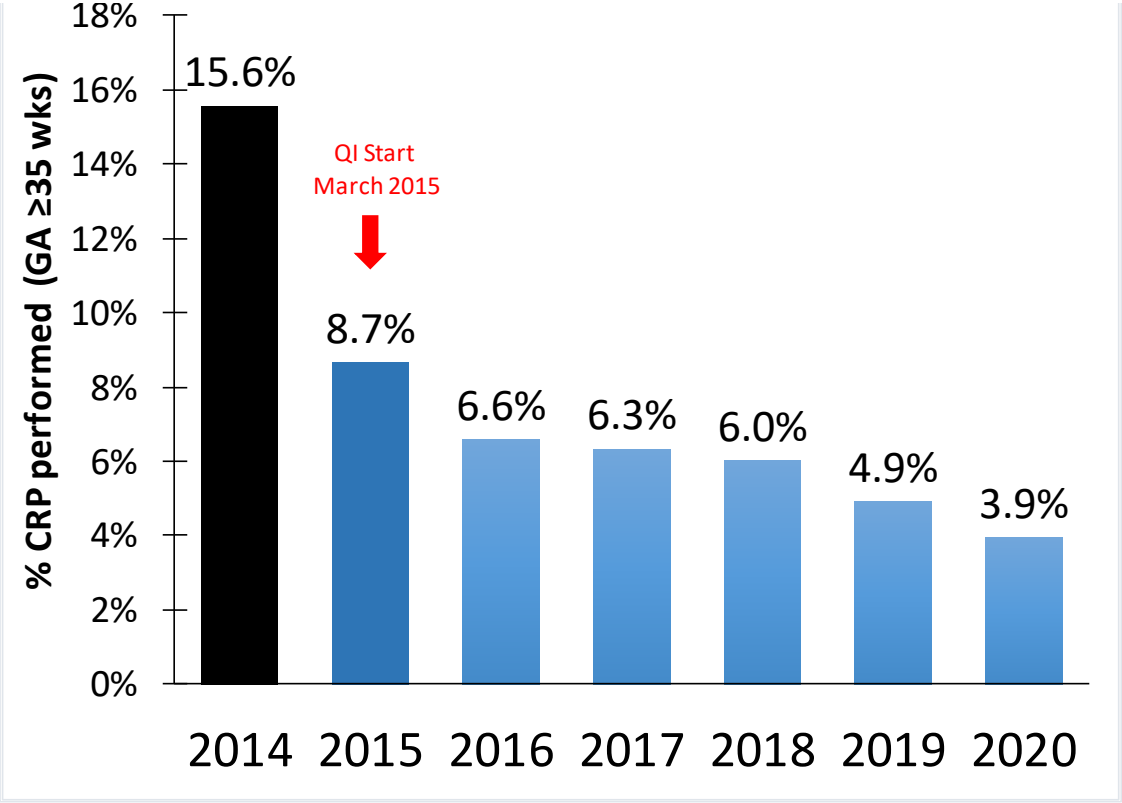


Ensure Adequate Education, Resources, Infrastructure

- Nursing staffing Ratio 1:3
- In-house Neonatal Hospitalist 24/7

Started August 2016

Impact at LPCH: Sepsis Lab Testing All Infants



>60% antibiotic reduction

58% Lab testing reduction

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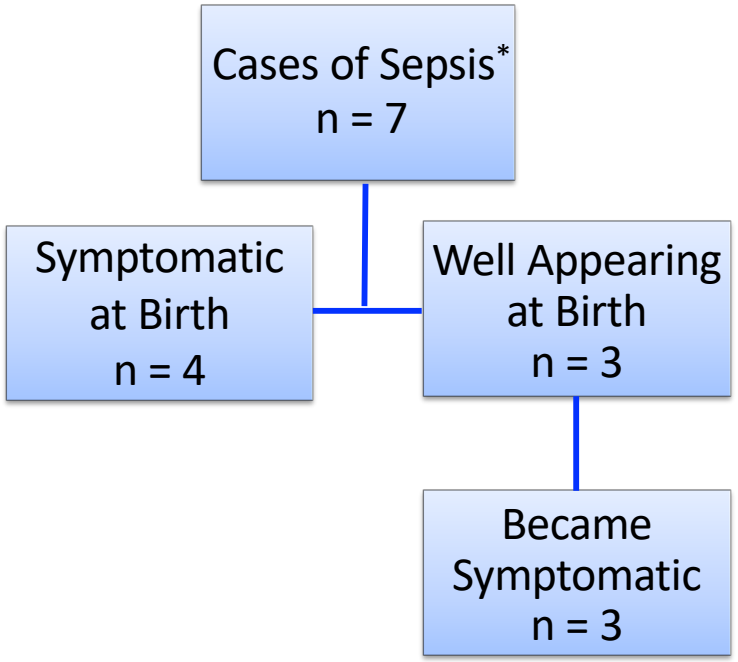
N=26,000+ births

EOS Cases at LPCH
All Infants GA ≥ 35 wk (2015-2020)

- 4 'symptomatic' at birth
- 3 'well appearing' at birth
  - Developed signs illness at 6, 24, and 36 hours of life
  - If used Kaiser calculator….
    - All were low risk at birth (<0.5 per 1000)
- Clinical Exam was key to identifying!



*Excludes one case of sepsis at 65 hol in setting of UVC placed for hypoglycemia. Sepsis screen at birth negative.

N=25,249 births
EOS risk 0.27 per 1000

Safety of a Clinical Exam Centered Approach

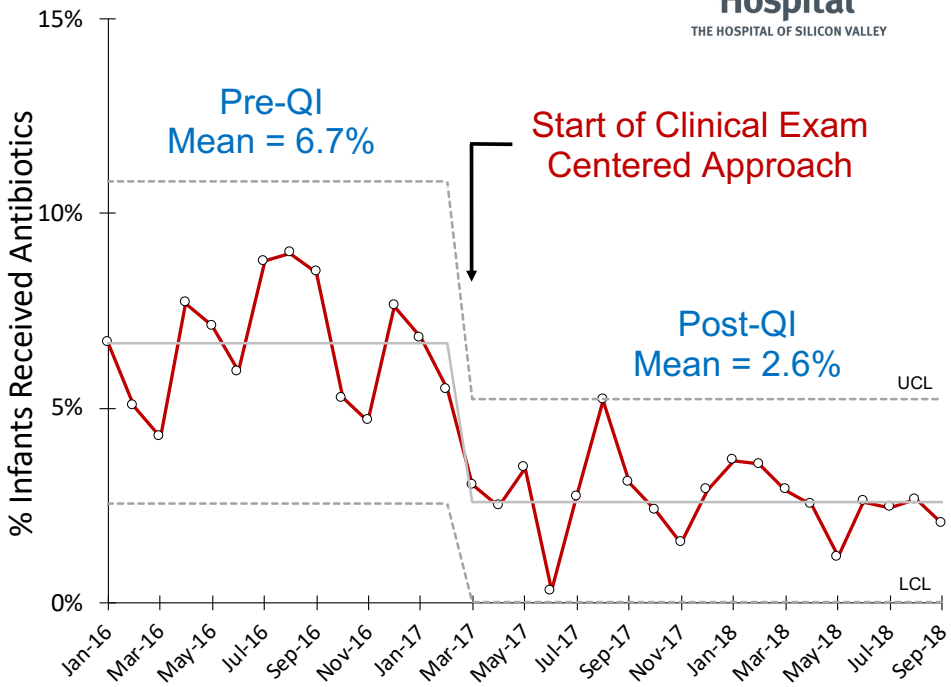
- LPCH experience (2015-2021)
  - Treated over n=27,000 newborns (7 EOS cases)
  - No clinically relevant delays in care or adverse outcomes
- Italian experience (2010-2016)
  - Treated over n=260,000 newborns* (48 EOS cases)
  - No change in rates meningitis, mortality, or mechanical ventilation
  - 'Safe and effective alternative'
- Kaiser Sepsis Calculator experience?

*Still drew CBC and BCx for 75% exposed to intrapartum fever

Berardi A. PLoS One. 2019;14(3):e0212784
Joshi N, *Pediatrics.* 2018 Apr;141(4). pii: e20172056
Joshi N, *Hosp Pediatr.* 2019;9:227-233.
Frymoyer A, *J of Pediatrics*, 2020;225:263-268.

Can Clinical Exam Centered Approach be Done at a Community Hospital?

- YES!!!
- El Camino Hospital
  - ~4500 deliveries/yr
  - Level III NICU
    - In-house neonatologist
- Antibiotic Use Decreased
  - 6.7% -> 2.6%



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Bain L, et al. PAS 2021

Lessons Learned

- Institutional support and buy-in critical!
  - Identify local champions, educate on evidence, demonstrate local problem (local data)
- Multi-disciplinary -> bring all to the table
  - Nurses, newborn physicians, neonatologists, OBs, units impacted

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- Multi-disciplinary -> bring all to the table
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- Incremental change may be needed
  - Fear of 'big' change, hard to do 180 degree, don't get stuck, compromise
  - Gain trust/confidence/skills, building blocks toward end target

Lessons Learned

- Institutional support and buy-in critical!
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- Incremental change may be needed
  - Fear of 'big' change, hard to do 180 degree, don't get stuck, compromise
  - Gain trust/confidence/skills, building blocks toward end target
- Study impact
  - Learn from experience -> Modify approach -> Re-deploy
  - Share successes -> keeps providers invested -> sustained improvement

Take Home Message

- Clinical exam central to identifying infected infants
  - Regardless of approach
  - Need framework in place to support repeated exams/assessments
  - Relevant to ALL care settings (tertiary, community, 'low' risk)
- Finding symptomatic babies is a CATCH, not a miss!
- "No sepsis algorithm can function without excellent clinical care!"
  - Karen Puopolo, MD - PAS 2016

Thank you!

Physician Leadership

- Neha Joshi, MD
- Arun Gupta, MD
- Bill Benitz, MD
- Jessie Allan, MD
- Ron Cohen, MD
- Julie Kim, MD
- Janelle Aby, MD

Nursing Leadership

- Sheryl Goldstein, RN
- Lou Filoteo, RN
- Beth Faulkner, RN

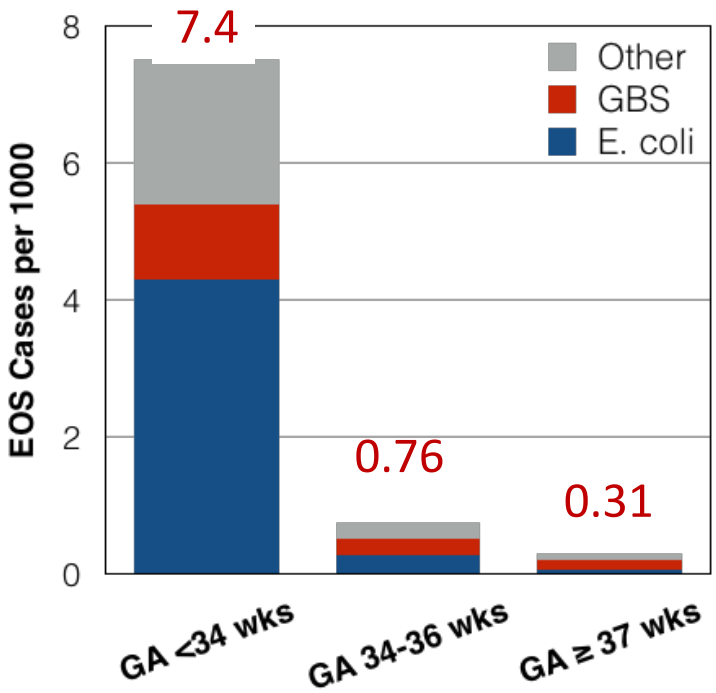
Providers at LPCH

- Nurses & Physicians in L&D, Newborn Nursery, NICUs

Food for Thought!
CPQCC 2010-2017

- Low overall EOS risk!
  - Term = 0.31 per 1000 births
- Of N=348 cases of GBS EOS 73% were born to GBS negative mothers!

CPQCC 2010-2017



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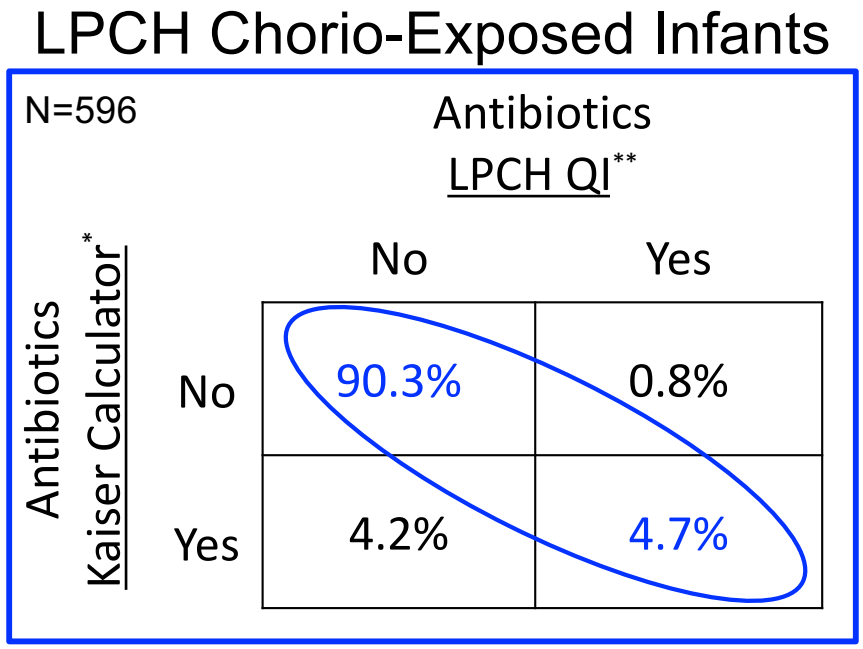
Joshi N. PAS 2020

Data represent CA 2010-2017
2.8+ million births & 1,700+ EOS cases

EXTRA

What if We Had Used the Kaiser Calculator?

- 95% Agreement
  - Kaiser Calculator recommended antibiotic use
  - LPCH QI actual antibiotic use
- Clinical exam strongest driver in Kaiser Calculator



* Risk >3 per 1000 after incorporating clinical exam
** Antibiotics started within first 24 hol

Joshi N, *Pediatrics.* 2018 Apr;141(4). pii: e20172056
Joshi N, *Hosp Pediatr.* 2019;9:227-233
Kuzniewicz MW. Jt Comm J Qual Patient Saf. 2016;42:232-9

First Reports of Potential Clinical Utility of Clinical Exam to Identify EOS in Infants

				Symptomatic infants			Well-appearing infants	
Source	Era	Gestation, wk	Births, n	n	Cases of EOS†	NNT	N	Cases of EOS†
Ottolini 2003[32]	1996-1999	≥35	19 320	300	8	38	19 020	0
Cantoni 2013[35]	2005-2006	≥37	7611	44	2	22	7567	0
Flidel-Rimon 2012[34]	2005-2008	All	22 215	434§	20	22	1661§	1
Hashavya 2011[33]	2005-2009	All	53 788	N.S.	11¶	-	N.S.	0¶
Berardi 2014[54]	2009-2011	≥35	19 504	80	16	5	N.S.	N.S.

- In those who remain well-appearing → Extremely low risk of infection
  - Only 1 case of culture positive sepsis (preterm infant, chorioamnionitis)
- Reduction in antibiotic exposure by 50-75% and lab testing by 70-85%

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Benitz W, Wynn J, Polin R. J Peds. 2015. 166 (4):1070-1074

Berardi *J. Matern Fetal Neonatal Med.* 2015 Jul;28(10):1123-7.

Berardi *J. World J Clin Pediatr.* 2016 Nov 8;5(4):358-364

Cantoni L. J Pediatr 2013;163:568-73