University of Colorado **Anschutz Medical Campus**

Sepsis in pregnancy: caring for two in the ICU

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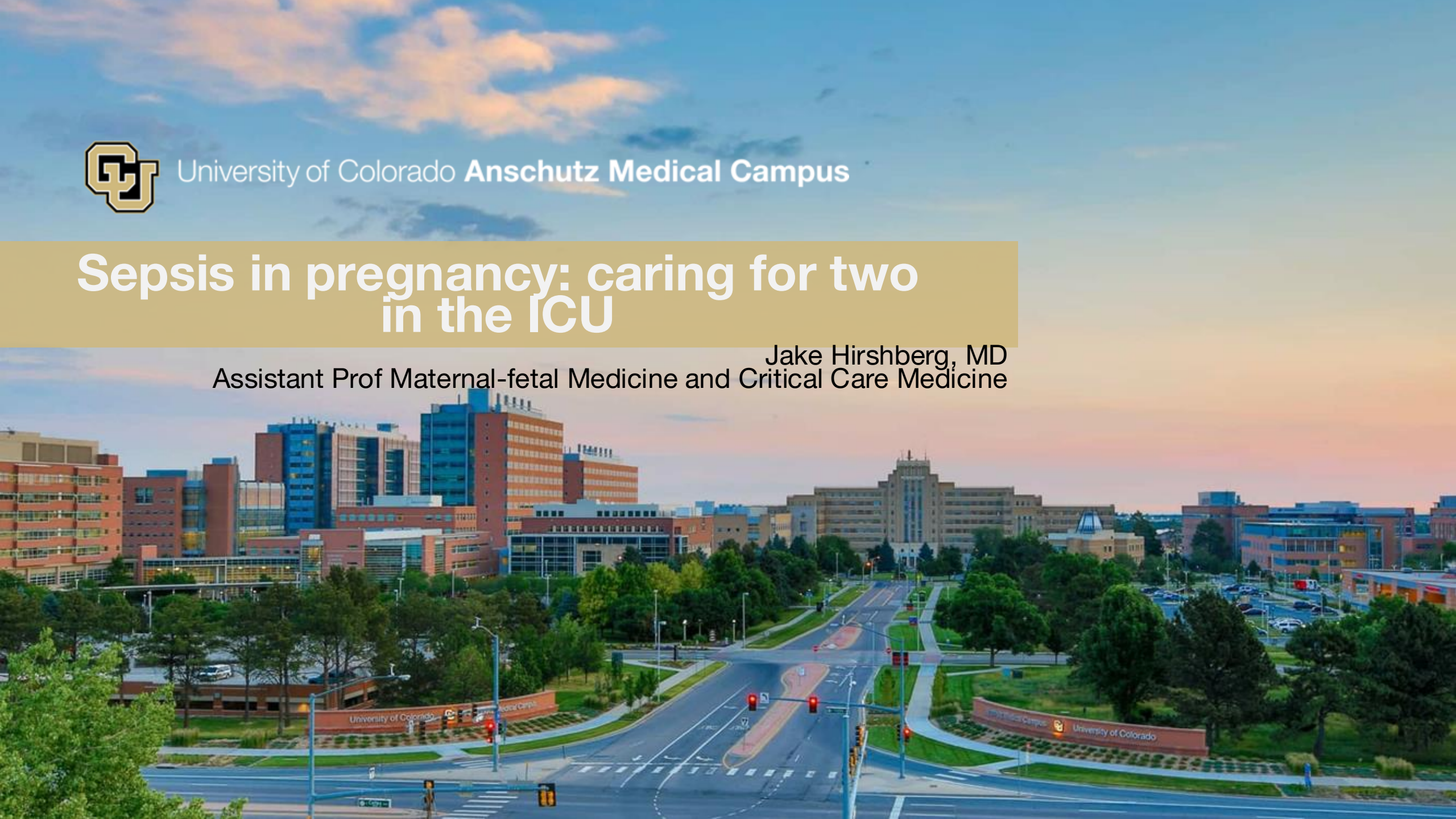


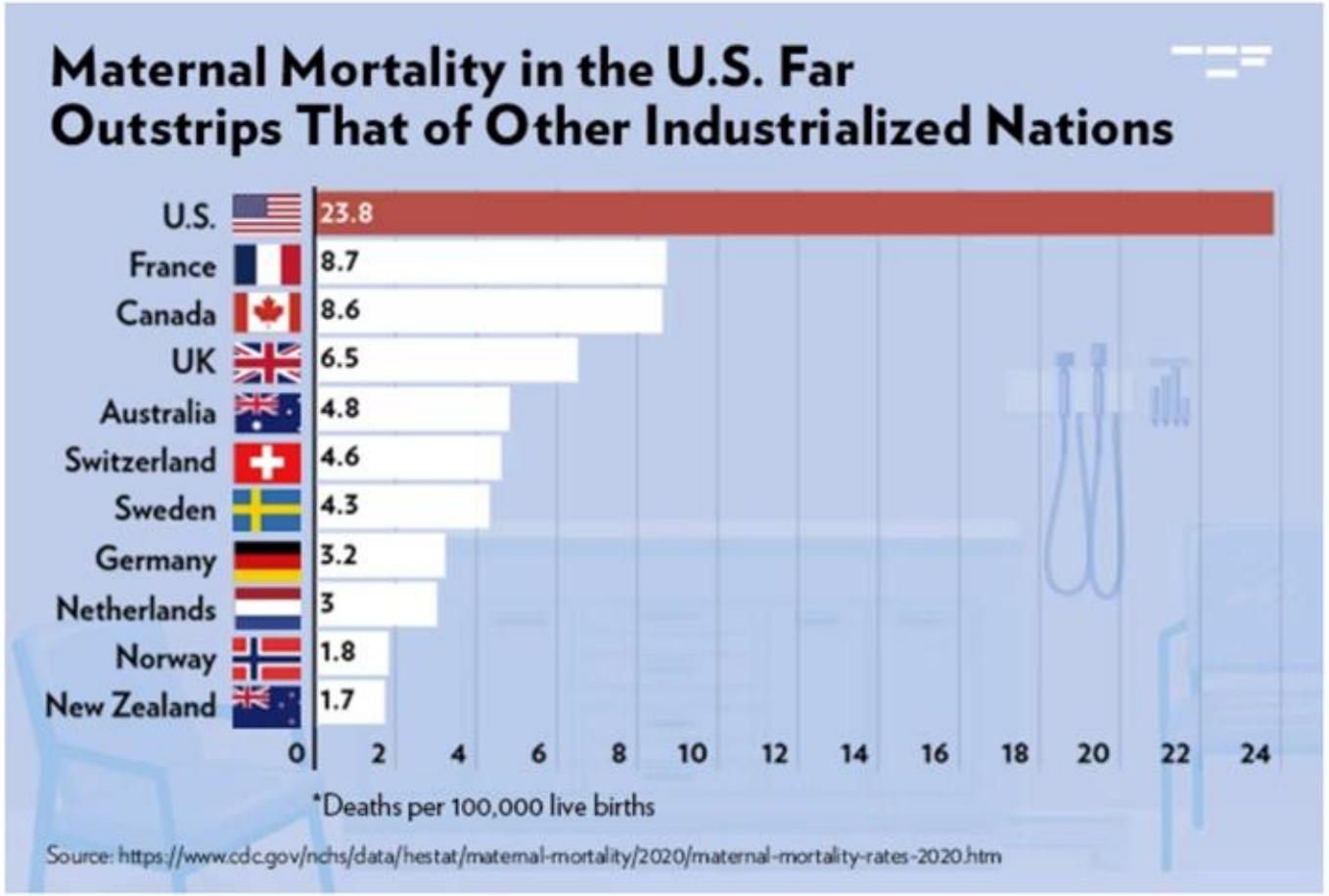
Disclosures

- None

Objectives

- Understand trends in maternal mortality
  - Review Colorado's newest Data
- Review physiologic changes in Pregnancy
- Apply these to the diagnosis and evaluation of sepsis in pregnancy
- Determine what alterations we need to make to sepsis care in pregnancy
- Master the care of puerperal sepsis

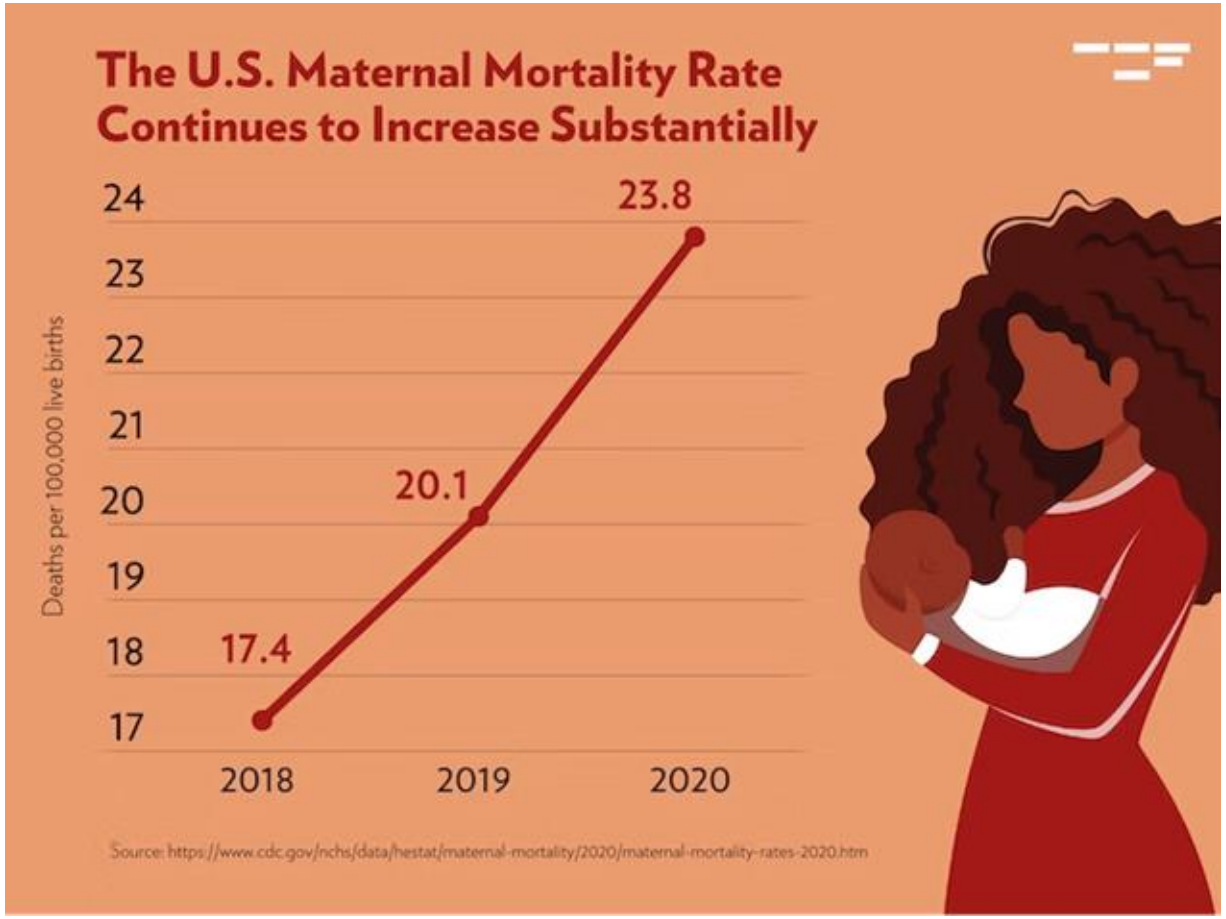
Maternal Mortality



Defining the problem

- The death of a person while pregnant or within 42 days of the end of pregnancy
- Can be pregnancy “related” or not
- The US outpaces all other “industrialized” nations
- 2/3 are preventable

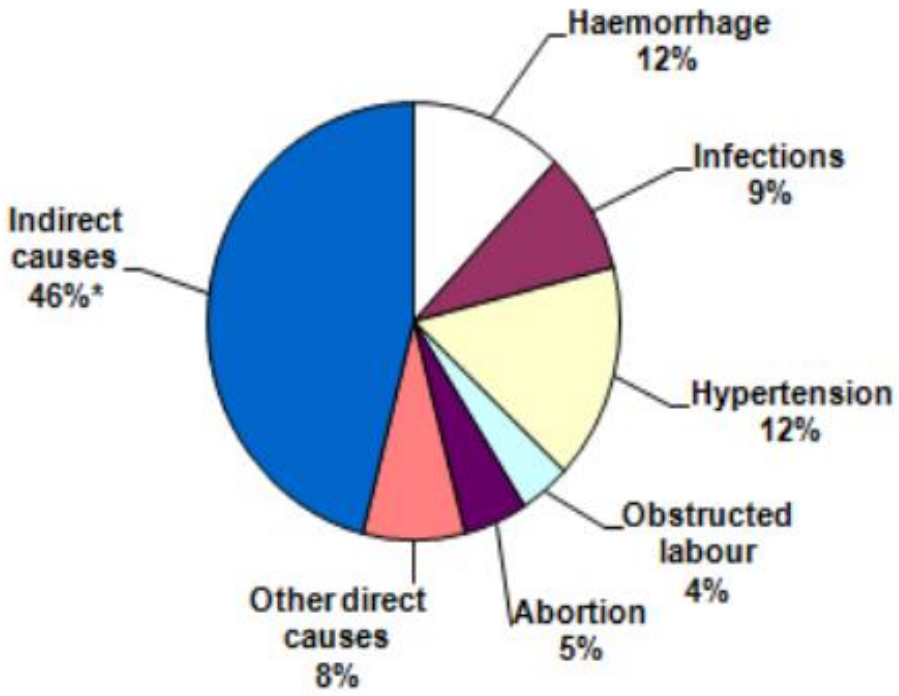
Maternal Mortality

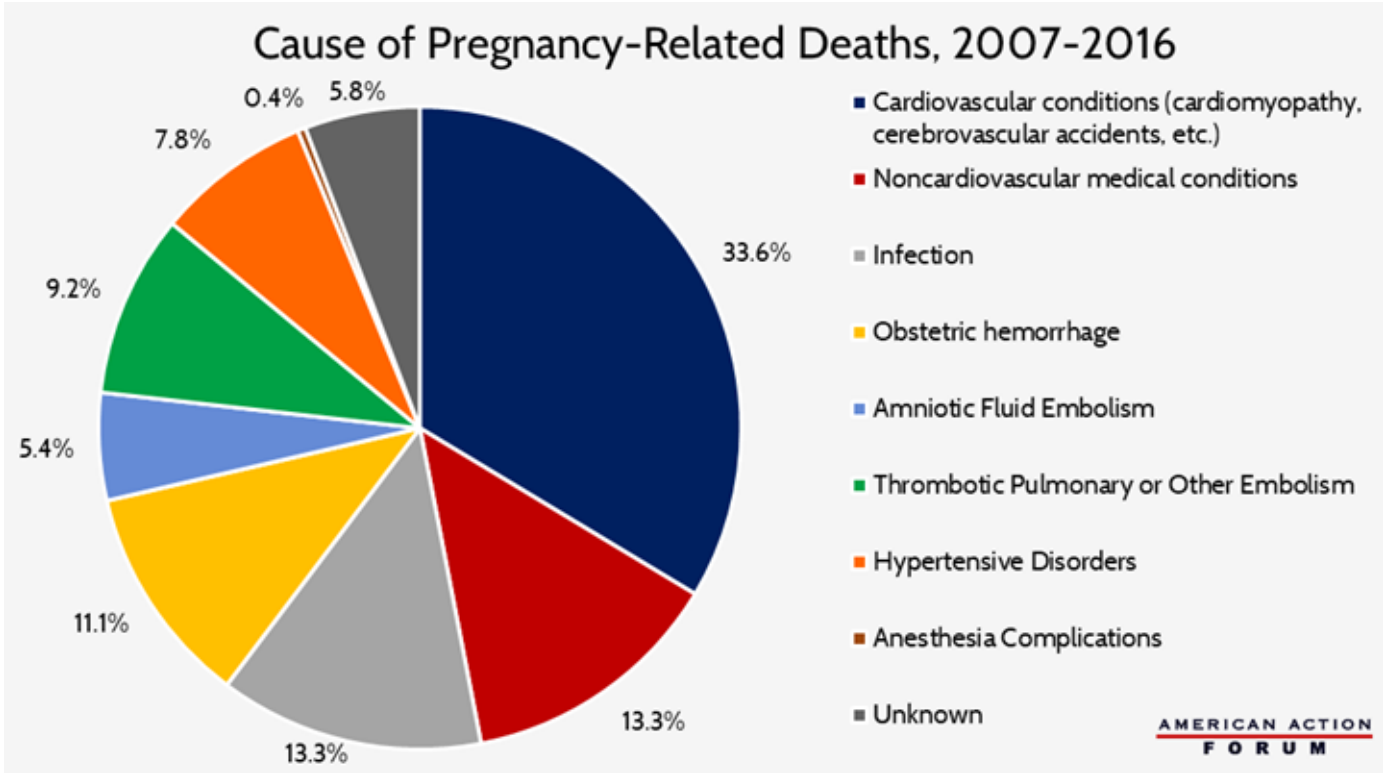


Trends over time

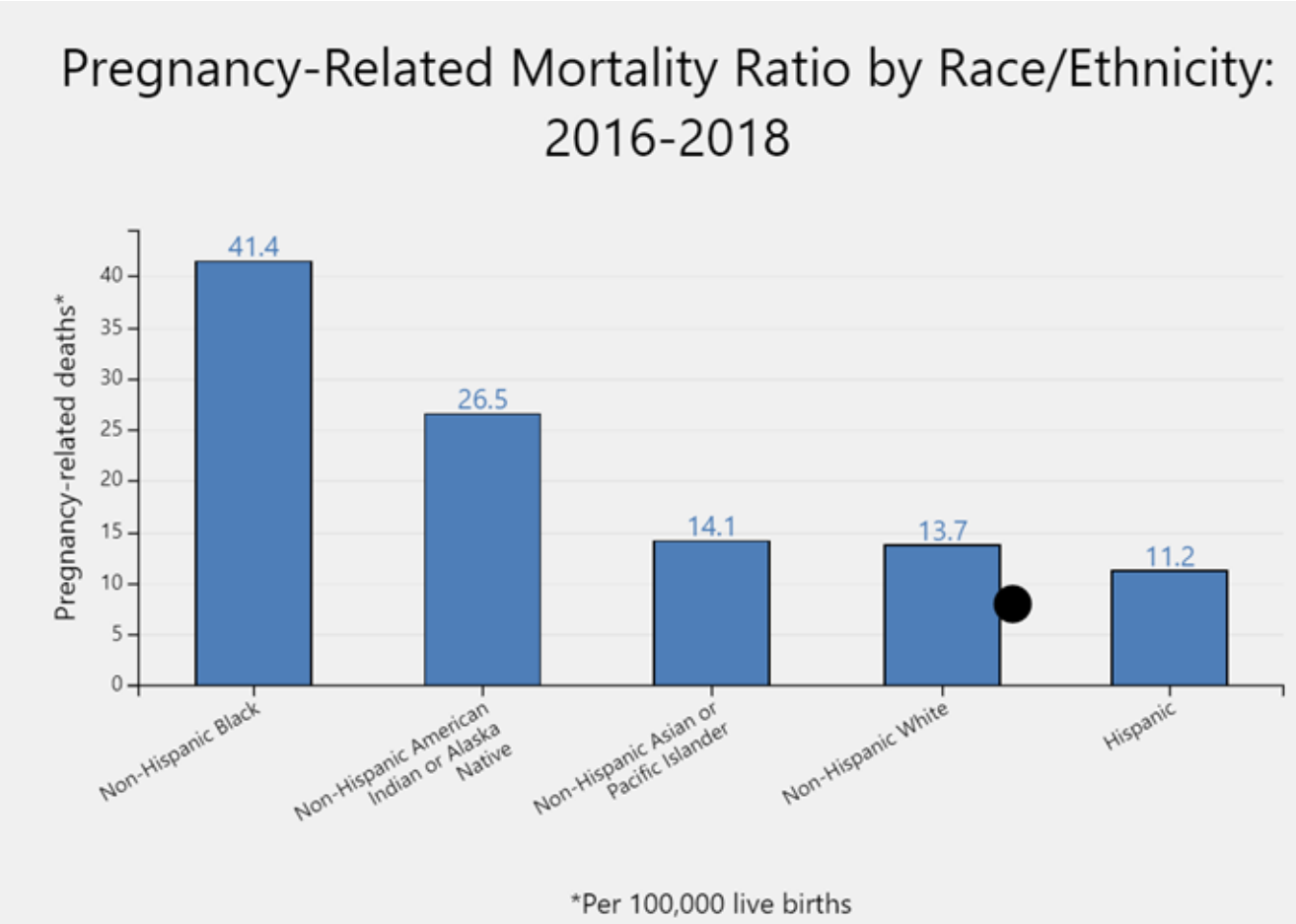
- Continues to worsen
- Data from 2022 shows another 22% increase
- Historic context
  - 1900: 600/100,000
  - 1600: 1200/100,000
  - Prehistoric: 1000/100,000

Maternal Mortality





Maternal Mortality



Disparities in outcomes

- Transcends economic and educational barriers
- Access to quality care
- Implicit bias
- Preexisting conditions
- Structural racism
- Historic context

Colorado: From 2017-2021 there were

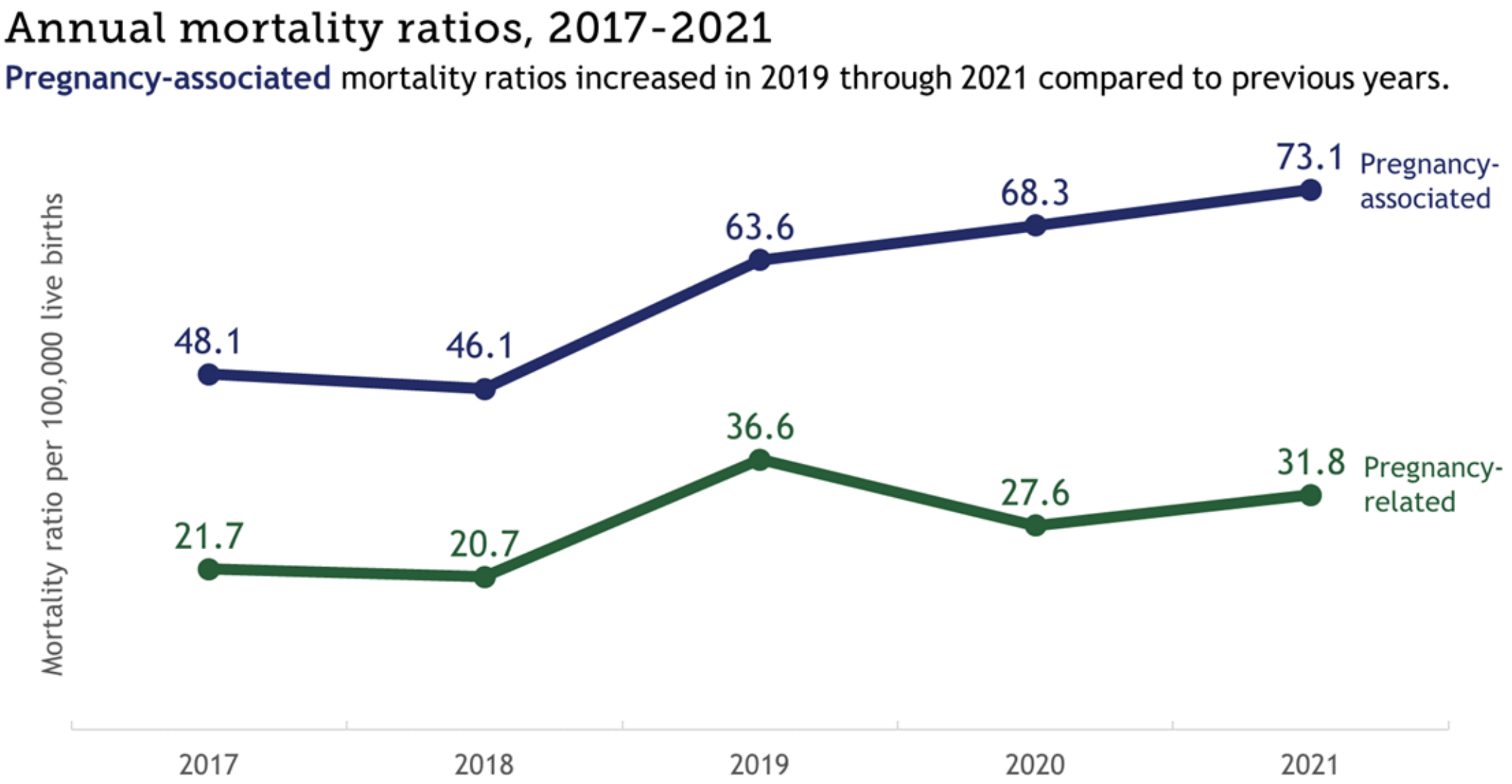
188 pregnancy-associated deaths

59.8 pregnancy-associated deaths per 100,000 live births

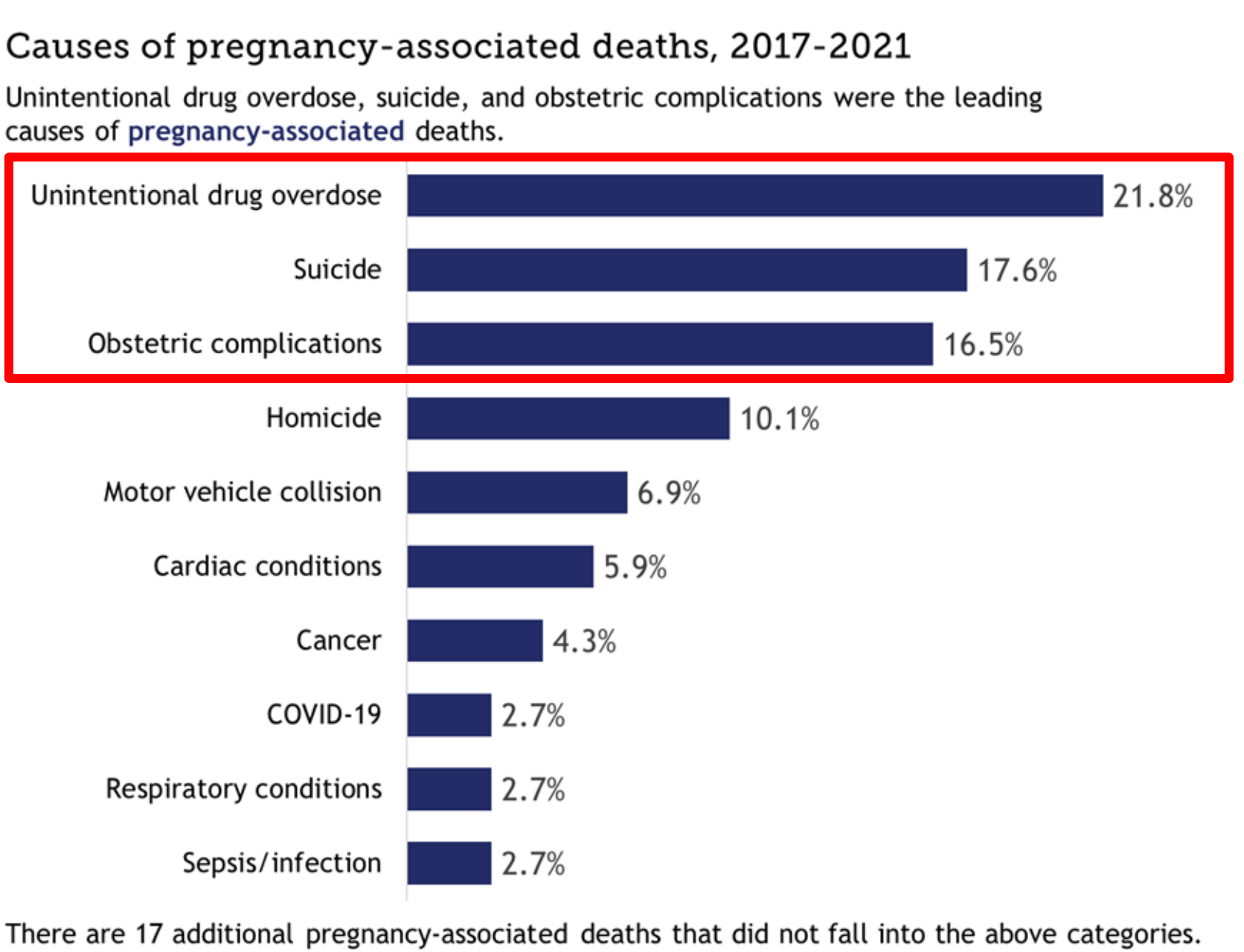
87 pregnancy-related deaths

27.7 pregnancy-related deaths per 100,000 live births

Mortality Ratios Over Time

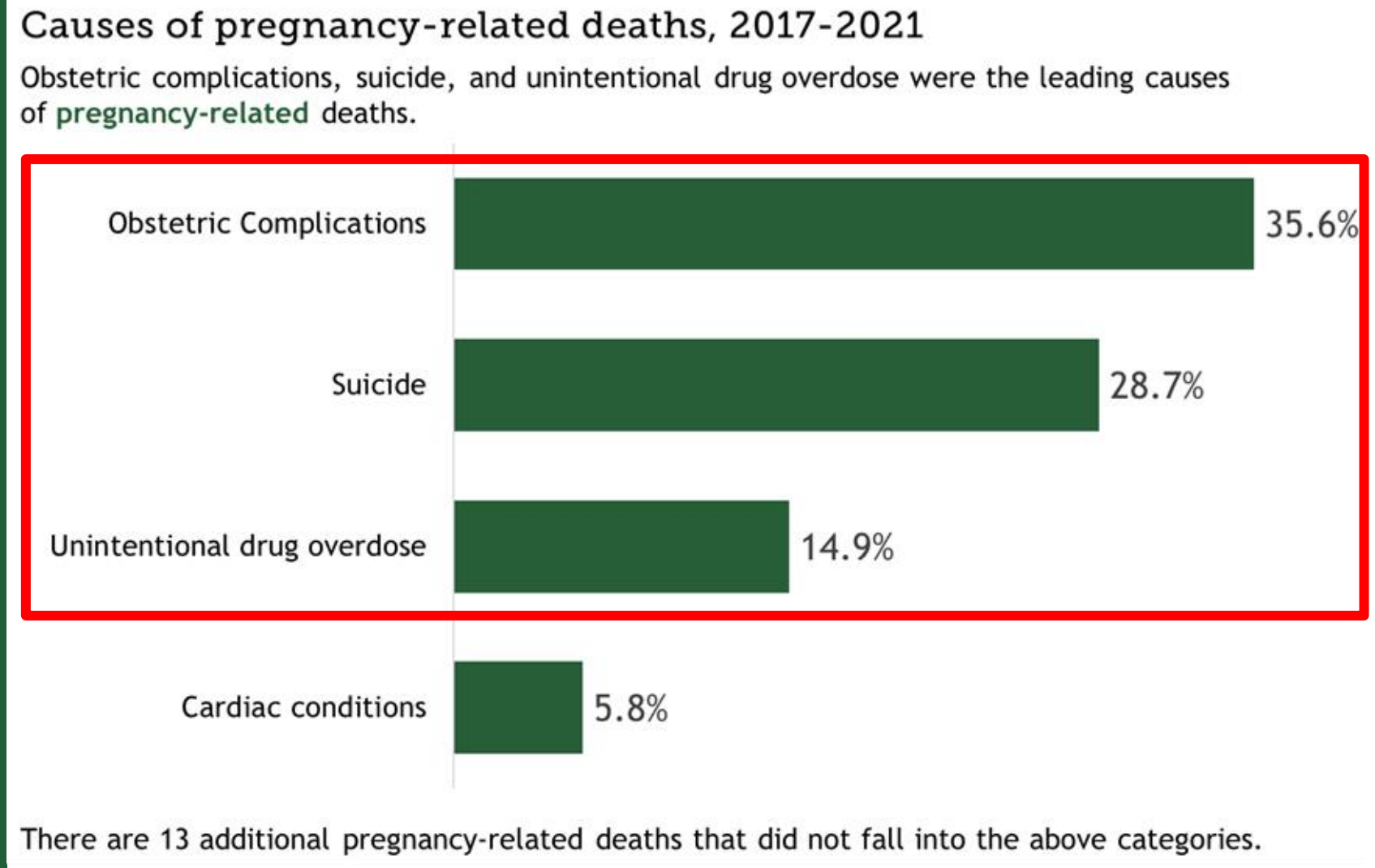


Causes of pregnancy-associated deaths, 2017-2021



Obstetric complications include hemorrhage, placenta accreta spectrum disorders, postpartum infections, obstetric sepsis, hypertensive complications of pregnancy (e.g., pre-eclampsia, eclampsia, and HELLP syndrome), pulmonary embolism, amniotic fluid embolism, anesthesia complications, and ruptured ectopic pregnancies

Causes of pregnancy-related deaths, 2017-2021



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Pregnancy Physiology-Cardiac

- Hemodynamic changes in pregnancy

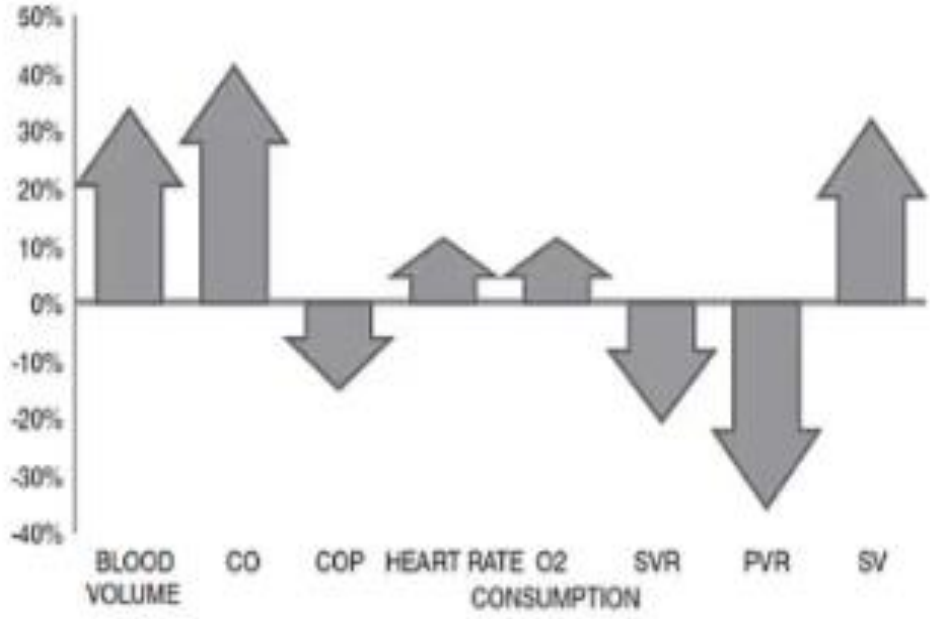
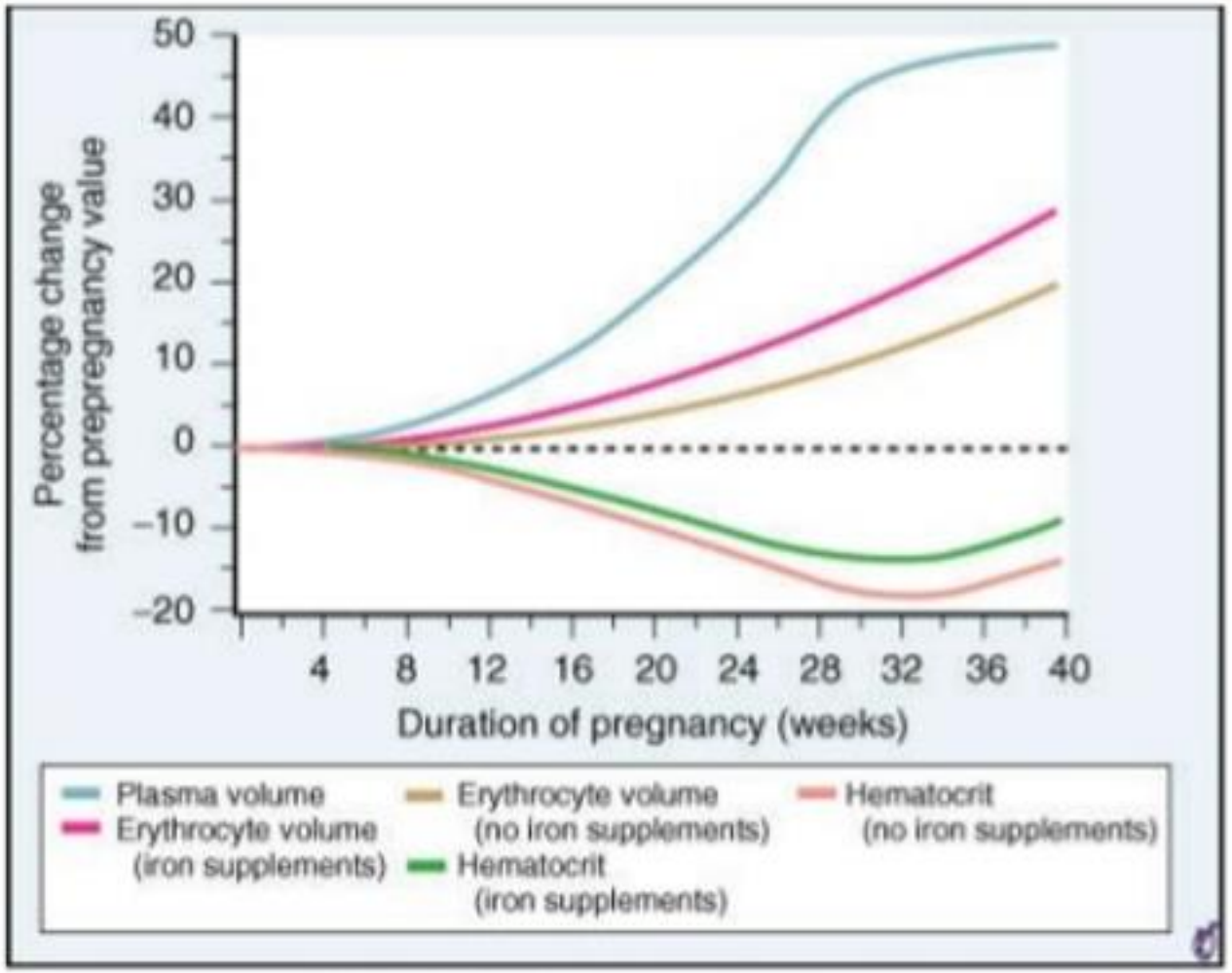
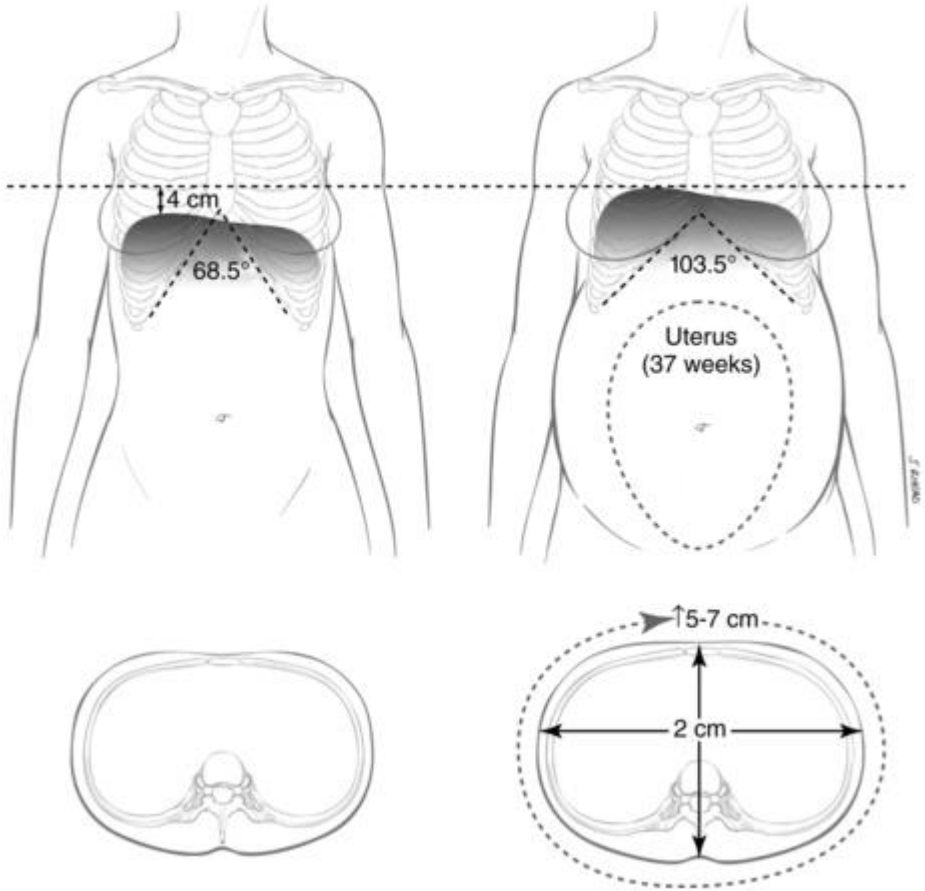


FIGURE 2. Hemodynamic alterations of pregnancy. CO indicates cardiac output; COP, colloid oncotic pressure; PVR, pulmonary vascular resistance; SV, stroke volume; SVR, stroke volume resistance.

Pregnancy Physiology-heme

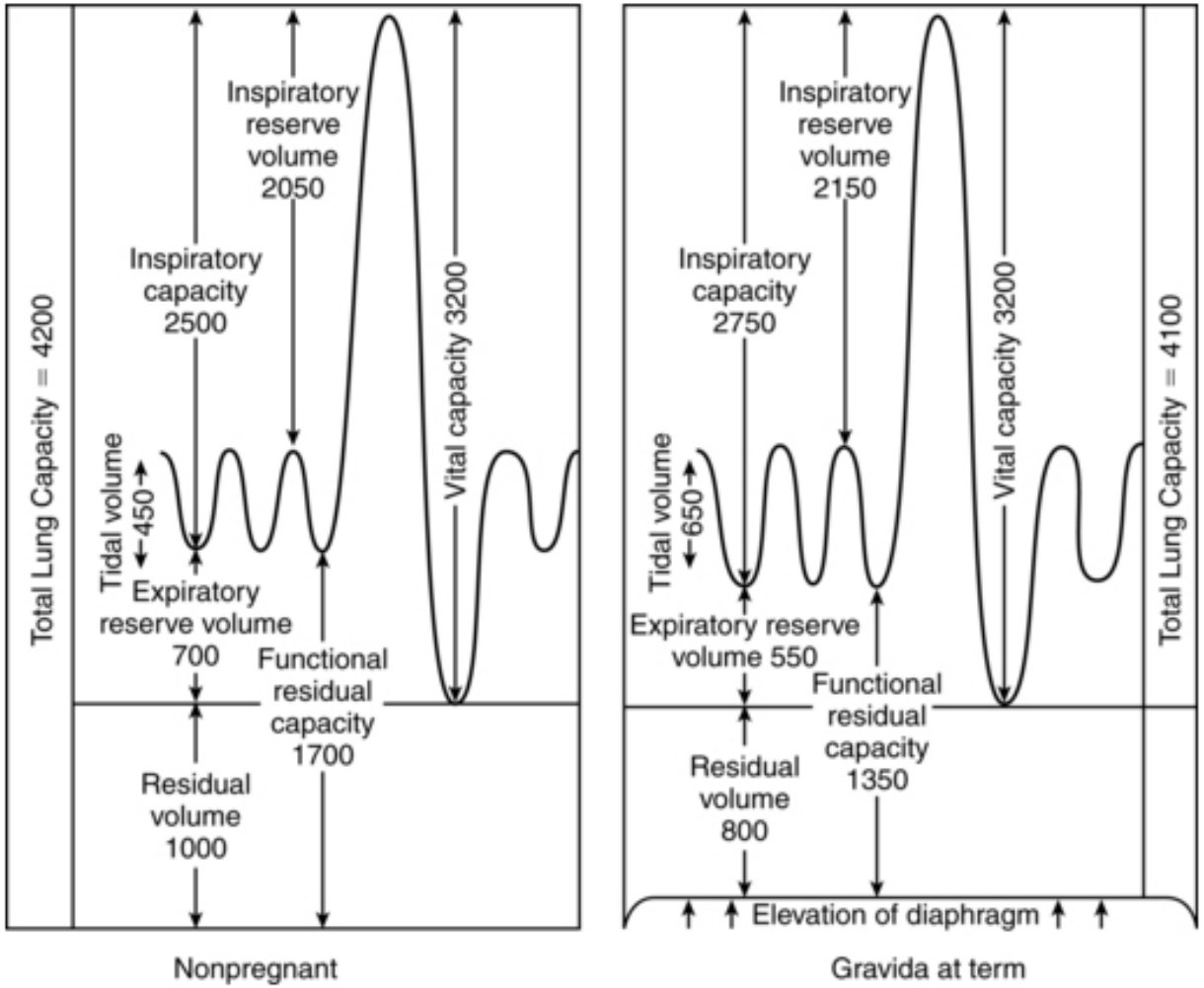


Pregnancy Physiology-pulm



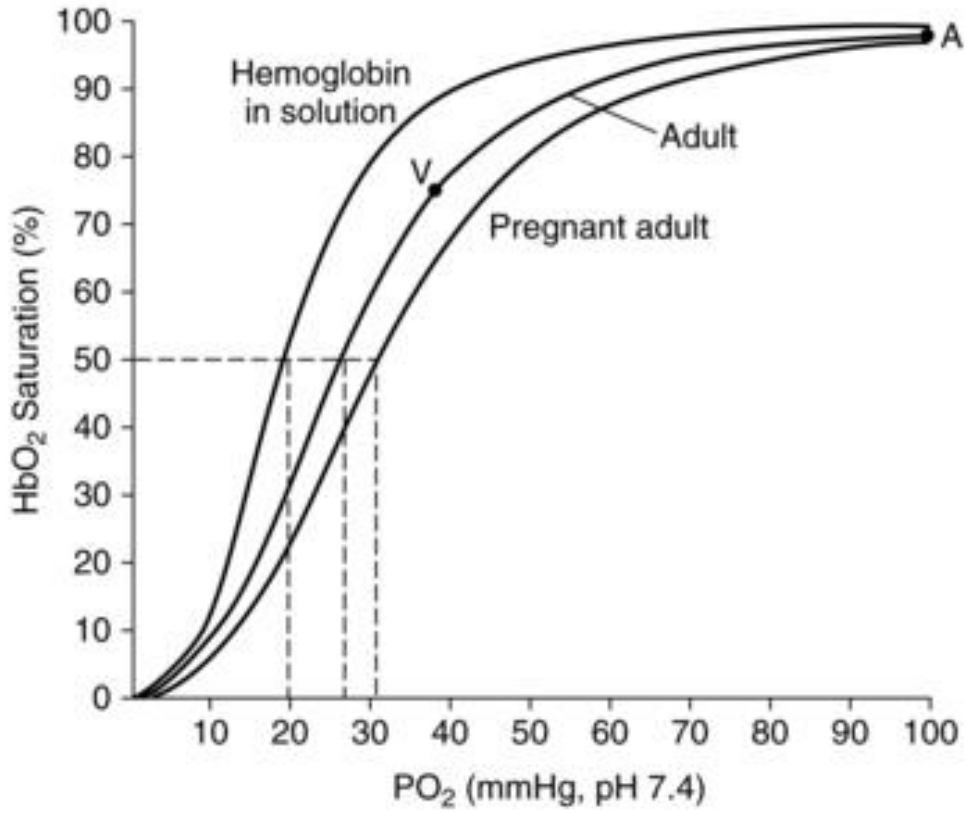
Hegewald, M.J. & Crapo, R.O. (2011). Respiratory physiology in pregnancy. *Clin Chest Med*, 32, 1.

Pregnancy Physiology-pulm

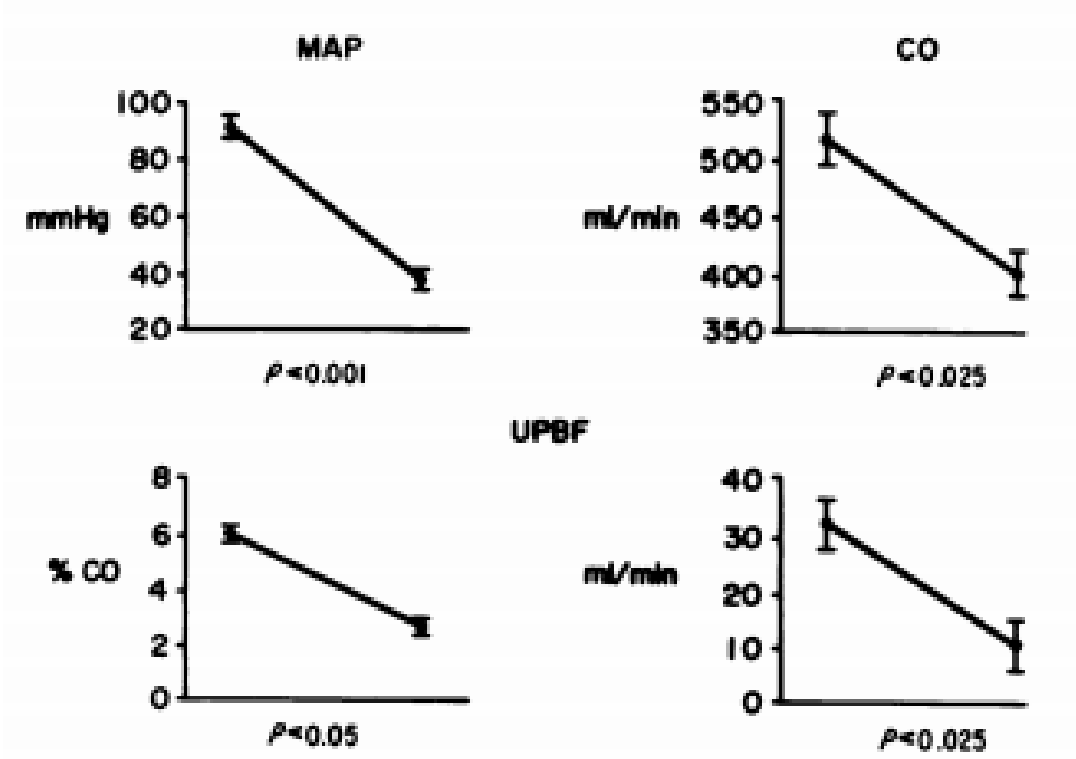


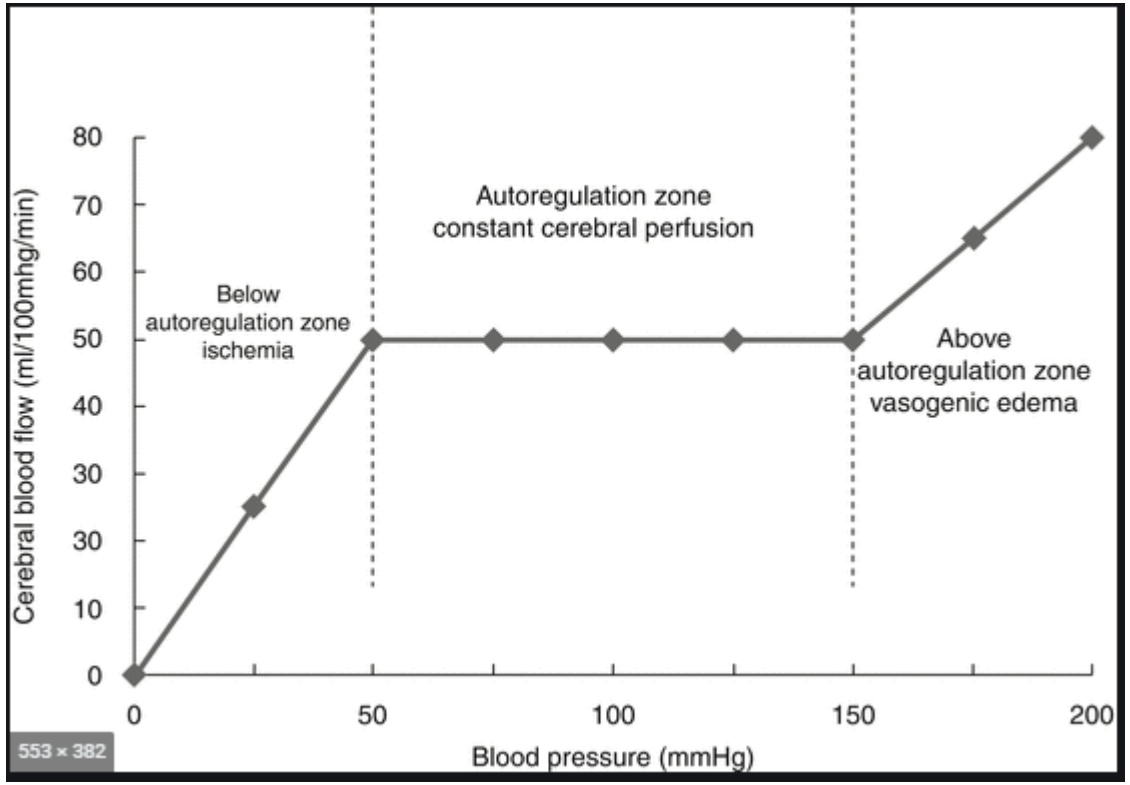
Pregnancy Physiology-pulm

Blood gas measurement	Non-pregnant adult	Third trimester
pH	7.38–7.44	7.39–7.45
Arterial partial pressure of oxygen (mmHg [kPa])	80–100 (11–13)	92–107 (12.3–14.3)
Arterial partial pressure of carbon dioxide (mmHg [kPa])	35–45 (4.7–5.9)	25–33 (3.3–4.4)
Bicarbonate (mmol/L or mEq/L)	21–30	16–22



Autoregulation of placental perfusion





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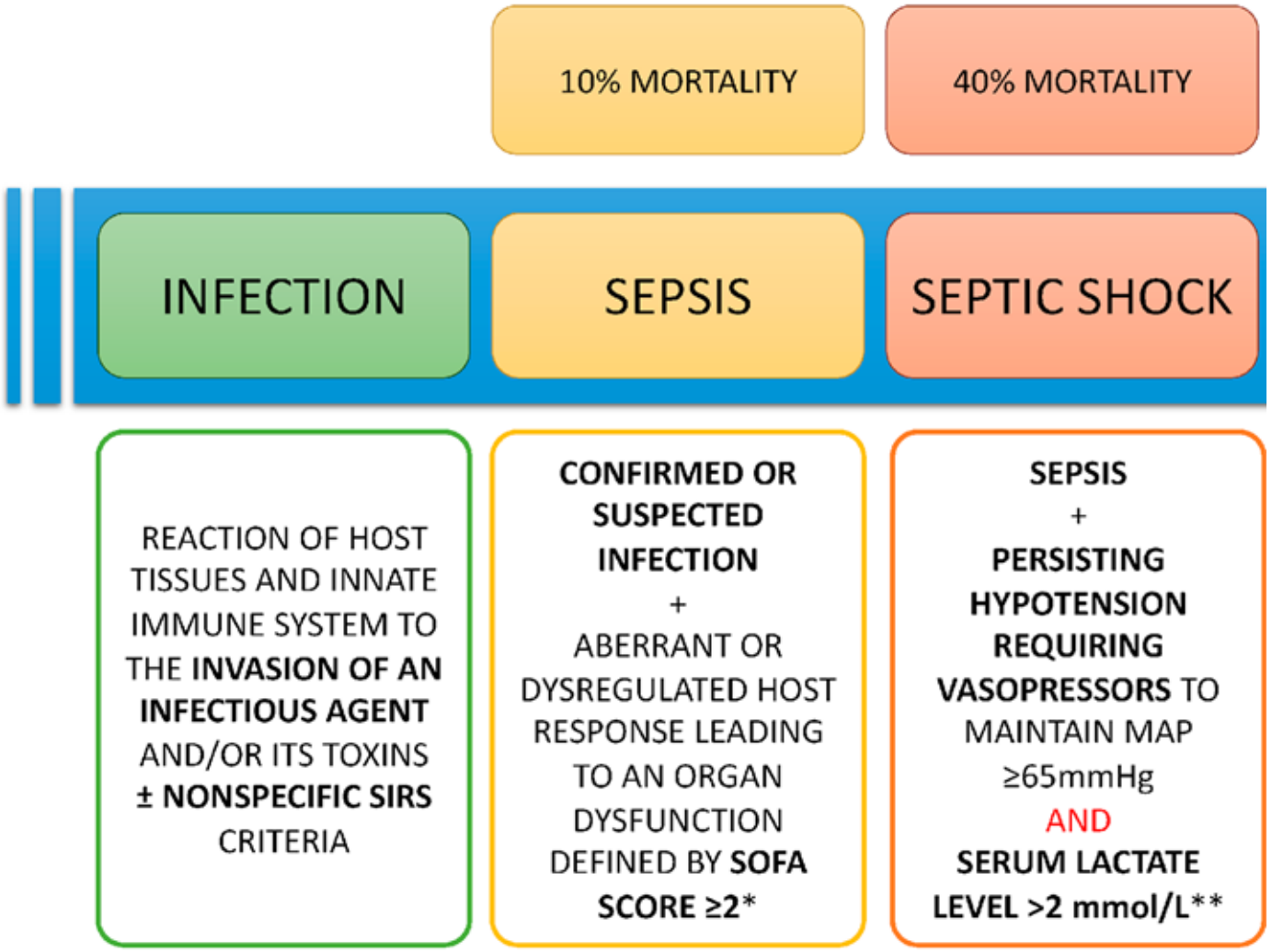
Sepsis-3



** or an increase of 2 points compared to the initial value of the SOFA*
*** Despite adequate volume/fluid resuscitation*

Maternal Sepsis evaluation

Identification and escalation of care

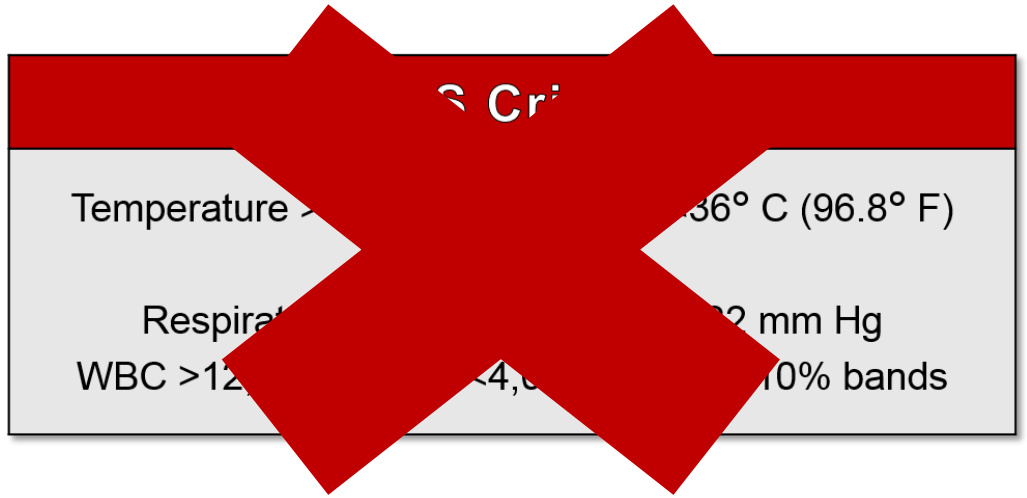


Table 1. Characteristics of Common Maternal Early Warning Systems for Sepsis

Pregnancy Scoring System	Parameters Evaluated	Threshold	Advantages	Disadvantages
MOEWS[16]	Heart rate, respiratory rate, oxygen saturation, systolic blood pressure, temperature, and mental status changes	Varies	Simple bedside screening tool	Marked variation of thresholds and formats Validated for chorioamnionitis Overdetects severe sepsis Need for secondary testing to identify true-positives Low specificity; low PPV
omqSOFA[18]	Systolic blood pressure, respiratory rate, and altered mental status	2	Simple bedside screening tool Uses only clinical data, allowing for rapid diagnosis	Altered mental status in criteria may have nonseptic causes in obstetric patients Need for secondary testing
S.O.S.[17],*	Temperature, heart rate, respiratory rate, oxygen saturation, systolic blood pressure, heart rate, leukocyte count, percentage of immature neutrophils, and lactic acid	6	Excellent NPV 98.6% Rapidly rules out need for ICU Does not use altered mental status in criteria	Complex scoring system with multiple variables Requires laboratory data, which can delay diagnosis

MOEWS, modified Obstetric Early Warning Signs; PPV, positive predictive value; omqSOFA, obstetric modified quick Sepsis-related Organ Failure Assessment; S.O.S, Sepsis in Obstetrics Score; NPV, negative predictive value; ICU, intensive care unit.
* Free online calculator available at https://www.perinatology.com/calculators/Sepsis%20Calculator.htm.

Maternal Sepsis

Source and pathogens

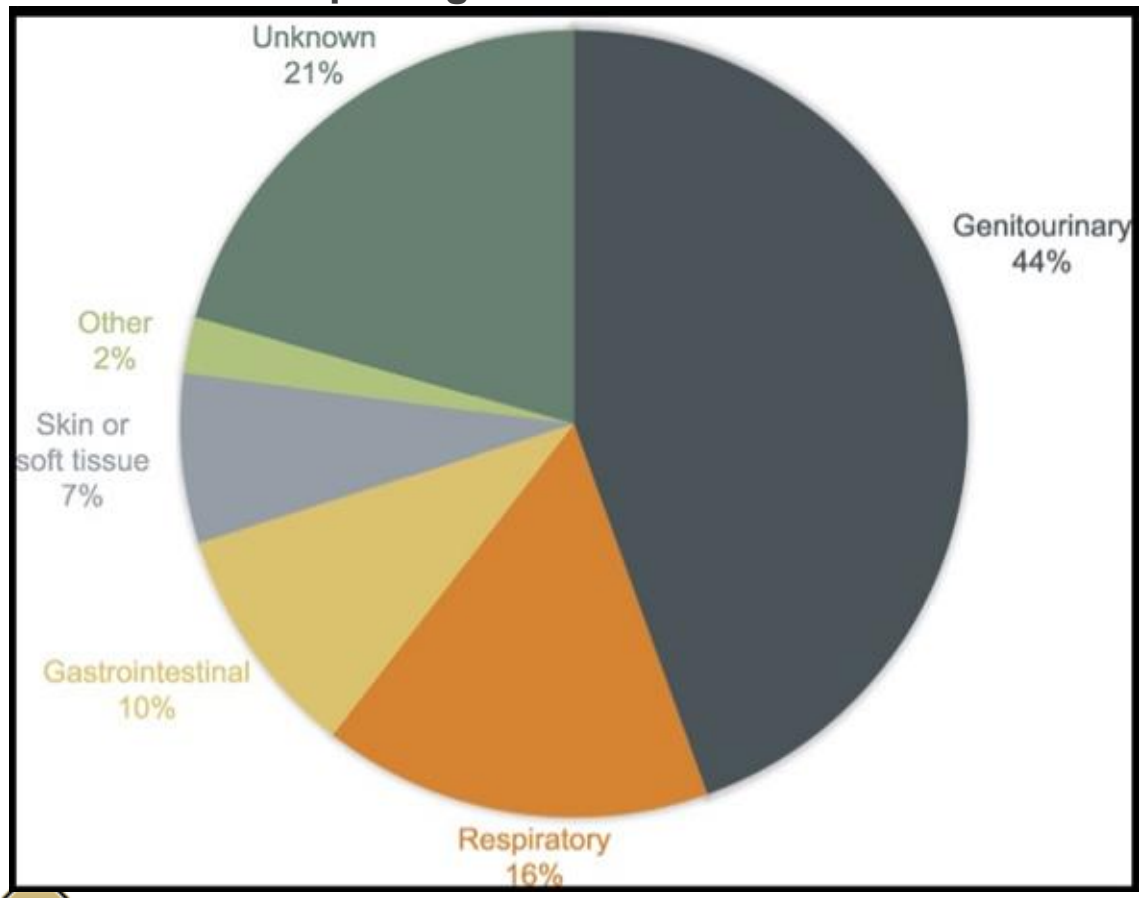


Table 1. Organisms isolated at each stage of pregnancy

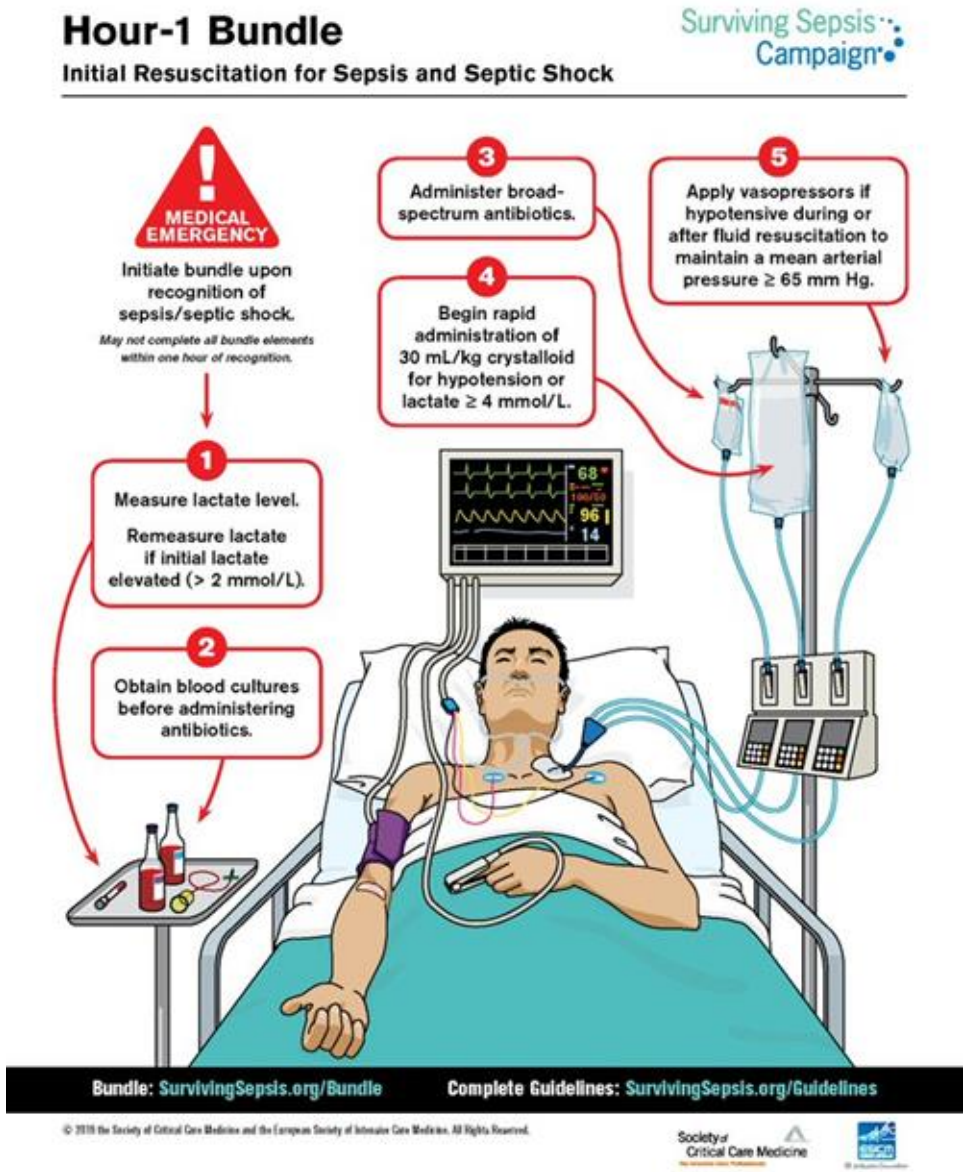
Organism	Antenatal	Intrapartum	Postnatal	All isolates
Escherichia coli	26	22	55	103
Group B *Streptococcus*	2	43	12	57
Anaerobes	4	8	11	23
Staphylococcus aureus	4	5	12	21
Enterococcus faecalis	2	5	6	13
Group A *Streptococcus*	0	2	10	12
Streptococcus milleri	1	4	4	9
Klebsiella pneumonia	1	2	2	5
Proteus mirabilis	0	3	2	5
Haemophilus influenzae	3	1	0	4
Streptococcus pneumoniae	1	0	3	4
Morganella morganii	0	0	3	3
Group C *Streptococcus*	0	1	2	3
Enterobacter species	1	0	2	3
Group G *Streptococcus*	0	0	2	2
Listeria monocytogenes	1	1	0	2
Moraxella species	0	0	2	2
Staphylococcus saprophyticus	0	1	1	2
Acinetobacter lwoffii	1	0	1	2
Streptococcus gallolyticus	0	1	0	1
Total	47	99	130	276

Obstetric sepsis

Treatment-2021 guidelines

	Shock is present	Shock is absent
Sepsis is definite or probable	✔ Administer antimicrobials ***immediately***, ideally within 1 hour of recognition.	✔ Administer antimicrobials ***immediately***, ideally within 1 hour of recognition.
Sepsis is possible	✔ Administer antimicrobials ***immediately***, ideally within 1 hour of recognition.	✔ Rapid assessment* of infectious vs. noninfectious causes of acute illness. ✔ Administer antimicrobials ***within 3 hours*** if concern for infection persists.

**Rapid assessment includes history and clinical examination, tests for both infectious and noninfectious causes of acute illness, and immediate treatment of acute conditions that can mimic sepsis. Whenever*



Antibiotics

"Go big so they can go home"

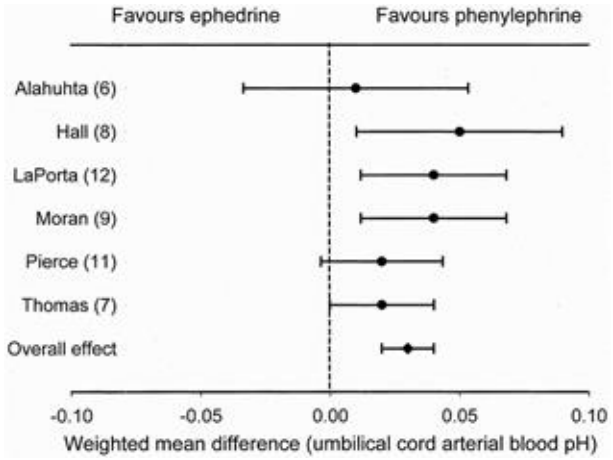
Table 3. Proposed broad-spectrum empiric antibiotic regimens of peripartum sepsis.

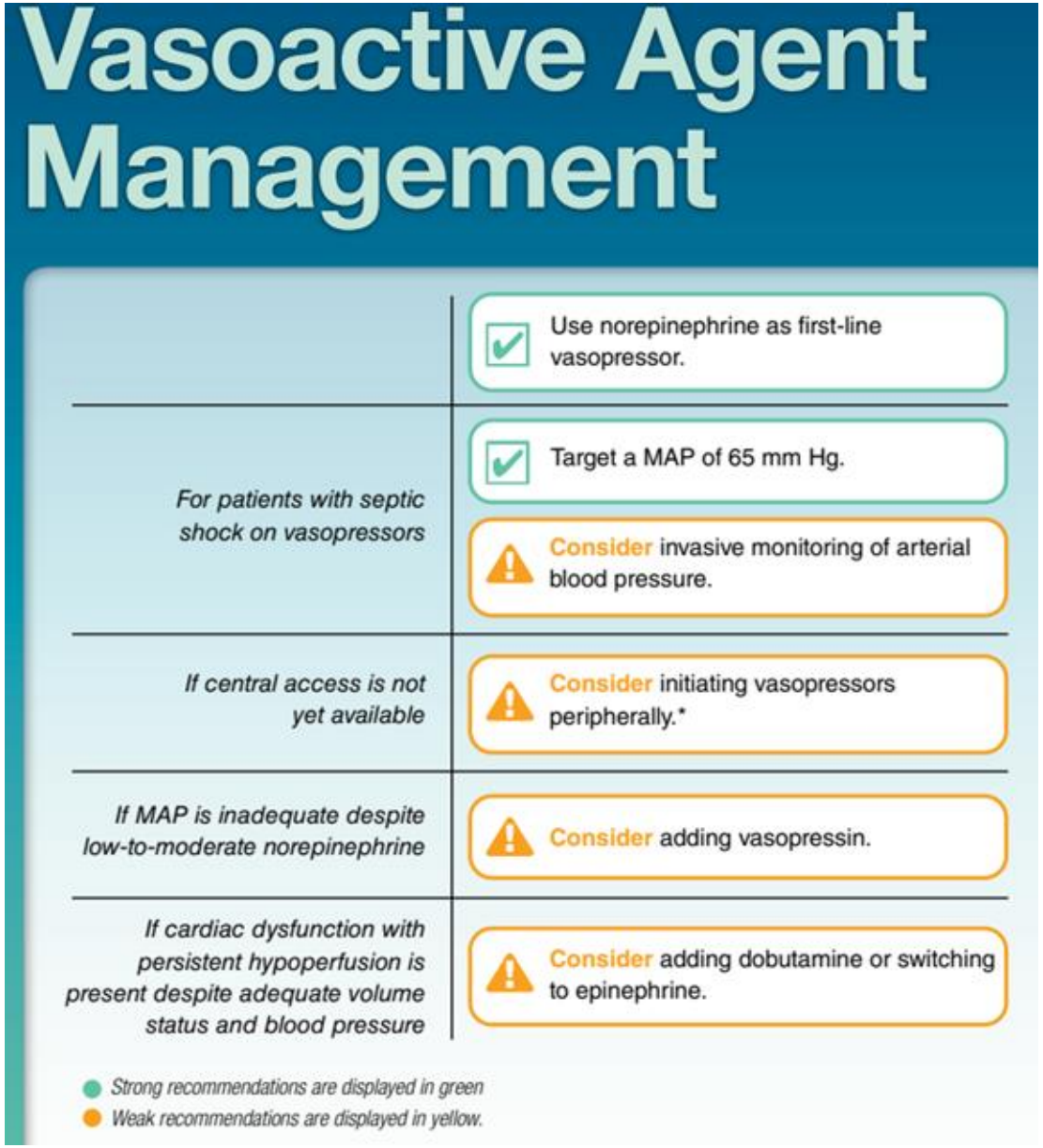
1.	**Gram-negative and anaerobic coverage** • Piperacillin/tazobactam 3.375 g IV q8h (extended infusion) or 4.5 g IV q6h **or** • Meropenem 1 g IV q8h (if recent hospitalization or concern for multi-drug resistant organisms) **or** • Cefepime 1–2 g IV q8h plus metronidazole 500 mg IV q8h **or** • Aztreonam 2 g IV q8h (for women with severe penicillin allergy) plus metronidazole 500 mg IV q8h **or** • Aztreonam 2g IV q8h plus clindamycin 900 mg IV q8h
	PLUS
2.	**Gram-positive coverage** • Vancomycin 15–20 mg/kg q8h–q12h (goal trough 15–20 mcg/mL) **or** • Linezolid 600 mg IV/PO q12h (for women with severe vancomycin allergy)

Obstetric sepsis

Treatment-2021 guidelines

- Levo is the preferred pressor in shock (and in pregnancy)
- Second line agent is controversial
  - Vasopressin may increase contractions
  - Phenylephrine improves UA blood flow
  - MAP goal is unknown

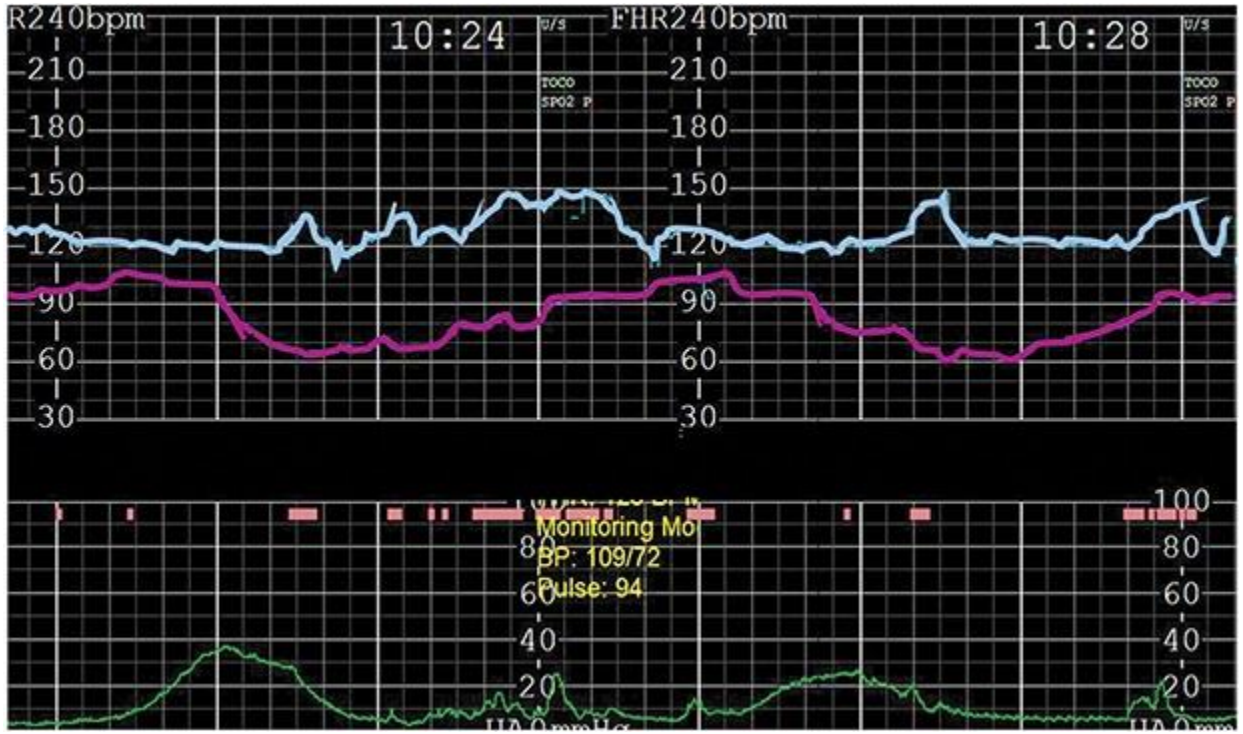




Obstetric Sepsis

Alterations in OB sepsis

- Increased rates of bacteremia for any given infection
  - Pylo=> 20-30% bacteremia
  - Transient bacteremia in labor
- Surviving sepsis guidelines
  - MAP>65?
  - Fluid tolerant
  - Often hypovolemic
- ScVO2 is lower in the 3rd trimester
- Fetal monitoring
- Don't miss GAS!
  - Surgical emergency



Group A Strep

1. TIME: Optimize rapid recognition and diagnosis of GAS

1. TOXIN: Understand medical management of GAS

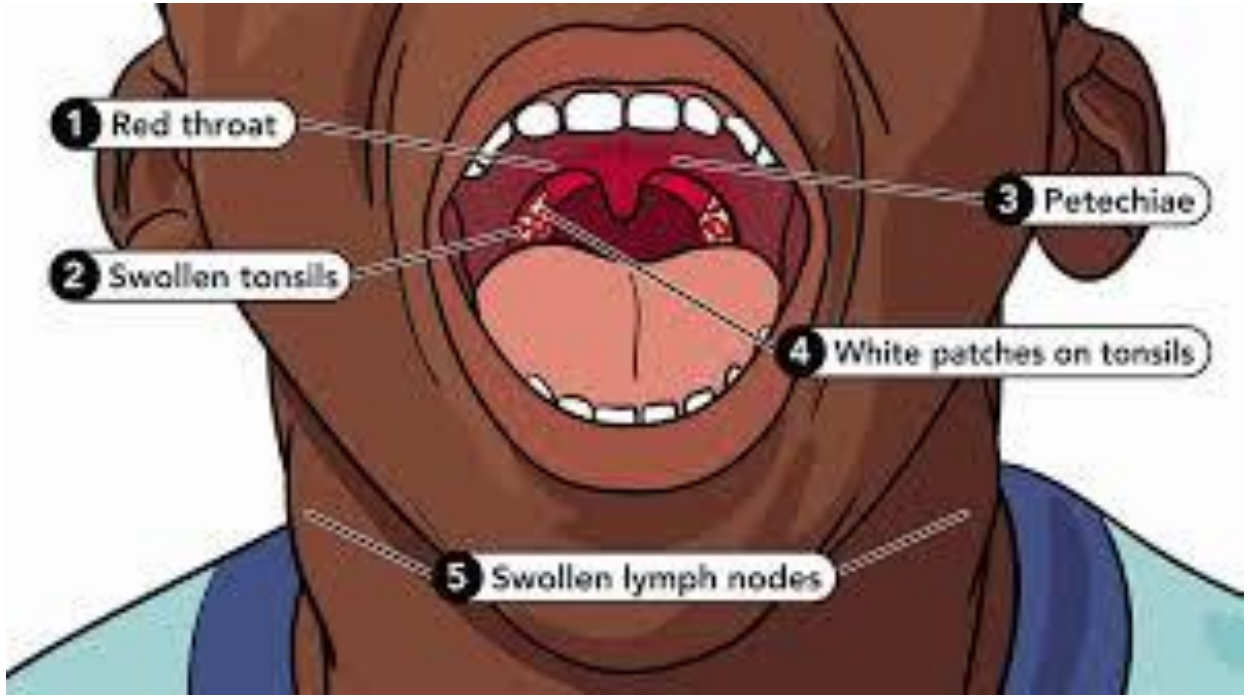
1. TISSUE: Recognize when surgical management of GAS is indicated.

1. TRAGEDY: Review Modern outcomes from GAS

TIME

Populations at risk:

- Recently postpartum/postabortive
- Prolonged ROM
- Preterm birth
- Cesarean delivery
- Multigravida
- GAS colonization/exposure



TIME

Signs and symptoms

Typical

- Pain out of proportion to exam
- Fever
- Malodorous vaginal discharge
- Tender/boggy uterus

Atypical

- Joint pain/swelling
- Nausea and vomiting
- Rash

TIME

Imaging and labs

Labs:

- Bandemia (>10%)
- Renal impairment (Cr >1.1 mg/dL)
- Liver injury (AST/ALT>2x uln)
- Coagulopathy (plts <100k, DIC)
- Endometrial biopsy?
- Bacteremia (50%)

Imaging:

- Not required for diagnosis
- Can be useful if source is unknown
- MRI without contrast antepartum
- CT with contrast for deep infections
- Ultrasound for superficial infections

Maternal Sepsis

identification

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* Free online calculator available at https://www.perinatology.com/calculators/Sepsis%20Calculator.htm.

TOXIN

Antimicrobials

Initial treatment should be broad

- Ampicillin-sulbactam is not adequate for Severe disease
- Gent/clinda is losing B fragilis activity

- Linezolid+Pip-Tazo/Carbapenem

or

- Vanc+pip-tazo/Cabbapenem+clinda

Once GAS is identified narrow coverage

- PCN+Clindamycin

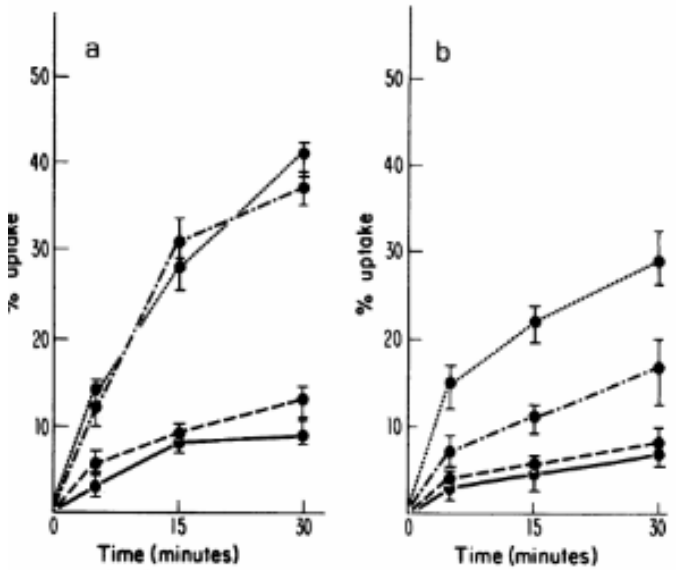

FIGURE 1 Phagocytosis of *S. pyogenes* S43 by PMN and MN. 4-h logarithmic-phase cultures grown in the presence or absence of clindamycin (1/2, 1/4, and 1/40 MIC) were used as targets for phagocytosis measured by following uptake of radiolabeled bacteria by PMN (*a*) and MN (*b*). —, streptococci grown in absence of clindamycin; ----, streptococci grown in presence of 0.025 μg/ml clindamycin (1/2 MIC); ·–·, streptococci grown in presence of 0.01 μg/ml clindamycin (1/4 MIC); – – –, streptococci grown in presence of 0.001 μg/ml clindamycin (1/40 MIC).

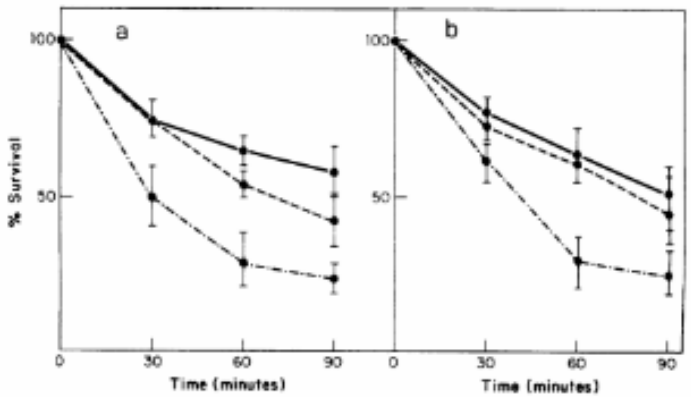

FIGURE 2 Killing of *S. pyogenes* S43 by PMN and MN. 4-h logarithmic-phase cultures grown in the presence or absence of clindamycin (1/2 and 1/4 MIC) were used as targets for killing by PMN (a) and MN (b). ——, streptococci grown in absence of clindamycin; –·–·, streptococci grown in presence of 0.025 μg/ml clindamycin (1/2 MIC); – – –, streptococci grown in the presence of 0.01 μg/ml clindamycin (1/4 MIC).

TOXIN

Treatment-2021 guidelines

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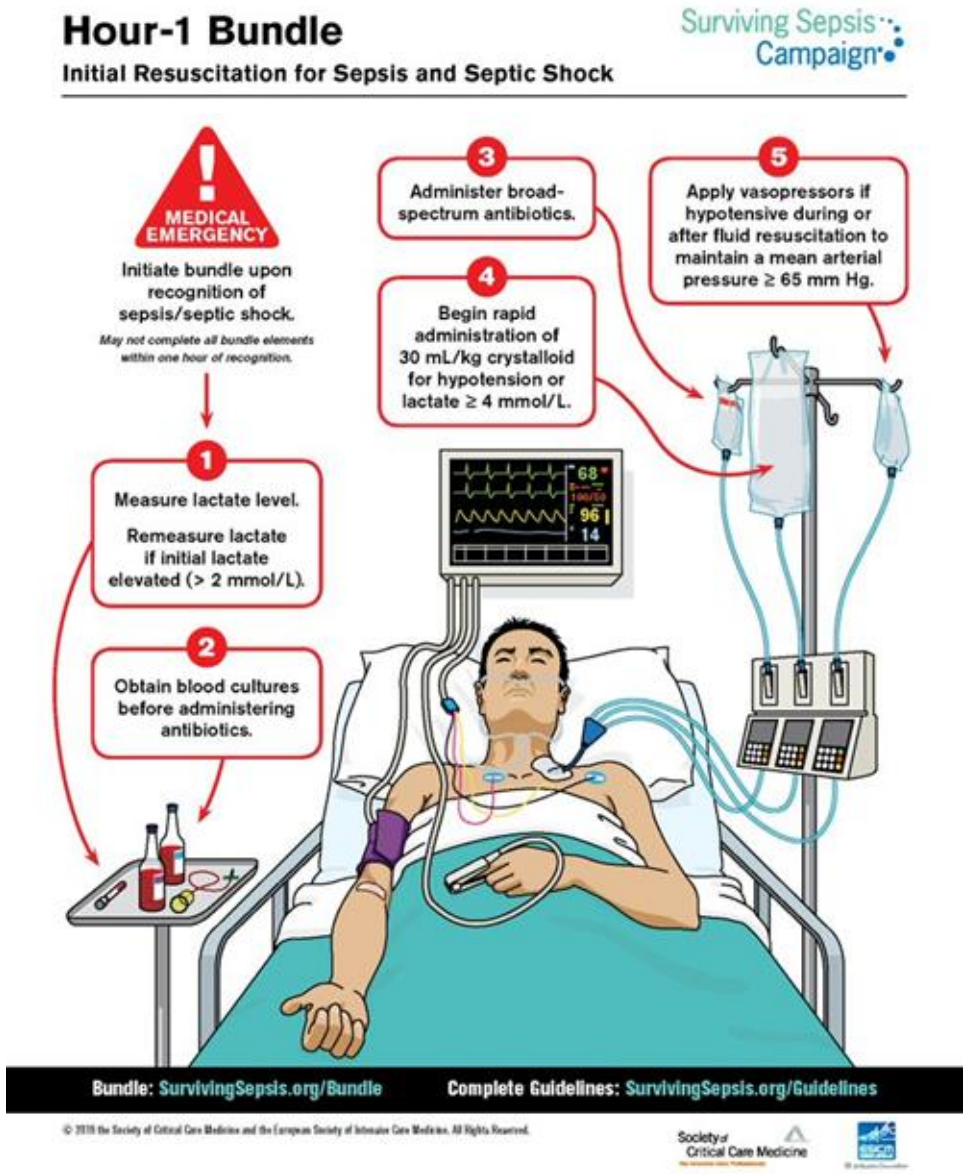


TOXIN

Adjuvants

IVIG

- Theory: neutralizes Toxin/superantigen
- Data: retrospective was promising, RCT showed no improvement
- IDSA guidelines: “Additional studies of the efficacy of IVIG are necessary before a recommendation can be made supporting its use in this setting.”

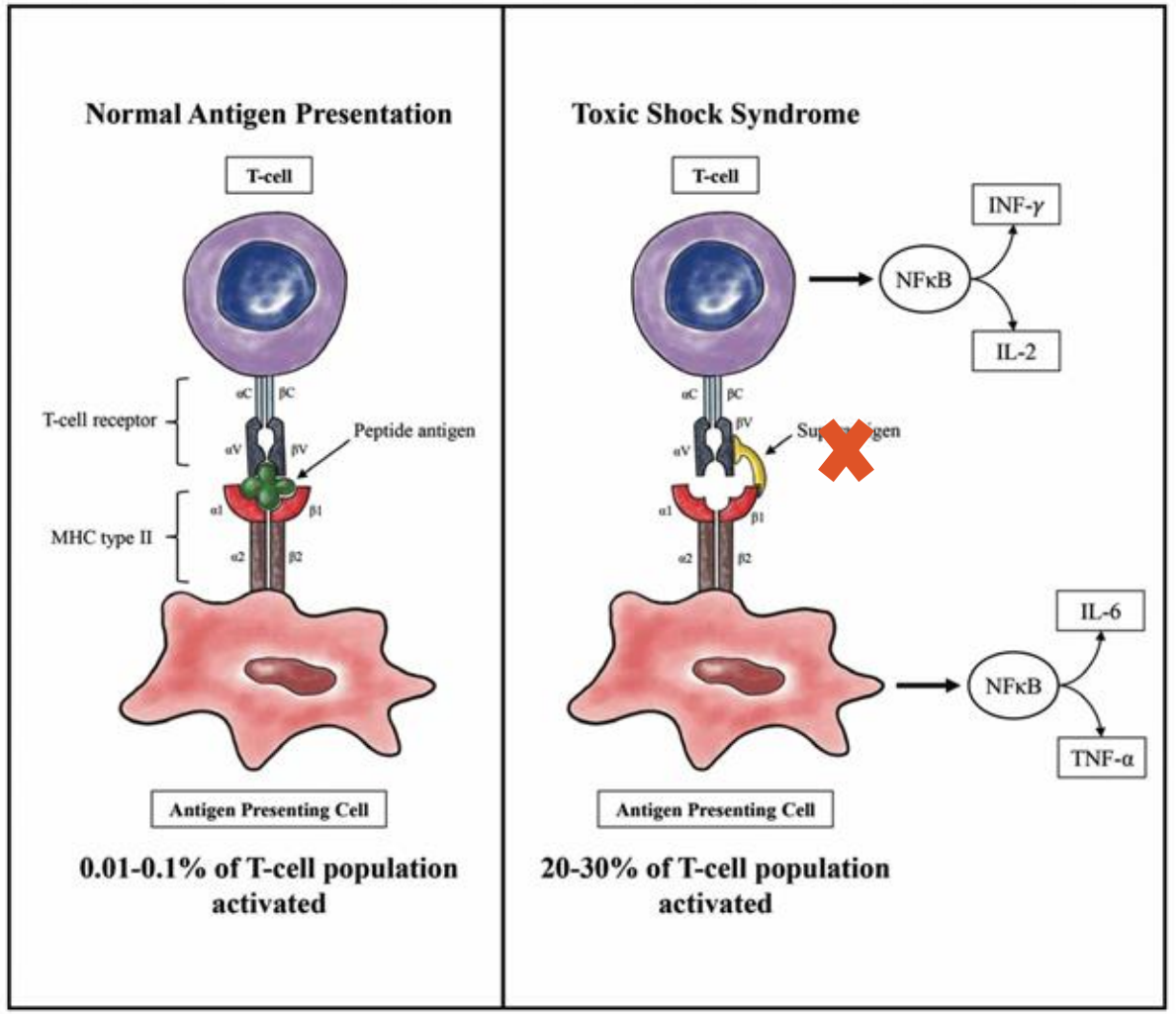


Fig. 4. Schematic of normal T-cell activation and abnormal T-cell activation induced by superantigen. Note that more inflammatory markers are secreted downstream than are shown in the figure.

Celie KB et al. PMID 33133879

TISSUE

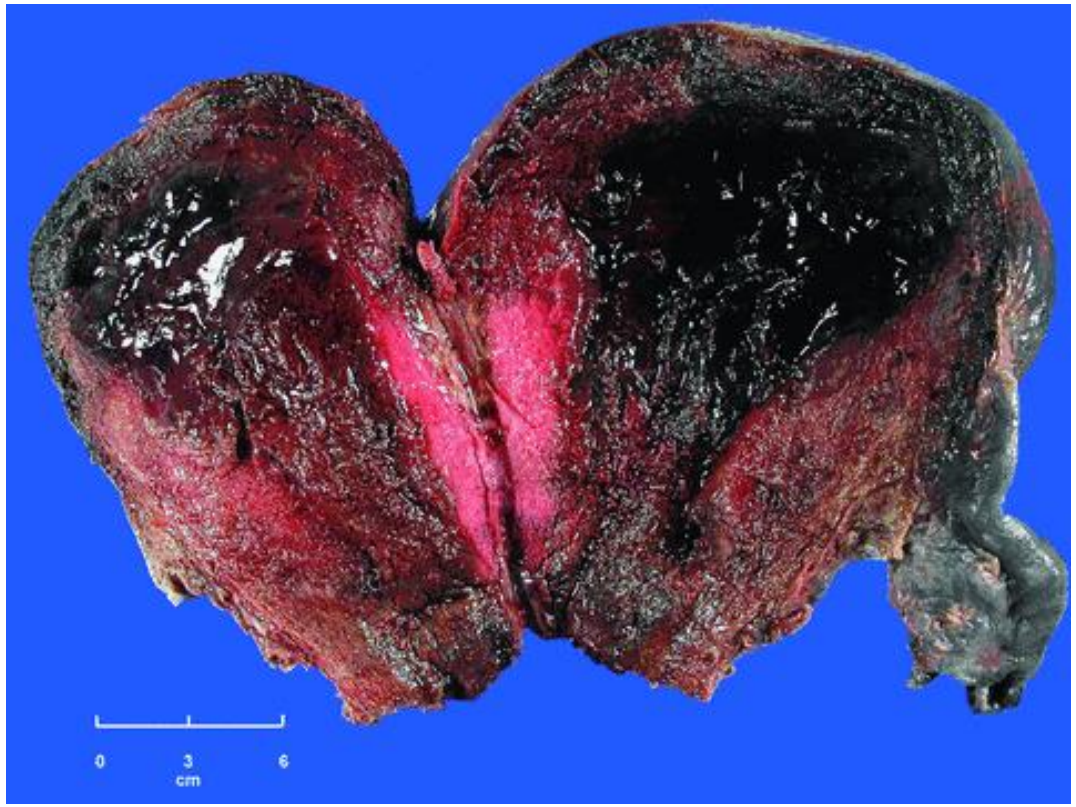
Who needs surgery?

CHIPS scoring system

	+4	+3	+2	+1	0	+1	+2	+3	+4
Temperature, °C	≥41	39-40.9		38.5-38.9	36-38.4	34-35.9	32-33.9	30-31.9	≤29.9
Mean Arterial Pressure, mm HG	≥160	130-159	110-129		70-109		50-69		≤49
Heart Rate	≥180	140-179	110-139		70-109		55-69	40-54	≤39
Respiratory Rate	≥50	35-49		25-34	12-24	10-11	6-9		≤5
White Blood Cell Count	≥40		20-39.9	15-19.9	3-14.9		1-2.9		≤1
Objective Concern for Capillary Leak (ARDS, Ascites, Pleural Effusion, Abdominal Distention)	Yes				No				

- From SSTI data: A 6 hr delay in surgical management leads to a 3x in mortality rates
- Calculating hysterectomy rate in puerperal sepsis score (CHIPS): The area under the ROC curve for the final model was 0.83. A score of 10 predicted a greater than 60% probability of hysterectomy, with specificity of over 90%. A score of 13 yielded specificity of 100%

TISSUE

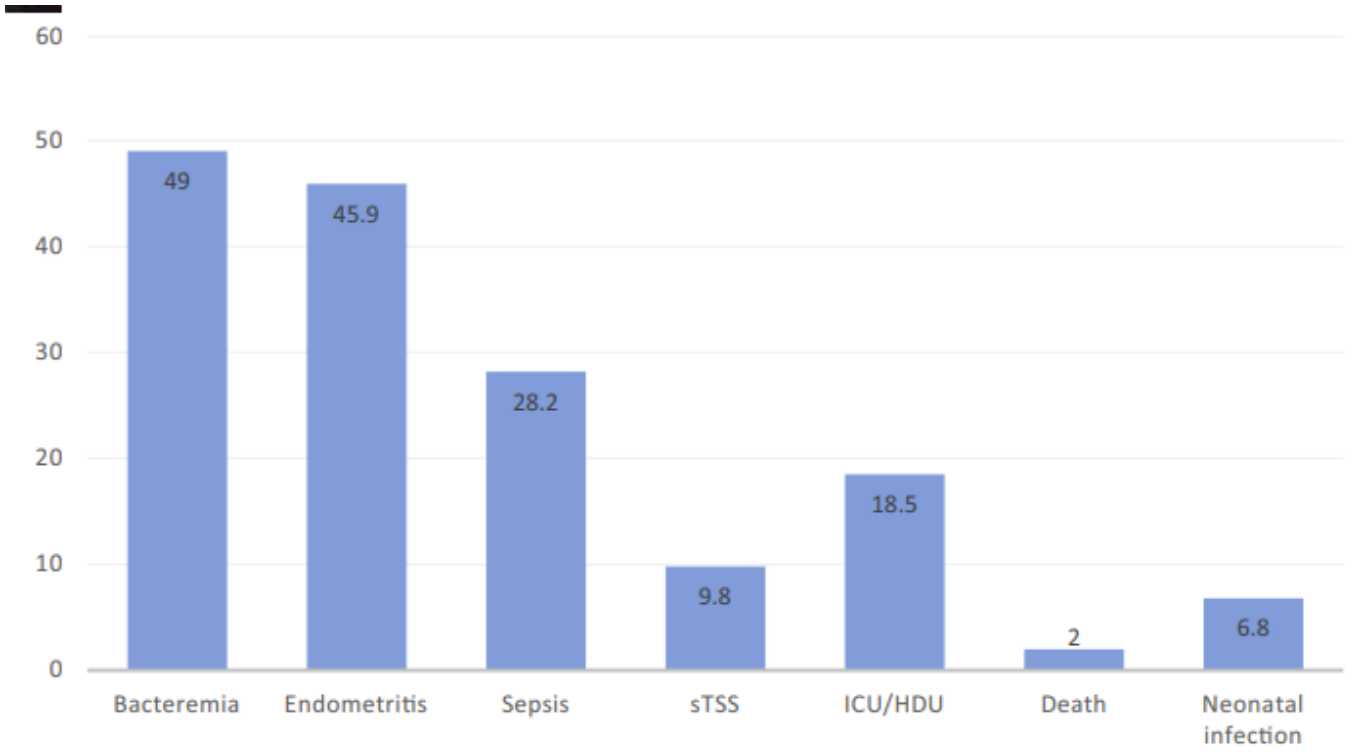


“Hysterectomy was not required in the majority of GAS cases (213/246; 86.6%), even in the context of puerperal sepsis and sTSS. In the described cases where hysterectomy was performed, there was often evidence of necrotizing fasciitis in addition to sepsis, sTSS and multiorgan failure. Most experts agree that a confirmed GAS infection in the presence of organ dysfunction should be managed surgically”

TRAGEDY

Outcomes

- Death occurs in 10–15% of all invasive cases, more than 35% of patients with streptococcal toxic shock syndrome, and approximately 25% of necrotizing fasciitis cases



ACLS in Pregnancy

Cardiac arrest epidemiology

In-hospital arrests

- 2-3:100,000 pregnancies
- Risks
  - Age
  - BMI
  - Mode of delivery
- Etiology: 27% anesthetic complications
- Survival: 58% (12% non preg)

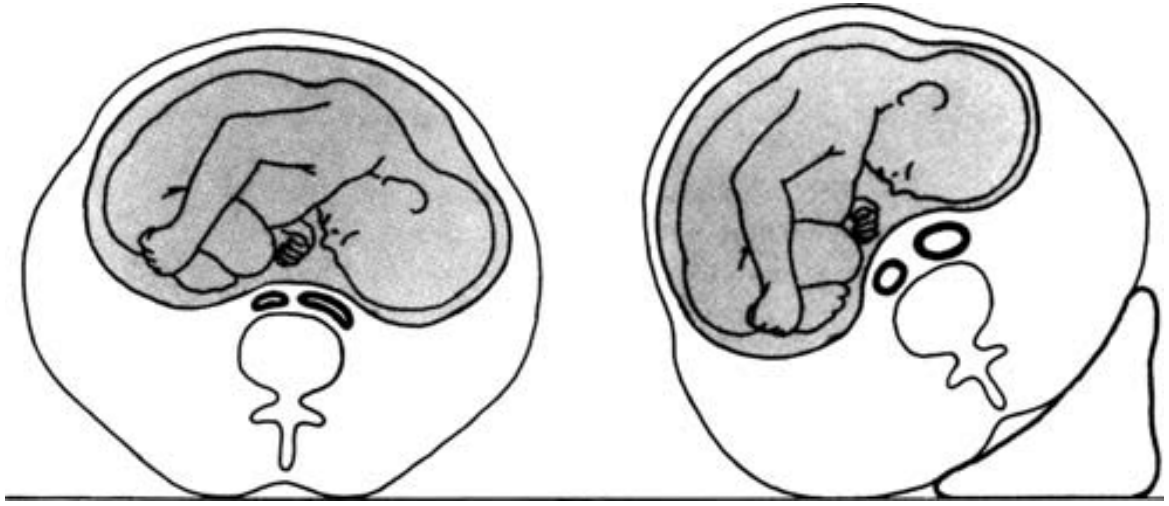
Table 4. Suspected and confirmed (at post mortem) causes for women who died and women who survived

Cause	Women who survived (n = 37)	Women who died (n = 22)
Presumed premortem causes (n = 59)		
Cardiac tamponade	1	0
Hypoxia	4	0
Hypovolaemia	5	8
Venous thromboembolism	1	7
Toxic drug cause	1	0
Anaphylaxis	1	0
Sepsis	0	1
Anaesthetic cause	17	0
Amniotic fluid embolism	5	3
Cardiac cause	5	1
Intracerebral bleed	0	3
Aortic dissection	0	2
Asthma	0	1
Pulmonary artery rupture	0	1
Postmortem causes of collapse (n = 19)		
Amniotic fluid embolism		6
Vessel bleed/rupture		5
Thrombembolic		3
Cardiomyopathy		2
Other		3

Data were available for 59 women. Some women were suspected of having more than one cause, where this is the case both causes have been recorded.

Perimortem Cesarean

- Who?
  - Any patient greater than 20 weeks gestation, or when the uterine fundus can be palpated at the umbilicus



Perimortem Cesarean

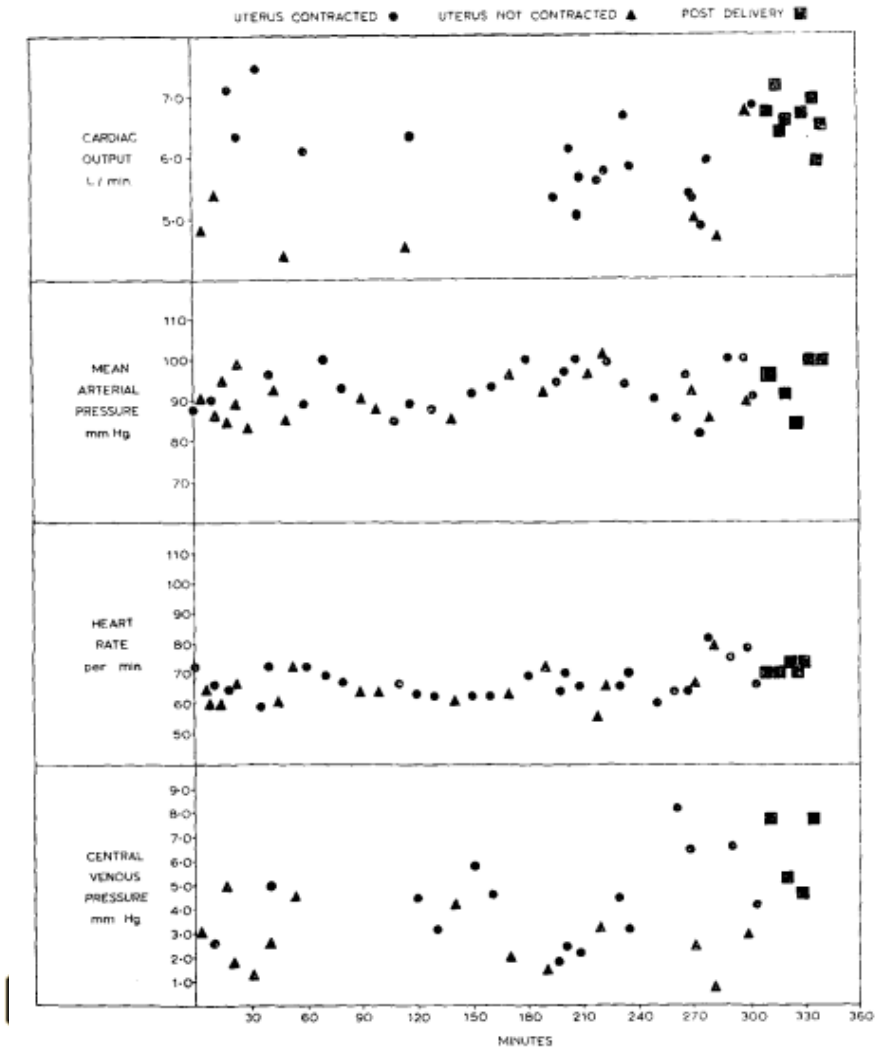


FIG. 2
Serial observations in a single case throughout 350 minutes of labour.

- Why?
  - Delivery leads to a massive maternal autotransfusion

Table 2. Time to emergency procedures in minutes, median (range), following maternal collapse

	Women who survived (n = 38)	Women who died (n = 28)	P-value
Collapse to BLS	0 (0–17)	0 (0–23)	0.28
Collapse to ALS	1 (0–36)	0 (0–24)	0.08
Collapse to PMCS	3 (0–39)	12 (0–67)	0.01

Mann–Whitney U tests for nonparametric data were applied.

Perimortem Cesarean

- When?
  - Initiate at 4 mins, delivery by 5 mins

Table 2. Postmortem Cesarean Deliveries With Surviving Infants With Reports of Time From Death of the Mother Until Delivery (From 1900–1985)

Cases	No. patients	Percent
0–5 min	42 (normal infants)	70
6–10 min	7 (normal infants)	13
	1 (mild neurologic sequelae)	
Subtotal	8	
11–15 min	6 (normal infants)	12
	1 (severe neurologic sequelae)	
Subtotal	7	
16–20 min	1 (severe neurologic sequelae)	1.7
21+ min	2 (severe neurologic sequelae)	
	1 (normal infant)	3.3
Subtotal	3	
Total	61	100

Perimortem Cesarean

- Where?
  - At the site of arrest

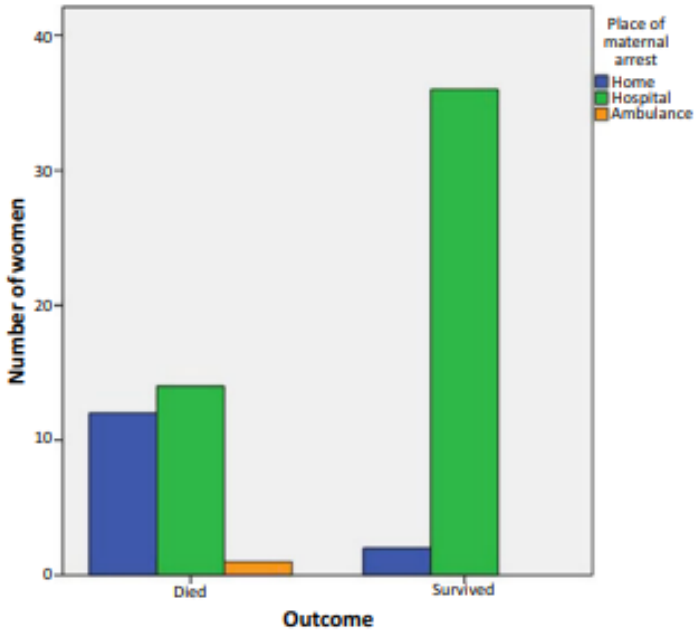


Figure 1. The place where the cardiac arrest occurred (n = 66). P < 0.001 chi-square test.

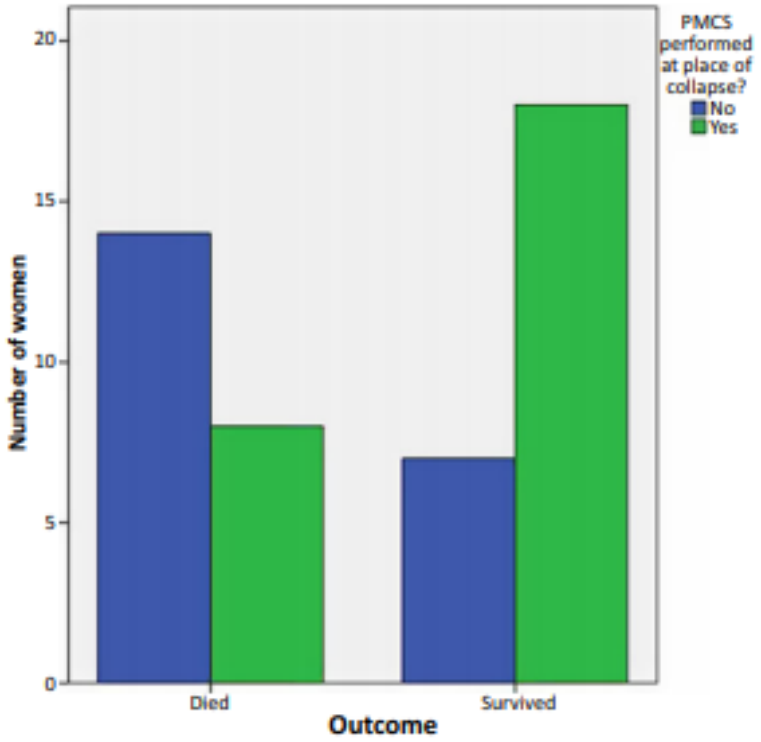
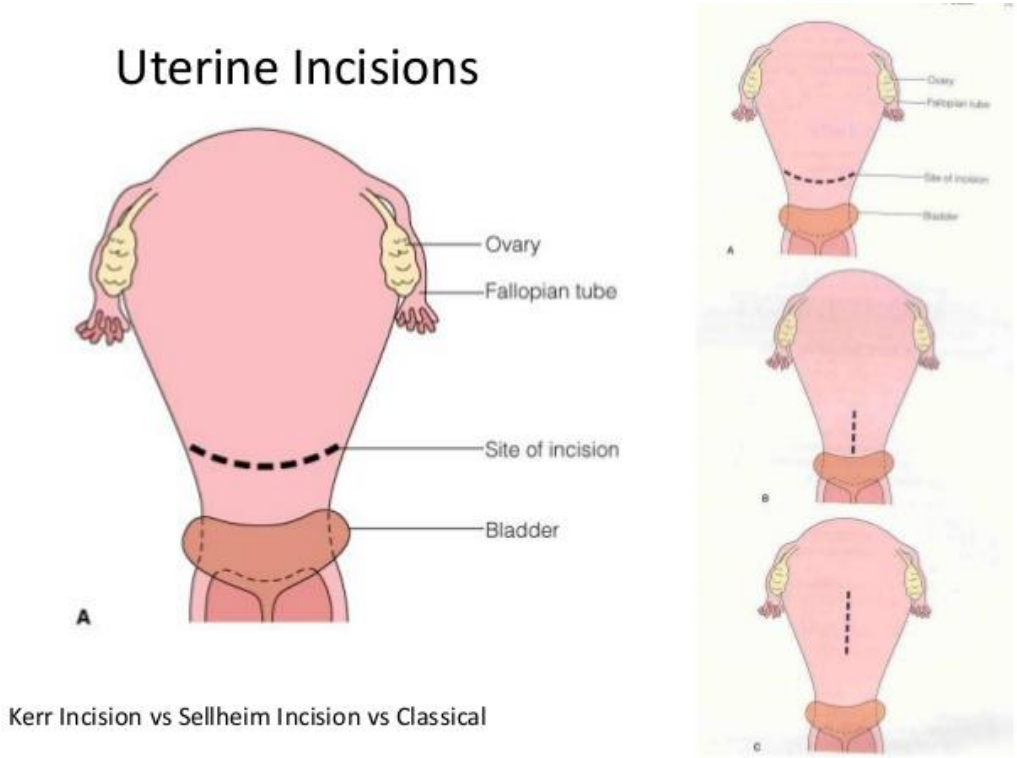


Figure 2. The site of perimortem caesarean section (n = 47, as data were missing for two cases of PMCS). P < 0.001 chi-square test.

Perimortem Cesarean

- How?
  - Midline vertical abdominal entry
  - Transverse or vertical uterine incision
  - Fetal delivery
  - Placenta can remain insitu until ROSC
  - Patient can be packed until ROSC



Kerr Incision vs Sellheim Incision vs Classical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Questions?