PROPHYLACTIC ANTIBIOTICS ON LABOR & DELIVERY

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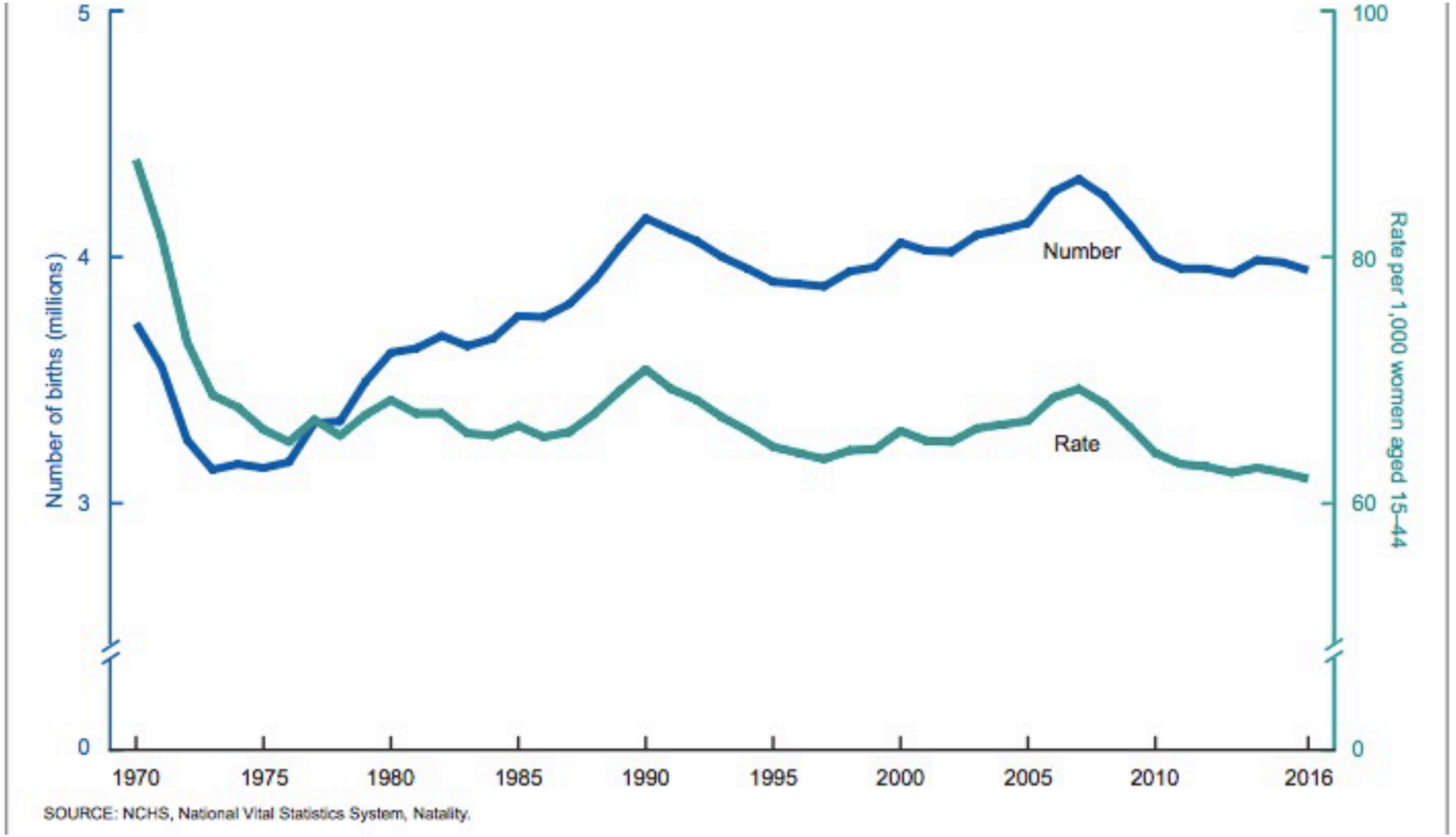
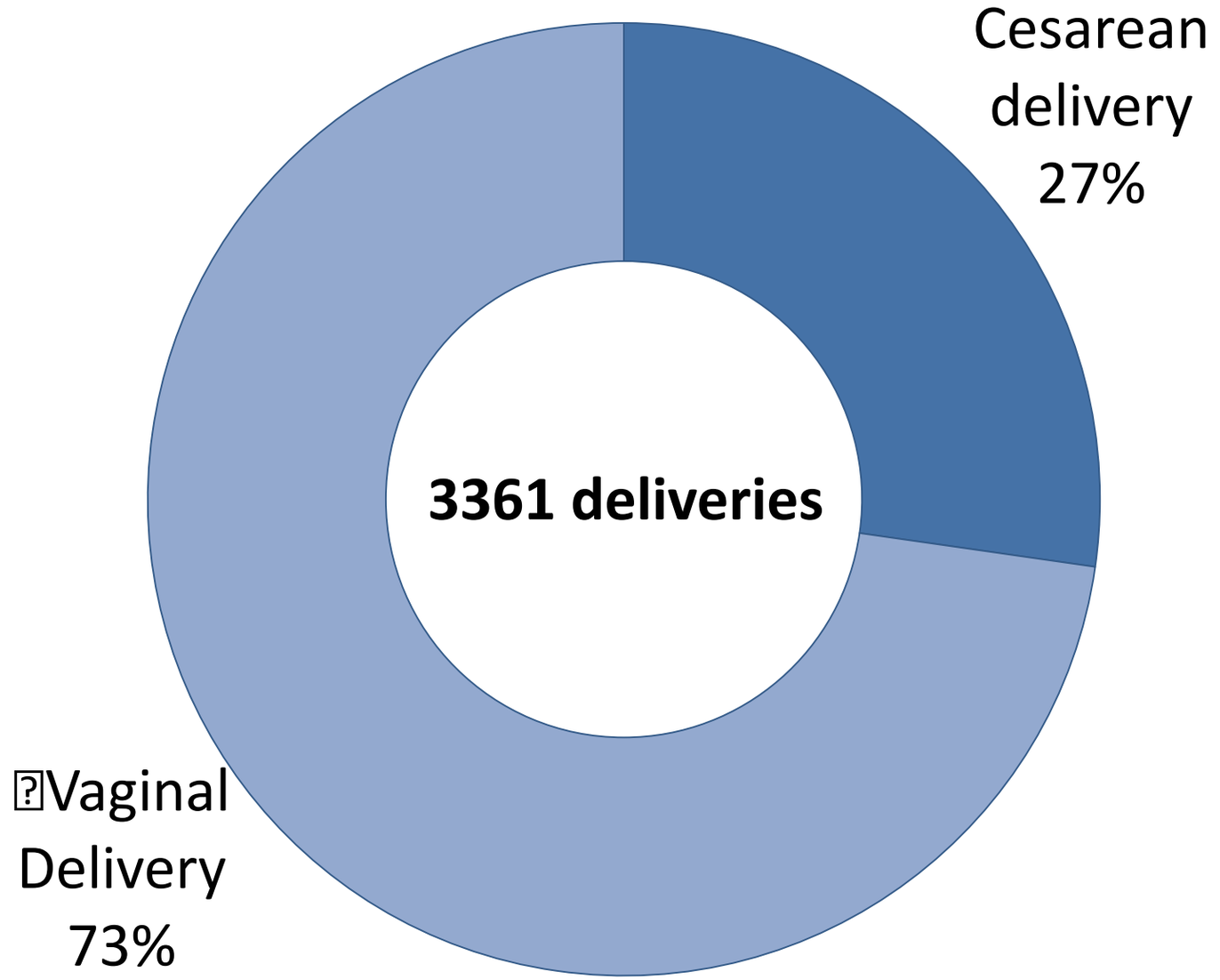
No disclosures

ANNUAL U.S BIRTHS



National Center for Health Statistics 2018

UNIVERSITY OF UTAH DELIVERIES (2017)



ANTIBIOTIC PROPHYLAXIS

- Goal is to have therapeutic tissue levels at time of microbial contamination

- Agent of choice should be **long acting**, **narrowly focused** on the likely bacteria, **inexpensive**, and have a **low incidence of adverse effects**

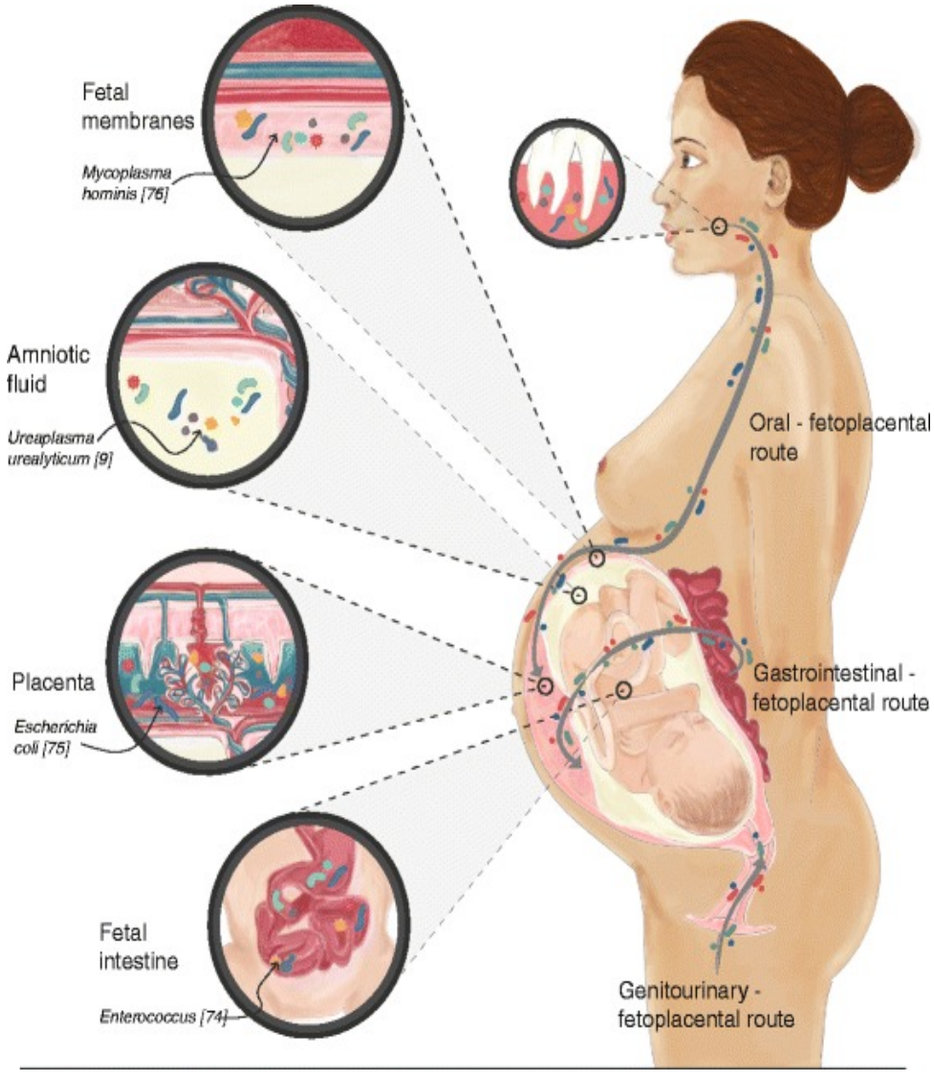
GENITOURINARY TRACT MICROBIOLOGY

Gram positive aerobic	Gram negative aerobic	Anaerobic	Mycoplasma	Other
GBS	E. coli	Peptostreptococcus	Mycoplasma	Chlamydia
S. auerus	Klebsiella	Peptococcus	Ureaplasma	
Enterococcus	Proteus	Bacteroides		
	Pseudomonas	Gardnerella		
	Enterobacter			

Gibbs, Am J Obstet Gynecol 1987

ANTIBIOTIC MISUSE

- Allergic reactions
- GI disturbance
- Unknown fetal effects
- Potential healthcare costs
- Antibiotic resistance



Ledger. BJOG 2013
Stiemsma. Pediatrics 2018

CLOSTRIDIUM DIFFICILE

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

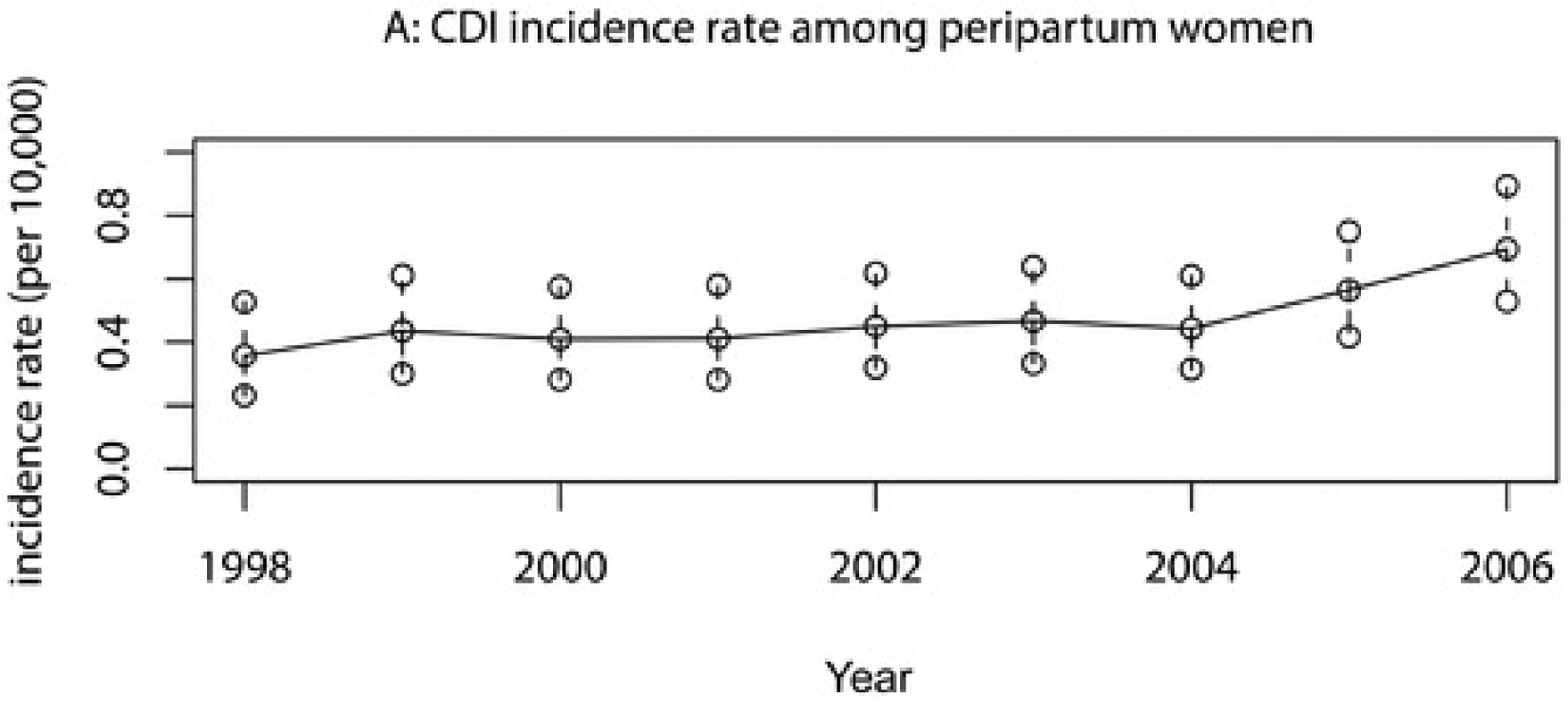
Burden of *Clostridium difficile* Infection in the United States

Fernanda C. Lessa, M.D., M.P.H., Yi Mu, Ph.D., Wendy M. Bamberg, M.D., Zintars G. Beldavs, M.S., Ghinwa K. Dumyati, M.D., John R. Dunn, D.V.M., Ph.D., Monica M. Farley, M.D., Stacy M. Holzbauer, D.V.M., M.P.H., James I. Meek, M.P.H., Erin C. Phipps, D.V.M., M.P.H., Lucy E. Wilson, M.D., Lisa G. Winston, M.D., Jessica A. Cohen, M.P.H., Brandi M. Limbago, Ph.D., Scott K. Fridkin, M.D., Dale N. Gerding, M.D., and L. Clifford McDonald, M.D.

ABSTRACT

Lessa et al. N Engl J Med 2015

C. DIFF AMONG PERIPARTUM WOMEN



Kuntz et al. Infect Control Hosp Epidemiol 2010

OBJECTIVES

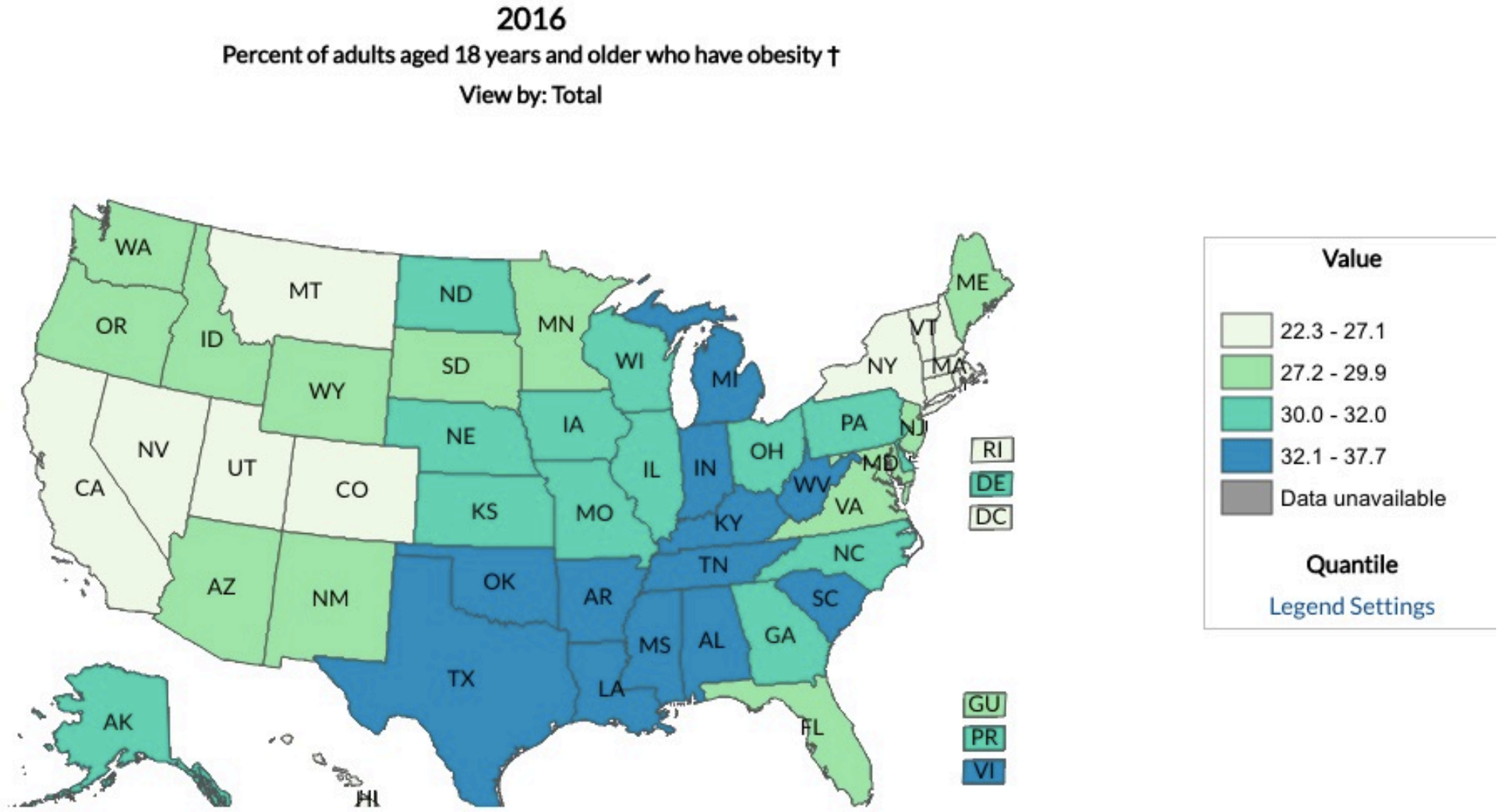
- Post-op antibiotics following cesarean in BMI > 30
- Cesarean complicated by Triple-I
- Manual placental removal
- Obstetric anal sphincter injury

CESAREAN AS RISK FACTOR FOR INFECTION

- Surgical site infection (SSI) following cesarean section:
  - reported rates of 3–20 %

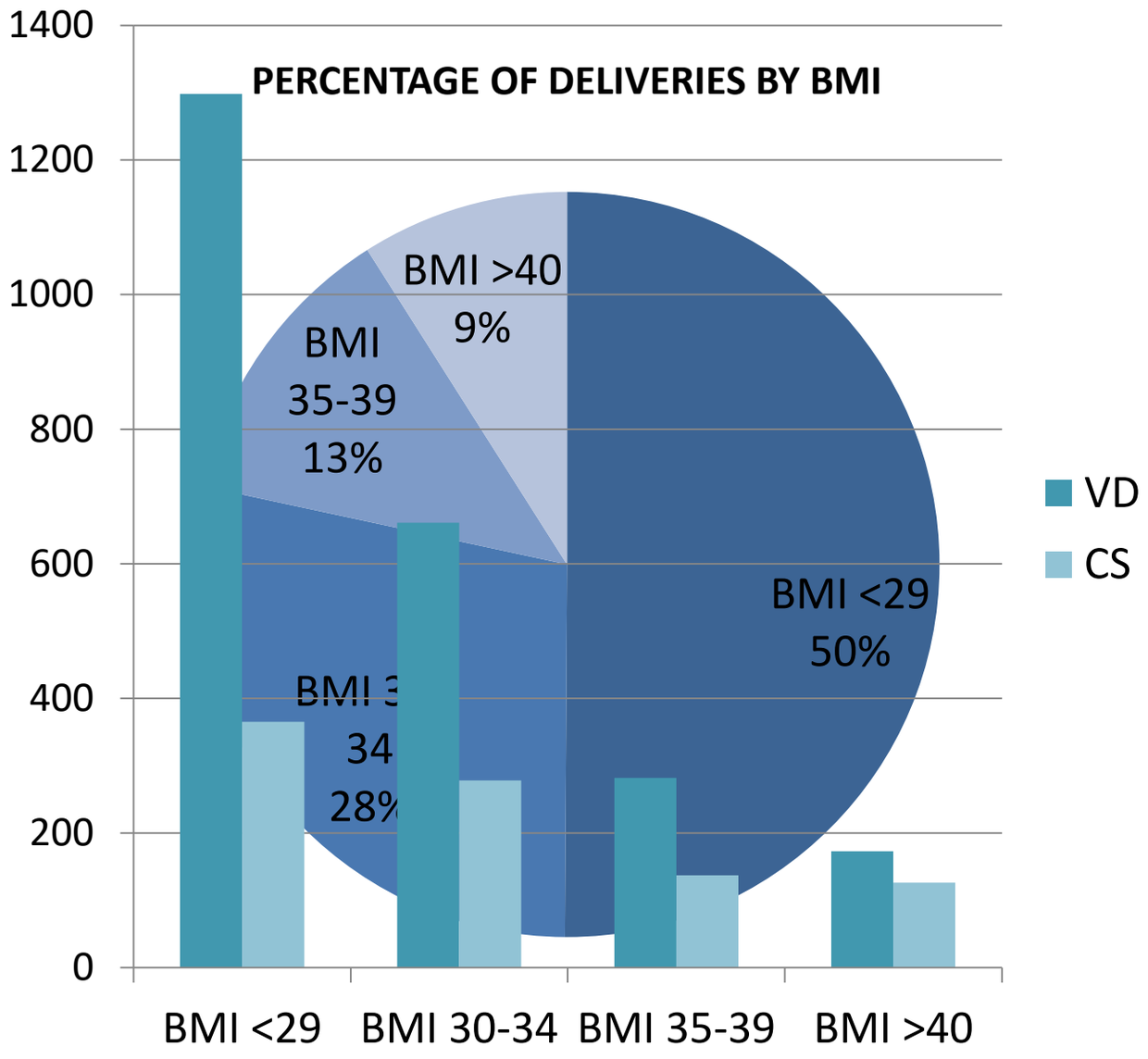
Costantine et al. Am J Obstet Gynecol 2008

OBESITY IN PREGNANCY



CDC. National Center for Chronic Disease Prevention and Health Promotion, 2018

UNIVERSITY OF UTAH – DELIVERY TYPE BY BMI



CEFAZOLIN DOSING FOR BMI > 30

- **Standard dose recommendation:** 2g cefazolin within 60 minutes of incision

Bratzler et al. Am J Health Syst Pharm 2013

Post-cesarean extended oral prophylaxis in BMI > 30

POST-CESAREAN ORAL KEFLEX AND FLAGYL

September 19, 2017

Effect of Post-Cesarean Delivery Oral Cephalexin and Metronidazole on Surgical Site Infection Among Obese Women

A Randomized Clinical Trial

Amy M. Valent, DO[1]; Chris DeArmond, RN[2]; Judy M. Houston, RPh[3]; et al

» Author Affiliations | Article Information

JAMA. 2017;318(11):1026-1034. doi:10.1001/jama.2017.10567

POST-CESAREAN ORAL KEFLEX AND FLAGYL

Table 2. Study Outcomes

Outcomes	No. (%) [95% CI] With Outcome		Mean Between-Group Difference, % (95% CI)	Relative Risk (95% CI)	*P* Value
	Cephalexin-Metronidazole (n = 202)	Placebo (n = 201)			
Primary outcome					
Surgical site infection[a]	13 (6.4) [3.0 to 9.8]	31 (15.4) [10.4-20.4]	9.0 (2.9 to 15.0)	0.41 (0.22-0.77)	.01
Secondary outcomes					
Incisional morbidity[b]	20 (9.9) [5.8 to 14.1]	32 (15.9) [10.8-21.0]	6.0 (−0.5 to 13.0)	0.61 (0.37-1.04)	.18
Fever of unknown etiology	9 (4.5) [1.6 to 7.3]	10 (5.0) [2.0-8.0]	0.5 (−3.6 to 4.6)	0.89 (0.37-2.14)	.94
Wound separation	16 (7.9) [4.2 to 11.7]	22 (10.9) [6.6-15.3]	3.0 (−2.7 to 8.8)	0.72 (0.39-1.33)	.56
Cellulitis	12 (5.9) [2.7 to 9.2]	27 (13.4) [8.9-18.2]	7.5 (1.7 to 13.0)	0.44 (0.23-0.84)	.04
Endometritis	2 (1.0) [−0.4 to 2.4]	8 (4.0) [1.3-6.7]	3.0 (−0.05 to 6.0)	0.24 (0.53-1.16)	.05

[a] Defined as any superficial incisional, deep incisional, or organ/space infection.

[b] Defined as any defect in the incisional integrity with or without the presence of an infection, including cellulitis, endometritis, and wound separation.

Valent et al. JAMA 2017

INTACT VS RUPTURED MEMBRANES

Table 3. Post Hoc Study Outcomes Stratified by Membrane Status[a]

Outcomes	No. (%) [95% CI] With Outcome		Mean Between-Group Difference, % (95% CI)	Relative Risk (95% CI)	*P* Value
	Cephalexin-Metronidazole	Placebo			
Ruptured Membranes (n = 126)					
Primary outcome	(n = 63)	(n = 63)			
Surgical site infection	6 (9.5) [2.1 to 16.9]	19 (30.2) [18.6 to 41.7]	20.6 (6.9 to 34.3)	0.31(0.13-0.71)	.008
Secondary outcomes					
Incisional morbidity	10 (15.9) [6.7 to 25.1]	19 (30.2) [18.6 to 41.7]	14.3 (0.5 to 29.0)	0.51 (0.26-0.99)	.10
Fever of unknown etiology	4 (6.3) [0.2 to 12.5]	7 (11.1))[3.2 to 19.0	4.8 (−5.2 to 14.8)	0.55 (0.17-1.79)	.46
Wound separation	8 (12.7) [4.3 to 21.1]	11 (17.5) [7.9 to 27.0]	4.8 (−7.9 to 17.5)	0.70 (0.30-1.62)	.54
Cellulitis	5 (7.9) [1.1 to 14.7]	15 (23.8) [13.1 to 34.5]	15.9 (3.2 to 28.6)	0.32 (0.13-0.83)	.03
Endometritis	2 (3.2) [−1.2 to 7.6]	8 (12.7) [4.3 to 21.1]	9.5 (0.06 to 19.0)	0.25 (0.06-1.13)	.048
Intact Membranes (n = 277)					
Primary outcome	(n = 138)	(n = 139)			
Surgical site infection	7 (5.0) [1.4 to 8.7]	12 (8.7) [4.0 to 13.4]	3.7 (−2.3 to 9.6)	0.58 (0.24-1.44)	.47
Secondary outcomes					
Incisional morbidity	10 (7.2) [(2.9 to 11.5]	13 (9.4) [4.5 to 14.3]	2.2 (−4.3 to 8.8)	0.77 (0.35-1.69)	.78
Fever of unknown etiology	5 (3.6) [0.5 to 6.7]	3 (2.2) [−0.3 to 4.6]	−1.4 (−5.4 to 2.5)	1.67 (0.41-6.83)	.75
Wound separation	8 (5.8) [1.9 to 9.7]	11 (8.0) [3.4 to 12.5]	2.2 (−3.8 to 8.2)	0.73 (0.30-1.75)	.75
Cellulitis	7 (5.0) [1.4 to 8.7]	12 (8.7) [4.0 to 13.4]	3.7 (−2.3 to 9.6)	0.58 (0.24-1.44)	.47
Endometritis	0	0			

[a] Analyses examining subgroups according to intact or ruptured membranes are post hoc and should be considered exploratory.

Valent et al. JAMA 2017

Cesarean section in the setting of Triple-I infection

TRIPLE-I TREATMENT

Antibiotic	Dose
Ampicillin	2g q6h PLUS
Gentamicin	5mg/kg daily OR 1.5mg/kg q8h
Ampicillin-sulbactam	3g q6h
Ticarcillin-clavulanate	3.1g q4h
Cefoxitin	2g q8h
Cefotetan	2g q12
Pipercillin-tazobactam	3.375g q6h

Hopkins. Cochrane Database Syst Rev 2002

CEPHALOSPORINS VS AMINOPENICILLINS

- First generation Cephalosporins vs Aminopenicillins
  - 7 studies; 1487 women
  - **No significant difference in maternal endometritis**
    - (RR = 1.09, CI 0.69 – 1.71)

Gyte. Cochrane Database of Syst Review 2014

UREAPLASMA COVERAGE IN TRIPLE-I

TABLE 1 Incidence of *Ureaplasma* infection, polymicrobial infections, and chorioamnionitis in women delivering preterm, late preterm, or at term[g]

Author(s) of reference (yr)	Reference no.	GA (wk)	Specimen type	*n*	Incidence, no. positive/no. total (%)			
					Ureaplasma infection	Polymicrobial infection	*Ureaplasma* spp.	
							With chorioamnionitis	Without chorioamnionitis
Viscardi et al. (2008)	222	<33	S/CSF	313	74/313 (23.6)	—[a]	30/46 (65.0)	16/46 (35.0)
Hassanein et al. (2012)	310	<35	CB	30	13/30 (43.3)	No polymicrobial infections	7/13 (53.8)	6/13 (46.2)
Gray et al. (1992)	311	<28	AF	2,461	8/2,461 (0.4)	—[b]	8/8 (100.0)	0/8 (0.0)
Yoon et al. (1998)	60	≤36	AF	120	25/120 (20.8)	11/120 (9.0)	5/25 (20.0)	
Yoon et al. (2003)	312	≤35	AF	252	23/252 (9.1)	—[c]		
Park et al. (2013)	136	<34	AF	56	35/56 (62.5)	7/56 (12.5)	26/47 (55.31)[f]	0/3 (0.0)
Kacerovsky et al. (2014)	16	24–36	AF	124	26/124 (21.0)	5/124 (4.0)[d]		
Romero et al. (2015)	313	≤35	AF	59	6/24 (25.0)	10/24 (41.7)	3/6 (50.0)	2/6 (33.3)[f]
Stepan et al. (2016)	314	24–34	AF	122	33/122 (27.0)	8/122 (6.6)	29/33 (87.9)	4/33 (12.1)
Musilova et al. (2015)	315	24–36	AF	166	40/166 (24.1)	19/166 (11.4)	26/40 (65.0)	14/40 (35.0)
Stepan et al. (2016)	316	24–36	AF	386	103/386 (26.7)	32/386 (8.3)	70/103 (68.0)[f]	16/103 (15.5)[f]
Berger et al. (2009)	317	≤33	AF/PL	114	32/114 (28.1)	—[a]	11/25 (44.0)[f]	14/25 (66.0)[f]
Hillier et al. (1988)	1	<37	PL	112	32/112 (28.6)	—[c]	19/29 (65.5)[f]	10/65 (15.4)[f]
Stein et al. (1994)	318	Any GA	PL	182	21/182 (11.5)	—[e]	11/16[f]	5/16[f]
Van Marter et al. (2002)	319	<36	PL	206	58/155 (37.4)	—[e]	51/77 (66.2)	7/78 (9.0)
Miralles et al. (2005)	320	<33	PL	14	5/14 (35.7)	5/14 (35.7)	4/5 (80.0)	1/5 (20.0)
Egawa et al. (2007)	135	<32	PL	83	4/83 (4.8)	5/83 (6.0)[b]	4/4 (100.0)	0/4 (0.0)
Olomu et al. (2009)	321	<28	PL	866	52/866 (6.0)	21/52 (40.4)	34/52 (65.4)	18/52 (34.6)
Kasper et al. (2010)	202	<34	AF	118	32/118 (27.1)	—[a]	5/19 (26.3)[f]	14/19 (73.7)[f]
Namba et al. (2010)	134	≤32	PL	151	63/151 (41.7)	13/151 (8.6)	52/63 (82.5)	11/63 (17.5)
Roberts et al. (2012)	4	>37	PL	195	2/195 (1.0)	1/195 (0.5)	0/2 (0.0)	2/2 (100.0)
Kundsin et al. (1984)	322	Various	PL	801	156/801 (19.5)	18/801 (2.2)[b]	32/53 (60.4)[f]	21/53 (39.6)
Sweeney et al. (2016)	62	>32	PL	535	42/535 (7.9)	4/57 (7.0)	26/38 (68.4)	12/38 (31.6)
Cox et al. (2016)	133	<37	PL	57	13/57 (22.8)		9/24 (37.5)	4/33 (12.1)

Sweeney at al. Clin Microbiol Rev 2017

MACROLIDE THERAPY AT TIME OF CESAREAN

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Adjunctive Azithromycin Prophylaxis for Cesarean Delivery

Alan T.N. Tita, M.D., Ph.D., Jeff M. Szychowski, Ph.D., Kim Boggess, M.D., George Saade, M.D., Sherri Longo, M.D., Erin Clark, M.D., Sean Esplin, M.D., Kirsten Cleary, M.D., Ron Wapner, M.D., Kellett Letson, M.D., Michelle Owens, M.D., Adi Abramovici, M.D., Namasivayam Ambalavanan, M.D., Gary Cutter, Ph.D., and William Andrews, M.D., Ph.D., for the C/SOAP Trial Consortium*

Antibiotic prophylaxis in the setting of manual placental removal

UNIVERSITY OF UTAH – MANUAL PLACENTAL REMOVAL

	Manual removal of placenta	**Cefazolin given**
2015	472	418 (89%)
2016	448	412 (92%)
2017	334	238 (71%)

ANTIBIOTICS AT TIME OF PLACENTAL REMOVAL

- NO RCTs to evaluate effectiveness of antibiotic prophylaxis to prevent endometritis after manual removal of placenta

Chongsomchai. Cochrane Database of Syst Reviews 2014

MANUAL REMOVAL – SYSTEMATIC REVIEW

Observational studies: systematic review

- Three eligible cohort studies (n=567)
- **Primary outcome:** puerpural fever or endometritis
- **Results:** no difference
  - (OR = 0.84, 95 % CI 0.38 to 1.85)
- **Limitations:**
  - small number of low quality non-randomized studies

Chibueze et al. BMC Pregnancy Childbirth 2015

Obstetric anal sphincter injuries (OASIS)

OASIS

- Anal sphincter injuries: up to 24% of obstetric vaginal lacerations
- Wound breakdown: 0.1- 5% of obstetric vaginal lacerations

Williams. Obstet Gynecol 2006

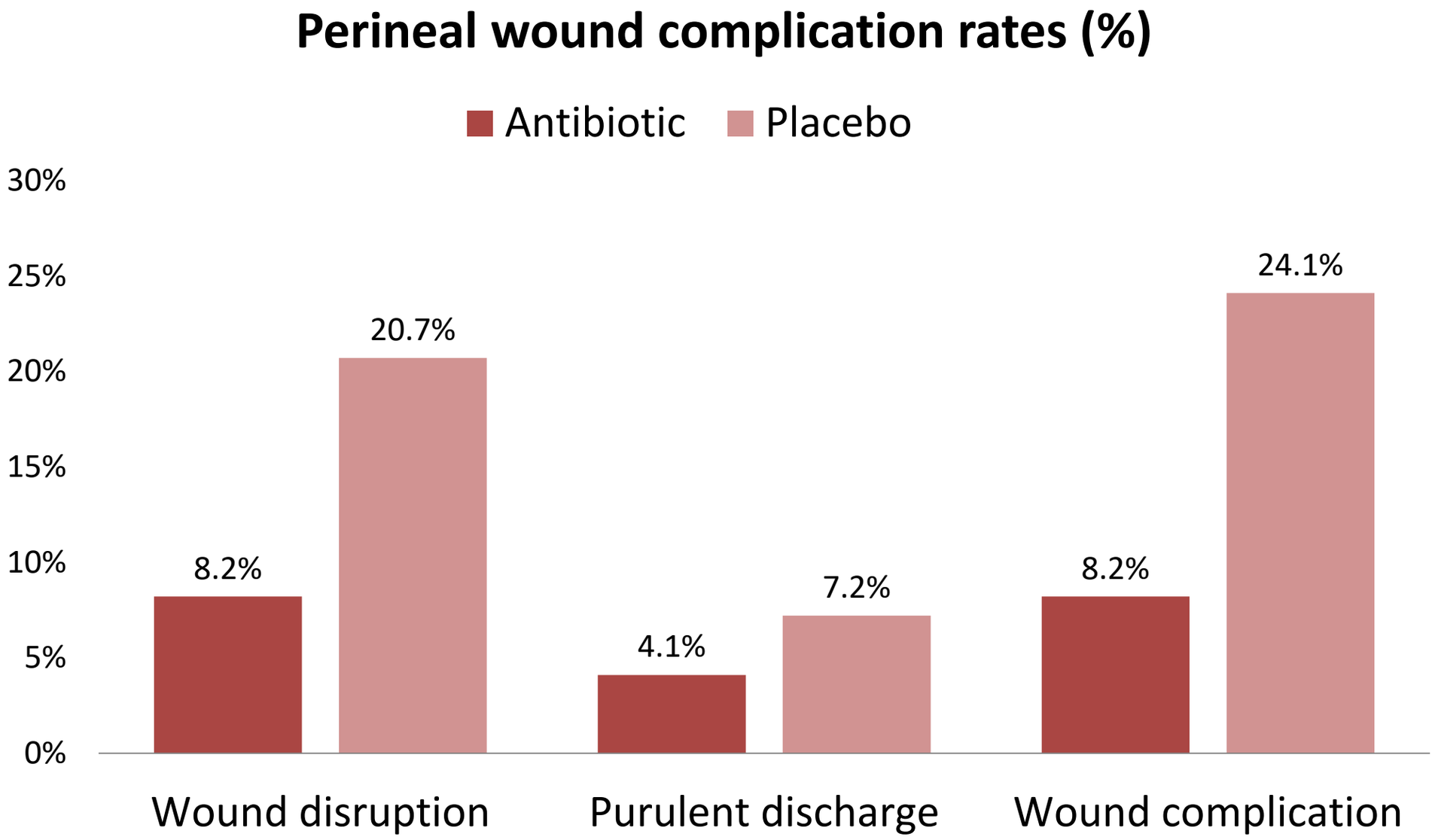
OBSTETRIC LACERATION PROPHYLAXIS - RCT

- **Intervention:** single dose of 2nd or 3rd generation cephalosporin at time of repair

- **Primary outcome:** evidence of a perineal wound complication at the 2-week postpartum visit

Duggal et al. Obstet Gynecol 2008

PERINEAL WOUND COMPLICATIONS



Duggal et al. Obstet Gynecol 2008

In Summary…

CESAREAN PROPHYLAXIS IN OBESITY

- 48 hours of Keflex and Flagyl requires additional studies

CESAREAN IN THE SETTING OF TRIPLE-I

- Add Clindamycin at time of cesarean
- Additional cephalosporin not necessary
- Azithromycin: probably beneficial, excellent research question

MANUAL PLACENTAL REMOVAL

- Antibiotics probably not necessary

- Another great research question!

OASIS

- Complications devastating
- Potential to reduce morbidity outweighs possible side effect of antibiotic administration

QUESTIONS?

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