

Early-onset Group B Streptococcal Disease Prevention: For Clinicians

Overview of CDC Prevention Guidelines, 2010

**National Center for Immunization and Respiratory Diseases
Division of Bacterial Diseases**

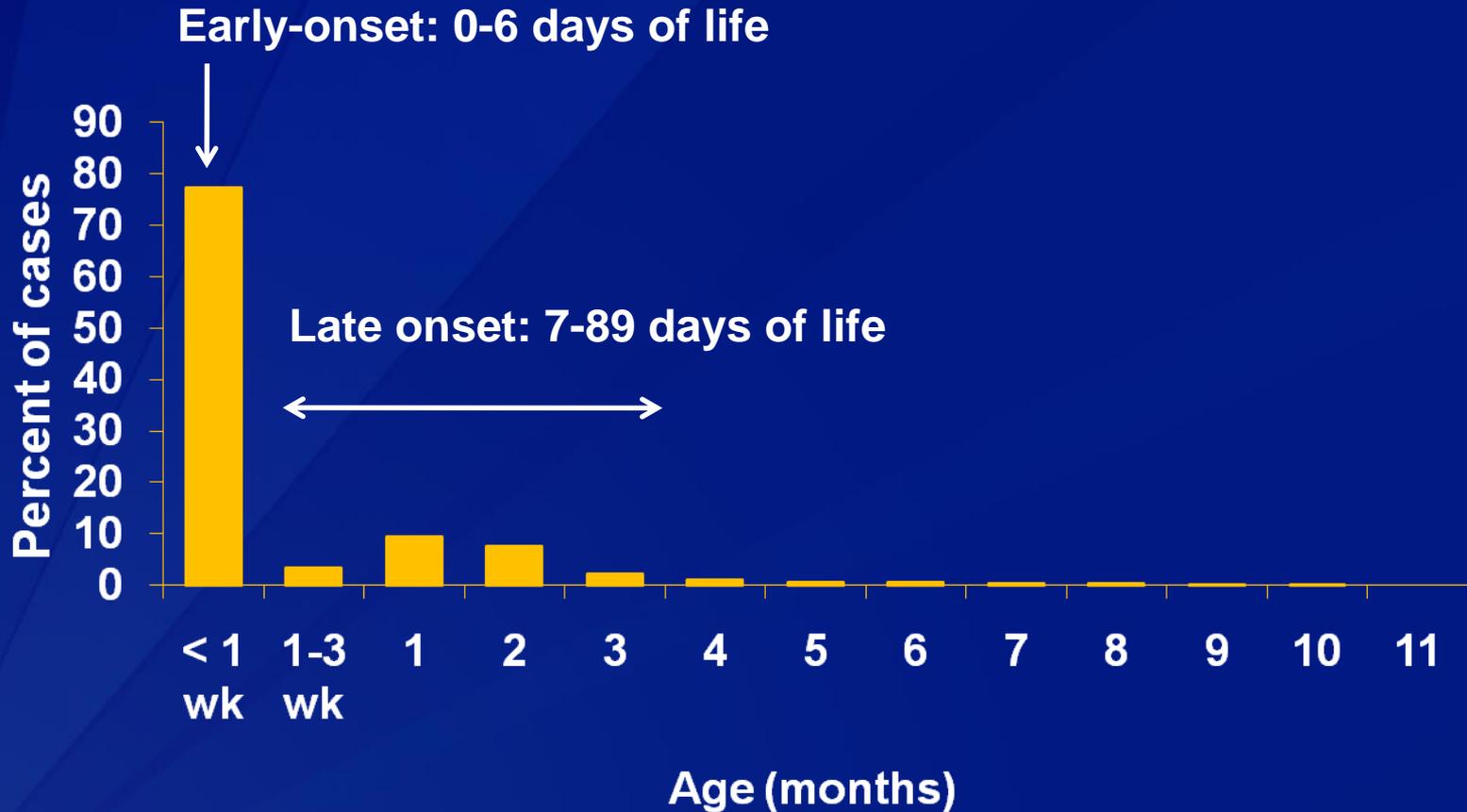
November 19, 2010

Background on Group B Streptococcal (GBS) Disease and Prevention

Group B Streptococcus

- **Gram positive, beta hemolytic bacteria**
- **Common colonizer of human gastrointestinal and genitourinary tracts**
- **Recognized as causing disease in humans in the 1930s**
- **Causes serious disease in young infants, pregnant women and older adults**
- **Emerged as most common cause of sepsis and meningitis in infants <3 months in the 1970s**

GBS Disease in Infants Before Prevention Efforts



A Schuchat. Clin Micro Rev 1998;11:497-513.

Early-onset GBS Disease (EOGBS)

- **Leading infectious cause of neonatal sepsis in U.S.**
 - Annual incidence in 2008: 0.28 cases / 1,000 live births
 - Estimated 1,200 cases in 2008
- **Clinical presentation**
 - Typically symptoms appear on day 0 or day 1 of life
 - Respiratory distress, apnea, signs of sepsis most common symptoms
 - Bacteremia most common form of disease (app. 80% of cases)
 - Pneumonia and meningitis less common
- **Case fatality rate**
 - 1970s: As high as 50%
 - 4-6% in recent years



Photo courtesy of Dr. Carol Baker
Baylor College of Medicine, Houston, TX



Photo courtesy of Dr. Carol Baker Baylor
College of Medicine, Houston, TX

GBS Maternal Colonization

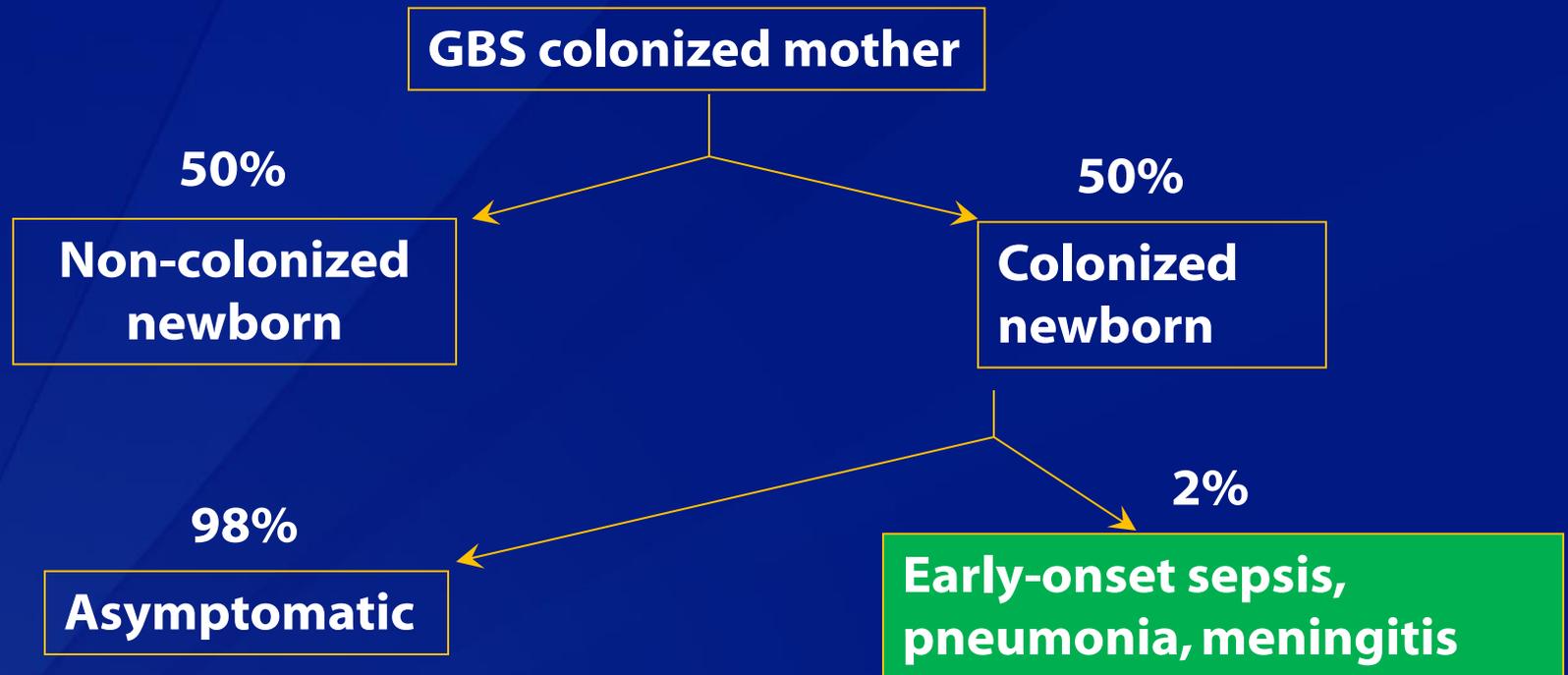
■ GBS Carriers

- 10% - 30% of women
- Higher proportion in African Americans and nonsmokers
- GBS usually live in gastrointestinal tract but can spread to the genital tract
- No symptoms or signs on examination
- Colonization comes and goes over months
- Not a sexually transmitted infection

■ **Risk factor for early-onset disease: GBS colonization during labor and delivery**

- Prenatal cultures late in pregnancy can predict delivery status

Mother to Infant Transmission of GBS



Additional Risk Factors for Early-onset GBS Disease

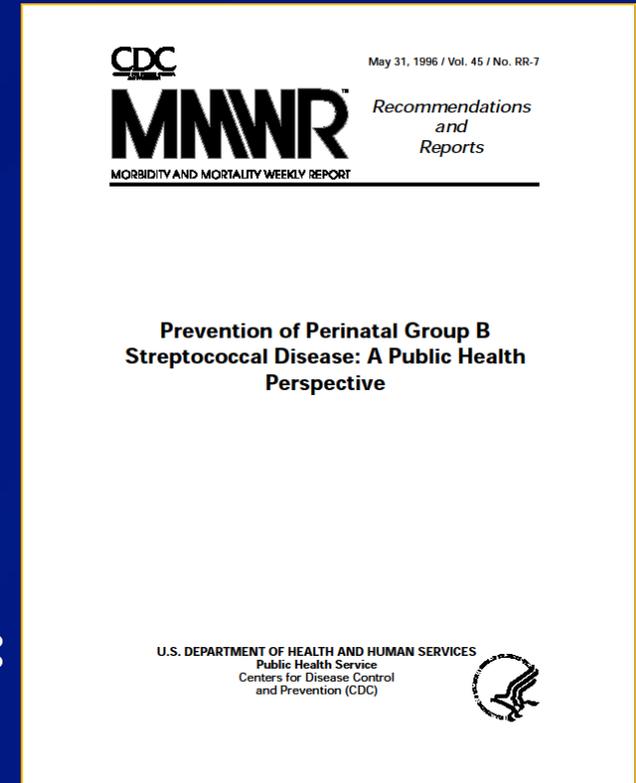
- **Obstetric risk factors:**
 - Preterm delivery
 - Prolonged rupture of membranes
 - Infection of the placental tissues or amniotic fluid / fever during labor
- **GBS in the mother's urine during pregnancy (marker for heavy colonization)**
- **Previous infant with GBS disease**
- **Low maternal levels of anti-GBS antibodies**
- **Demographic risk factors**
 - African American
 - Young maternal age

Prevention of Early-onset GBS Disease

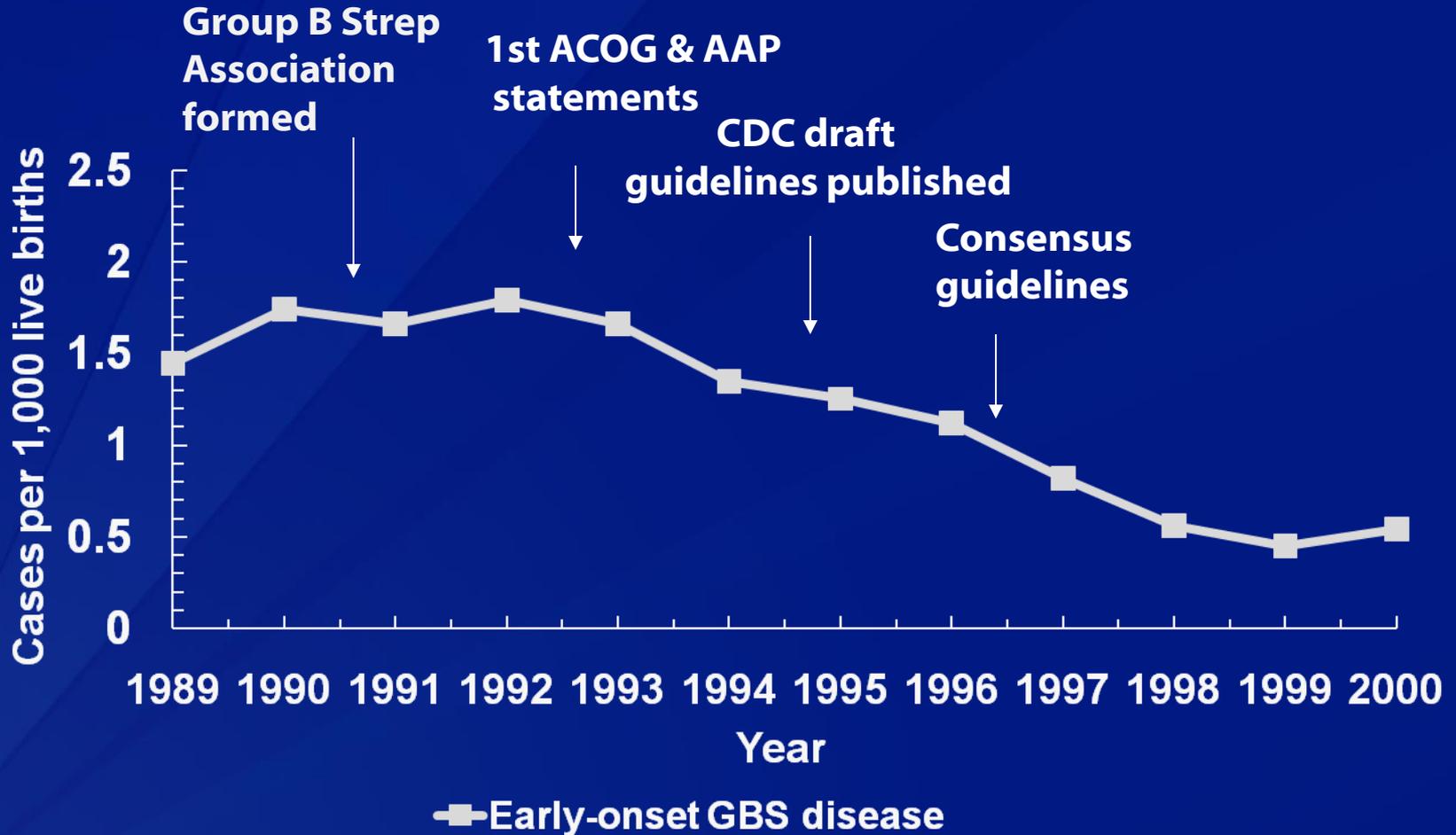
- **Intrapartum antibiotics (IAP)**
 - Highly effective at preventing early-onset disease in women at risk of transmitting GBS to their newborns
 - Efficacy in clinical trials: 100%
 - Effectiveness in observational studies: 86-89%
- **Challenge: How best to identify women who should receive IAP?**

1996 Consensus Guidelines for GBS Prevention

- **Screening-based approach:**
 - Vaginal-rectal culture at 35-37 wks
 - IAP for GBS carriers
 - IAP for preterm delivery (unless negative culture result available)
- **Risk-based approach :**
 - No vaginal-rectal culture
 - IAP for preterm deliveries, membrane rupture ≥ 18 hours, or intrapartum fever ($T \geq 38^{\circ}\text{C}$)
- **Both strategies - IAP to women with:**
 - GBS bacteriuria during pregnancy
 - Previous infant with GBS disease



Rate of Early-onset GBS Disease in the 1990s, United States

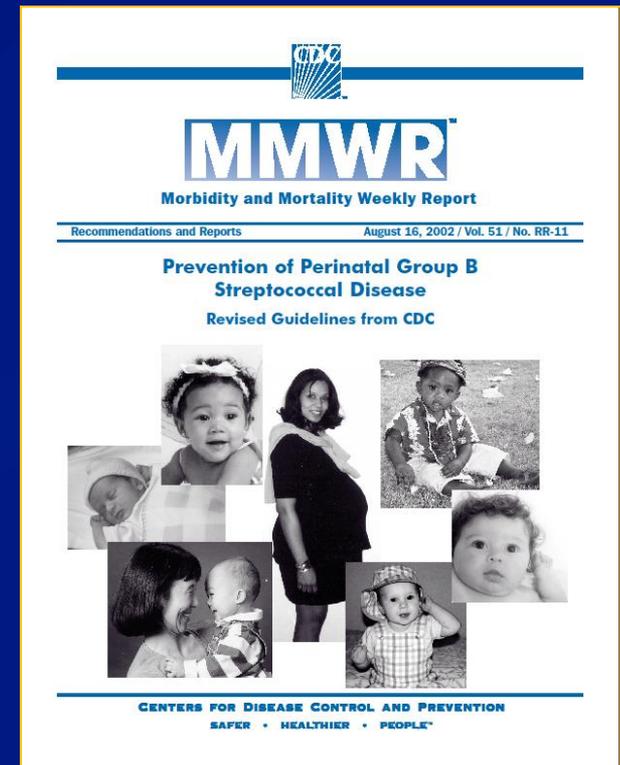


Screening for GBS Protects More Infants from Early-onset GBS than Relying on Risk Factors

- **Infants whose mothers are screened for GBS are less than half as likely to develop early-onset GBS disease as mothers who are not screened**
- **Screening identifies colonized women without obstetric risk factors (18% of all deliveries in 1990s)**

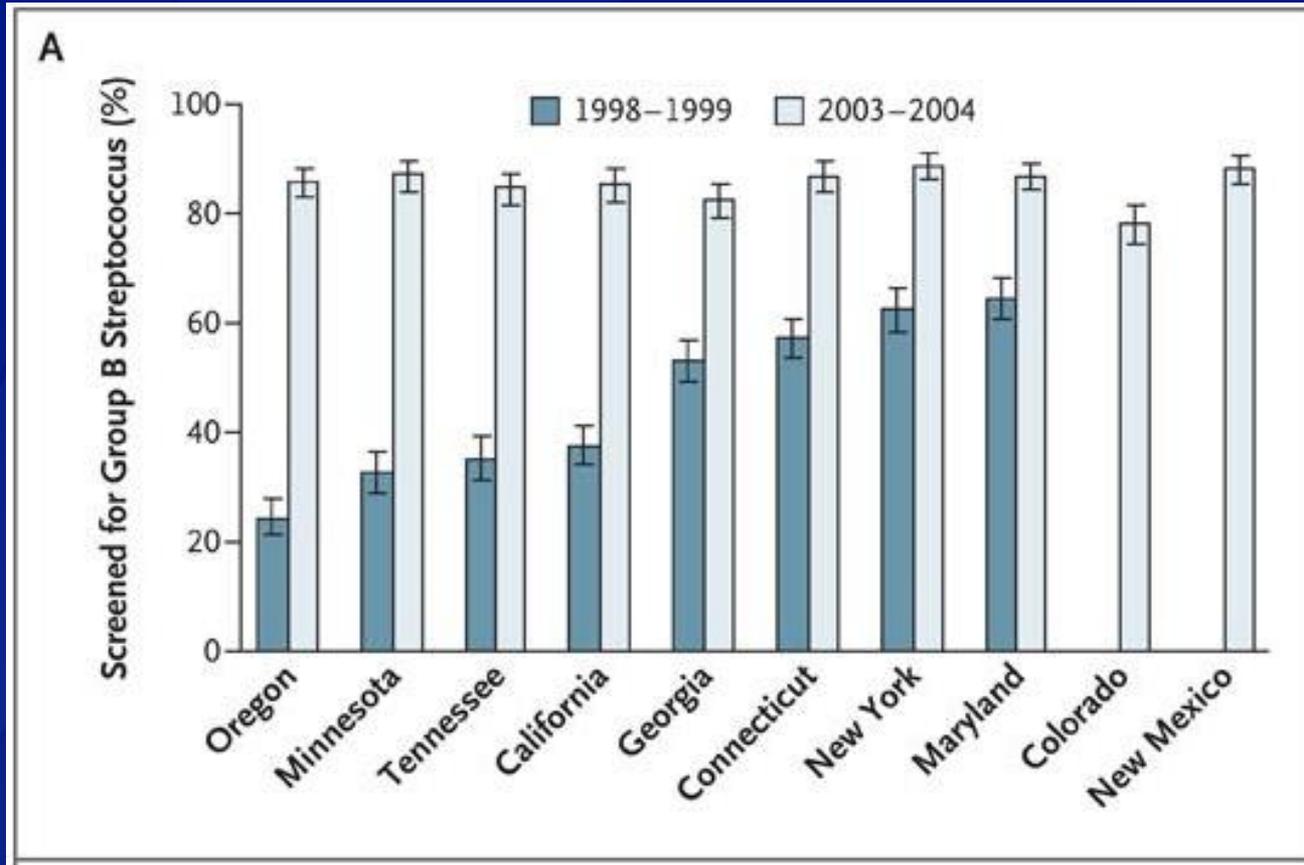
2002 GBS Guidelines: Key Changes

- **Single strategy for identifying candidates for IAP: universal screening by culture at 35-37 wks**
- **IAP agents for penicillin-allergic**
 - Cefazolin, except for women at high risk of anaphylaxis
- **No routine IAP for planned cesarean deliveries**
- **GBS screening and IAP for threatened preterm deliveries**
- **More detail on specimen collection and handling**
- **Neonatal management**
 - Addition of chorioamnionitis



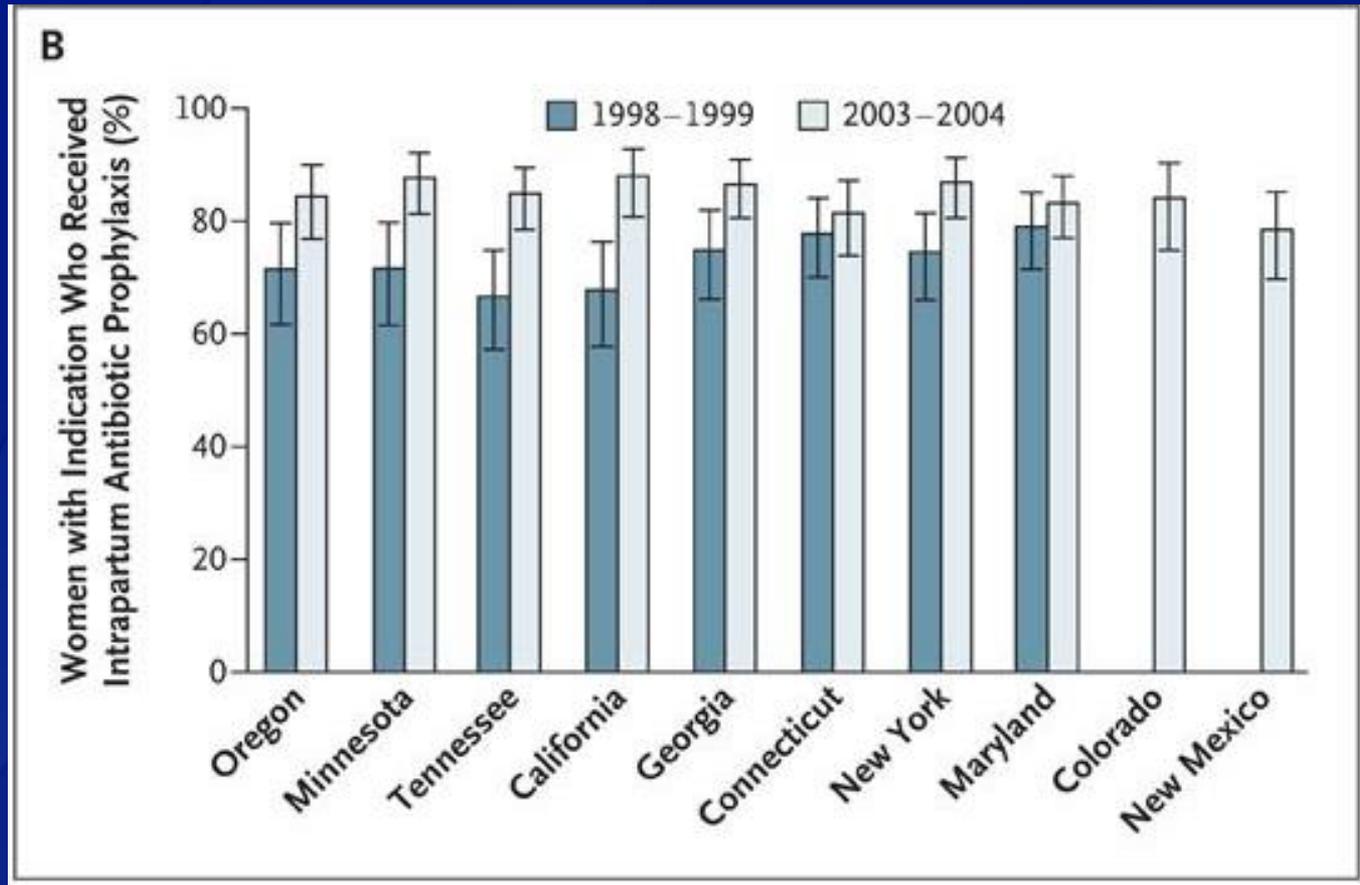
Implementation and Impact of Early-onset GBS Disease Prevention Guidelines

Proportion of Women Screened for GBS Colonization



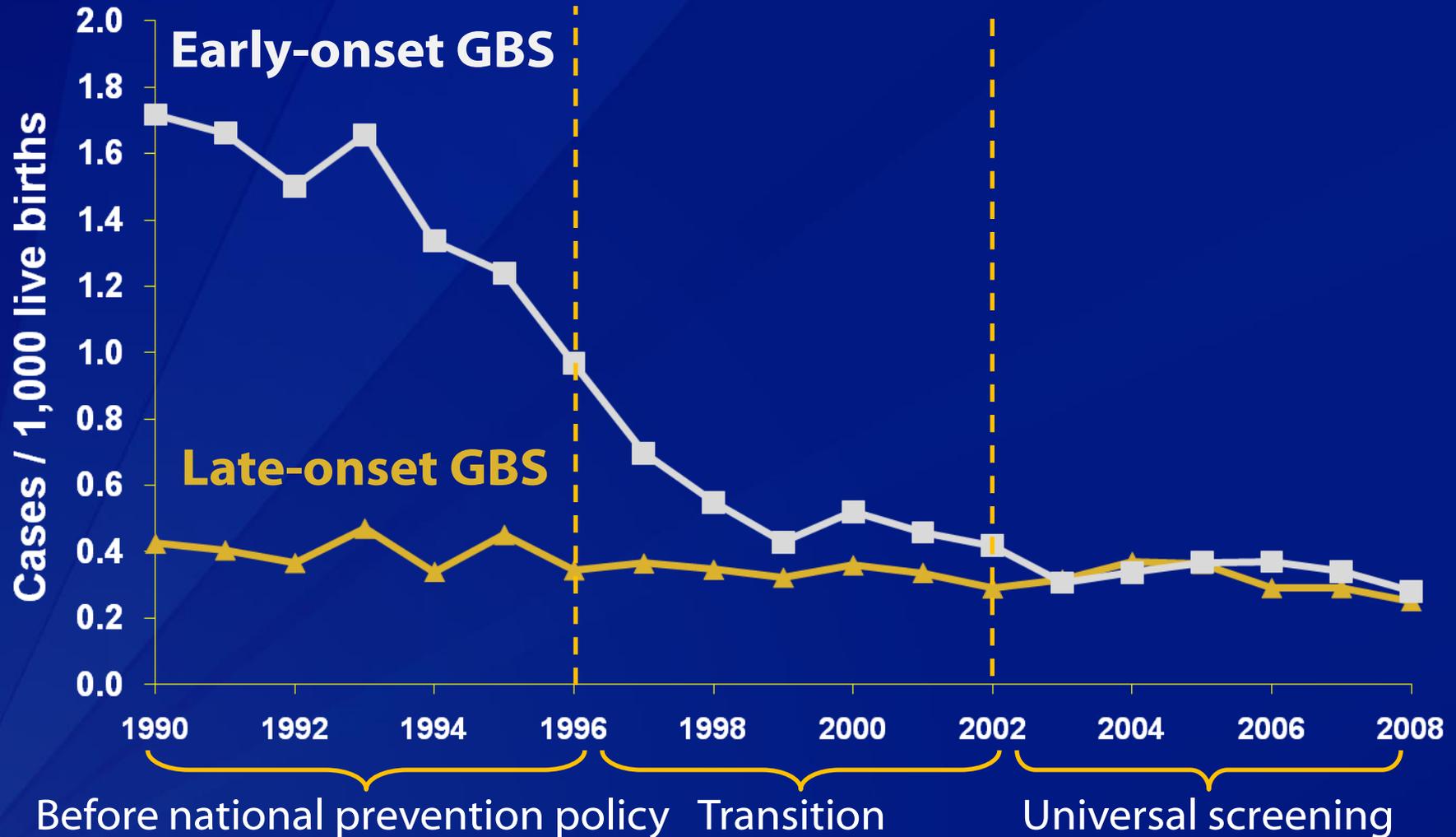
- Proportion of women screened increased from 48% to 85%
- 98% of women screened had available result at labor

Proportion of Women with an Indication for GBS IAP Who Received GBS IAP



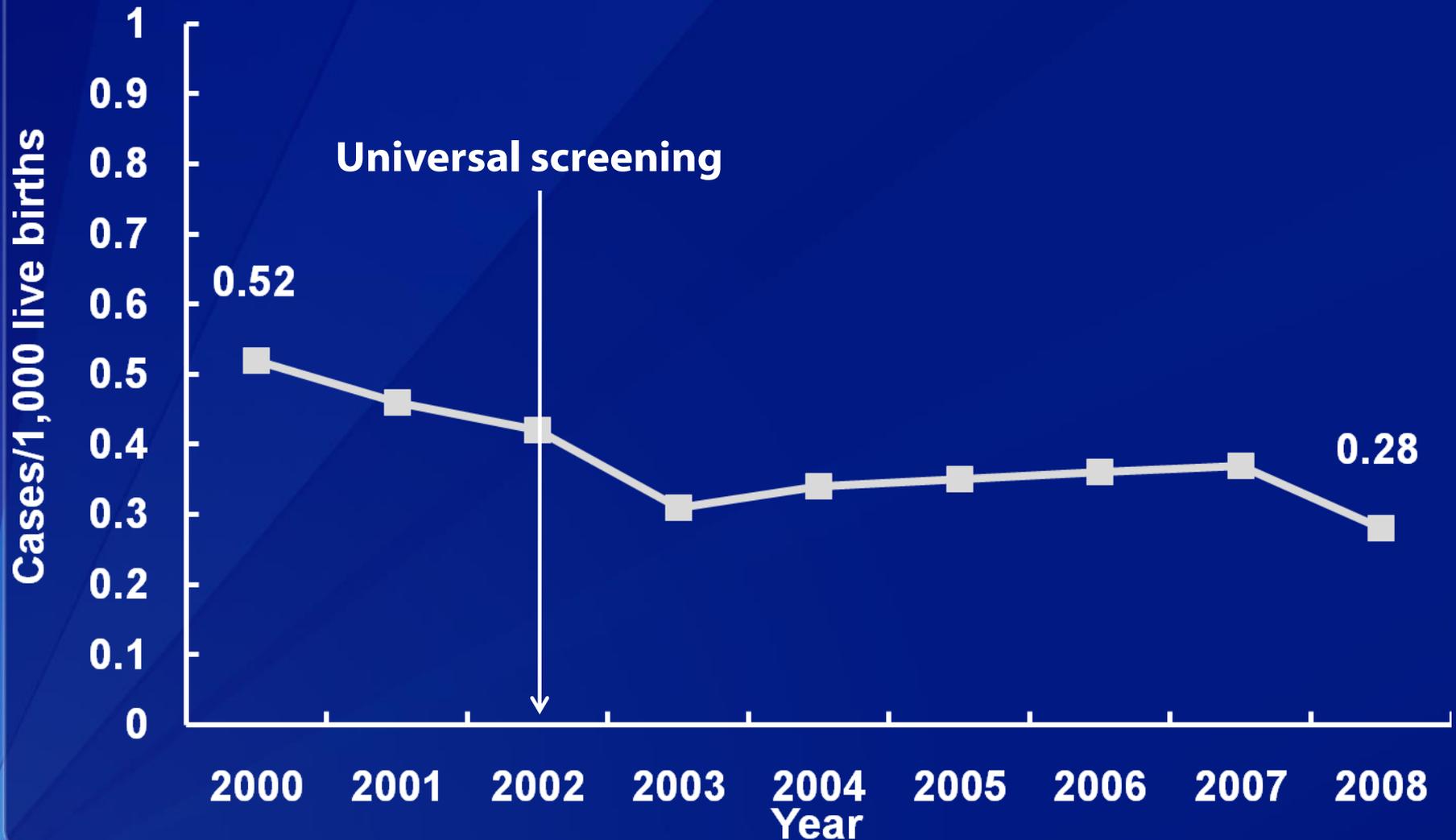
•Proportion of women with an indication for IAP who then received IAP increased from 74% to 85%

Rate of Early- and Late-Onset GBS, 1990-2008



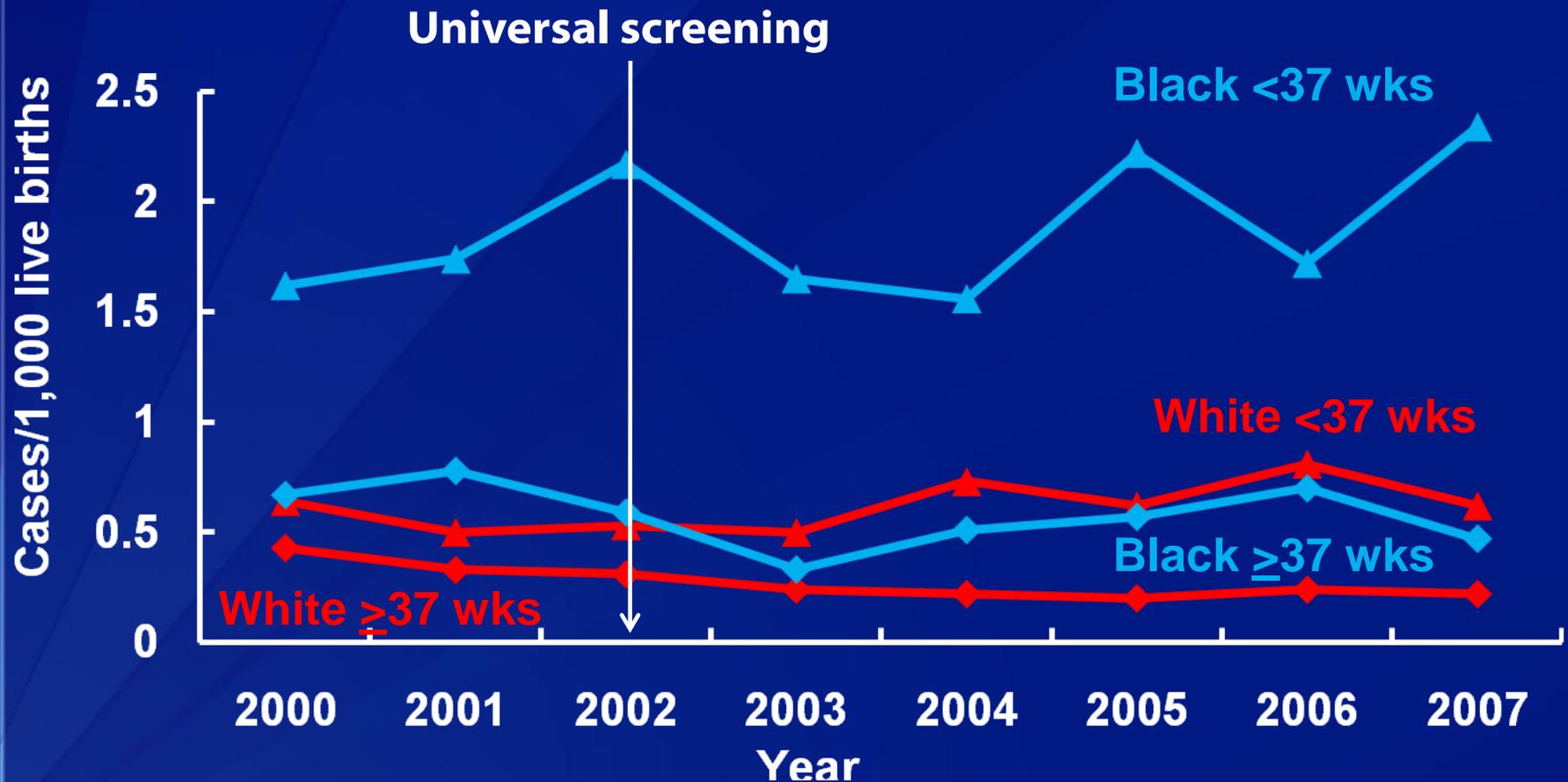
Source: Active Bacterial Core surveillance / Emerging Infections Program

Early-onset GBS Disease in the U.S., 2000-2008



Source: Active Bacterial Core surveillance / Emerging Infections Program

Rate of Early-onset GBS Disease by Race and Gestational Age, 2000-2007

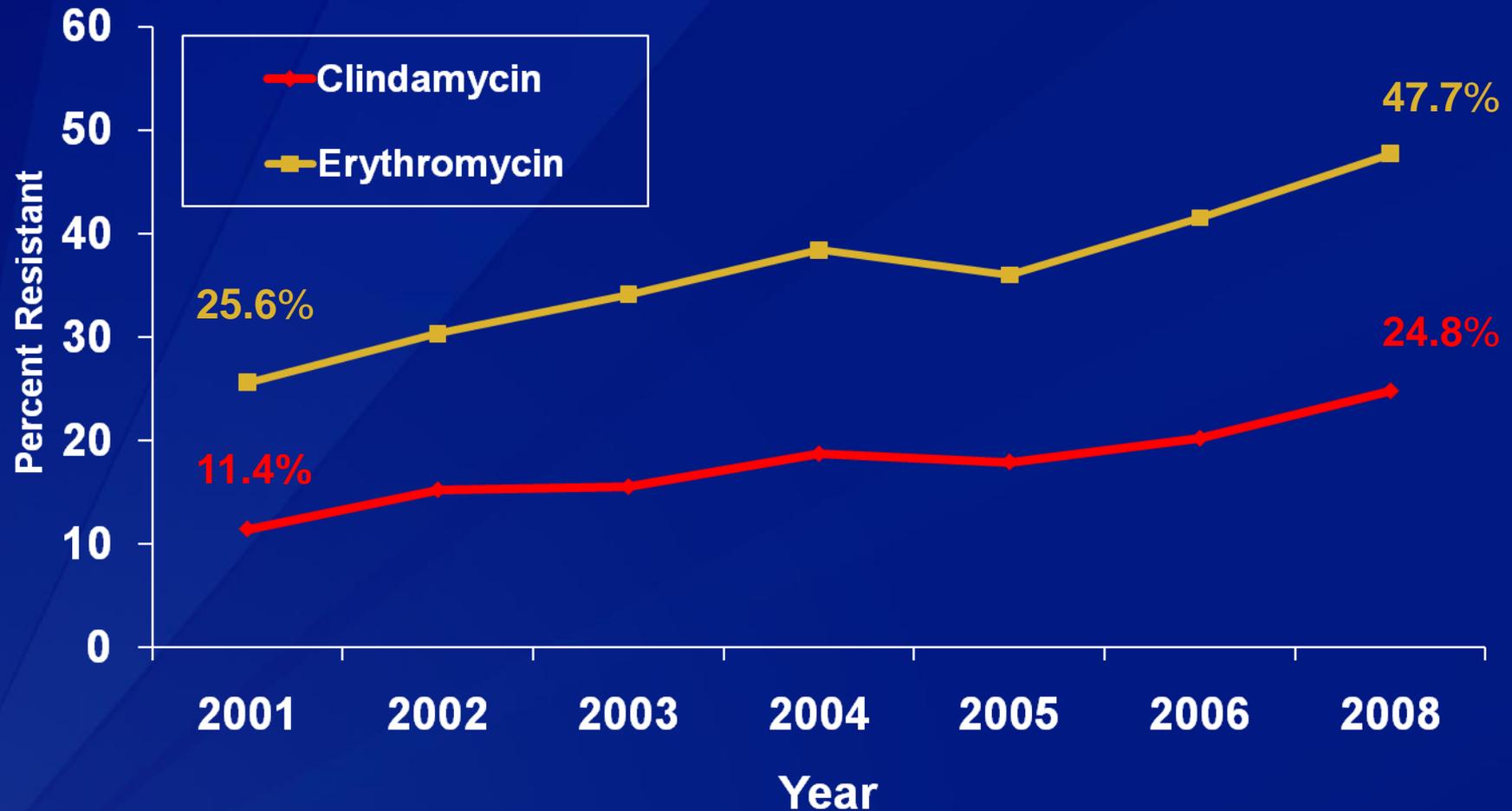


Source: Active Bacterial Core surveillance / Emerging Infections Program

Implementation Challenges

- **Missed prevention opportunities among infants born preterm**
 - 50% screened prior to admission
 - Only 18% of GBS unknown screened on admission
 - Preterm 20% less likely to receive IAP when indicated than term
 - Receipt of ≥ 4 hours IAP protective (78% effective, 95% CI 44-91)
- **Penicillin-allergic women**
 - Only 14% at low risk for anaphylaxis received cefazolin
 - 70% at low risk for anaphylaxis received clindamycin even though
 - <5% had susceptibility testing
 - No data on efficacy/effectiveness of clindamycin to prevent EOGBS

GBS Resistance: Clindamycin and Erythromycin All Ages, 2001-2008*



*Isolates are from CO, GA, MD, MN, NY, and OR. 2007 data excluded since only early-onset isolates were tested.

Source: Active Bacterial Core surveillance / Emerging Infections Program

Potential Unintended Consequences of GBS Prevention Guidelines

- **Adverse drug reactions**
 - Anaphylaxis among women receiving GBS IAP very rare
 - Two studies reviewing >12,000 births found one non-fatal case
 - Four published case reports in U.S. since 1996
- **Impact on non-GBS sepsis**
 - Stable or decreasing rates in most studies
 - *E.coli* sepsis may be increasing among pre-term infants, but trends not consistent across studies
- **Health services utilization for neonates**
 - Studies conducted during 1996-2002 reported increased, stable, or decreased use of health services for neonates whose mothers received IAP
 - No studies on the impact of the 2002 guidelines

2010 GBS Guidelines

Organizations Endorsing CDC's 2010 GBS Guidelines

- **American College of Obstetricians and Gynecologists**
- **American Academy of Pediatrics**
- **American College of Nurse-Midwives**
- **American Academy of Family Physicians**
- **American Society for Microbiology**

2010 GBS Guidelines: Methods

- **Key stakeholders convened late 2008**
 - American Academy of Pediatrics, American Academy of Family Physicians, American College of Nurse-midwives, American College of Obstetricians and Gynecologists, Centers for Disease Control and Prevention, Society for Hospital Epidemiology of America, American Society for Microbiology, microbiologists, pharmacologists, state health departments, parent organizations
- **Reviewed relevant data**
- **Identified areas of guidelines that needed changes or clarifications**
- **Made evidence-based revisions to guidelines**





MMWR™

Morbidity and Mortality Weekly Report

www.cdc.gov/mmwr

Recommendations and Reports

November 19, 2010 / Vol. 59 / No. RR-10

Prevention of Perinatal Group B Streptococcal Disease

Revised Guidelines from CDC, 2010



Continuing Education Examination available at <http://www.cdc.gov/mmwr/cms/conted.html>

DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION

The Recommendations

MMWR, Vol 59 (RR-10)

Key Prevention Strategies Remain Unchanged in 2010

- **Universal screening of pregnant women for GBS at 35-37 weeks gestational age**
- **Intrapartum antibiotic prophylaxis for:**
 - GBS positive screening test
 - GBS colonization status unknown with
 - Delivery <37 weeks
 - Temperature during labor $\geq 100.4^{\circ}$ F ($\geq 38.0^{\circ}$ C)
 - Rupture of membranes ≥ 18 hours
 - Previous infant with GBS disease
 - GBS in the mother's urine during current pregnancy
- **Penicillin preferred drug for IAP**
 - Ampicillin acceptable alternative
 - Cefazolin preferred for penicillin-allergic at low risk of anaphylaxis

Identification of Candidates for IAP in the 2010 GBS Guidelines

Indications for Intrapartum GBS Prophylaxis

- **Previous infant with invasive GBS disease**
- **GBS bacteriuria during current pregnancy**
- **Positive GBS screening test during current pregnancy**
- **Unknown GBS status AND any of the following:**
 - Delivery at <37 weeks' gestation
 - Amniotic membrane rupture ≥ 18 hours
 - Intrapartum temperature $\geq 100.4^{\circ}\text{F}$ ($\geq 38.0^{\circ}\text{C}$)

Intrapartum GBS Prophylaxis Not Indicated

- **Colonization with GBS during a previous pregnancy**
 - Unless another indication during the current pregnancy
- **GBS bacteriuria during a previous pregnancy**
 - Unless another indication during the current pregnancy
- **Negative vaginal and rectal GBS screening test during the current pregnancy**
 - Regardless of intrapartum risk factors
- **Cesarean delivery performed before labor onset on a woman with intact amniotic membranes**
 - Regardless of maternal GBS test status
 - **Regardless of gestational age**

Bacteriuria

- **GBS in urine during pregnancy**
 - GBS found in urine of 2%-7% of pregnant women
 - Marker of heavy vaginal-rectal colonization
 - Risk factor for early-onset GBS disease in the newborn
 - Antibiotic treatment of GBS bacteriuria during pregnancy does not eliminate GBS from the genitourinary and gastrointestinal tracts, and recolonization after a course of antibiotics is typical
- **Clinicians must inform laboratories when submitted urine specimens are from pregnant women**
- **Women with symptomatic or asymptomatic GBS urinary tract infections detected during pregnancy should be treated according to current standards of care**
- **Women with GBS isolated from the urine at any time during the current pregnancy should receive IAP**

Prenatal GBS Sample Collection

- **Site: vagina and rectum**
 - Single swab or two swabs
 - Lower 1/3 of vagina
 - Through anal sphincter
 - Collection: NOT by speculum
 - Self collection an option
- **Timing: 35 to 37 weeks**
- **Transport: Nonnutritive transport medium**
 - Examples - Stuart's or Amies
 - With or without charcoal
 - Results most sensitive if processed within 24 hours of collection
 - Results most sensitive if refrigerated before processing

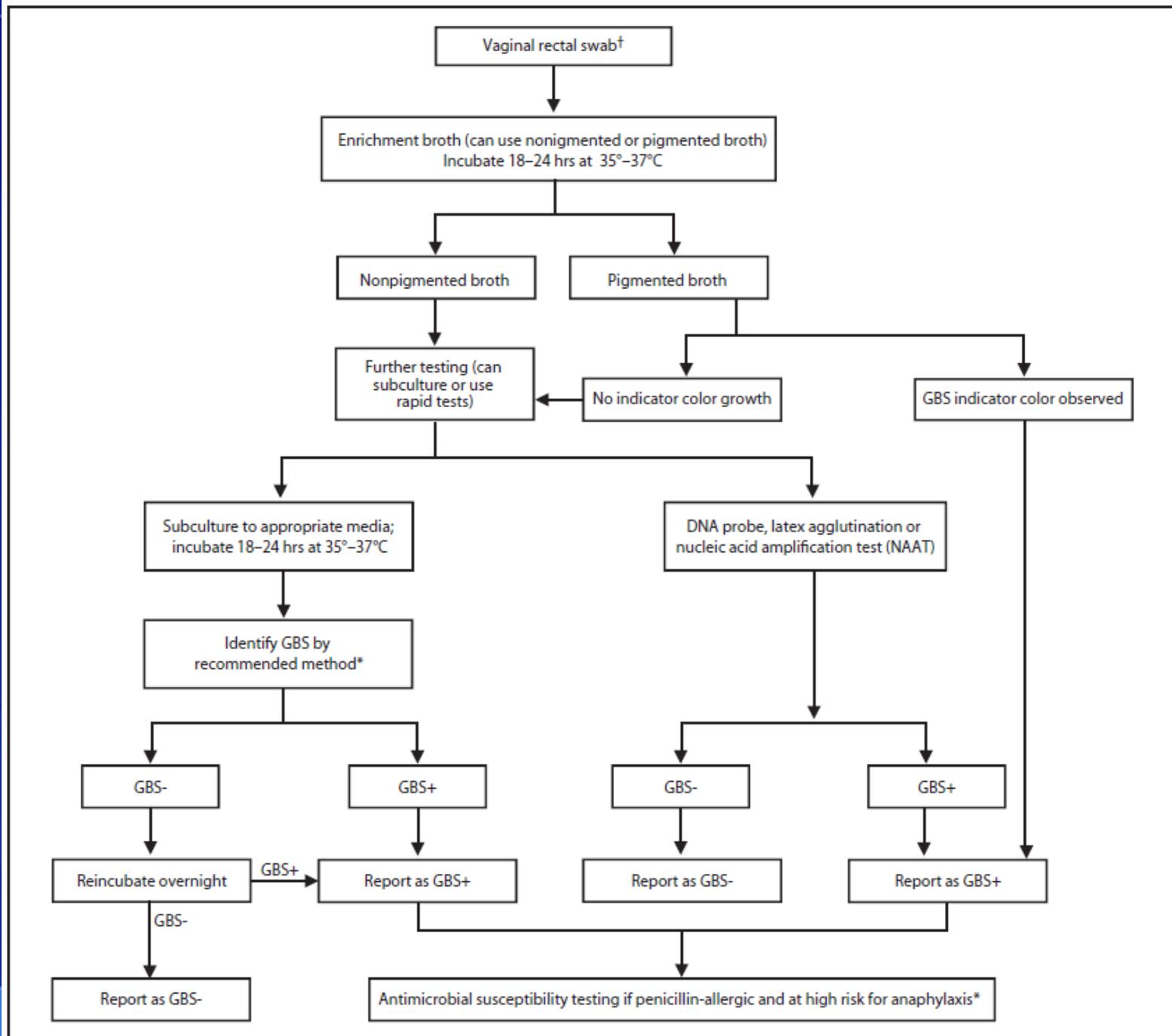
Antimicrobial Susceptibility Testing for Penicillin-Allergic Women at High Risk of Anaphylaxis

- **Many isolates from invasive GBS disease are resistant to clindamycin or erythromycin**
 - Resistance to erythromycin is associated frequently but not always with resistance to clindamycin
 - Some isolates susceptible to clindamycin but resistant to erythromycin may have inducible clindamycin resistance
- **Antimicrobial susceptibility testing should be performed on antenatal GBS isolates from penicillin-allergic women at high risk for anaphylaxis**
 - Should include testing for inducible resistance (e.g. D-zone test)
- **Specimens from penicillin allergic women at high risk for anaphylaxis should be clearly labeled**

Intrapartum testing for GBS

- **Nucleic acid amplification tests (NAAT) such as PCR an option for intrapartum GBS testing for women who are GBS unknown at labor onset and have no risk factors**
- **Lower sensitivity for direct specimens (no enrichment)**
 - Positive result: Administer IAP
 - Negative result and patient does not develop intrapartum temperature $\geq 100.4^{\circ}\text{F}$ ($\geq 38.0^{\circ}\text{C}$) or have ROM ≥ 18 hours: No IAP
 - Negative result and patient develops intrapartum temperature $\geq 100.4^{\circ}\text{F}$ ($\geq 38.0^{\circ}\text{C}$) or has ROM ≥ 18 hours: Administer IAP
- **Additional slides on changes affecting laboratories in the 2010 GBS prevention guidelines can be found at:**
<http://www.cdc.gov/groupbstrep/lab.html>

FIGURE 7. Algorithm for recommended laboratory testing for prenatal screening for group B streptococcal (GBS) colonization*



Threatened Preterm Delivery

- **Separate algorithms are presented for GBS prophylaxis in the setting of threatened preterm delivery, one for spontaneous preterm labor (PTL) and one for preterm premature rupture of membranes (pPROM)**
- **Women with PTL or pPROM should all receive:**
 - Screening on admission for GBS if GBS status unknown
 - Antibiotics for GBS prophylaxis
- **Antibiotics to prolong latency in pPROM can serve as GBS IAP if certain criteria are met**
 - Ampicillin 2 g IV followed by 1 g IV every 6 hours for 48 hours
 - Delivery occurs while the mother is receiving that antibiotic regime

FIGURE 5. Algorithm for group B streptococcus (GBS) intrapartum prophylaxis for women with preterm* labor (PTL)

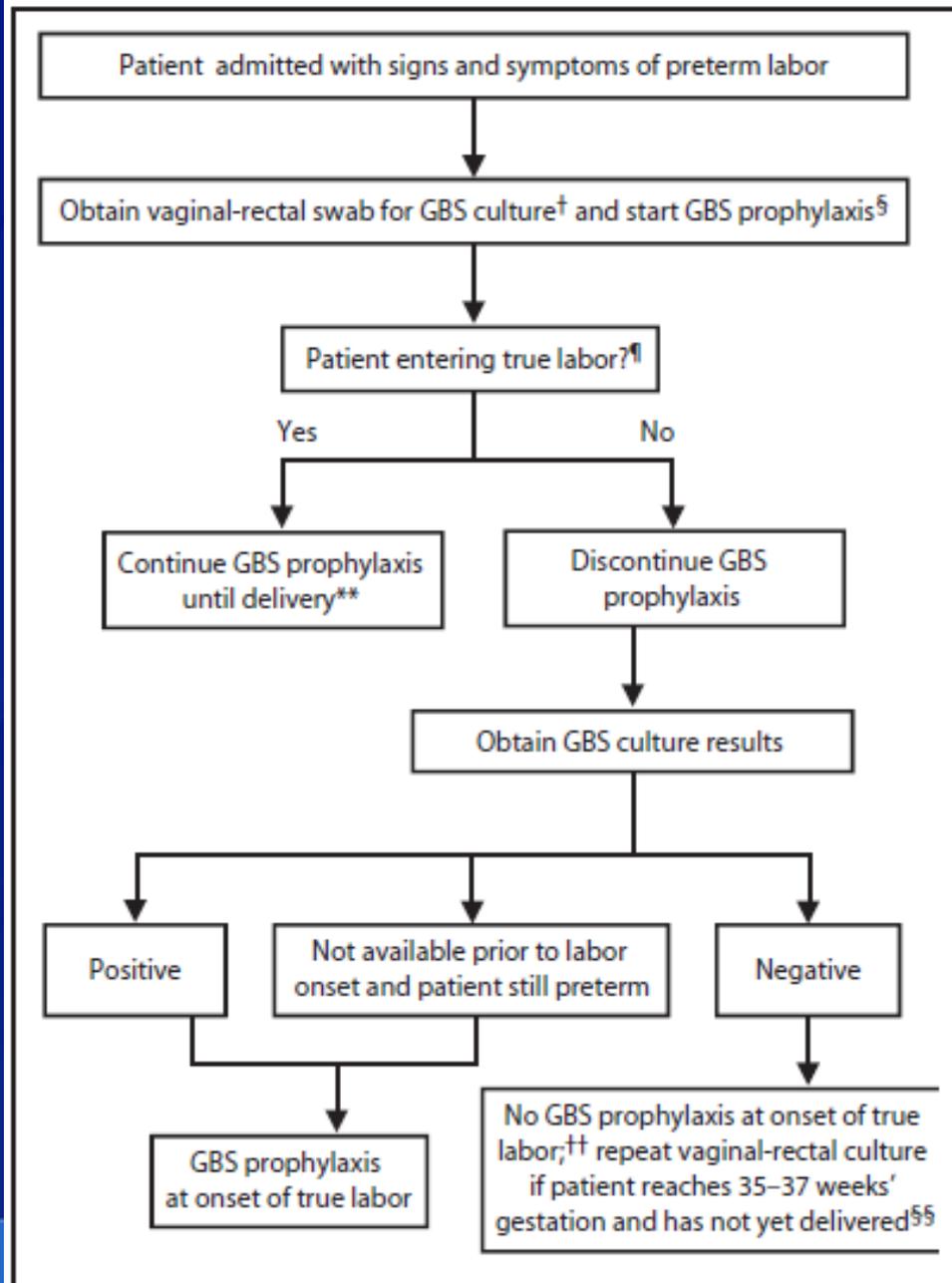
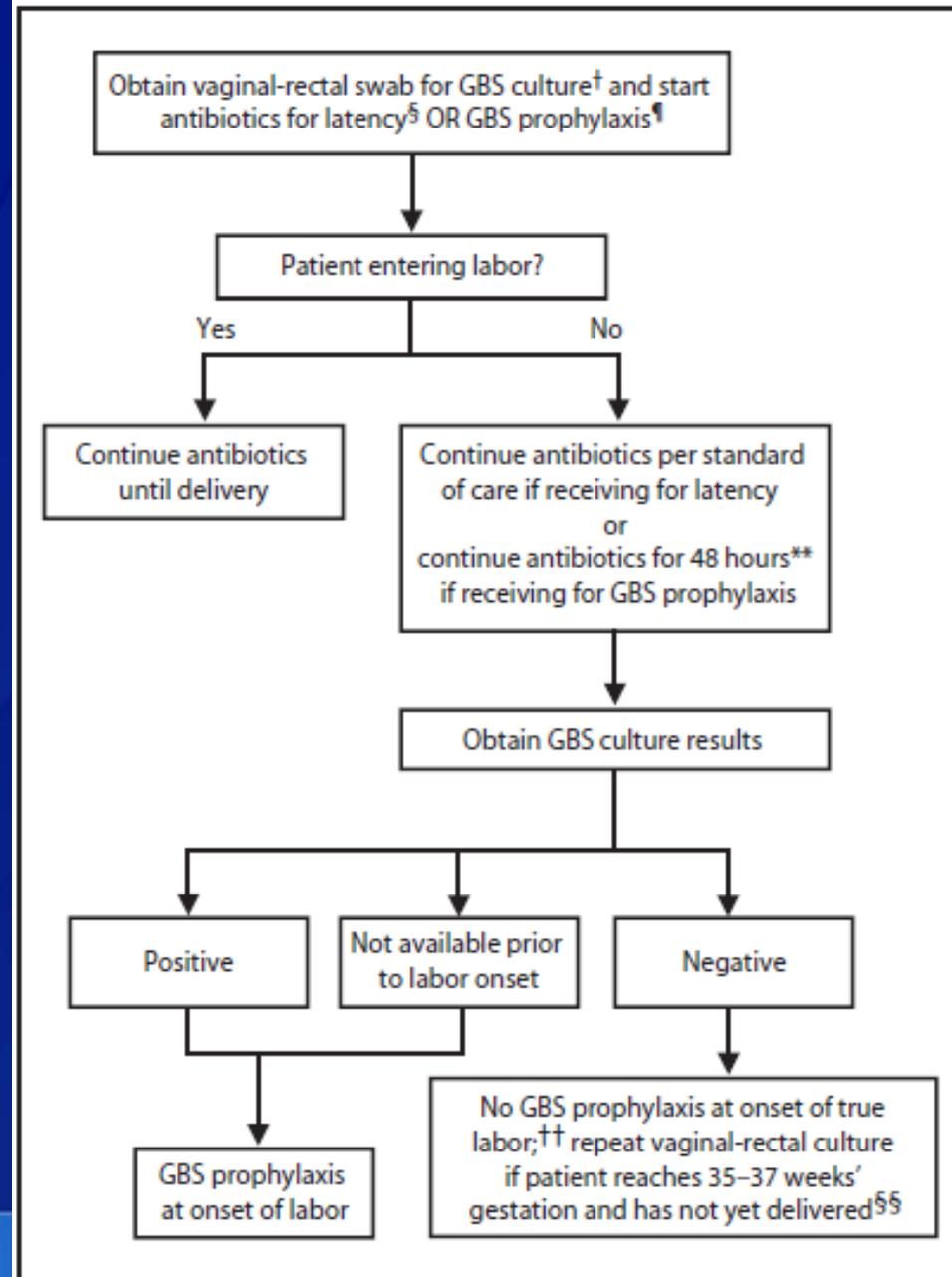


FIGURE 6. Algorithm for group B streptococcus (GBS) intrapartum prophylaxis for women with preterm* premature rupture of membranes (pPROM)



Antibiotic Selection in the 2010 GBS Guidelines

Antibiotics for IAP

- **Penicillin the first-line agent for IAP**
 - Dosage: 5 million IU IV then 2.5-3.0 million IU IV every 4 hours
 - Revised dose (2.5-3.0 million IU) consistent with available penicillin formulations
- **Ampicillin an acceptable alternative**

Data on Antibiotics for Intrapartum GBS Prophylaxis

Antibiotic	Efficacy (clinical trials)	Effectiveness (observational studies)	Favorable pharmacokinetics in pregnancy
Penicillin	yes	yes	yes
Ampicillin	yes	yes	yes
Cefazolin	no	yes	yes
Clindamycin	no	no	no
Erythromycin	no	no	no
Vancomycin	no	no	limited

Antibiotics for IAP in Women Allergic to Penicillin

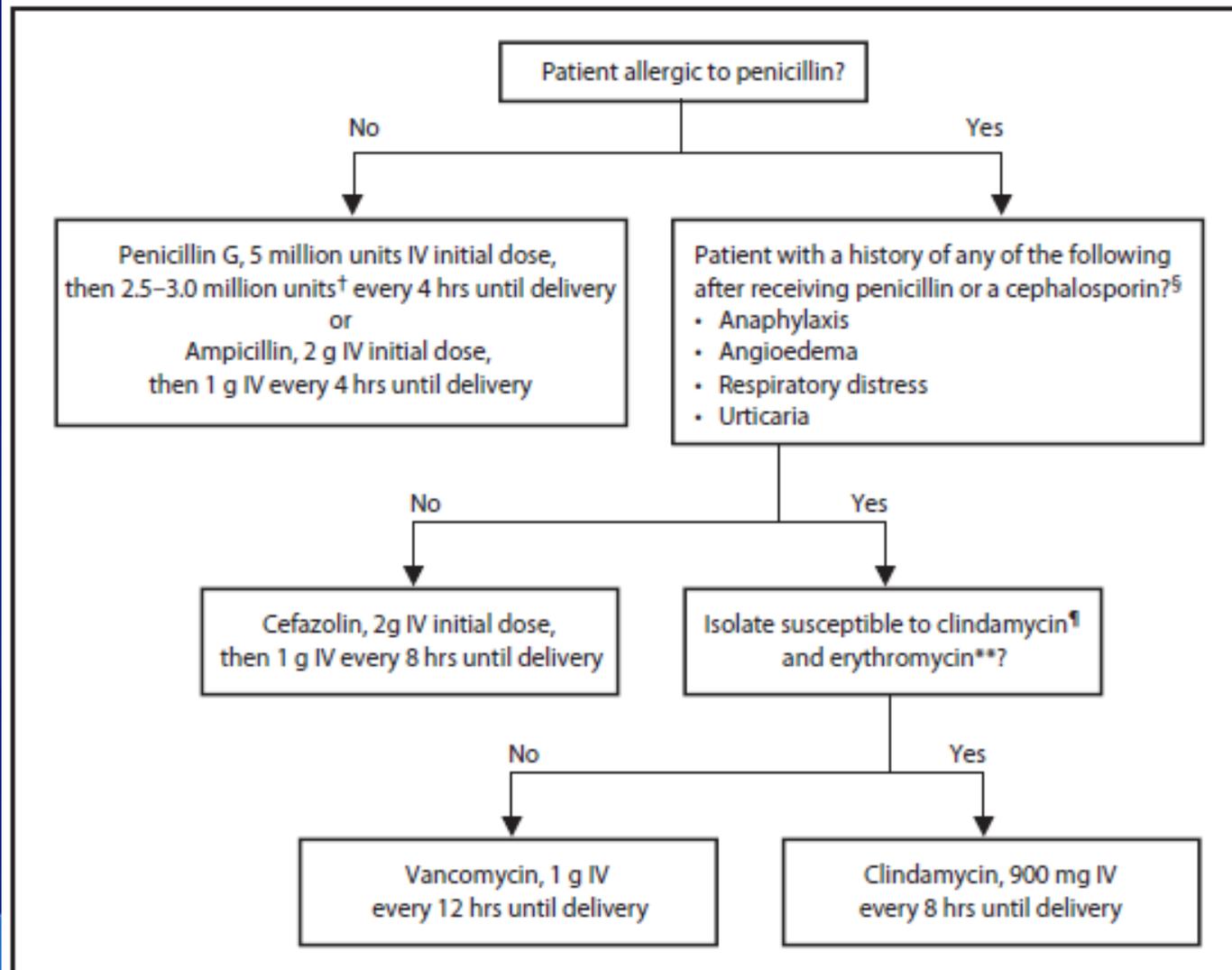
- **Cefazolin best option for a woman allergic to penicillin but not at high risk for anaphylaxis**
- **Drugs with less evidence for effectiveness (e.g. clindamycin, vancomycin) only for women at high risk of anaphylaxis**
 - High risk for anaphylaxis defined as history of anaphylaxis, angioedema, respiratory distress or urticaria following penicillin
- **Erythromycin no longer included as option**

Antibiotics for IAP in Women Allergic to Penicillin

- **Women at high risk for anaphylaxis following penicillin or a cephalosporin may receive CLINDAMYCIN for GBS IAP if:**
 - Their GBS isolate is susceptible to clindamycin and erythromycin OR
 - Their GBS isolate is susceptible to clindamycin but resistant to erythromycin and testing for inducible resistance is negative
- **Women at high risk for anaphylaxis following penicillin or a cephalosporin may receive VANCOMYCIN for GBS IAP if:**
 - Their GBS isolate is intrinsically resistant to clindamycin OR
 - Their GBS isolate shows inducible resistance to clindamycin OR
 - Their GBS isolate's susceptibility to clindamycin and erythromycin is unknown

2010 GBS Guidelines: Algorithm for Selecting IAP Regimens

FIGURE 8. Recommended regimens for intrapartum antibiotic prophylaxis for prevention of early-onset group B streptococcal (GBS) disease*

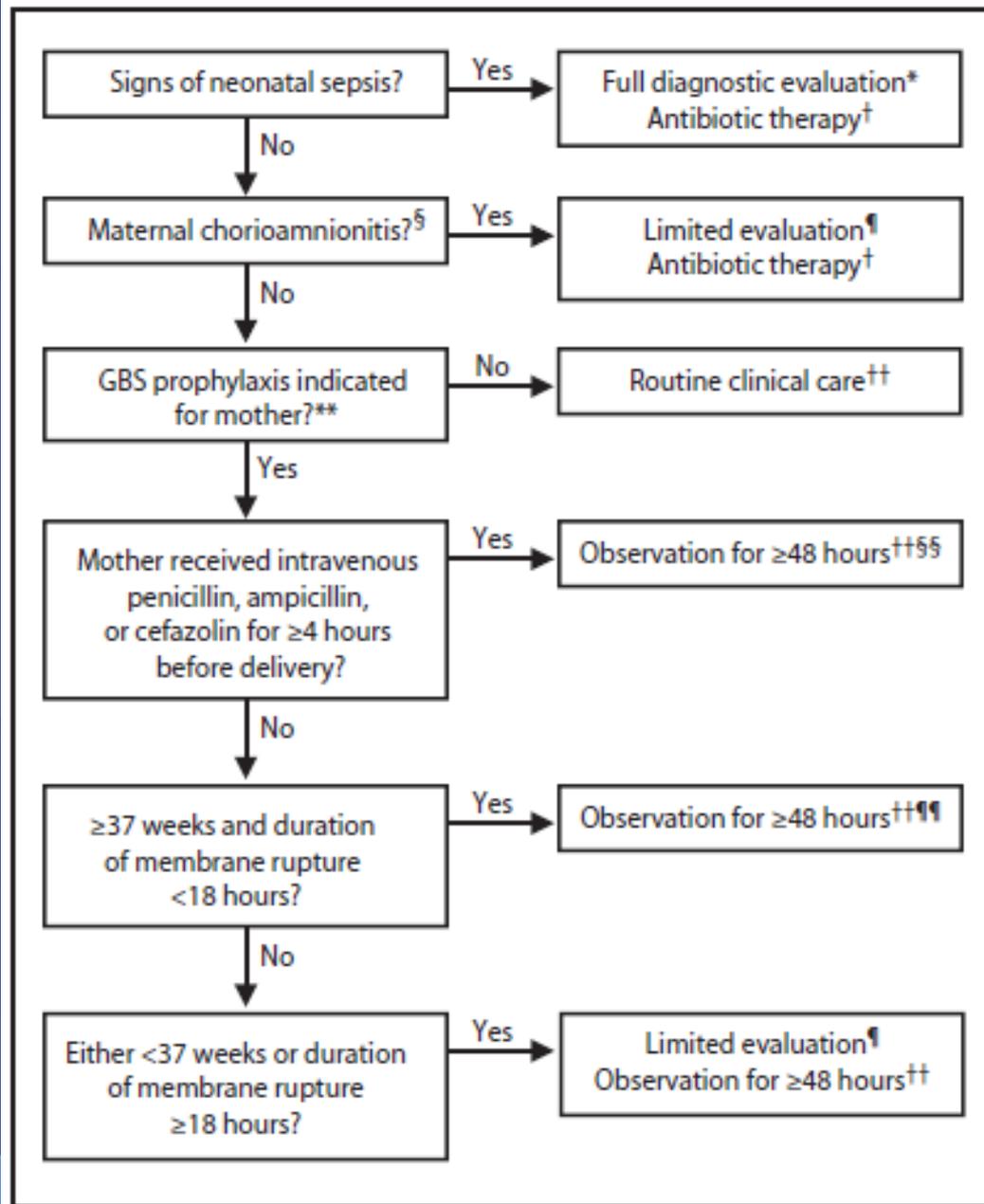


Newborn Management in the 2010 GBS Guidelines

Revised Neonatal Management Algorithm

- **Applies to all newborns**
 - Regardless of whether mother received IAP
- **Management based on clinical appearance, risk factors (maternal chorioamnionitis, prolonged rupture of membranes, preterm), and adequacy of IAP if indicated for mother**
- **Adequate IAP clarified**
 - ≥ 4 hours of IV penicillin, ampicillin, or cefazolin before delivery
 - All other agents or durations are considered inadequate for purposes of neonatal management
- **Aims to reduce unnecessary evaluations and antibiotics in newborns at relatively low risk for early-onset GBS disease**

FIGURE 9. Algorithm for secondary prevention of early-onset group B streptococcal (GBS) disease among newborns



Recommended Management: 2002 vs. 2010

Clinical scenario	2002	2010
Newborn with signs of sepsis, no IAP	No guidance	Full evaluation +antibiotics
Well appearing newborn, maternal chorioamnionitis	No guidance	Limited evaluation +antibiotics
Well appearing newborn, GBS+ mother, no IAP	No guidance	Depends on GA and ROM
Well appearing newborn, mother w/ indication for IAP, received clindamycin or vancomycin	No guidance	Depends on GA and ROM
Well appearing newborn, mother w/ indication for IAP, received ampicillin, penicillin or cefazolin <4 hrs	Limited evaluation	Depends on GA and ROM
Well appearing newborn, mother w/ indication for IAP, received ampicillin, penicillin or cefazolin ≥4 hours, GA 35-36 weeks	Limited evaluation	Observation for ≥48 hours

What Can You Do to Help?

- **Make sure your OB, Peds, FP, Midwife, and Microbiology colleagues know the new guidelines are out**
- **Check to see if your lab is following the new guidelines for laboratory methods**
- **Form a committee to plan steps needed for implementation in your facility**

Early-onset GBS Disease Web Resources

- Centers for Disease Control and Prevention
 - <http://www.cdc.gov/groupbstrep>
- American College of Obstetricians and Gynecologists
 - <http://www.acog.org>
- American Academy of Pediatrics
 - <http://www.aap.org>
- American College of Nurse-Midwives
 - <http://www.midwife.org>
- American Academy of Family Physicians
 - <http://www.aafp.org>
- American Society for Microbiology
 - <http://www.asm.org/>
- Group B Strep Association
 - <http://www.groupbstrep.org>

Acknowledgments

GBS Technical Team:

Kathryn Arnold, Barbara Stoll, Yun Wang, Carol Baker, Carrie Byington, Richard Polin, Ronald Gibbs, Jeanne Jordan, Sarah Kilpatrick, Geraldine Hall, Tekoa King, Ruth Lynfield, Marti Perhach, Laura Riley, Pablo Sanchez, Pamela Simms, Julie Wood, Rex Astles, Bernard Beall, Roberta Carey, Janine Corey, Tarayn Fairlie, Lee Hampton, Denise Jamieson, Melissa Lewis, Lesley McGee, Michael Miller, Christine Olson, Alison Patti, Stephanie Schrag, Jennifer Verani, Emily Weston, Cynthia Whitney, Elizabeth Zell

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