
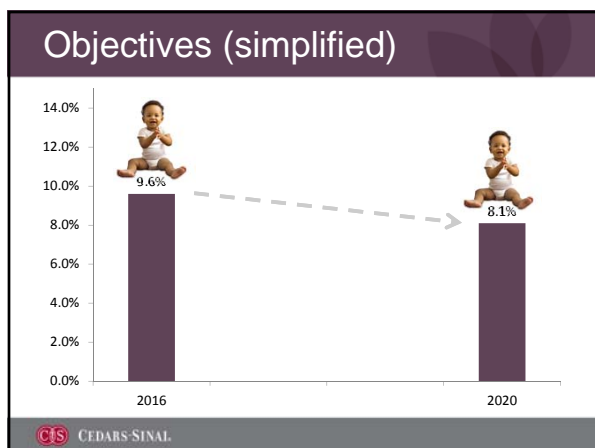




Objectives

- Discuss the current rate of preterm birth locally, nationally, and worldwide.
- Review the March of Dimes Roadmap Interventions.
- Highlight two tools for prevention of spontaneous preterm birth in at-risk women:
 - Intramuscular progesterone
 - Short cervix identification and treatment

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PRETERM BIRTH

How are we doing?

CIS CEDARS SINAI

Preterm birth: a global epidemic.

CIS CEDARS SINAI

Blencowe, Lancet 2012.

U.S. Preterm Birth Rates

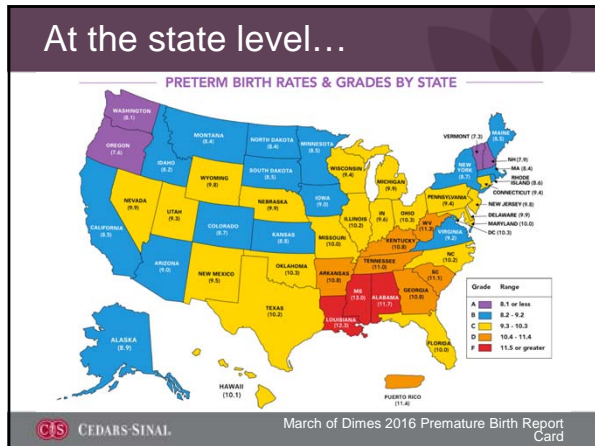
Year	Rate (%)	Method
1990	10.6	LMP-based
1995	11.0	LMP-based
2000	11.6	LMP-based
2005	12.7	LMP-based
2006	12.7	LMP-based
2007	12.7	LMP-based
2008	12.3	LMP-based
2009	12.2	LMP-based
2010	12.0	LMP-based
2011	11.7	LMP-based
2012	11.5	LMP-based
2013	11.4	LMP-based
2014	9.57	OE-based
2015	9.62	OE-based
2020 Goal	8.1	Goal
2030 Goal	5.5	Goal

LMP=gestational age based on date of mother's last menstrual period
OE=gestational age based on clinical estimate
2015 and 2016 goals based on OE gestational age
Preterm is less than 37 weeks gestation
Source: National Center for Health Statistics, 1990-2014 final and 2015 preliminary natality data.
Prepared by March of Dimes Perinatal Data Center, June 2016.

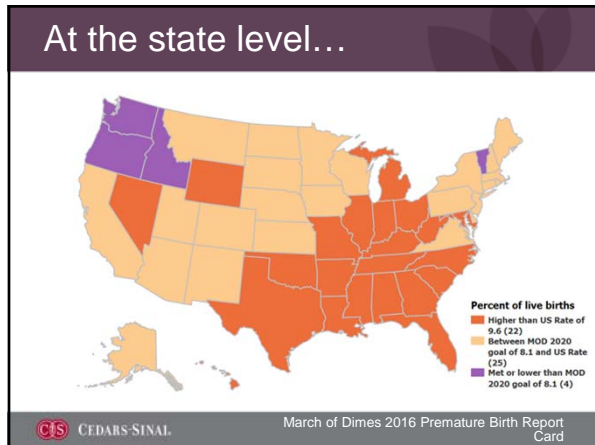
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National Vital Statistics Report / MOD PeriStats

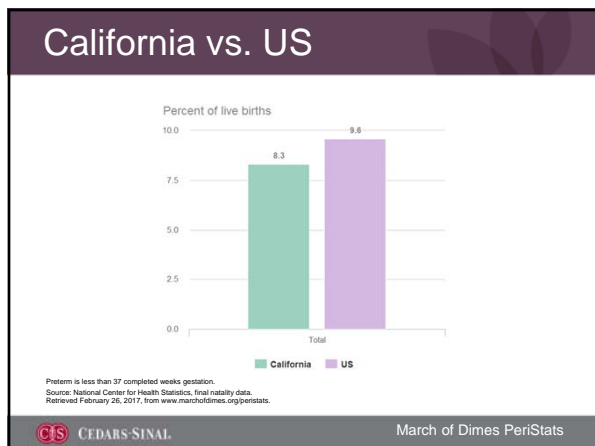
At the state level...

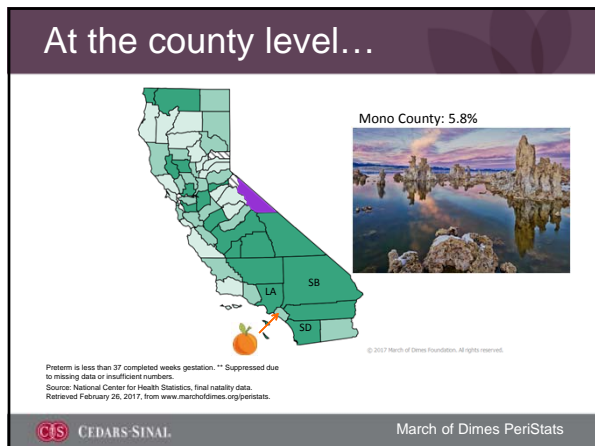


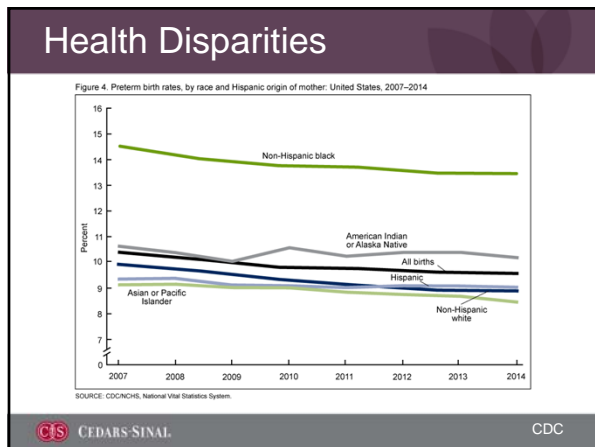
At the state level...

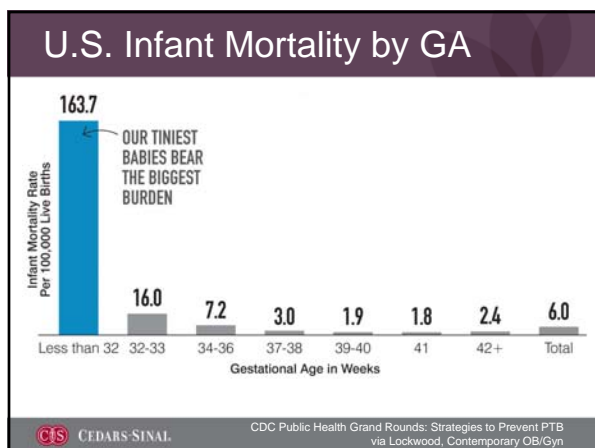


California vs. US









8.1%


ROADMAP INTERVENTIONS

March of Dimes

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Social Determinants of Health



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Dahlgren and Whitehead, 1991

Roadmap Interventions

- 
1. Reduce elective deliveries < 39 weeks.
 2. Increase progesterone use among women with a history of preterm birth.
 3. Reduce tobacco use among pregnant women.
 4. Encourage women to space pregnancies at least 18 months apart.
 5. Increase use of low-dose aspirin to prevent preeclampsia.
 6. Advance interventions for women with a short cervix.
 7. Reduce multiple gestation births via ART.
 8. Expand group prenatal care.

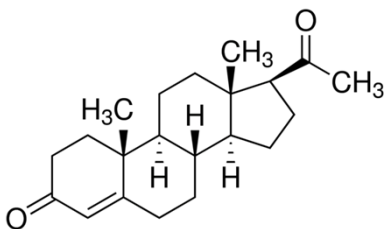
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ROADMAP INTERVENTIONS

Progesterone for prevention of recurrent preterm birth.


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Progesterone



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Progesterone in Pregnancy




Early

- Pregnancy support until the placenta takes over (7-9 weeks)
- Progesterone = progestational steroid ketone.

Late

- Maintain uterine quiescence (?)
- Anti-inflammatory (?)

 CEDARS-SINAI Dodd & Crowther, IJWH 2009

Wonder womb drug

Maintain the Peace



Defend against Infection



 CEDARS-SINAI DC Comics

Wonder womb drug(progesterone)



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Progesterone to Prevent PTB

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1902 JUNE 12, 2003 VOL. 349 NO. 24
Prevention of Recurrent Preterm Delivery
by 17 Alpha-Hydroxyprogesterone Caproate

Reif J, Meis, M.D., Mark Wilkerson, M.D., Elizabeth Thom, Ph.D., Mitchell P. Dombrowski, M.D., Beha Sital, M.D.,

- Double-blind placebo-controlled RCT
- 19 clinical centers in NICHD / MFM-U
- Spontaneous PTB in prior pregnancy
- From 16-36 weeks, randomized to receive either
 - Weekly IM 17-OH-progesterone
 - Placebo

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Meis, NEJM 2003

Progesterone ↓ recurrent PTB

	Progesterone (n=306)	Placebo (n=153)	Outcome
Delivery < 37 wks	36.3%	54.9%	Risk reduced by 34%
Delivery < 35 wks	20.6%	30.7%	Risk reduced by 33%
Delivery < 32 wks	11.4%	19.6%	Risk reduced by 42%

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Meis, NEJM 2003

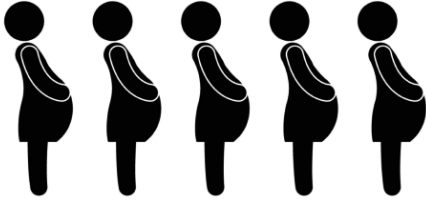
...and babies benefit!

	Progesterone (n=306)	Placebo (n=153)	Outcome
Supplemental O2 needed	14.9%	23.8%	Risk reduced by 38%
IVH	1.3%	5.2%	Risk reduced by 75%
NEC	0%	2.6%	N/A

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Meis, NEJM 2003

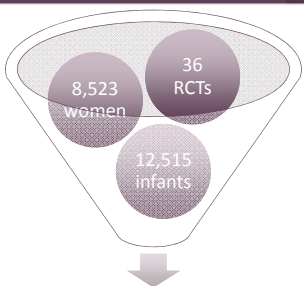
How many women would need to be treated to prevent one preterm birth < 37 weeks?



Only five.

CIS CEDARS-SINAI Meis, NEJM 2003

Other studies agreed!



BENEFITS

CIS CEDARS-SINAI Dodd, Cochrane 2013.

Progesterone improved...

Obstetric	Neonatal
• PTB < 37 weeks	• Perinatal death
• PTB < 34 weeks	• Neonatal death
	• NICU admission
	• Assisted ventilation
	• NEC

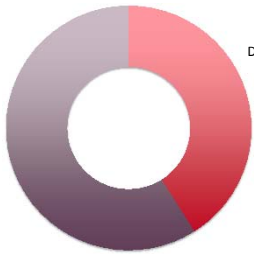
CIS CEDARS-SINAI Dodd, Cochrane 2013.

**SO, EVERYBODY'S USING IT,
RIGHT?**


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Provider Survey

Among patients for whom 17-OHP was indicated...



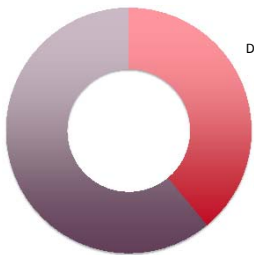
Category	Percentage
Received	59%
Did not receive	41%

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Rebarber, 2013.

Provider Survey #2: MFM-U sites

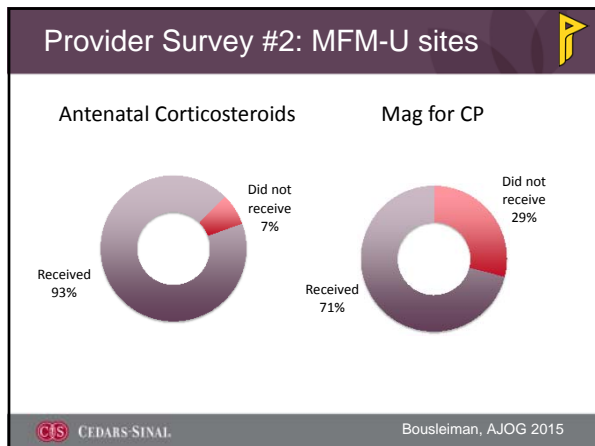
Among patients for whom 17-OHP was indicated...



Category	Percentage
Received	61%
Did not receive	39%

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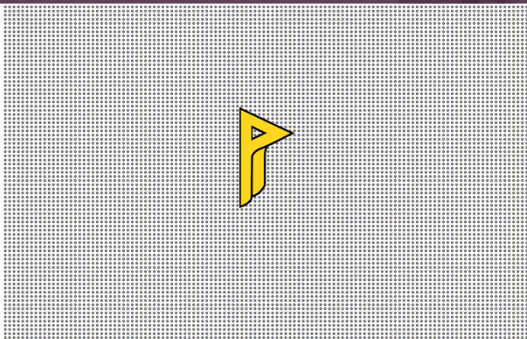
Bousleiman, AJOG 2015





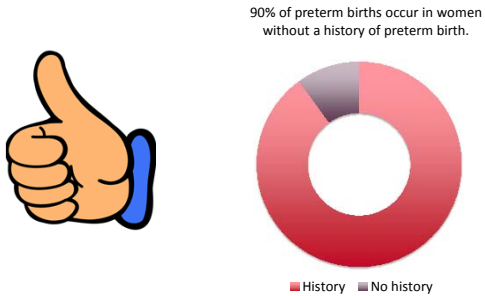


How many fewer preterm births per year?



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So, we're good?



90% of preterm births occur in women without a history of preterm birth.

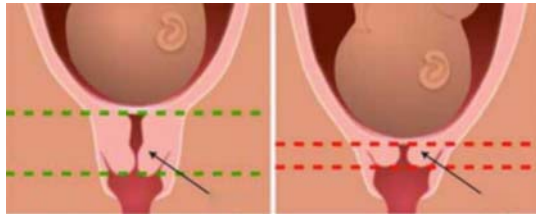
History No history

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ROADMAP INTERVENTIONS
Identification / Treatment of Short Cervix

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What is a short cervix?

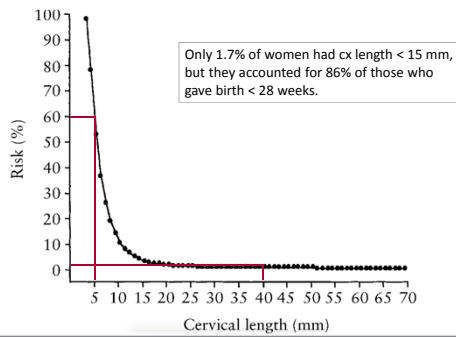


Normal Length Cervix

Short Cervix

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Risk of Delivery < 32 weeks by Cervical Length



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Heath, UOG 1998

Management: The Tools



IM
Progesterone



Vaginal
Progesterone



Cerclage



Pessary

CEDARS-SINAI

Intramuscular vs vaginal?



- 250 mg IM

- Weekly

- Patients with history of preterm birth



- 200 mg pill or 90 mg vaginal gel

- Nightly

- Short cervix

CIS CEDARS-SINAI

Vaginal Progesterone



ORIGINAL ARTICLE

Progesterone and the Risk of Preterm Birth among Women with a Short Cervix

Eduardo R. Fonseca, M.D., Ebru Celik, M.D., Mauro Parra, M.D.

	Progesterone (n=125)	Placebo (n=125)	Outcome
Spont delivery < 34 wks	19.2%	34.4%	Risk reduced by 44%
Delivery < 34 wks	20.8%	36%	Risk reduced by 42%

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Fonseca, NEJM 2007.

Vaginal Progesterone



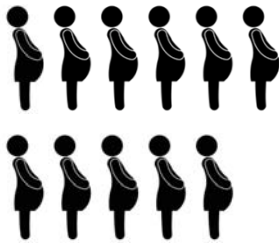
- Meta-analysis of five RCTs involving 974 women w/ short cx
- Variety of vaginal preparations (capsules, gel, suppositories)

	Progesterone	Placebo	Outcome
Preterm birth < 34 wks	18%	27.5%	Risk reduced by 34%
Preterm birth < 28 wks	5.5%	10.9%	Risk reduced by 49%
Composite neo morb/mortality	7.9%	13.6%	Risk reduced by 42%
NICU	13.4%	24.3%	Risk reduced by 42%
RDS	4.6%	10.3%	Risk reduced by 55%

CIS CEDARS-SINAI

Romero, UOG 2016.

How many women would need to be treated to prevent one preterm birth < 34 weeks?



Only eleven.

CEDARS-SINAI Romero, UOG 2016.

Management: The Tools



IM
Progesterone



Vaginal
Progesterone




Cerclage



Pessary

CEDARS-SINAI

Cerclage



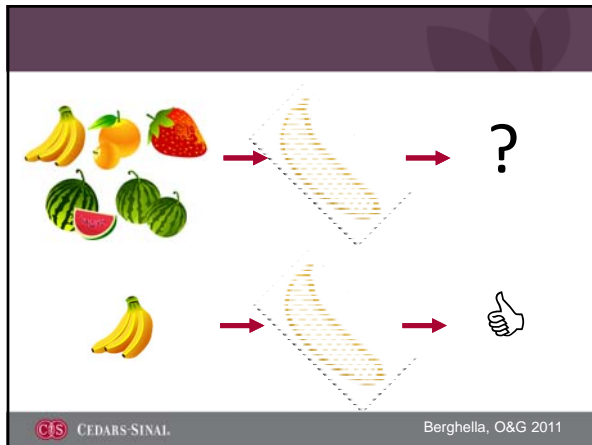
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Cerclage

- History-indicated
- Exam-indicated
- Short cervix
 - In women with a history of preterm birth
 - With a singleton pregnancy
 - At < 24 weeks
 - Whose cervix is <25 mm

CIS CEDARS-SINAI

Berghella, O&G 2011.



CIS CEDARS-SINAI

Berghella, O&G 2011

Cerclage

- Meta-analysis of five RCTs involving 908 women w/ short cx, singleton pregnancy, and previous PTB

	Cerclage	No cerclage	Outcome
Preterm birth < 35 wks	28.4%	41.3%	Risk reduced by 30%
Preterm birth			Risk reduced by
< 37	42%	60.6%	30%
< 32	19.2%	29.5%	34%
< 28	12.8%	20.1%	36%
< 24	5.2%	11%	52%
Composite neo morb/mortality	8.6%	17.6%	Risk reduced by 48%

CIS CEDARS-SINAI

Romero, UOG 2016.

Management: The Tools



IM
Progesterone



Vaginal
Progesterone



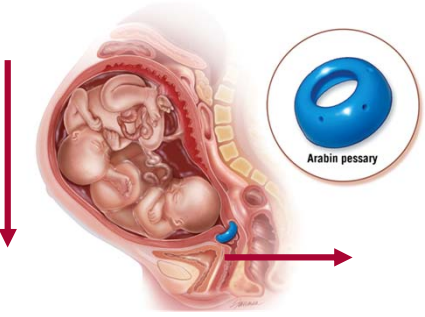
Cerclage





Pessary

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Cervical Pessary




Arabin pessary

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Cervical Pessary: not quite yet

 Society for Maternal-Fetal Medicine
high-risk pregnancy experts

The role of cervical pessary placement to prevent preterm birth in clinical practice


Society for Maternal-Fetal Medicine (SMFM) Publications Committee

The practice of medicine continues to evolve, and individual circumstances will vary. This publication reflects information available at the time of its submission for publication and is neither designed nor intended to establish an exclusive standard of perinatal care. This publication is not expected to reflect the opinions of all members of the Society for Maternal-Fetal Medicine.

There has been renewed interest in the use of the cervical pessary as an intervention to prevent preterm birth (PTB) in women at high-risk for preterm birth. Multiple randomized clinical trials (RCTs) have been published in the last several years, with conflicting results. The purpose of this statement is to summarize the findings of recent RCTs studying the use of the cervical pessary to prevent PTB and to provide guidance regarding the role of cervical pessary use in clinical practice.

SMFM Statement


smfm.org

 CrossMark

neonatal or child outcomes. Serious adverse events (eg, cervical ischemia) are rare. Reported side effects from other pessaries, including other ring devices and the Smith-Hodge lever design, are limited but appear similar to those trials involving the Arabin pessary.¹

Cervical pessary in singleton gestations

Two large RCTs have recently been performed in singleton gestations, with conflicting results. The Pessario

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Management: The Tools



IM
Progesterone



Vaginal
Progesterone




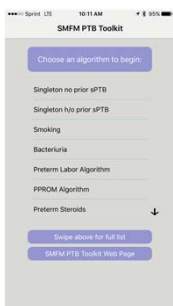
Cerclage




Pessary

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There's an app for that!

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iOS Store: "SMFM Preterm"

So, we're good?



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To-Do List...

- Cervical length screening timing?
- Multiples?
- Shortening despite IM progesterone?
- Some shortening, but not < 20 mm?
- Risk factor screening?
- Shortening despite vaginal progesterone?
- What if PTL has started?
- Any pessary role?

CIS CEDARS-SINAI

March 7th!

ISUOG @ISUOG · Mar 7
 Vaginal progesterone decreases morbidity and mortality in twin pregnancy with short cervix #UOGjournal bit.ly/2lFpzG @AJOGEd_RR

TWEETS 1,808 FOLLOWING 818 FOLLOWERS 3,916 LIKES 475

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Management: The Tools

IM Progesterone

Vaginal Progesterone

Cerclage

Pessary

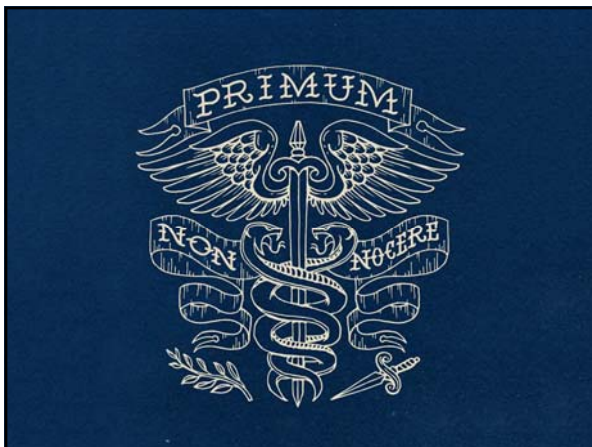
CIS CEDARS-SINAI

So, should we screen?

DISEASE should be	✓
• Clinically important and clearly defined	
• Prevalent and have an early asymptomatic phase	
SCREENING technique should be	✓
• Well-described, safe, and acceptable	
• Have a reasonable cut-off, with accurate/reproducible results	
INTERVENTION should be	✓
• Most effective when implemented early	
• Cost-effective to screen/treat abnormal	
FACILITIES are available for	±
• Screening	
• Treatment	

SMFM Statement

- Cervical length screening should be performed at for women with
 - Singleton pregnancy
 - History of spontaneous preterm birth
- Cervical length screening can be considered in all women at 18 – 23 6/7 weeks.



Objectives

- Discuss the current rate of preterm birth locally, nationally, and worldwide.
- Review the March of Dimes Roadmap Interventions.
- Highlight two tools for prevention of spontaneous preterm birth in at-risk women:
 - Intramuscular progesterone
 - Short cervix identification and treatment



A Statewide Progesterone Promotion Program



lams, O&G 2017.



Thank you.



 CEDARS-SINAI

References



<http://goo.gl/12L5YP>

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