



Adoption of the IADPSG in the U.S.: What Is Holding Us Back?

November 7, 2013

Catherine Kim, M.D. M.P.H.

Overview

- ACOG (current) vs. IADPSG (new)
- Objections to criteria changes: the perspective of the single hospital
 - Reproducibility
 - Resource allocation
 - Return on investment



The International Association
of the Diabetes and Pregnancy Study Groups [IADPSG]

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ACOG (currently used) vs. IADPSG (new)

- ACOG criteria (current):
 - Cumbersome: 3 hours, 4 blood draws
 - Based on maternal risk of postpartum diabetes
 - Incompatible with cross-country comparisons
- IADPSG (new):
 - Less cumbersome: 2 hours, 3 blood draws
 - Based on fetal outcomes
 - Based on international, multicenter study

**ACOG i.e. Carpenter &
Coustan**

IADPSG (new)

	ACOG i.e. Carpenter & Coustan	IADPSG (new)
Who	With risk factors or universal	High risk women for “overt diabetes” Fasting 7.0 mmol/l OR HbA1c \geq 6.5 OR Random or 2-hour \geq 11.1 mmol/l

	ACOG i.e. Carpenter & Coustan	IADPSG (new)
Who	With risk factors or universal	High risk women for “overt diabetes” Fasting 7.0 mmol/l OR HbA1c \geq 6.5 OR Random or 2-hour \geq 11.1 mmol/l
When	24-28 weeks	24-28 weeks for everyone else

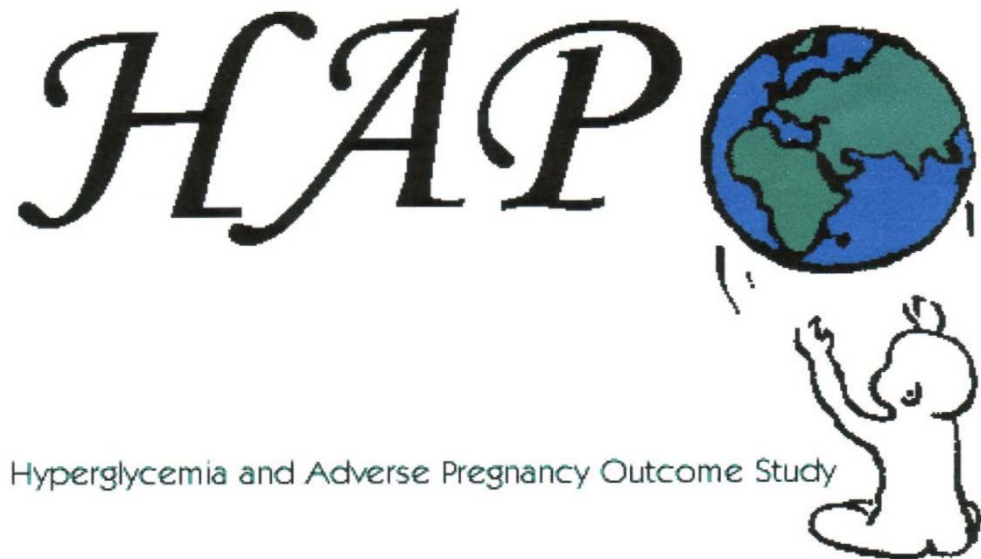
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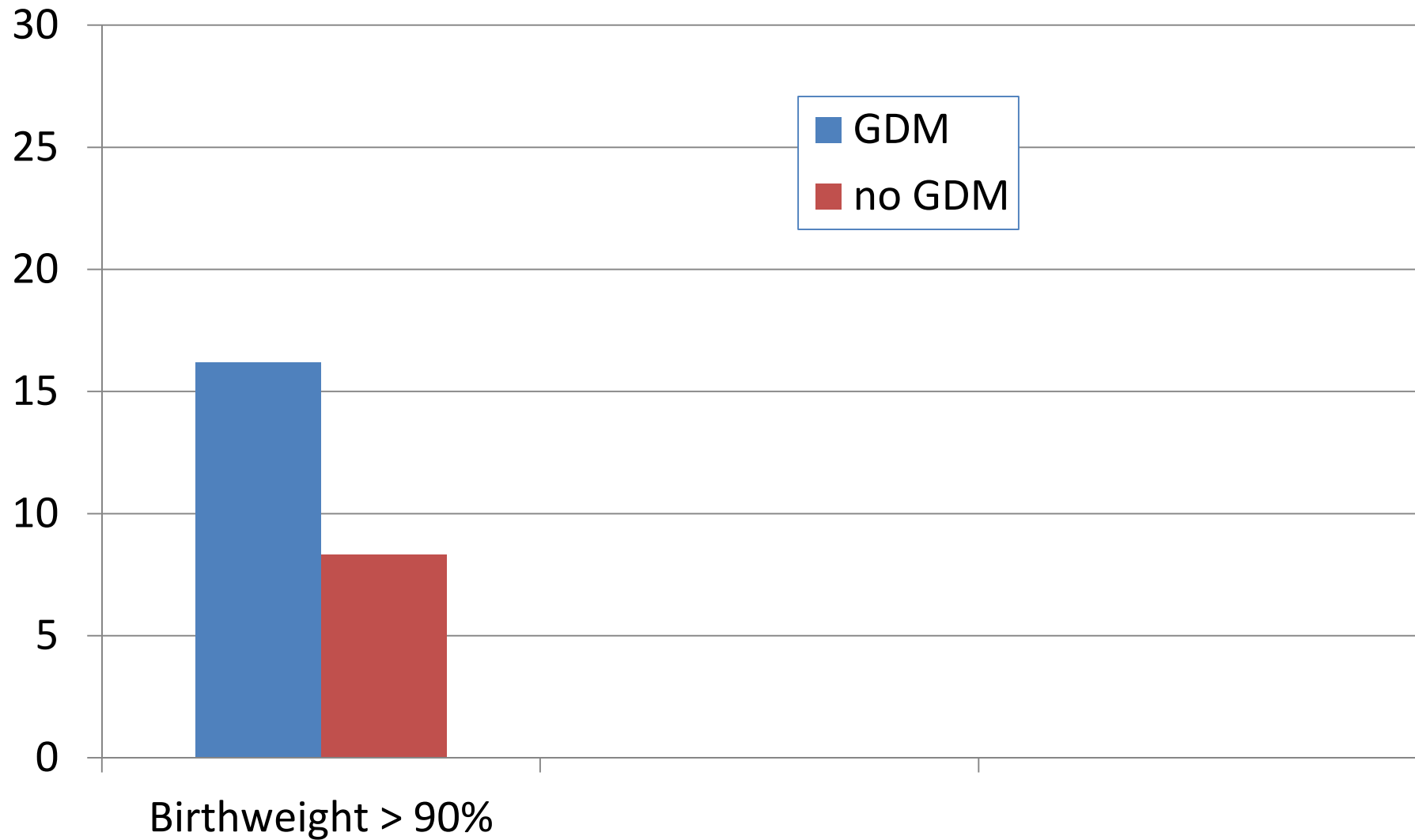
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When	24-28 weeks	24-28 weeks for everyone else
Step 1	50 gram, 1 hour test	--
Step 2	100 gram 3-hour OGTT \geq 2 elevations	75 gram 2-hour OGTT \geq 1 elevation
	Fasting \geq 5.3 mmol/l (95 mg/dl)	Fasting \geq 5.1 mmol/l (92 mg/dl)
	1 hour \geq 10 mmol/l (180 mg/dl)	1 hour \geq 10 mmol/l (180 mg/dl)
	2 hour \geq 8.6 mmol/l (155 mg/dl)	2 hour \geq 8.5 mmol/l (153 mg/dl)
	3 hour \geq 7.8 mmol/l (140 mg/dl)	

IADPSG (new) derived from HAPO

- Prospective cohort study
- 25,505 pregnant women
- 15 centers
- 9 countries
- Published 2008
- IADPSG cutpoints derived from an odds ratio of 1.75 for primary outcomes

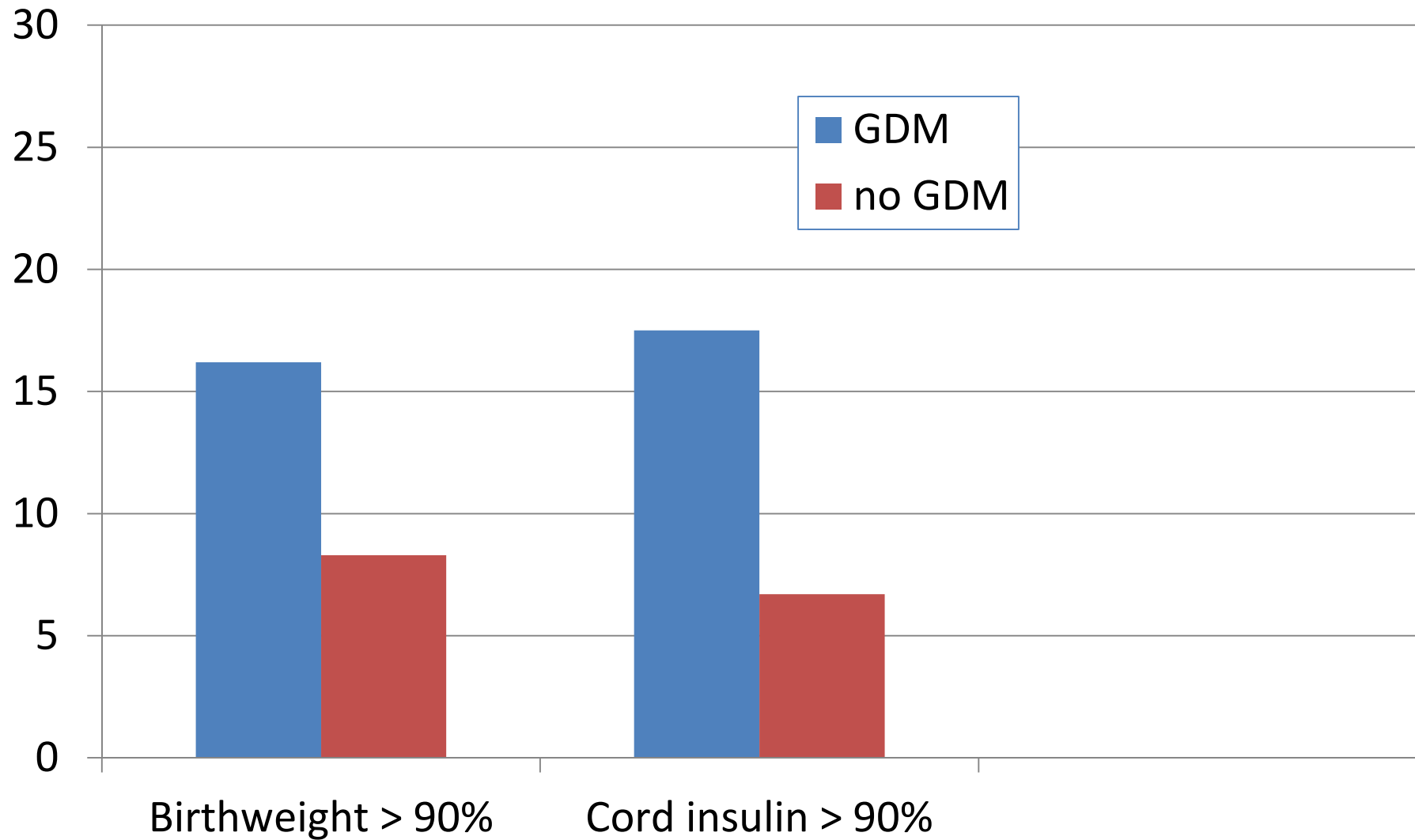


Incidence of primary outcomes in women with and without GDM using IADPSG criteria in HAPO



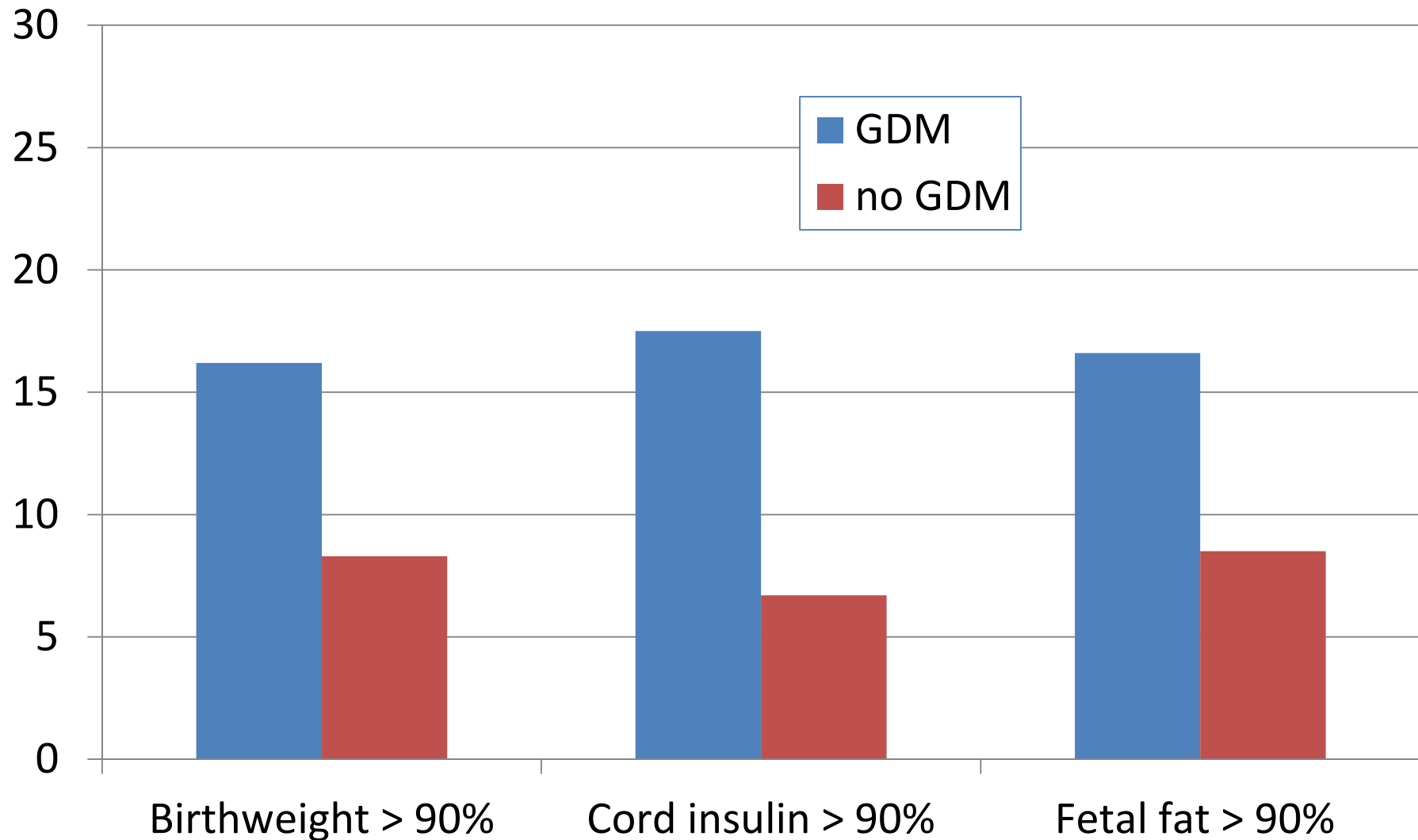
HAPO, N Engl J Med, 2008.

Incidence of primary outcomes in women with and without GDM using IADPSG criteria in HAPO



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Incidence of primary outcomes in women with and without GDM using IADPSG criteria in HAPO



HAPO, N Engl J Med, 2008.

What is the risk of adverse outcomes with the new criteria?

	New (IADPSG) Risk Ratio	
Macrosomia	2.09	
LGA	1.86	



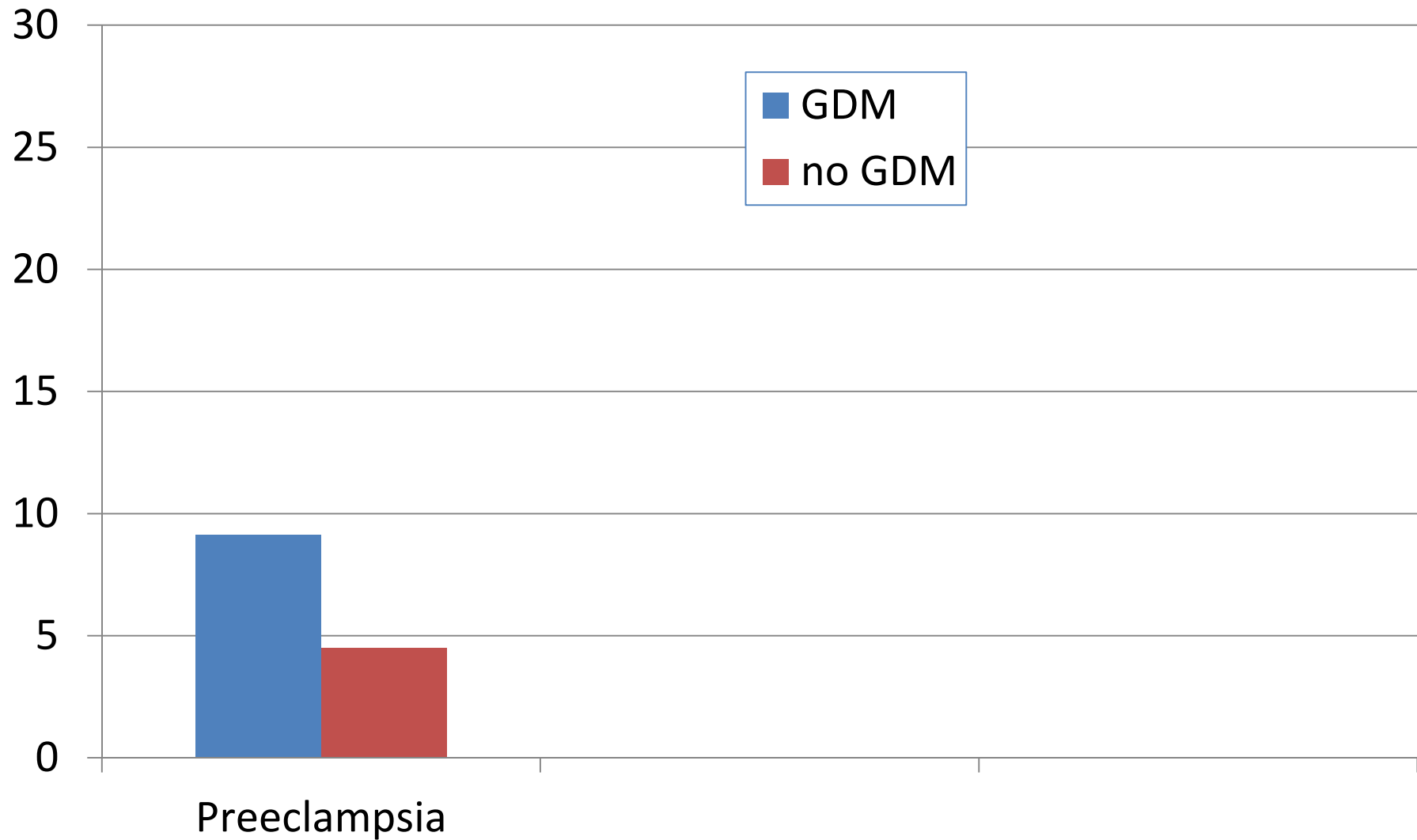
Donovan and Hartling, NIH Consensus Conference, 2013.

What is the risk of adverse outcomes with the current criteria?

	New (IADPSG) Risk Ratio	Current (ACOG) Risk Ratio
Macrosomia	2.09	1.61
LGA	1.86	2.18

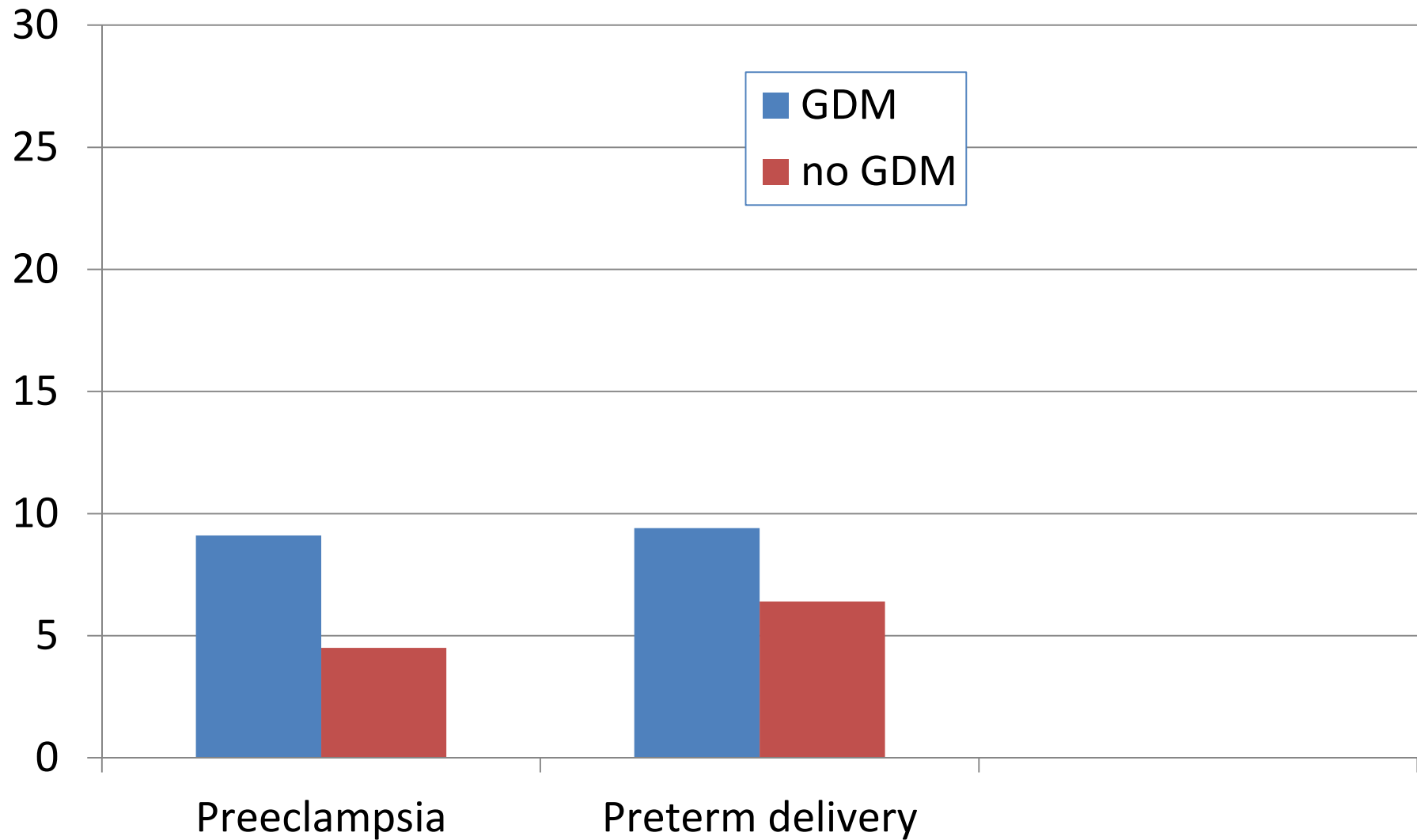
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Incidence of secondary outcomes in women with and without GDM using IADPSG criteria in HAPO



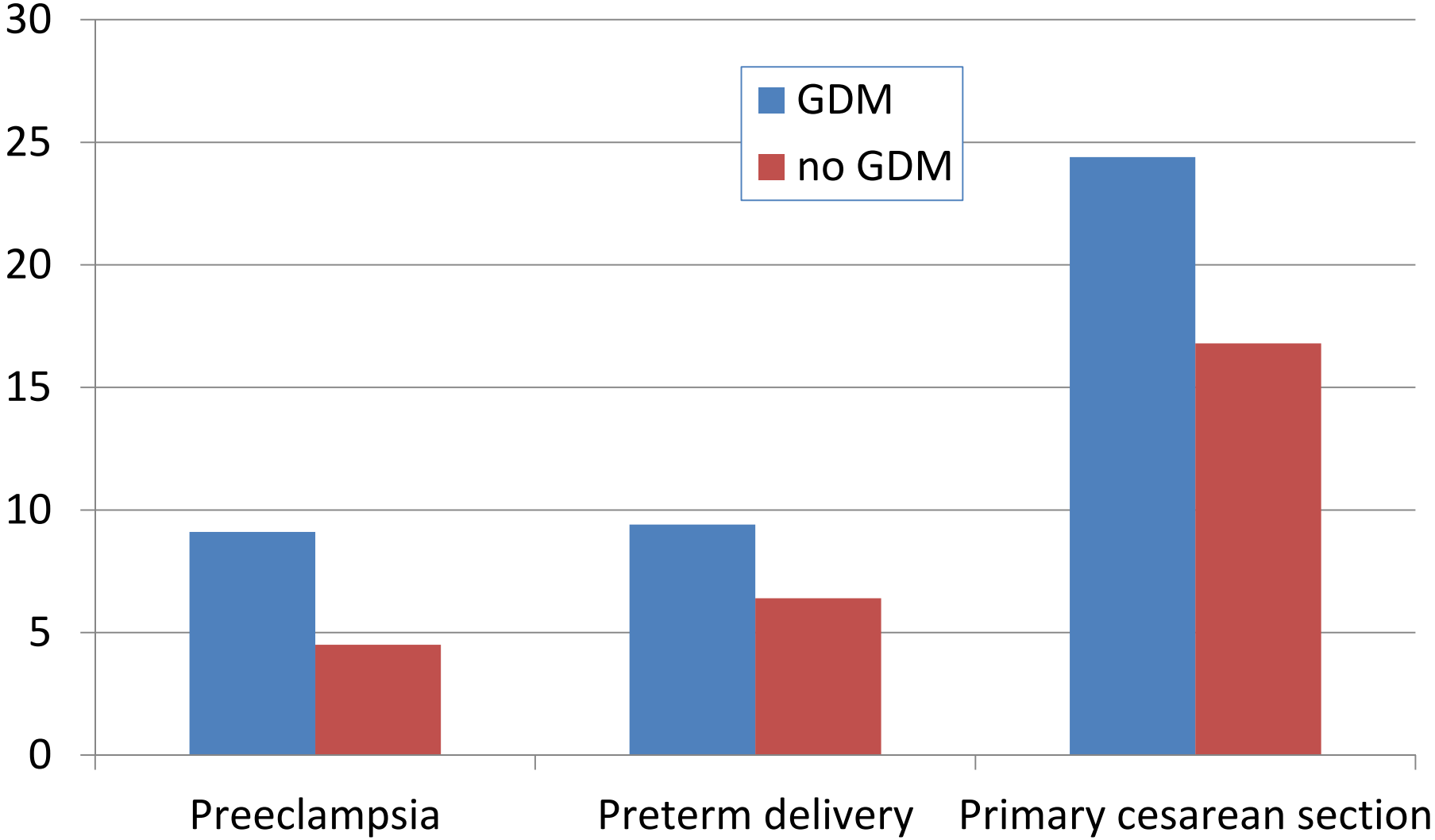
HAPO, N Engl J Med, 2008.

Incidence of secondary outcomes in women with and without GDM using IADPSG criteria in HAPO



HAPO, N Engl J Med, 2008.

Incidence of secondary outcomes in women with and without GDM using IADPSG criteria in HAPO



HAPO, N Engl J Med, 2008.

What is the risk of adverse outcomes with the new criteria?

	New (IADPSG) Risk Ratio	
Cesarean delivery	1.38	



Donovan and Hartling, NIH Consensus Conference, 2013.

What is the risk of adverse outcomes with the current criteria?

	New (IADPSG) Risk Ratio	Current (ACOG) Risk Ratio
Cesarean delivery	1.38	1.32



Donovan and Hartling, NIH Consensus Conference, 2013.

ACOG (current) vs. IADPSG (new)

- ACOG criteria more cumbersome than IADPSG
- ACOG criteria have similar prediction for key perinatal outcomes compared to IADPSG

Overview

- ACOG (current) vs. IADPSG (new)
- **Objections to criteria changes: the perspective of the single hospital**
 - **Reproducibility in other cohorts**
 - Resource allocation
 - Return on investment



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Reproducibility: are new criteria associated with adverse outcomes in other cohorts?

The perspective of the single hospital

How do new criteria perform in other cohorts?

	GDM (n=186)	No GDM (n=372)	P-value
LGA	9.1%	5.9%	0.19



Bodmer Roy et al, Obstet Gynecol, 2012. 120: 746-752.

New GDM criteria are not associated with LGA, any neonatal complication at delivery

	GDM (n=186)	No GDM (n=372)	P-value
LGA	9.1%	5.9%	0.19
Any neonatal complication at delivery	13.4%	9.7%	0.20

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New GDM criteria are not associated with neonatal metabolic complications

	GDM (n=186)	No GDM (n=372)	P-value
LGA	9.1%	5.9%	0.19
Any neonatal complication at delivery	13.4%	9.7%	0.20
Neonatal metabolic complications	10.8%	14.2%	0.29

Bodmer Roy et al, Obstet Gynecol, 2012. 120: 746-752.

New GDM criteria are associated with MORE Cesareans

	GDM (n=186)	No GDM (n=372)	P-value
LGA	9.1%	5.9%	0.19
Any neonatal complication at delivery	13.4%	9.7%	0.20
Neonatal metabolic complications	10.8%	14.2%	0.29
Cesarean	37.1%	25.3%	0.004
Repeat Cesarean	12.9%	6.7%	0.018

Bodmer Roy et al, Obstet Gynecol, 2012. 120: 746-752.

**Are new criteria associated with
adverse outcomes in other cohorts?**

Yes in meta-analyses that included HAPO

No in 1 study that did not, except for Cesareans

Power? Milder GDM?

The single hospital perspective

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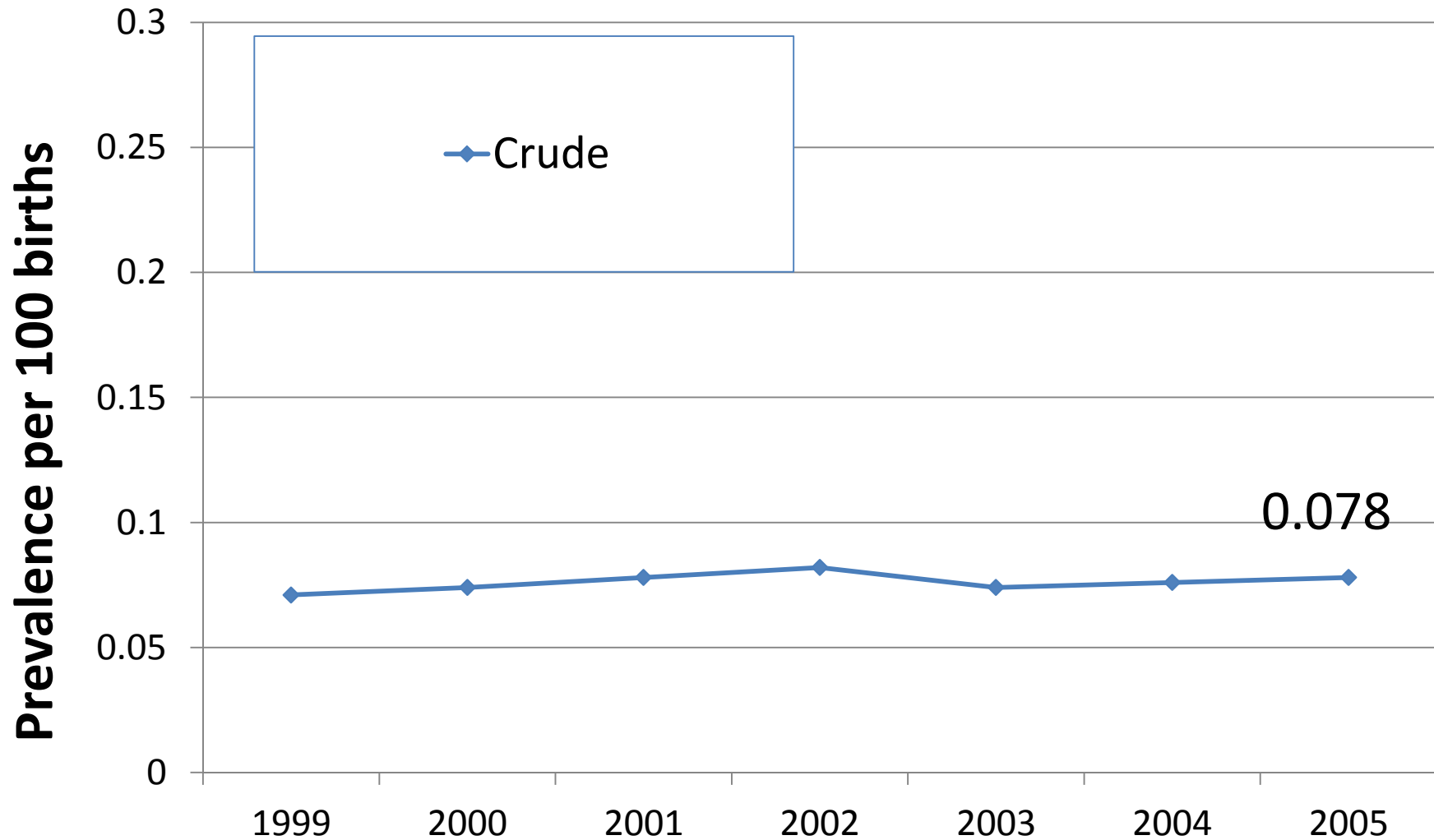
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Resource allocation

Prevalence of GDM with new criteria
would double

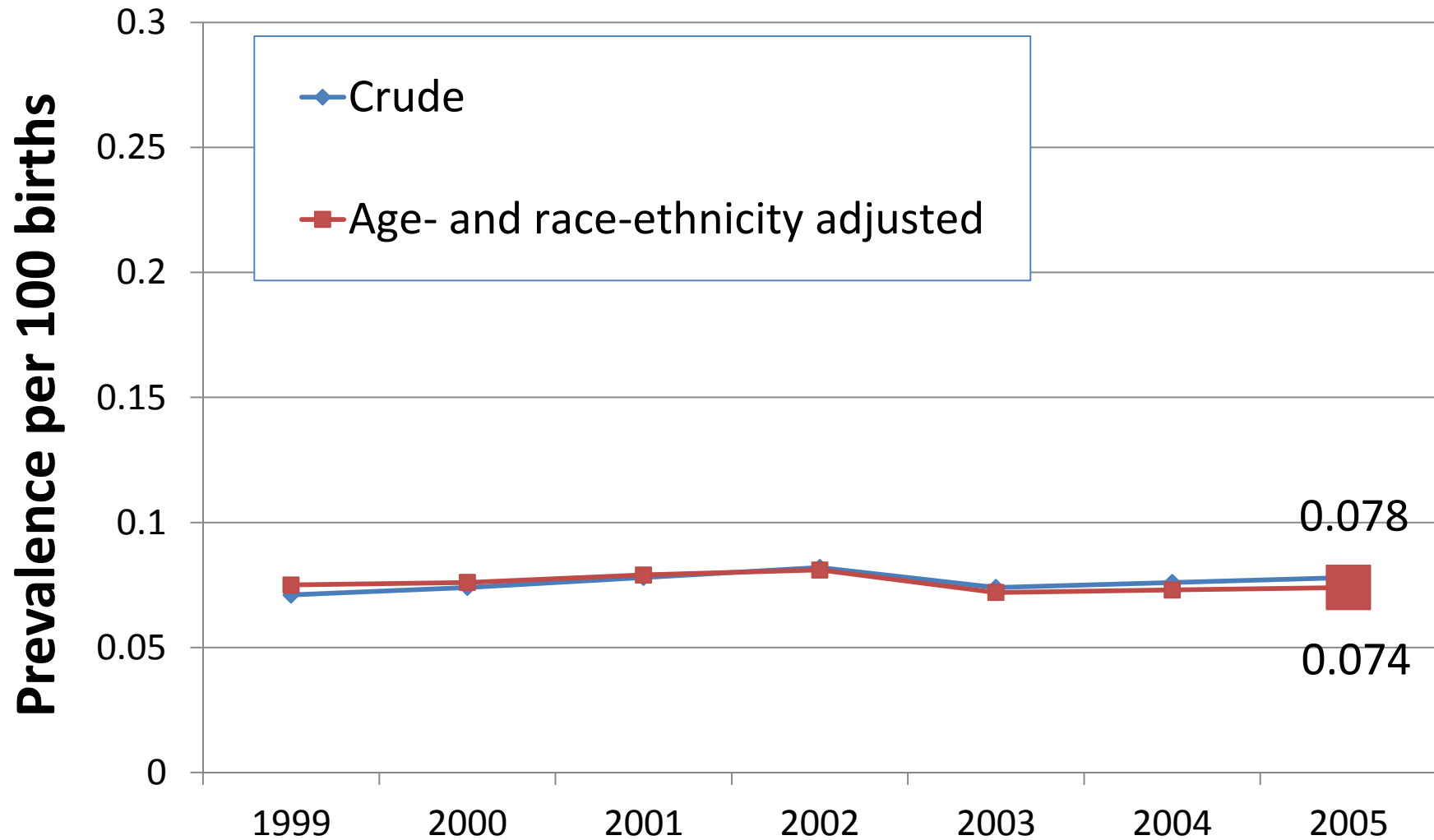


Prevalence of GDM in Southern California, 1999-2005



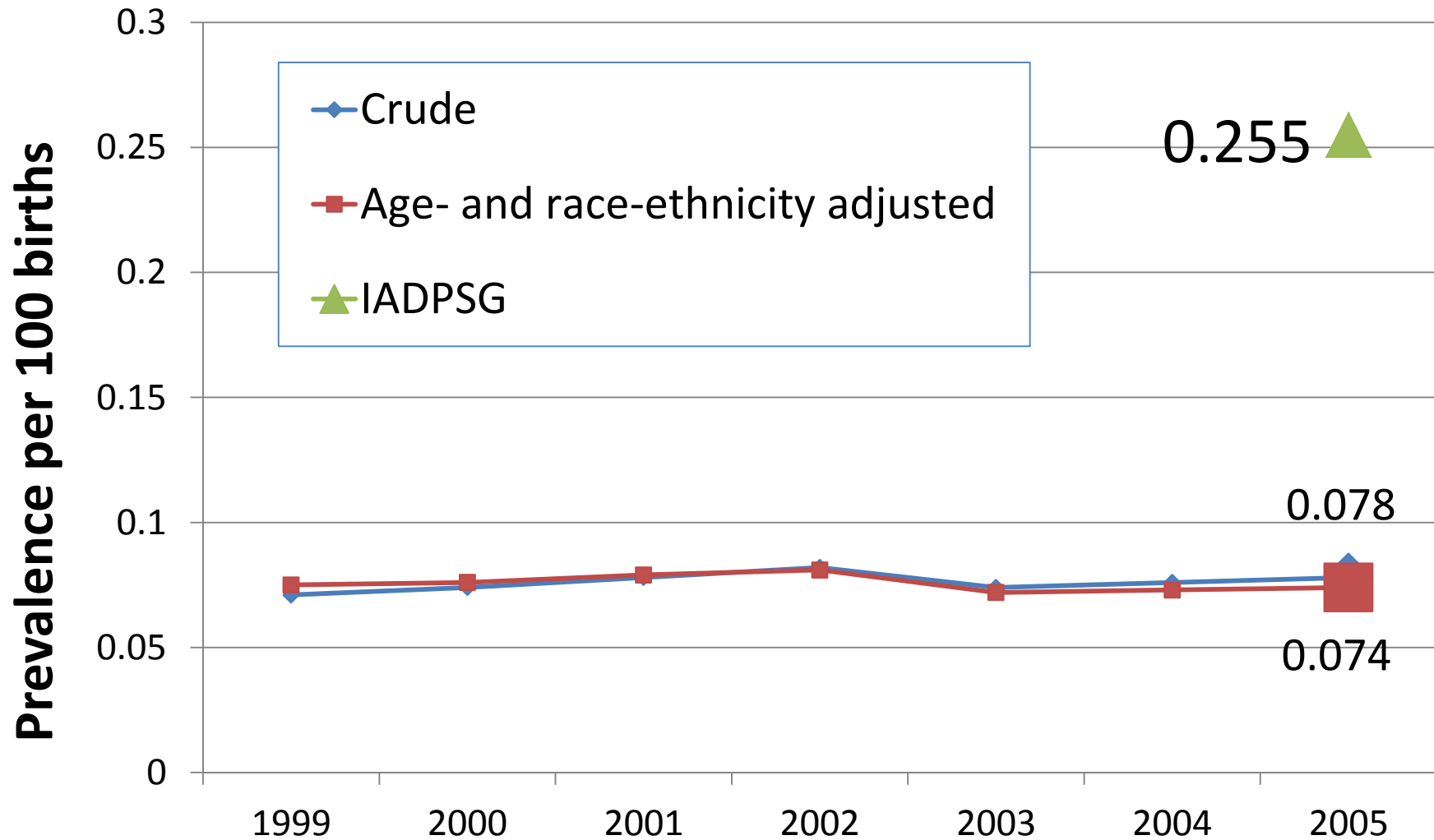


Prevalence of GDM in Southern California, 1999-2005





Prevalence of GDM in Southern California, 1999-2005



GDM at UT Southwestern

- 15,000 deliveries per year
- 2 half day clinics per week
- 120-150 women with GDM per week
- 8,000 clinic visits per year
- 8 nurses
- 2 diabetes educators
- 1 CNM
- 10-12 APNs
- 1-2 residents
- 1 MFM fellow
- 3 MFM faculty
- ***“Doubling or tripling the diagnosis is going to crush us. It is going to be devastating. We couldn’t do a good job for women who are most at risk.”***



What are costs of GDM in the U.S.?

Annual cost due to GDM: \$636 million in 2007

- **\$355 million (56%) by private insurers**
- \$230 million (36%) by U.S. government
- \$51 million (8%) by self-pay, charity

Treating GDM dxed by IADPSG can be cost-effective. . .

TABLE 1

Probabilities, costs, and utilities used in model

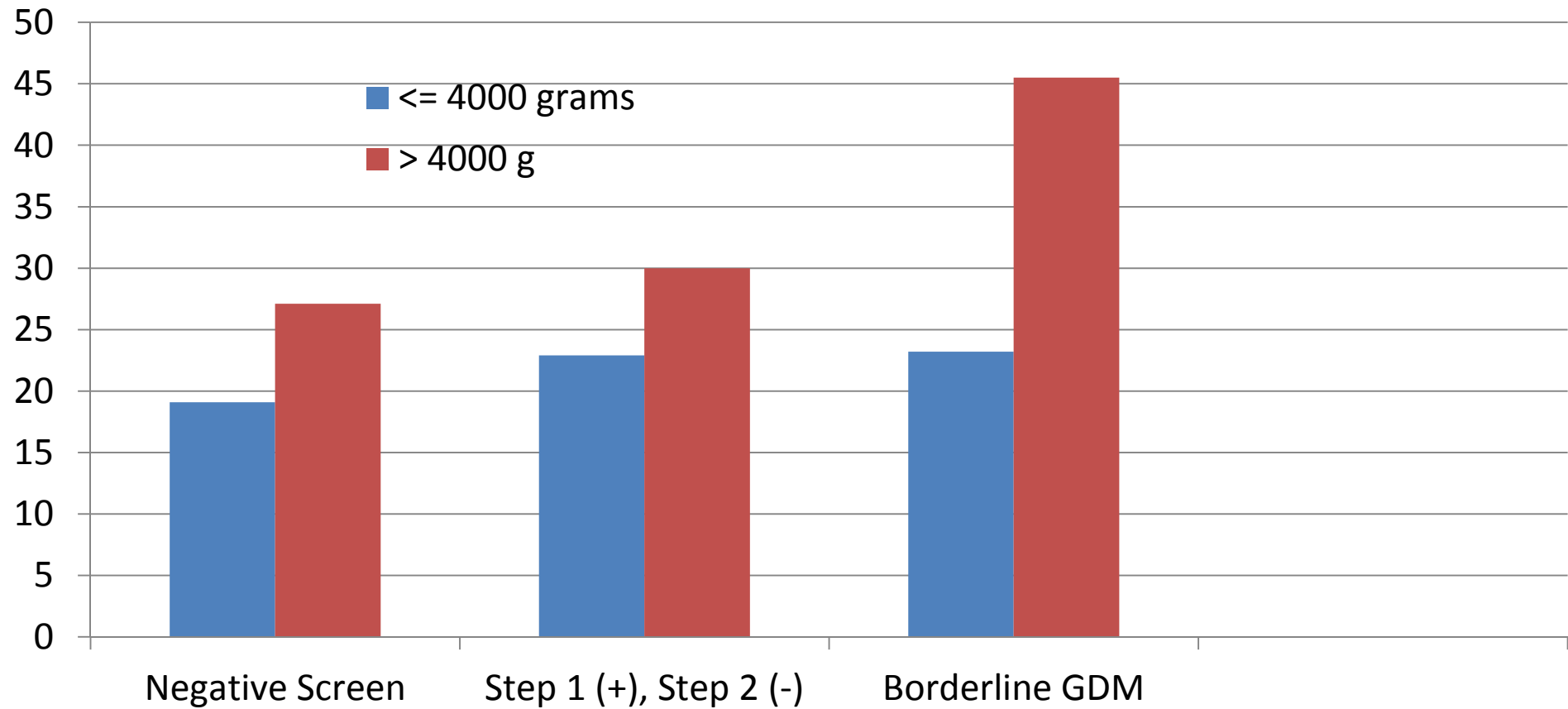
Parameter	Probabilities
GDM treatment	

But depends upon C-sections being lower with diagnosis and treatment

GDM diagnosis with IADPSG	Group 1		Group 2	
	No treatment	Treatment	No treatment	Treatment
GDM diagnosis with IADPSG	.054			
Maternal outcomes				
Preeclampsia	.136	.086	.0679	.0312
Cesarean delivery	.338	.338	.228	.180

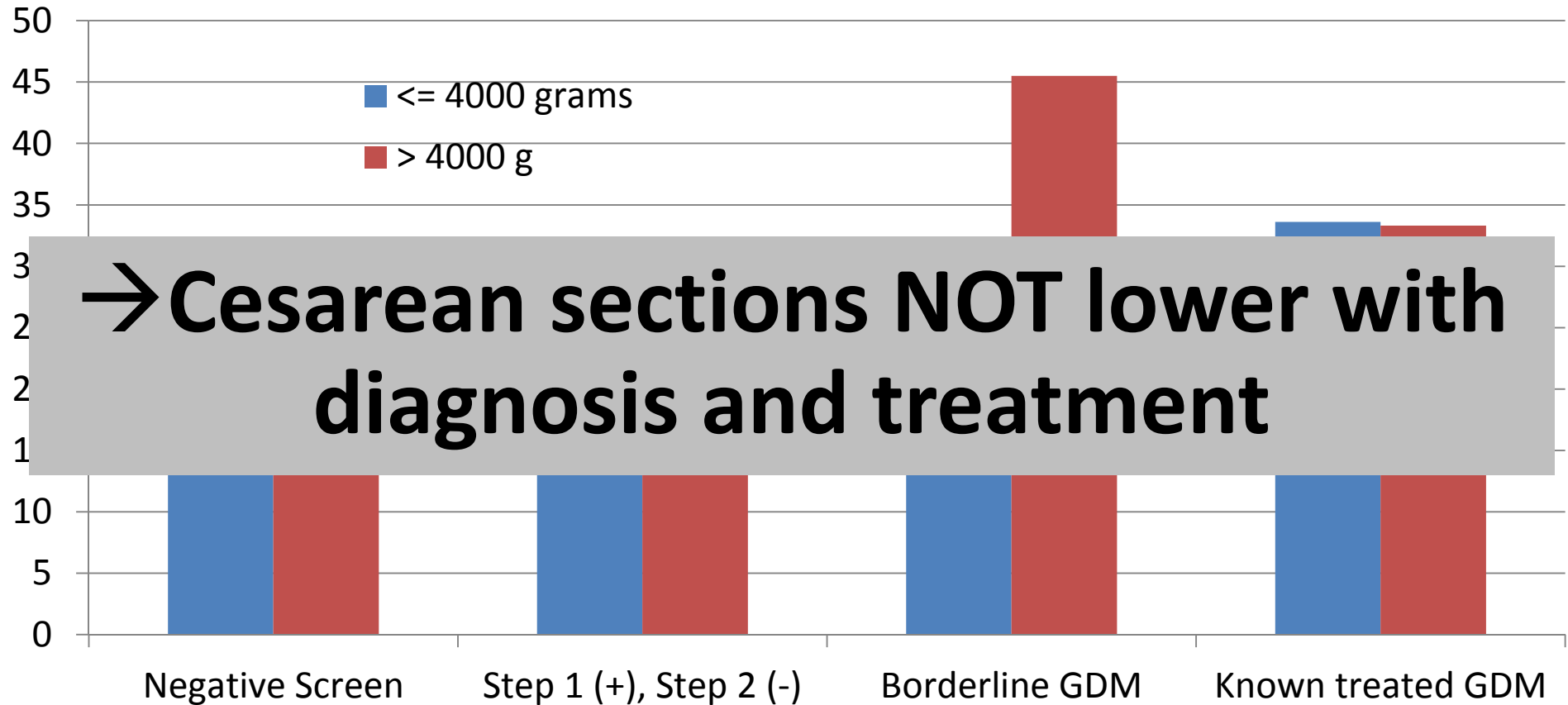
Mission et al, Am J Obstet Gynecol, 2012.

Are C-sections lower with diagnosis and treatment?



Naylor et al, JAMA, 1996.

Are C-sections lower with diagnosis and treatment?



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Maternal outcomes				
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Cesarean delivery	.338	.338	.228	.180

Mission et al, Am J Obstet Gynecol, 2012.

Resource allocation

Prevalence of GDM with IADPSG would double

Current cost-effectiveness analyses based on assumption that C-sections would decrease with GDM diagnosis

Past studies suggest that C-sections actually increase with GDM diagnosis

Overview

- ACOG (current) vs. IADPSG (new)
- **Objections to criteria changes**
 - Reproducibility
 - Resource allocation
 - **Return on investment: What does intervention do?**



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Return on investment: what does intervention do?

ACHOIS (moderate GDM)

MFMU (mild GDM)



Treatment for moderate GDM

		ACHOIS-moderate GDM
Age		30.5 years
BMI (kg/m ²)		26.4 (1 st trimester)
GCT		7.8 mmol/l
		75 gram OGTT
FPG		7.8 mmol/l
1 hour		Not done
2 hour		11.0 mmol/l
3 hour		Not done

Crowther et al 2005

Treatment for moderate GDM

		ACHOIS-moderate GDM
Primary Outcome		Any serious complication (n=524, 1% vs. 4%) Death Shoulder dystocia Fracture Nerve palsy NICU admission (n=321) Phototherapy

Crowther et al 2005

Treatment for moderate GDM

		ACHOIS-moderate GDM
Primary Outcome		Any serious complication (n=524, 1% vs. 4%) Death Shoulder dystocia Fracture Nerve palsy NICU admission (n=321) Phototherapy
Secondary Outcome		Birthweight, LGA (22%), Macrosomia (21%), Hypoglycemia, Neonatal Seizure, RDS

Crowther et al 2005

Treatment for moderate GDM

		ACHOIS-moderate GDM
Primary Outcome		NNT: 34
Secondary Outcome		C-section: 31 vs. 32%

Landon et al 2011; Crowther et al 2010

Treatment for mild GDM

	MFMU-mild GDM	ACHOIS-moderate GDM
Age	29.1 years	30.5 years
BMI (kg/m ²)	30.2 (3 rd trimester)	26.4 (1 st trimester)
GCT	7.5-11.1 mmol/l	7.8 mmol/l
	100 gram OGTT	75 gram OGTT
FPG	5.3 mmol/l	7.8 mmol/l
1 hour	10.0 mmol/l	Not done
2 hour	8.6 mmol/l	11.0 mmol/l
3 hour	7.8 mmol/l	Not done

Landon et al 2009; Crowther et al 2005

Treatment for mild GDM

	MFMU-mild GDM	ACHOIS-moderate GDM
1° Outcome	Composite (n=473, 32 % vs. 37%) Hypoglycemia, Hyperbilirubinemia Elevated C-peptide Stillbirth/death Birth Trauma	Any serious complication (n=524, 1% vs. 4%) Death Shoulder dystocia Fracture Nerve palsy NICU admission (n=321) Phototherapy
2° Outcome		Birthweight, LGA (22%), Macrosomia (21%), Hypoglycemia, Neonatal Seizure, RDS

Landon et al 2009; Crowther et al 2005

Treatment for mild GDM

	MFMU-mild GDM	ACHOIS-moderate GDM
1° Outcome	Composite (n=473, 32% vs. 37%) Hypoglycemia, Hyperbilirubinemia Elevated C-peptide Stillbirth/death Birth Trauma	Any serious complication (n=524, 1% vs. 4%) Death Shoulder dystocia Fracture Nerve palsy NICU admission (n=321) Phototherapy
2° Outcome	Birthweight, LGA (14.5%), Macrosomia (14.3%), Fat mass, Pre-term delivery, NICU admission, RDS, Hypoglycemia	Birthweight, LGA (22%), Macrosomia (21%), Hypoglycemia, Neonatal Seizure, RDS

Landon et al 2009; Crowther et al 2005

Treatment for mild GDM

	MFMU-mild GDM	ACHOIS-moderate GDM
Primary Outcome	No difference by randomization arm	NNT: 34
Secondary Outcome		C-section: 31 vs. 32%

Landon et al 2009; Crowther et al 2005

Treatment for mild GDM

	MFMU-mild GDM	ACHOIS-moderate GDM
Primary Outcome	No difference by randomization arm	NNT: 34
Secondary Outcome	NNT for macrosomia: 12 NNT for shoulder dystocia: 40 NNT for cesarean: 14 27% vs. 34% NNT for preeclampsia: 20	C-section: 31 vs. 32%

Landon et al 2009; Crowther et al 2005

Summary

- Treatment of **moderate GDM** leads to reduction in serious complications (1% vs. 4%)
- Treatment of **mild GDM** leads to reduction in macrosomia, macrosomia-related complications, pre-eclampsia, C-section
- → **Will treatment of even milder GDM (IADPSG) lead to benefit?**

Comparison of 2 interventions and HAPO

	ACHOIS- moderate GDM	MFMU- mild GDM	HAPO- Even milder GDM
Age (years)	30.5	29.1	31.0
BMI (kg/m ²)	26.4 (1 st trimester)	30.2 (3 rd trimester)	29.9 (3 rd trimester)

Comparison of 2 interventions and HAPO

	ACHOIS-moderate	MFMU-mild	HAPO-even milder
Age (years)	30.5	29.1	31.0
BMI (kg/m ²)	26.4 (1 st trimester)	30.2 (3 rd trimester)	29.9 (3 rd trimester)
	2 abnormal	2 abnormal	1 abnormal

Comparison of 2 interventions and HAPO

	ACHOIS-moderate	MFMU-mild	HAPO-even milder
Age (years)	30.5	29.1	31.0
BMI (kg/m ²)	26.4 (1 st trimester)	30.2 (3 rd trimester)	29.9 (3 rd trimester)
	2 abnormal	2 abnormal	1 abnormal
FPG mmol/l	4.8	4.8	4.9
1 hour mmol/l	Not done	10.7	9.6
2 hour mmol/l	8.6	9.7	7.6
3 hour mmol/l	Not done	7.6	Not done

Does treatment of women with only 1 abnormal value change outcomes?

	Treated (n=63)	Untreated (n=63)
Macrosomia (p<0.05)	6%	24%



Langer et al. Am J Obstet Gynecol, 1989.

Does treatment of women with only 1 abnormal value change outcomes?

	Treated (n=63)	Untreated (n=63)
Macrosomia (p<0.05)	6%	24%
Hypertensive disorder (NS)	2%	3%

Langer et al. Am J Obstet Gynecol, 1989.

Does treatment of women with only 1 abnormal value change outcomes?

	Treated (n=63)	Untreated (n=63)
Macrosomia (p<0.05)	6%	24%
Hypertensive disorder (NS)	2%	3%
Primary Cesarean section (NS)	6%	7%

Langer et al. Am J Obstet Gynecol, 1989.

Does treatment of macrosomia benefit children?

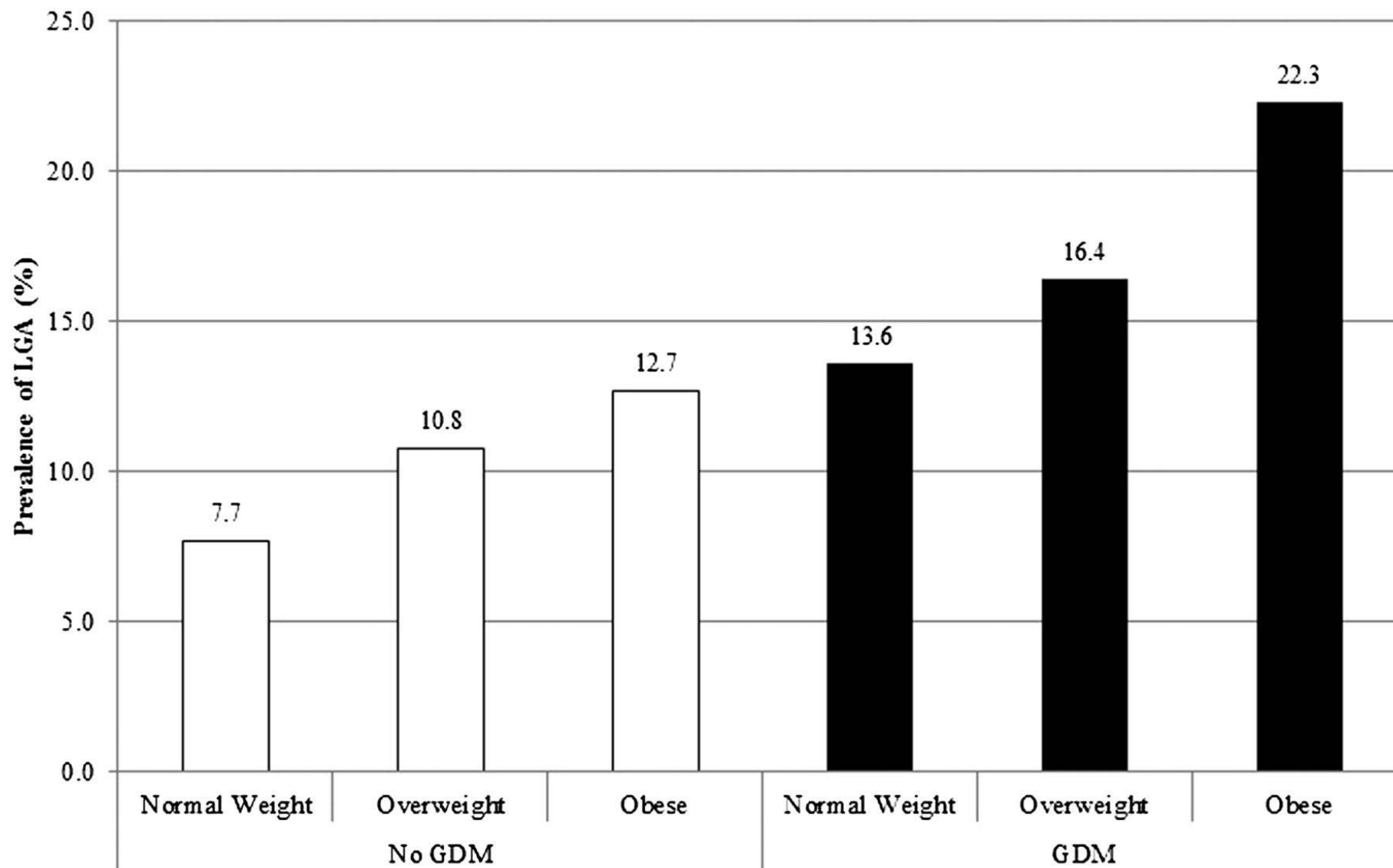
- ACHOIS: Body weight at 4 years similar by randomization arm
- HAPO: Body weight at 2 years similar by

Studies differ as to how much macrosomia is associated with future child body weight

response to glucose challenge

- Pima: Body weight at 5-24 years higher by response to glucose challenge

Maternal BMI and GDM both contribute to increased risk of macrosomia



Black M H et al. Dia Care 2013;36:56-62

In heavier populations, most macrosomia due to maternal BMI

- Among women without GDM, 21.6% of LGA infants were attributable to maternal overweight and obesity
- Combination of being overweight or obese and having GDM accounted for 23.3% of LGA infants

-->Treatment of GDM may have less effect upon macrosomia than treatment of maternal body weight in heavy populations (such treatment does not exist yet)

Return on investment: what does intervention do?

We can change outcomes for more severe hyperglycemia

Unclear if we can significantly change outcomes for mild hyperglycemia, except for macrosomia

Is it worth it to only reduce macrosomia, and not cesareans or other complications?

Are these reductions seen at the level of the single hospital?

Summary

- ACOG (current) vs. IADPSG (new)
 - **→ IADPSG less cumbersome**
- Objections to criteria changes: the perspective of the single hospital
 - Reproducibility
 - **Only higher C-sections were reproduced in another study**
 - Resource allocation
 - **New criteria would require more resources**
 - **New criteria cost-effective ONLY if Cesareans reduced**
 - Return on investment
 - **Treating moderate GDM beneficial**
 - **Treating mild GDM beneficial**
 - **Impact on Cesareans, in particular, is unclear**
 - **Unclear if treating even milder GDM affects outcomes other than macrosomia in single center-based studies**
 - **Center-based benefit is important to many**

Which way forward?

- Higher cutpoints?
 - Corresponding to odds ratio of 2.0
- Retain 1 hour 50 gram test?
- 2 abnormal values instead of 1?
- → Acceptance easier if cutpoints show benefit at the **center level** and for outcomes other than **cesarean and macrosomia**.

ACOG

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