Should induction of labor be routinely offered at 39 weeks?

William Grobman, MD,MBA
Arthur Hale Curtis Professor
Department of Obstetrics and Gynecology
Feinberg School of Medicine
Northwestern University

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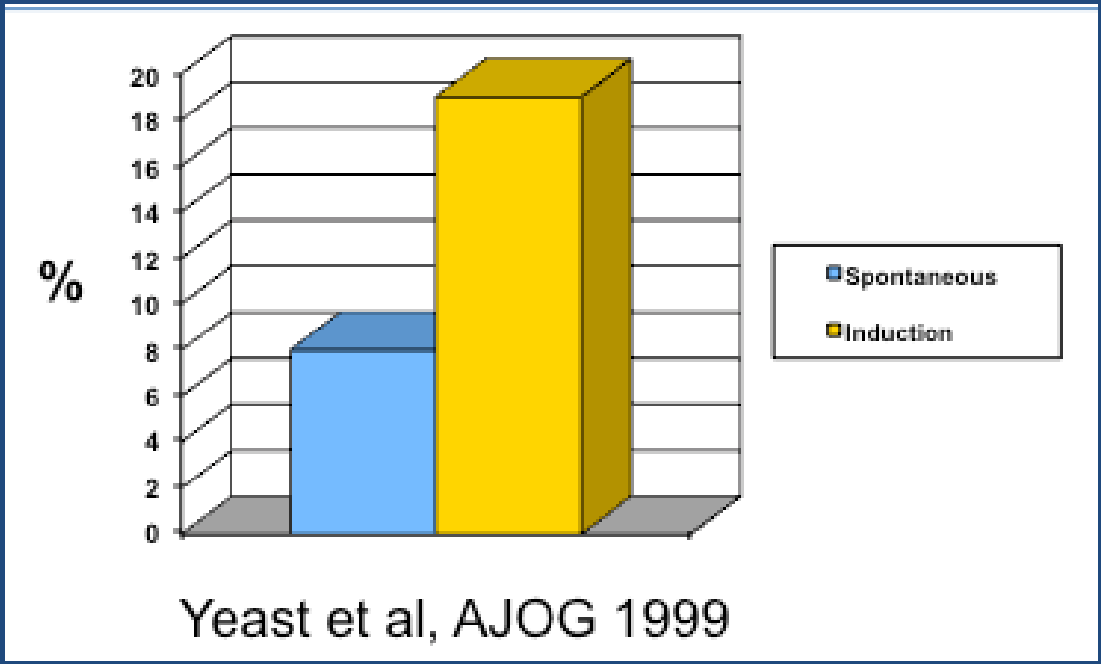
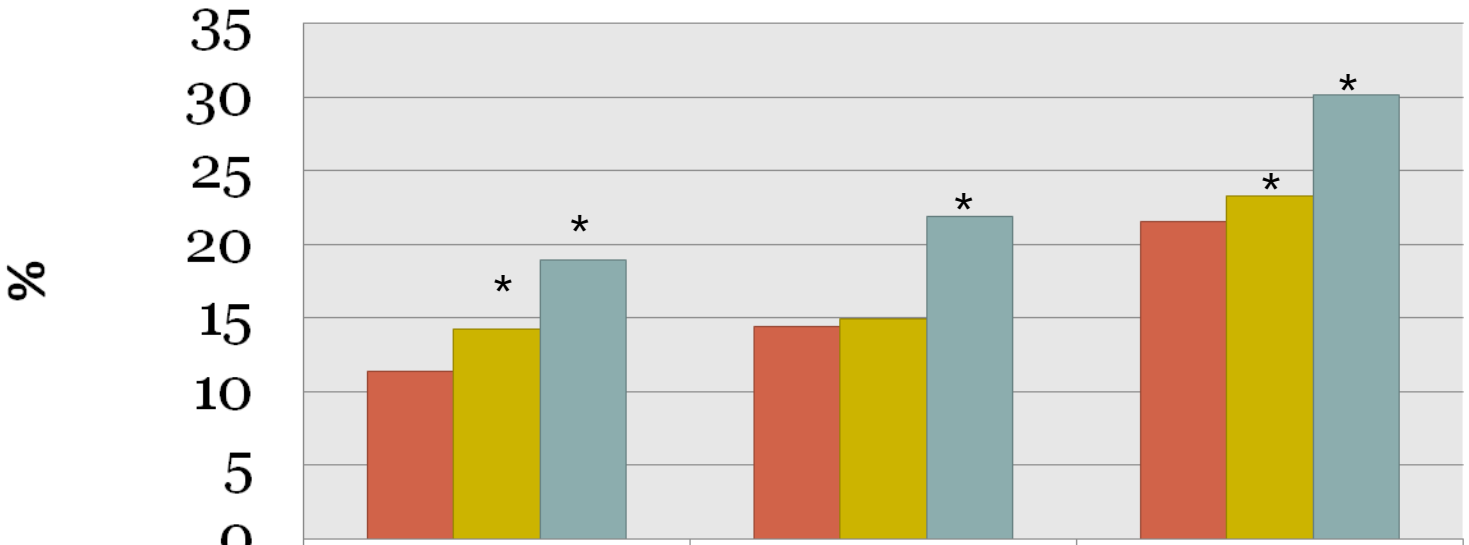
Induction and cesarean delivery: Long-standing belief

- Retrospective cohort studies
  - Induction of labor is associated with an approximately doubled risk of cesarean delivery in nulliparous women



Increasing maternal and perinatal risks after 39 weeks

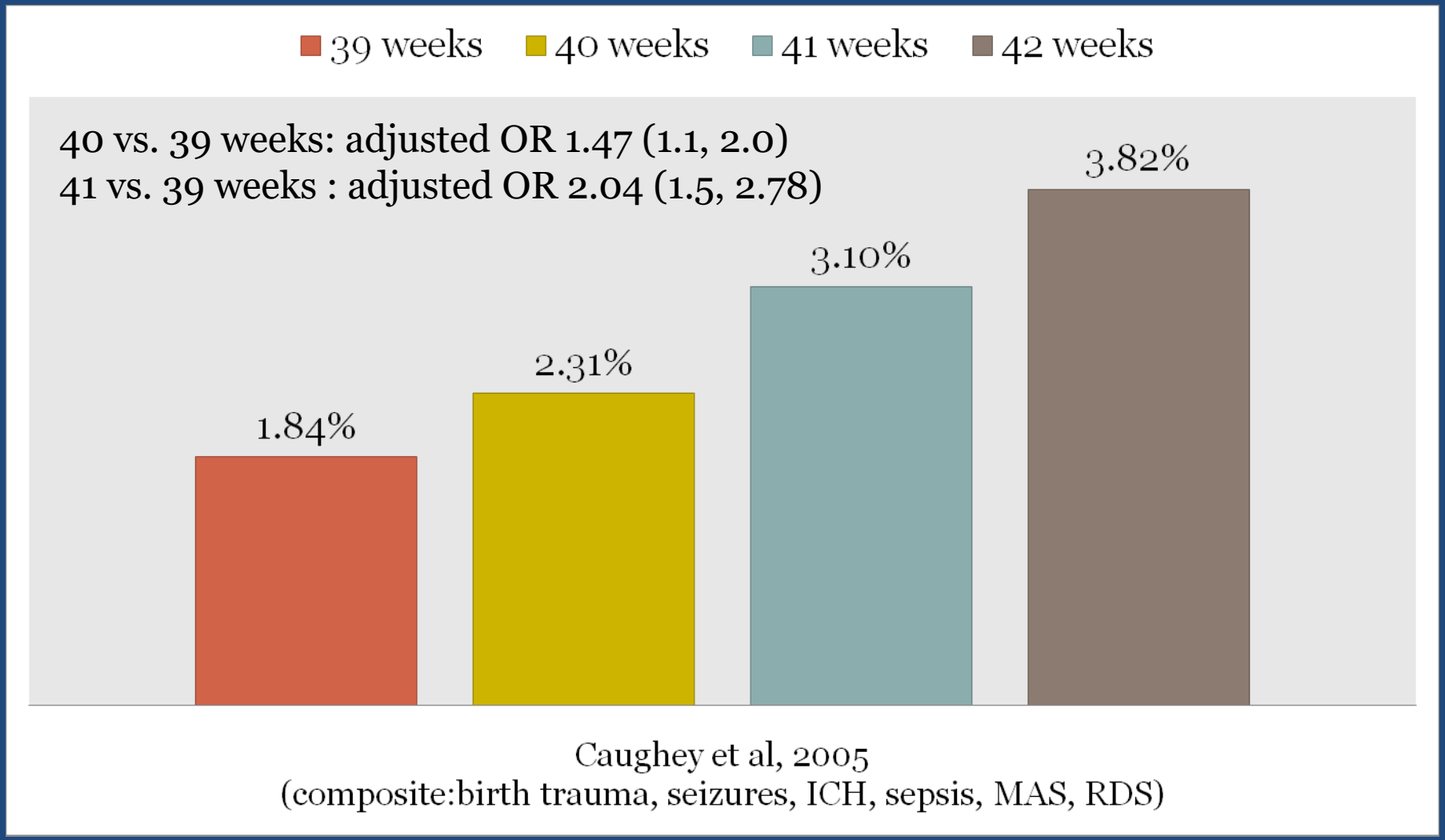
Cesarean Delivery by Gestational Age



	Caughey 2006	Caughey 2007	Cheng 2008
39 weeks	11.4	14.4	21.5
40 weeks	14.2	14.9	23.3
41 weeks	18.9	21.9	30.1

*p<.05

Severe Neonatal Complications



Caughey et al, 2005
(composite:birth trauma, seizures, ICH, sepsis, MAS, RDS)

A RANDOMIZED TRIAL OF INDUCTION OF LABOR VERSUS EXPECTANT MANAGEMENT AMONG LOW-RISK NULLIPAROUS WOMEN (ARRIVE)

NIH Eunice Kennedy Shriver National Institute of Child Health and Human Development

DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

unded by the National Institutes of Health

Methods

- Randomized, controlled, parallel group, unmasked trial
- Inclusion criteria
  - Nulliparous women
  - Singleton gestations
  - Reliably dated
  - No contraindication to vaginal delivery
  - Low risk

Methods

- Randomized between $38^{0/7}$ and $38^{6/7}$ wks
  - IOL
    - 39 weeks 0 days – 39 weeks 4 days
  - EM
    - Forego elective delivery < 40 weeks 5 days
    - Be delivered ≤ 42 weeks 2 days

Results: Patient characteristics

	IOL N = 3062	EM N = 3044
Maternal age – yr.	24 (21-28)	23 (20-28)
Race and ethnicity		
Non-Hispanic white	1329 (43.4)	1359 (44.7)
Non-Hispanic black	707 (23.1)	699 (23.0)
Asian	87 (2.8)	106 (3.5)
Hispanic	866 (28.3)	808 (26.5)
Other or unknown	73 (2.4)	72 (2.4)
Private insurance for prenatal care	1404 (45.9)	1335 (43.9)
Previous pregnancy loss	698 (22.8)	778 (25.6)
BMI ≥30 kg/m^2 at randomization	1633 (53.6)	1575 (52.0)
Modified Bishop score at randomization <5	1919 (62.7)	1954 (64.2)

Data are presented as median (interquartile range) or N (%)

Results: Primary perinatal composite

IOL N = 3059	EM N = 3037	RR	95% CI	P*
4.3%	5.4%	0.80	0.639 - 0.999	0.049

* P<0.046 was considered to indicate statistical significance

Results: Perinatal outcomes

	IOL %	EM %	RR	95% CI
Respiratory support	3.0	4.2	0.71	0.55 - 0.93
Perinatal death	0.1	0.1	0.66	0.12 - 3.33
Apgar ≤ 3 at 5 minutes	0.4	0.6	0.66	0.32 - 1.37
HIE	0.4	0.6	0.68	0.34 – 1.37
Seizure	0.4	0.1	2.73	0.91 – 8.12
Infection	0.3	0.4	0.74	0.31 - 1.76
MAS	0.6	0.9	0.65	0.35 - 1.19
Birth trauma	0.5	0.6	0.77	0.38 - 1.55
ICH or subgaleal hemorrhage	0.3	0.2	1.28	0.48 - 3.42
Hypotension	0.1	0.2	0.40	0.06 – 1.79

Results: Cesarean delivery

IOL N = 3059	EM N = 3037	RR	95% CI	P
18.6%	22.2%	0.84	0.76 - 0.93	< .001

Results: Maternal outcomes

	IOL %	EM %	RR	95% CI
Hypertensive disorder of pregnancy	9.1	14.1	0.64	0.56 - 0.74
Chorioamnionitis	13.3	14.1	0.94	0.83 - 1.07
Third or fourth degree perineal laceration	3.4	2.9	1.15	0.87 - 1.52
Postpartum hemorrhage	4.6	4.5	1.03	0.82 - 1.29
Postpartum infection	1.6	2.1	0.76	0.53 - 1.10
ICU admission	0.1	0.3	0.50	0.13 – 1.55

Results: Maternal outcomes

	IOL	EM	P
Labor Agentry Score after delivery	168 (148-183)	164 (143-181)	<.001
Labor Agentry Score 6 wk after delivery	176 (157-189)	174 (154-188)	.01
Worst labor pain	8 (7-10)	9 (8-10)	<.001
Overall labor pain	7 (5-8)	7 (5-9)	<.001

All data are presented as medians (interquartile range)

Concerns

- This population is not identical to others
  - There are particular subgroups of individuals for whom this won't hold
- The results won't be replicable during routine care
- This is so much more resource intensive
- The long-term outcomes are not known
- This is so different than everything that has come before

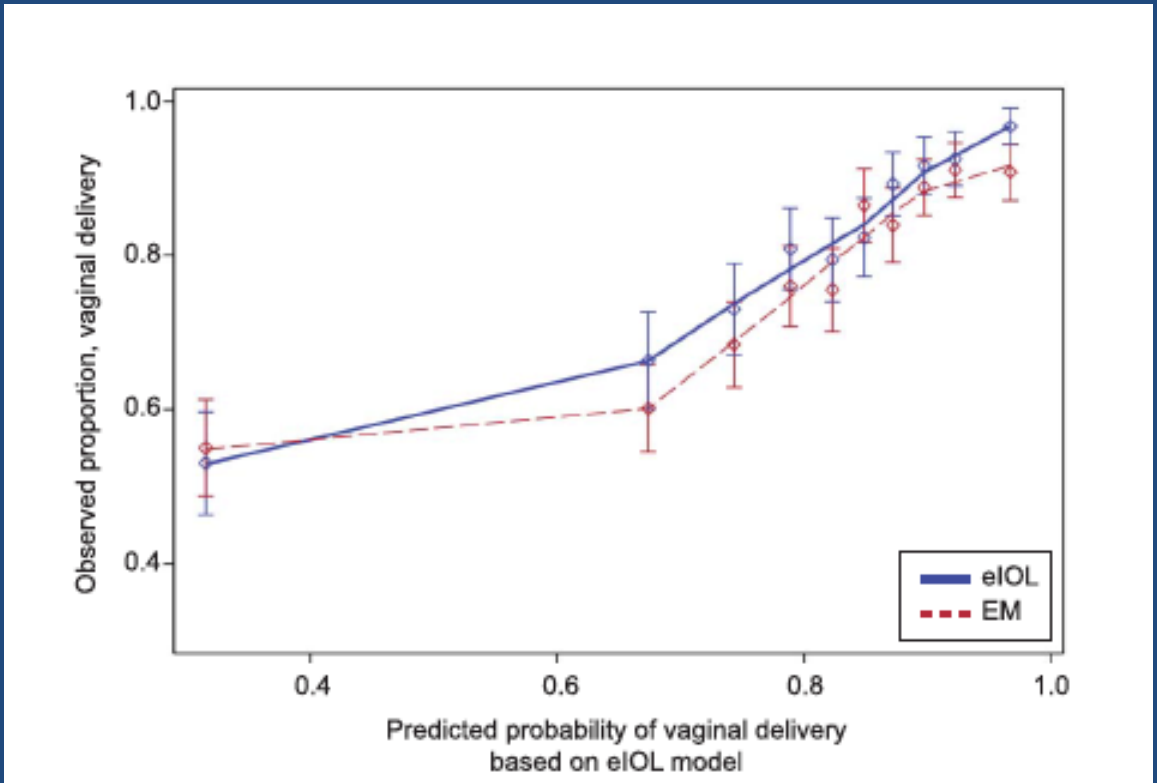
"In generalizing the results of a randomized trial, the assumption is not that the patient population studied is representative of all patients but rather that the proportional effects of the treatment studied on each specific health outcome should be similar in different circumstances, unless there is good reason to expect otherwise."

Collins et al, NEJM 2020

This population is not identical to others

Perinatal composite Cesarean delivery
Self-reported race/ethnicity
Modified Bishop score < 5
Body mass index ≥ 30 kg/m^2
Maternal age > 35 years

There are subgroups of individuals for whom the result won't hold



Silver et al, Obstet Gynecol 2020

There are subgroups of individuals for whom the result won't hold

- No ability to reliably predict adverse maternal (PPH, severe perineal laceration) or perinatal composite outcome based on:
  - Maternal age
  - SES factors
  - Substance use
  - Prior pregnancy loss < 20 weeks
  - ART
  - Modified Bishop score

El-Sayed et al, Obstet Gynecol 2020

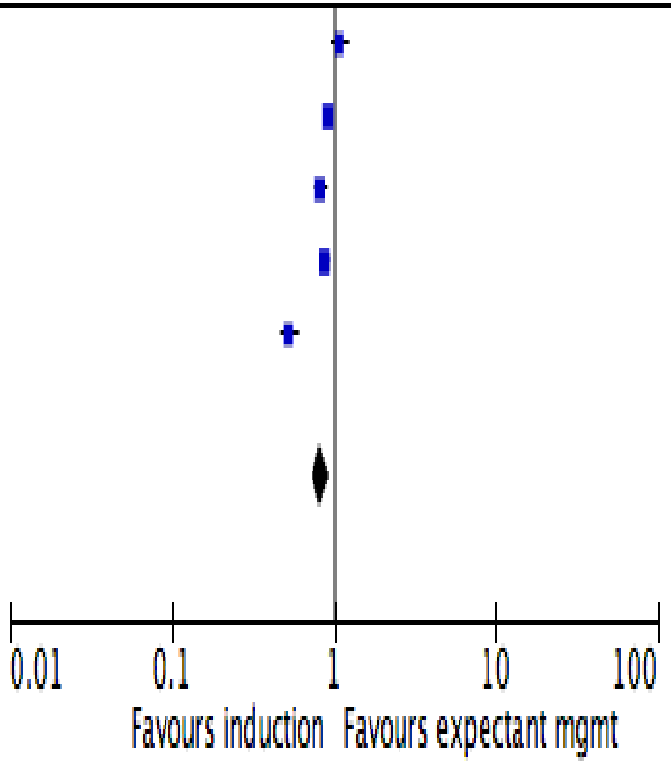
The results won’t be replicable during routine care

Cesarean Delivery

Study or Subgroup	Induction Events	Induction Total	Expectant management Events	Expectant management Total	Weight	Risk Ratio M-H, Random, 95% CI
Bailit	210	815	5532	23212	18.2%	1.08 [0.96, 1.22]
Cheng	11205	42769	79116	278578	22.1%	0.92 [0.91, 0.94]
Darney	498	2186	20530	74115	20.3%	0.82 [0.76, 0.89]
Gibbs	1416	3942	16673	40667	21.6%	0.88 [0.84, 0.91]
Gibson	220	1557	6619	24605	17.9%	0.53 [0.46, 0.59]
Total (95% CI)		**51269**		**441177**	**100.0%**	**0.83 [0.74, 0.93]**
Total events	13549		128470			

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 95.41$, df = 4 ($P < 0.00001$); $I^2 = 96\%$

Test for overall effect: Z = 3.08 (P = 0.002)



Grobman and Caughey, AJOG 2019

Neonatal respiratory compromise

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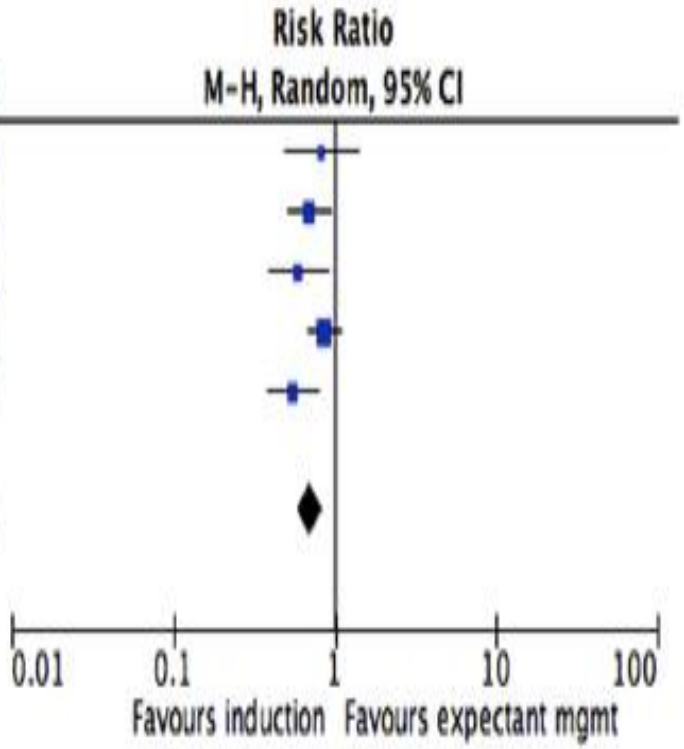
Study or Subgroup	Induction Events	Total	Expectant management Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Baillit	14	815	482	23212	10.2%	0.83 [0.49, 1.40]
Cheng	47	18890	363	100892	23.8%	0.69 [0.51, 0.94]
Darney	22	2186	1260	74115	14.8%	0.59 [0.39, 0.90]
Gibbs	74	3942	888	40667	32.4%	0.86 [0.68, 1.09]
Gibson	30	1553	863	24508	18.7%	0.55 [0.38, 0.79]
Total (95% CI)		**27386**		**263394**	**100.0%**	**0.71 [0.59, 0.85]**
Total events	187		3856			

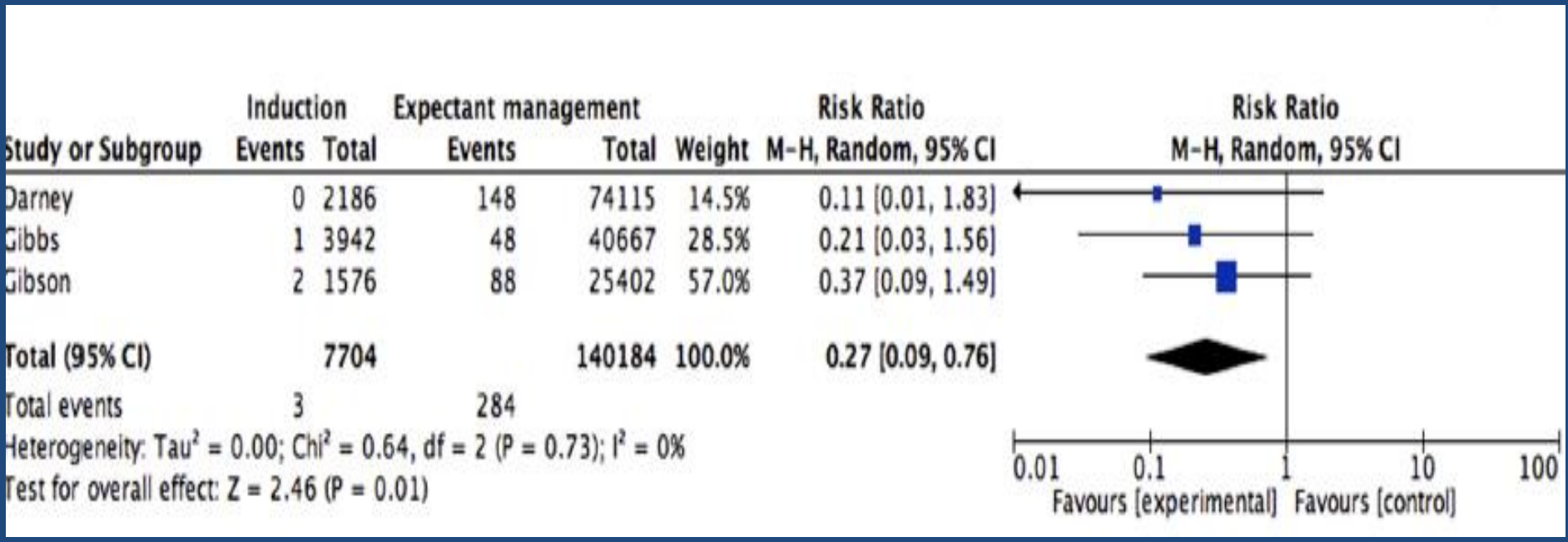
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 5.59$, df = 4 (P = 0.23); $I^2 = 28\%$

Test for overall effect: Z = 3.73 (P = 0.0002)



Grobman and Caughey, AJOG 2019

Perinatal mortality

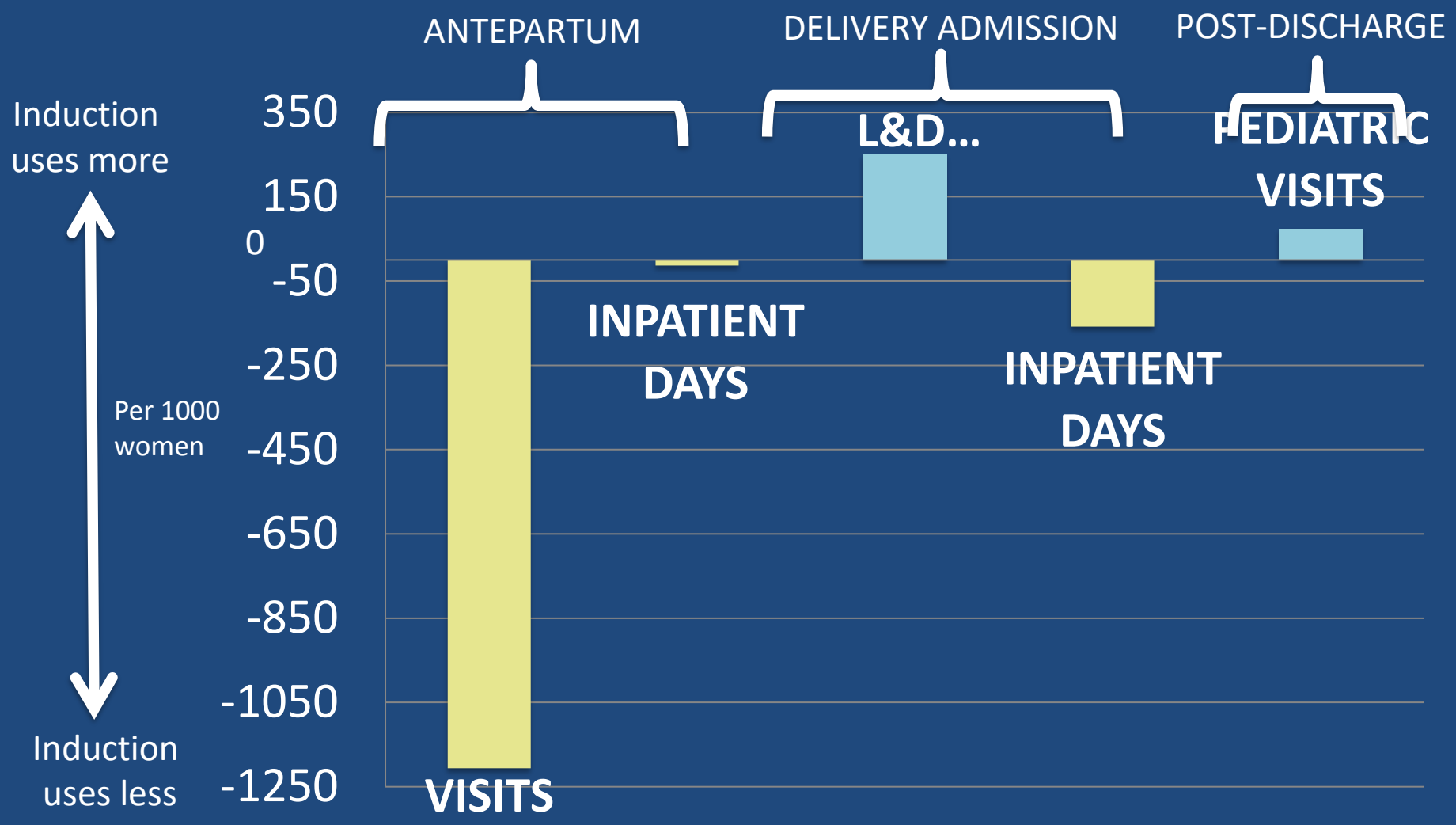


Grobman and Caughey, AJOG 2019

This is so much more resource intensive

There will be longer time on L&D

	IOL	EM	P
L&D duration (median IQR)	20 (13 – 28)	14 (9 - 20)	<.001



Grobman et al, AJOG 2020

Resource utilization

- Vijgen, BJOG 2010 (Hypitat)
  - Induction 11% cheaper (€831)
- Walker et al, BJOG 2017
  - Induction £236 cheaper
- Einerson et al, Obstet Gynecol 2020
  - No difference in cost between EIOL and EM in ARRIVE participants (mean difference +4.7%, 95% CI 22.1% to +12.0%, P=0.18)

Long-term outcomes are not known

- Reflect on regular practice
- Cohort studies with long-term follow-up
  - Werner et al. JAMA Network Open 2020
    - Math proficiency aRR 1.07 (95% CI, 0.97-1.18)
    - Reading proficiency aRR 0.98 (95% CI, 0.88-1.08)
  - Yisma et al. Ultrasound Obstet Gynecol 2020
    - No differences in reading, writing, spelling, grammar, and numeracy at 8 years of age

This is so different than everything that has come before

- Hannah et al
- Hypitat
- Boulvain et al
- Walker et al
- Wennerholm et al

Implementation

- Proper counseling in the outpatient setting
  - Shared decision making
  - Equity
- L&D organization
  - Ripening
  - Hours for induction admission

QUESTIONS

w-grobman@northwestern.edu