Cost-effective Treatment in the USA

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Cost-effective Infertility Treatments in the United States - Limitations

- IVF registry – has limitations
- No IUI registry
- Center – specific reports

Cost-effective Infertility Treatments in the United States

History –

In 1994, estimated cost per delivery for IVF ranged from $44,000 - $211,940

IVF pregnancy rate – 12%

Charges – $8,000/cycle

Neumann et al
NEJM 1994;331:239-43

Cost-effective Infertility Treatment – University of Iowa

- All charges and outcomes from infertility care
- Treatment charges until pregnancy confirmed including early complications
- Did not factor in multiple gestations

Fertil Steril 1995;64:647-50
Fertil Steril 1997;67:830-6
Fertil Steril 1998;70:995-1005

Cost-Effectiveness of Common Infertility Treatments

Procedure	No. of couples	No. of procedures	No. (%) of deliveries		Multiple birth rate (%)	Cost per delivery ($)
IUI	54	103	6	(5.8)	0	8,674
CC-IUI	91	188	12	(6.3)	8.3	7,808
HMG-IUI	52	80	14	(17.5)	21.0	10,282
ART	136	155	43	(27.7)	30.0	37,028

Fertil Steril 1997;67:830-6

Conclusions – UIHC Studies

- In general, IUI cycles more cost-effective than IVF

  Factors leading to worsened cost-effectiveness ratios
  - Advanced maternal age (all treatments)
  - Low sperm counts (IUI, not IVF)

Factors affecting IUI cost-effectiveness; a retrospective cohort study

Objectives: Identify factors affecting prognosis for infertility treatments

Study cost-effectiveness based on these factors

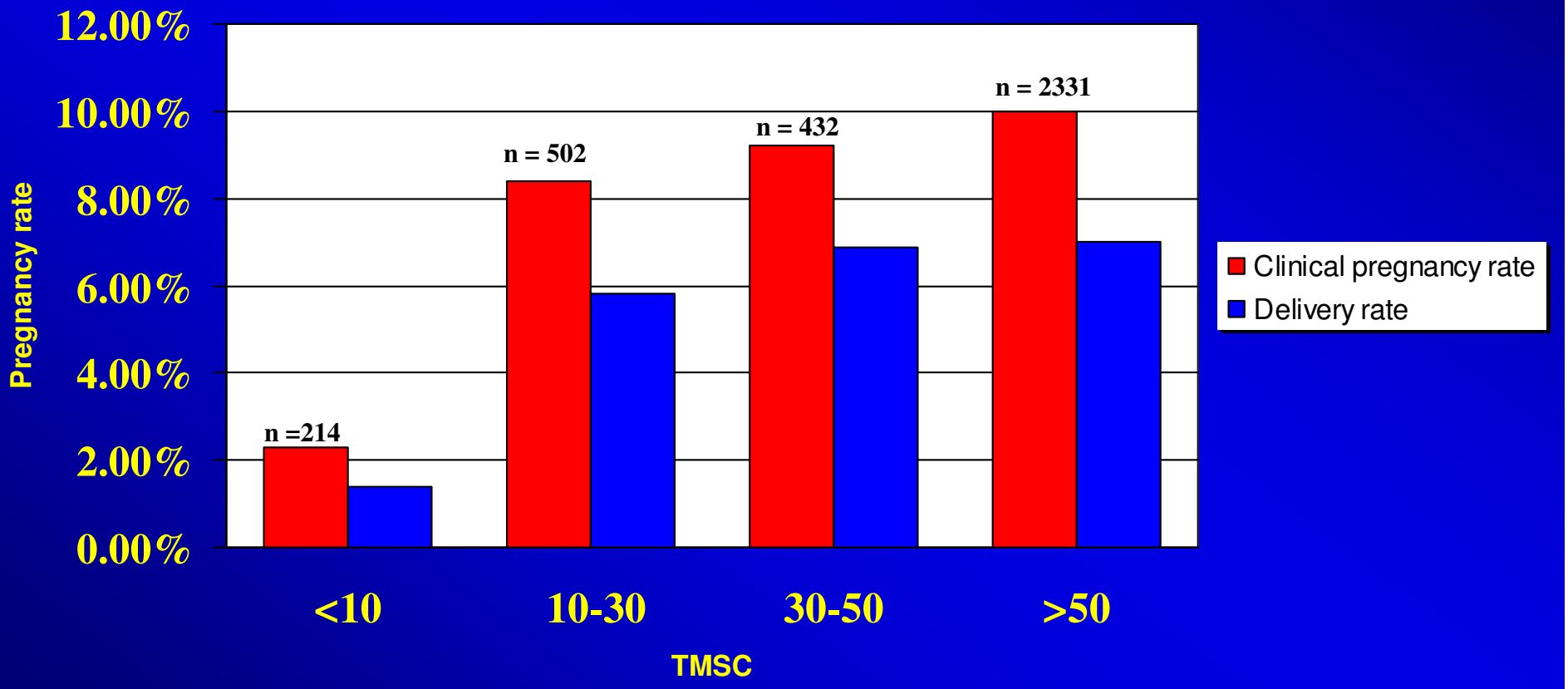
Fertil Steril 2001;75:661-8

Male Factor Infertility and IUI

- Meta analysis of trials demonstrated a 50% reduction in pregnancy rate with male factor infertility.
- How to define male factor infertility?
  - Total motile sperm count (TMSC)
    - Ejaculate (volume x concentration x motility)
    - Inseminate
- Best predictor – average TMSC in ejaculate

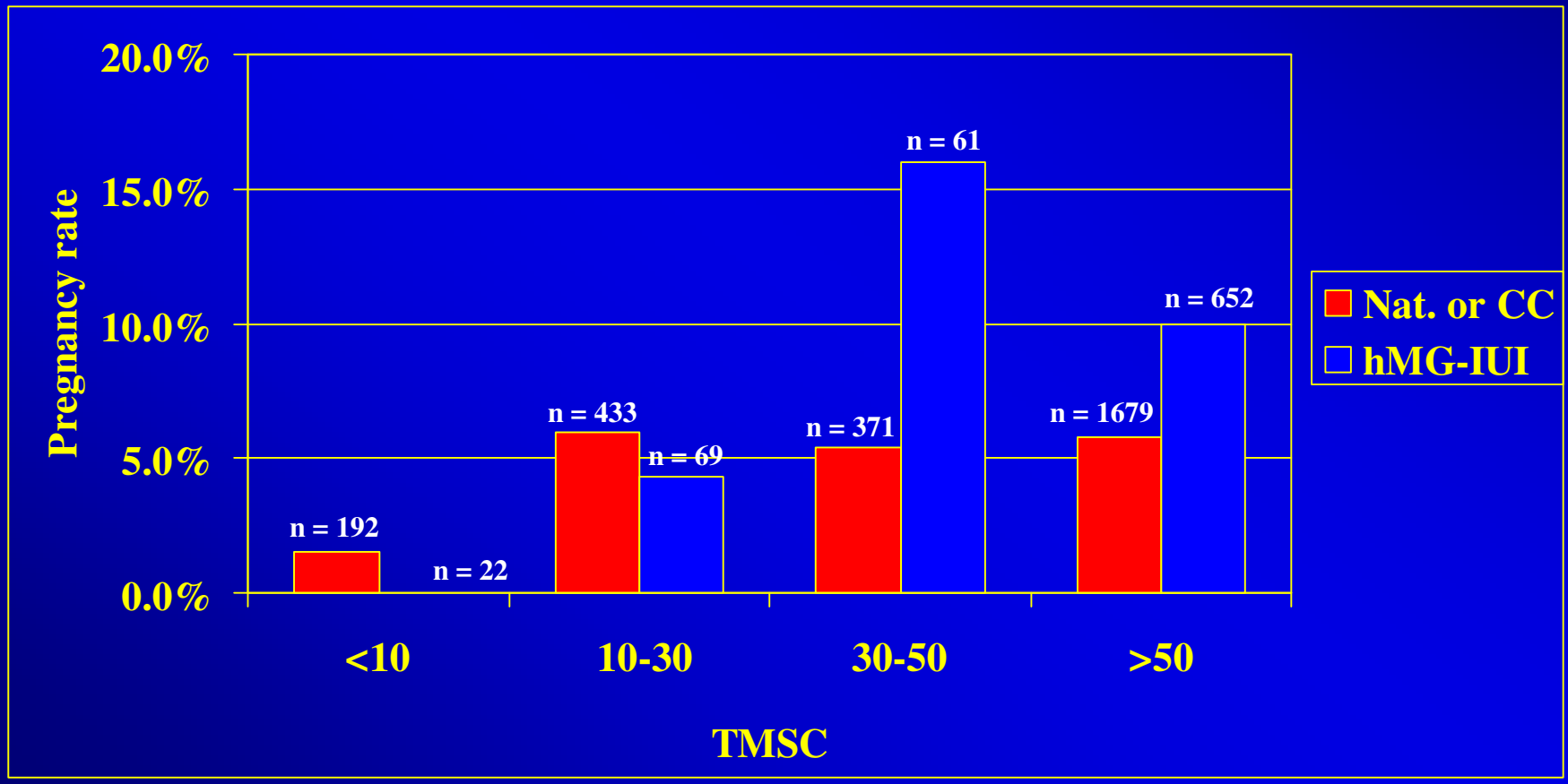
Fertil Steril 2001;75:661-8

IUI Pregnancy Rate by Sperm Count



Fertil Steril 2001 75:661-8

Delivery Rate After IUI by TMSC



Fertil Steril 2001;75:661-8

Factors Predicting Pregnancy after IUI

Factor (increment of comparison)	Odds ratio
Female age (1 year)	.95 (.91-.99)
Average total motile sperm count	
≥ 10 million	1.0 (Referent)
< 10 million	.13 (0.02-0.9)
Treatment type	
Natural IUI	1.0 (Referent)
CC – IUI	1.7 (1.01-2.9)
hMG – IUI	2.2 (1.2-3.9)
Nulligravid	.7 (0.4-0.99)

Fertil Steril 2001;75:661-8

Sperm Counts and Cost-Effectiveness of Infertility Treatments

	Average Total Motile Sperm Count			
	≤ 10 million		**> 10 million**	
Procedure	Delivery/Cycle	Cost/Delivery	Delivery/Cycle	Cost/Delivery
Natural IUI	.8%	$57,997	3.7%	$13,827
CC-IUI	2.5%	$22,248	7.1%	$ 7,951
hMG-IUI	-	-	10%	$19,092
All IUI	.4%	$48,129	6.8%	$12,744
IVF cycles	32.3%	$32,869	35.8%	$28,639

Fertil Steril 2001;75:661-8

Cut-off Values Total Motile Sperm Count Associated with Poor IUI Outcome

	TMC	
Reference	Ejaculate	Inseminate
Dickey et al [1]	5 million	
Van Voorhis et al [2]	10 million	
Horvath et al [3]		1 million
Campana et al [4]		1 million

[1] F&S 1999;71:864-9
[2] F&S 2001;75:661-8
[3] F&S 1989;52:288-94
[4] Hum Reprod 1996;11:732-6

Meta-Analysis of Total Motile Sperm Count

- 16 studies of TMC at insemination
- Cut-off value ranged from .8-5 million motile sperm (post wash)
- Poor sensitivity
- High specificity (predicts failure to conceive) ~ 100%
- Exact cut-off chosen based on lab and sperm prep technique

Fertil Steril 2004;82:612-62-

"The treatment of infertility usually does not make the difference between conceiving and not conceiving - the difference lies in conceiving sooner rather than later."

TeVelde and Cohlen.
NEJM 1999;340:224-225

Fast Track and Standard Treatment Trial

TRIAL

Fast Track	Standard Treatment
CC (100 mg) + IUI X 3 ↓ IVF – up to 6 cycles	CC (100 mg) + IUI X 3 ↓ FSH (150 IU) + IUI X 3 ↓ IVF up to 6 cycles

Reindollar et al.
Fertil & Steril (in press)

Fastt Trial

Entrance criteria

- Women's age 21-39
- Unexplained infertility
- Ovarian reserve normal (FSH + E_2)
- Sperm concentration - ≥15 million motile sperm

Fastt Trial

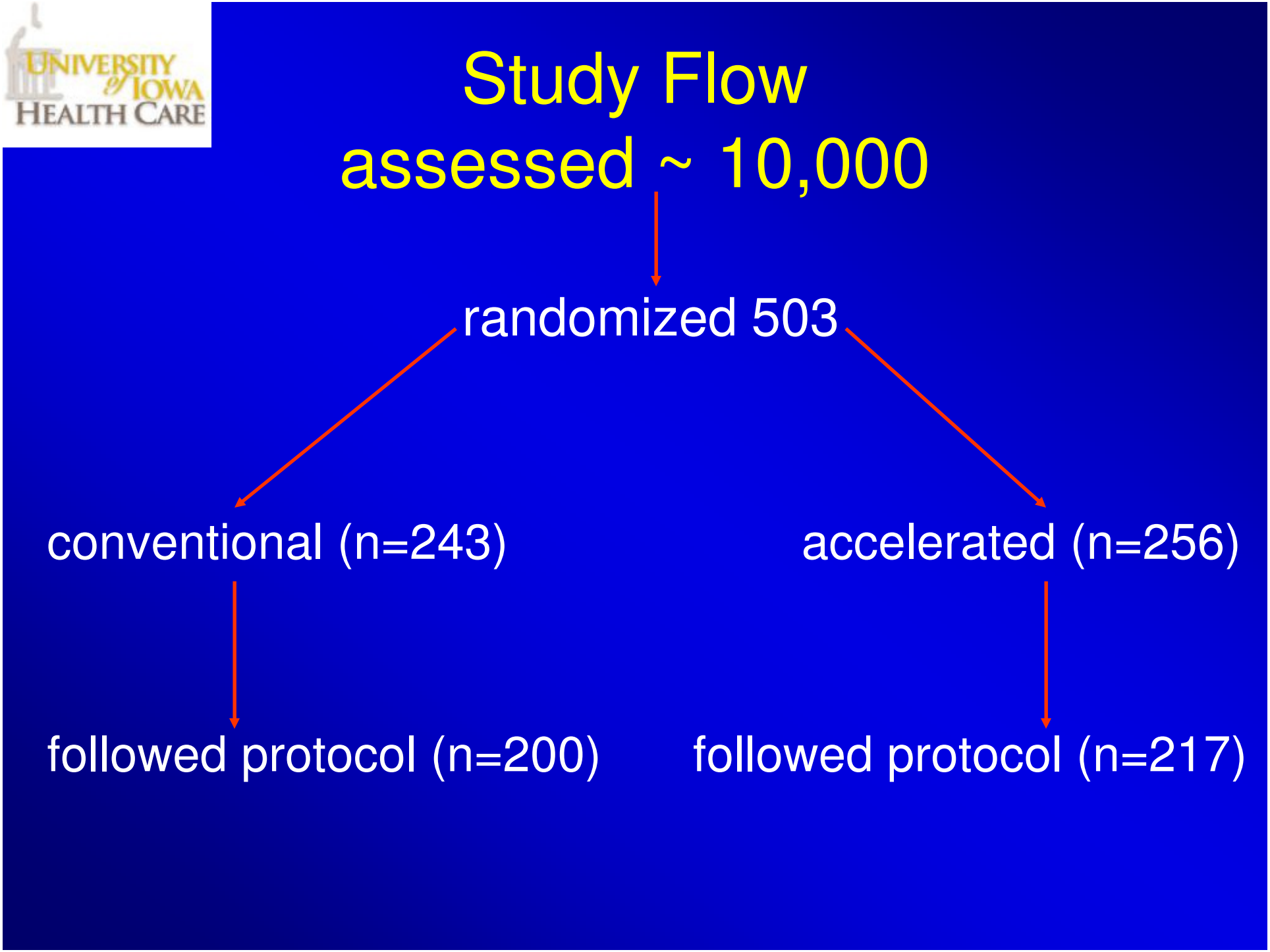
Outcomes

- Length of time from randomization to date of pregnancy
- Cost effectiveness – sum of insurance charges divided by number of couples delivering at least 1 child. Charges from randomization through hospital discharge of both mother and baby or until 1 year after protocol without pregnancy

+

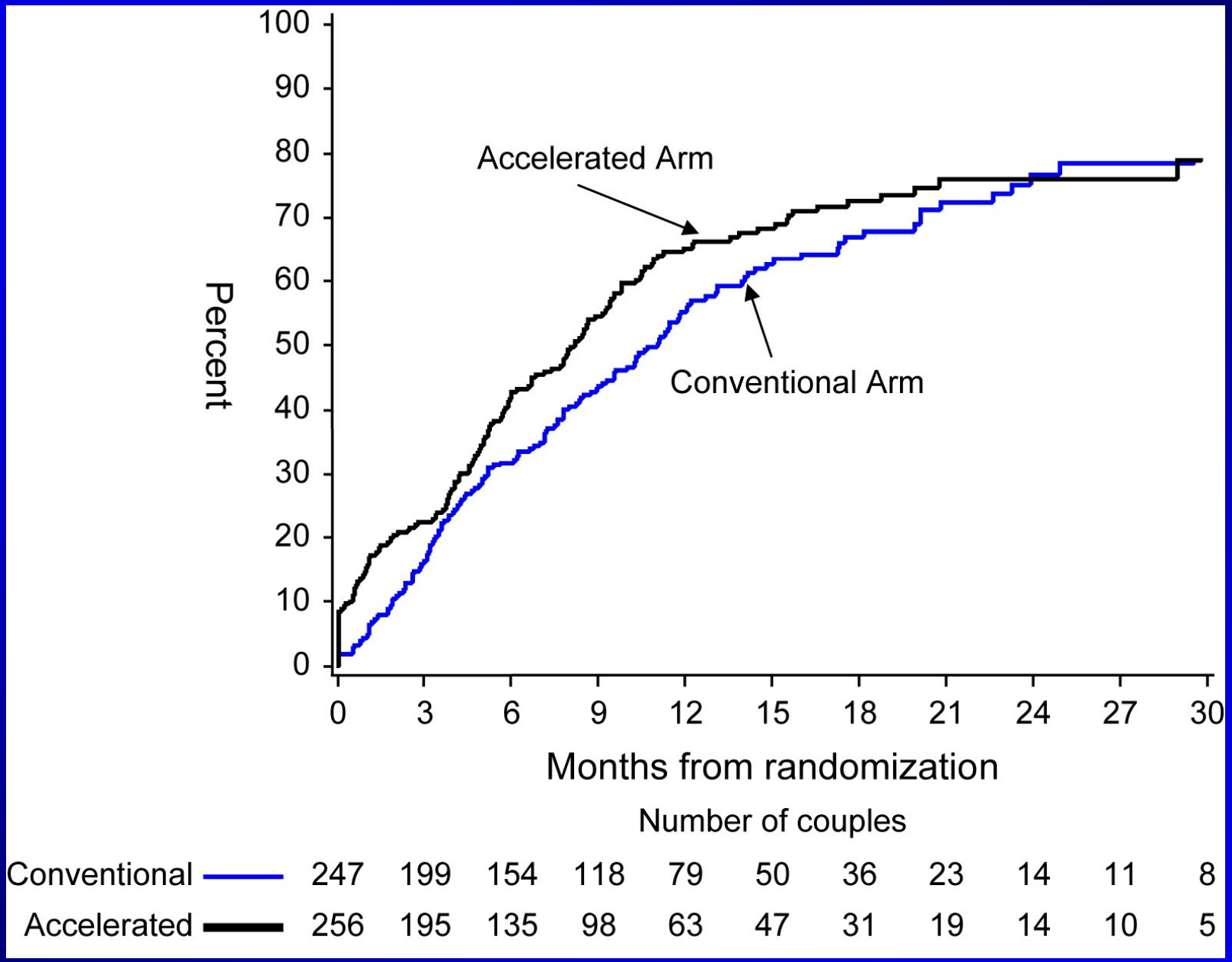
estimated indirect costs

Reindollar et al.
Fertil Steril (in press)


Study Flow
assessed ~ 10,000
randomized 503
conventional (n=243)
accelerated (n=256)
followed protocol (n=200)
followed protocol (n=217)

Outcomes

	Conventional	Accelerated
N	247	256
Delivered a child	150 (61%)	171 (67%)
Time to pregnancy	11 months	8 months*
Multiple birth	21%	23%
Charges per delivery	$71,399 €47,600	$61,553 €41,000



Reindollar et al. Fertil Steril (In press)

Effectiveness and Charges

Delivery rates	Charges
CC/IUI = 7.6%	$500 (€333)
FSH / IUI = 9.8%	$2,500 (€1,667)
IVF = 30.7%	$15,000 (€10,000)

14% of pregnancies were treatment independent.

Conclusions

1. In this paradigm, use of FSH/IUI was of no added value
2. Couples in accelerated arm were pregnant faster, with fewer treatment cycles and with less cost (as long as IVF cycles cost less than $17,749 - €11,800)

Prematurity and Multiple Gestations

- In the United States – 36% increase in prematurity in the last 25 years
  - One major cause – multiple gestations from infertility treatments
  - Cost estimate - $1 billion/year to pay for pre-term IVF deliveries

New York Times

University of Iowa
Cost-effective Infertility Treatments

	Delivery rate		Charge/cycle		Multiple rate	
Treatment	1992	2007	1992	2007	1992	2007
IUI	5.8%	7.8%	$505	$497	0	0
CC-IUI	6.3%	11%	$530	$515	8.3%	12.8%
hMG-IUI	17.5%	14.8%	$1800	$2300	21%	20%
IVF	27.7%	43%	$10,275	$14,295	30%	13%

Observations on Cost-effective Infertility Care

- Pregnancy rates with IVF improving, not for IUI
- Multiple birth is key driver from societal perspective
  - IVF has clear solution- SET
  - IUI not as clear (? improved stimulation protocols)
- Many couples value time more than cost
- Trend towards faster IVF in United States

Are mild stimulations the answer?

hMG Injection Protocol

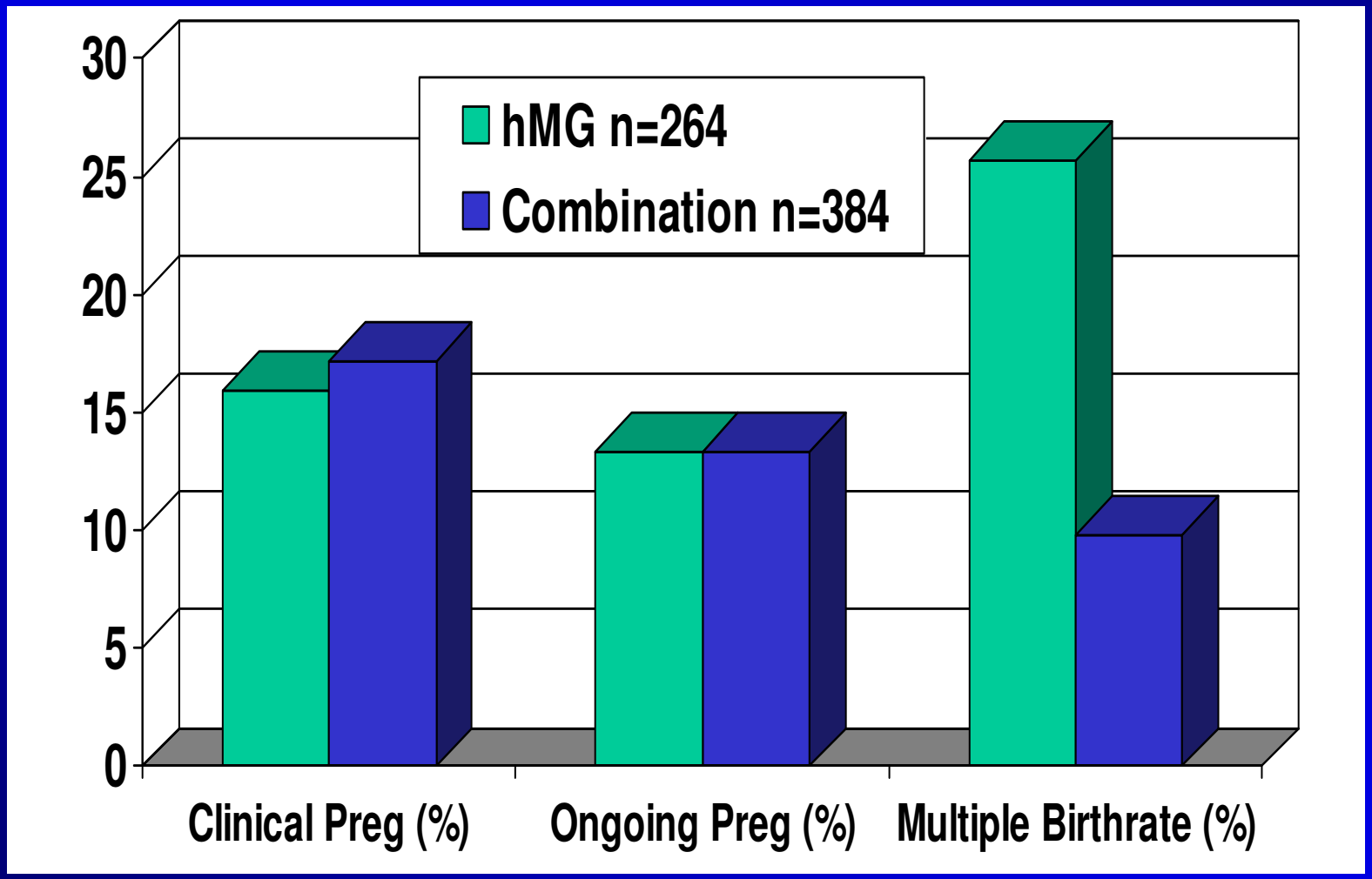
hMG Injections			X	X	X	X	X	X	X	X					
											hCG ↓		IUI ↓		
	Menses														
Cycle Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15

Combination Protocol

hMG Injections							X	X	X	X	X				
Oral Medications			X	X	X	X	X								
												hCG ↓		IUI ↓	
	Menses														
Cycle Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15

ASRM 2004

Outcomes of different ovulation induction protocols before IUI – all treatment cycles



Conclusions

Combination protocols more cost-effective than hMG protocols

- Fewer injections
- Less hMG used
- Similar delivery rates
- ? lower multiple rates

J Reprod Med 2005;50:963-50

Desire for Multiple Births

Survey of 464 infertile women:

- 20% of infertile couples desired multiple gestations over singleton (94% twins, 2% triplets, 4% quadruplets)
- 30% of IVF couples desired multiple gestations over a singleton

Ryan Fertil Steril 2004;81:500-4

Time is a Critical Factor

- 25% consider treatment a failure if not pregnant in 6 months
- 63% consider treatment a failure if not pregnancy in 1 year
- 16% had no time limit as long as pregnancy achieved

Prognostic Variables

- Female age, gravidity / parity
- Diagnosis

Treatment Variables

- Type of stimulation

Outcome (1st cycle only)

- Clinical pregnancy rate
- Delivery rates
- Cost-effectiveness- Charges as a surrogate for costs

Fertil Steril 2001;75:661-8

	IUI	IVF
Patients	1039	424
Cycles	3479	551
Age	31.8 ± 4.6	32.8 ± 4.1
Mean total motile sperm (millions)	123 ± 134	128 ± 123
Female infertility diagnosis		
Ovulatory	28%	13%
Tubal	12%	46%
Endometriosis	12%	8%
No female diagnosis	47%	32%