

FERTILITY THERAPY IN WOMEN WITH CARDIAC DISEASE

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OBJECTIVES

1. Infertility and assisted reproductive technologies
2. Adverse outcomes in pregnancies conceived with fertility therapy
3. Outcomes in women with heart disease

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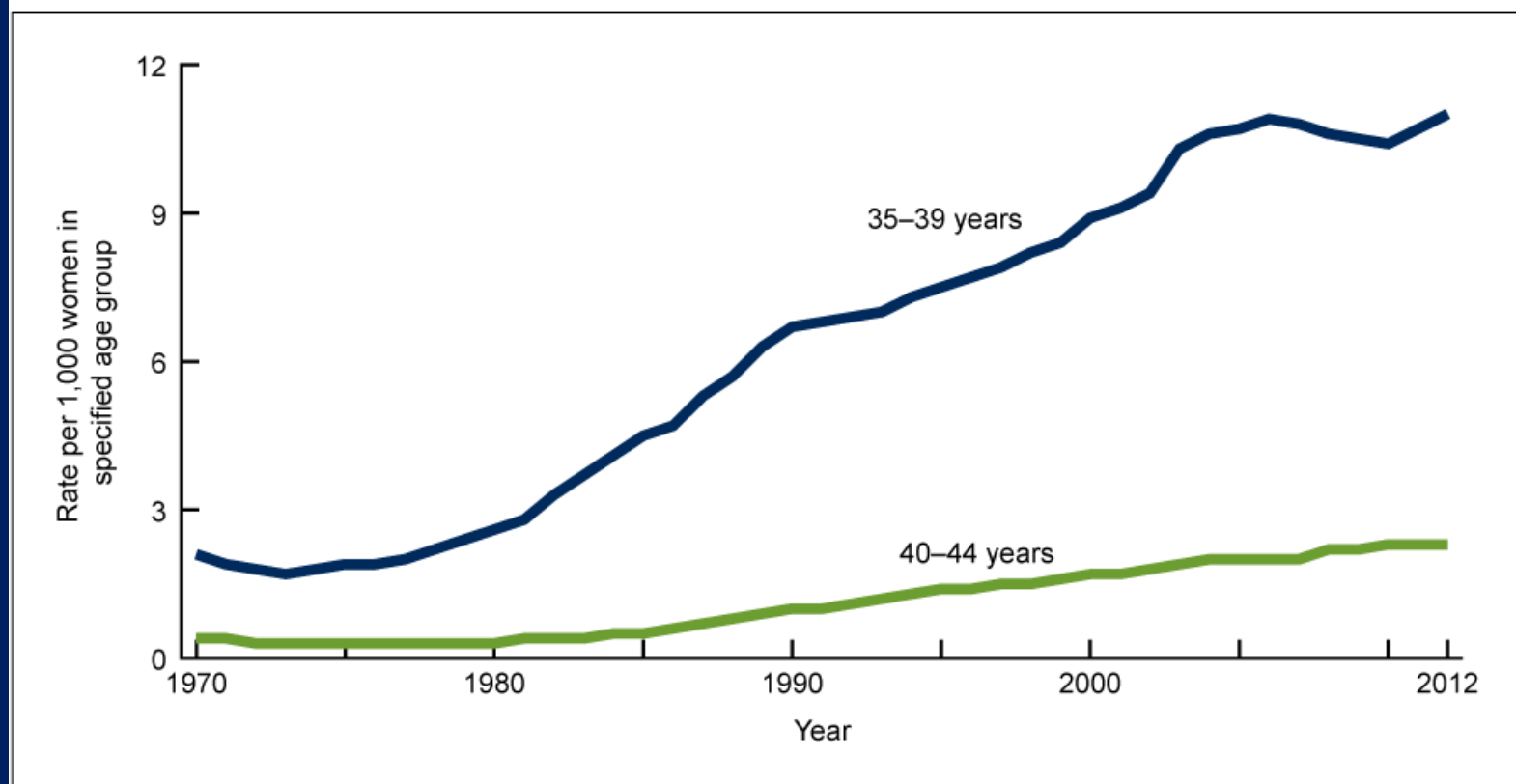
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ART NUMBERS, USA 2012

- ~ 6% infants conceived using ovarian stimulation treatments
- 1.5% infants conceived using assisted reproductive technologies (ART)

FIRST BIRTH RATES

Figure 1. First birth rates by selected age of mother: United States, 1970–2012



NOTE: Access data table for Figure 1 at: http://www.cdc.gov/nchs/data/databriefs/db152_table.pdf#1.

SOURCE: CDC/NCHS, National Vital Statistics System.

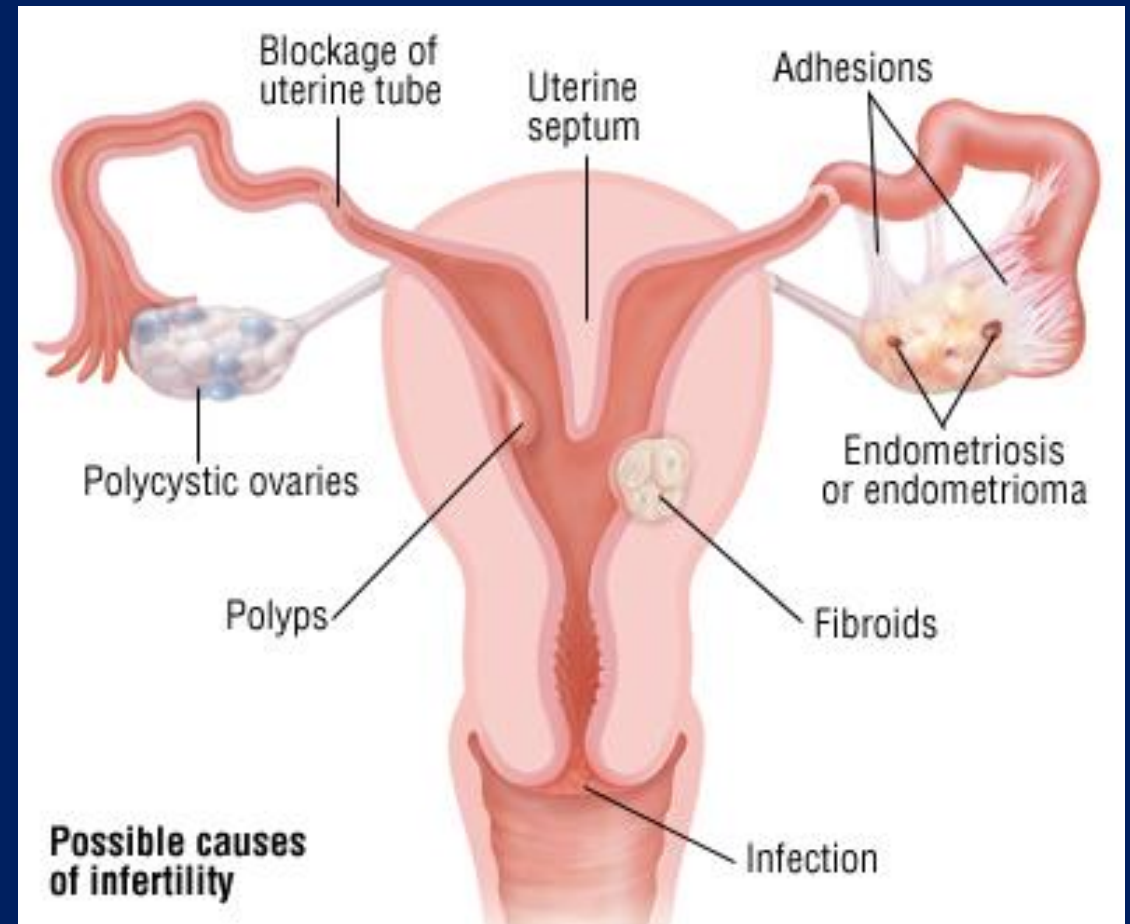
CAUSES OF INFERTILITY

Female Causes of Infertility

- Polycystic ovary syndrome
- Primary ovarian failure
- Salpingitis
- Endometriosis
- Uterine fibroids
- Hormonal disorders
- Cancers
- Thyroid disease, celiac disease, Cushing's disease, sickle cell disease, kidney disease or diabetes

Male factors

Mixed female/male factors



CARDIAC CONDITIONS ASSOCIATED WITH SUBFERTILITY/INFERTILITY

- Fontan operation
- Cyanotic heart disease
- Tetralogy of Fallot
- Genetic conditions: Turner syndrome

- Medications: anticoagulants

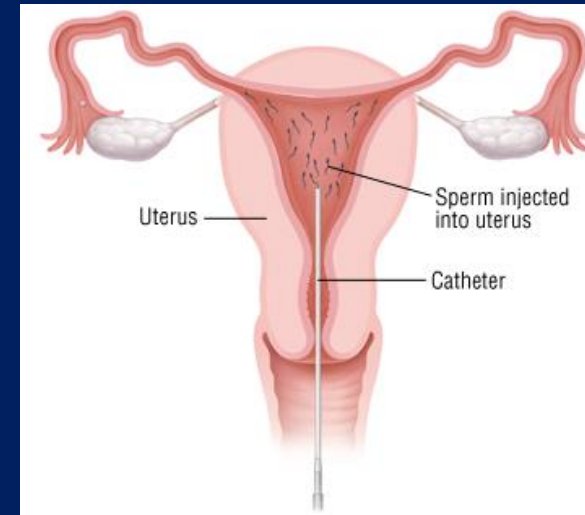
ASSISTED REPRODUCTIVE THERAPIES

Medications

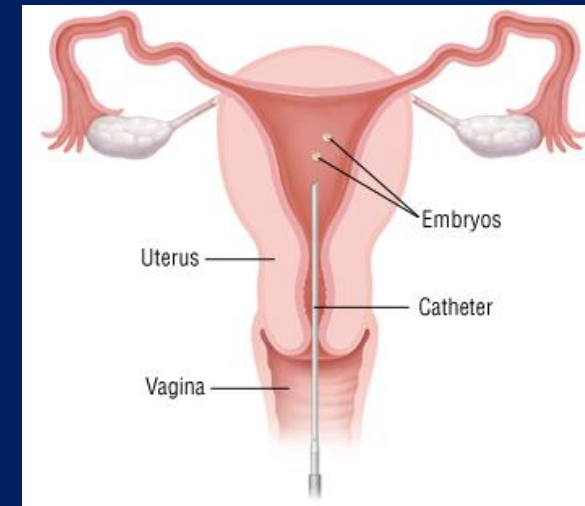
- Ovulation-inducing drugs

Procedures

- Intrauterine insemination (IUI)
 - +/- ovarian stimulation
 - catheter injection of sperm directly into the uterus
- In vitro fertilization (IVF)
 - procedures in which eggs and sperm are manipulated with the purpose of establishing a pregnancy



**INTRAUTERINE
INSEMINATION**



**INVITRO
FERTILIZATION**

COMPLICATIONS OF TREATMENT

Treatment	Complication
IVF	Multiple pregnancy OHSS
Clomiphene citrate	Multiple pregnancy
Laparoscopy Operative hysteroscopy	Cardiac and respiratory intolerance to pneumoperitoneum Excess fluid absorption and electrolyte imbalance.

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1. Infertility and assisted reproductive technologies
2. Adverse outcomes in pregnancies conceived with fertility therapy
 1. Risks associated with infertility/subfertility
 2. Risks of fertility drugs and procedures
 3. Consequences of multiple gestation
3. Outcomes in women with heart disease

RISK: SUBFERTILITY

Study		Outcome	Odds Ratio
Thomson et al. 2005	1437 subfertile women	Preeclampsia	1.9
	21688 control patients	Placenta previa	3.9
		Abruption	1.8
		Induction of labor	1.5
		Caesarean section	2.1
		Instrumental delivery	2.2
Jaques et al. 2010	2171 singletons to subfertile women with no ART	Hypertension/PE	1.29
	4363 spontaneous pregnancy control subjects	Antepartum hemorrhage	1.41
		Caesarean section	1.56

RISK: OVARIAN HYPERSTIMULATION SYNDROME (OHSS)

- Iatrogenic complication related to ovarian stimulation
- Vascular permeability and acute fluid shift into the extravascular space
- Ascites, localized or generalized peritonitis, edema, hydrothorax, hydropericardium, hypotension and/or hypovolemia, hypercoagulable state, electrolyte imbalances, acute renal failure

RISKS: EGG RETRIEVAL

- Risks related to the egg retrieval procedure
 - Removing eggs through an aspirating needle entails a risk injury to pelvic organs, bleeding, and infection
 - Ovarian torsion
- Risks of sedation

RISKS: MULTIFETAL PREGNANCIES

- **36% of twin births were attributable to medically assisted conceptions**
- **77% of triplet and higher-order births were attributable to medically assisted conceptions**

RISKS: MULTIFETAL PREGNANCY

Outcomes	Multiples n=44,674	Singletons n=165,188	RR
In hospital death	5	9	2.05
Preeclampsia	4407	5872	2.78
Gestational diabetes	1633	5387	1.12
MI	37	37	3.70
Heart failure	7	2	12.94
Stroke	1	1	3.70
PE	54	28	7.13

HEMODYNAMICS OF TWIN PREGNANCIES

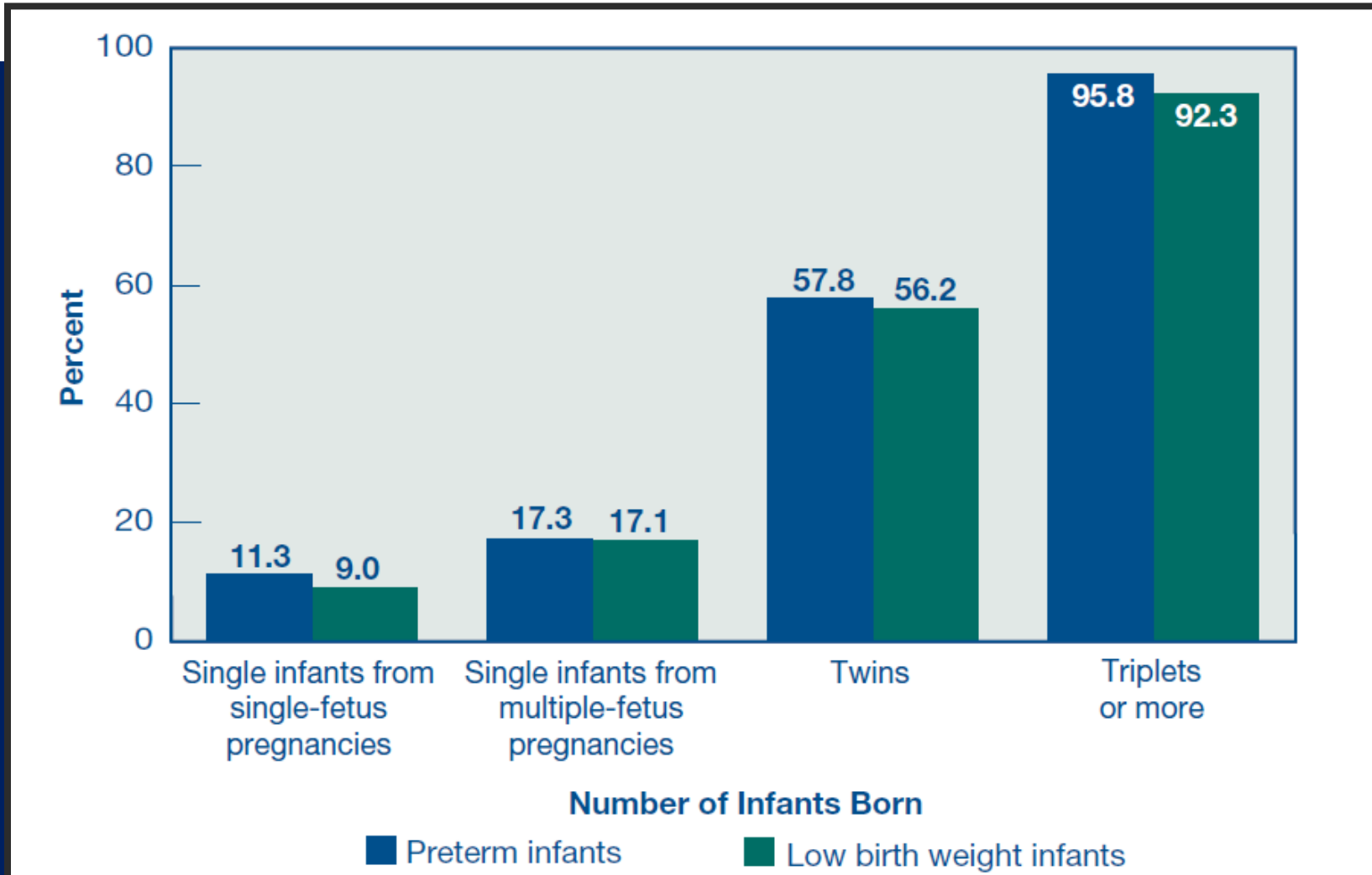
Significantly higher cardiac output and heart rate in twin pregnancies when compared to singleton pregnancies

Robson et al AJOG 1989

Women with heart disease who have twin pregnancies are at higher risk for developing heart failure

Fu et al Int J Gynaecol Obstet 2015

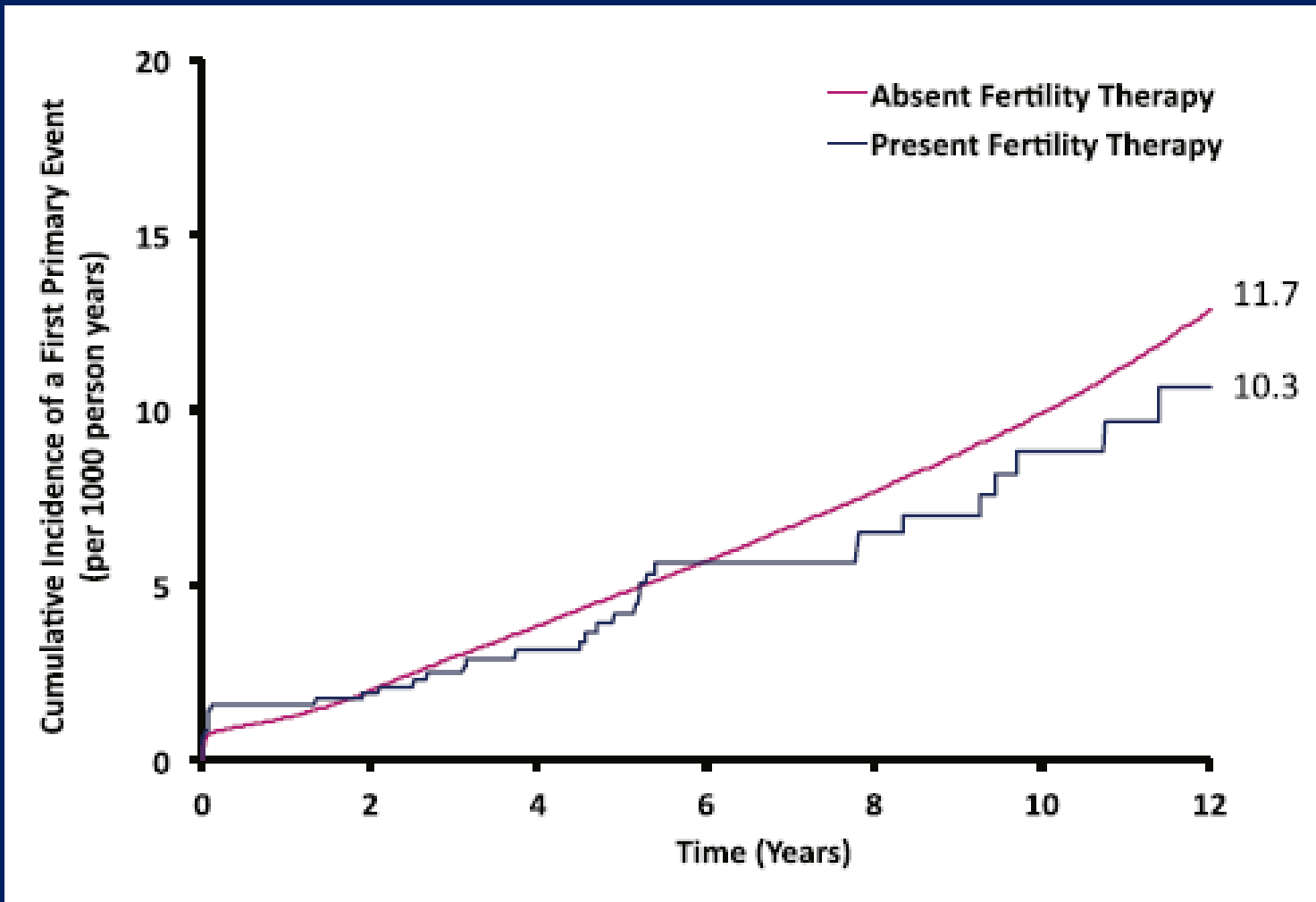
RISKS: PRETERM OR LOW BIRTH WEIGHT INFANTS



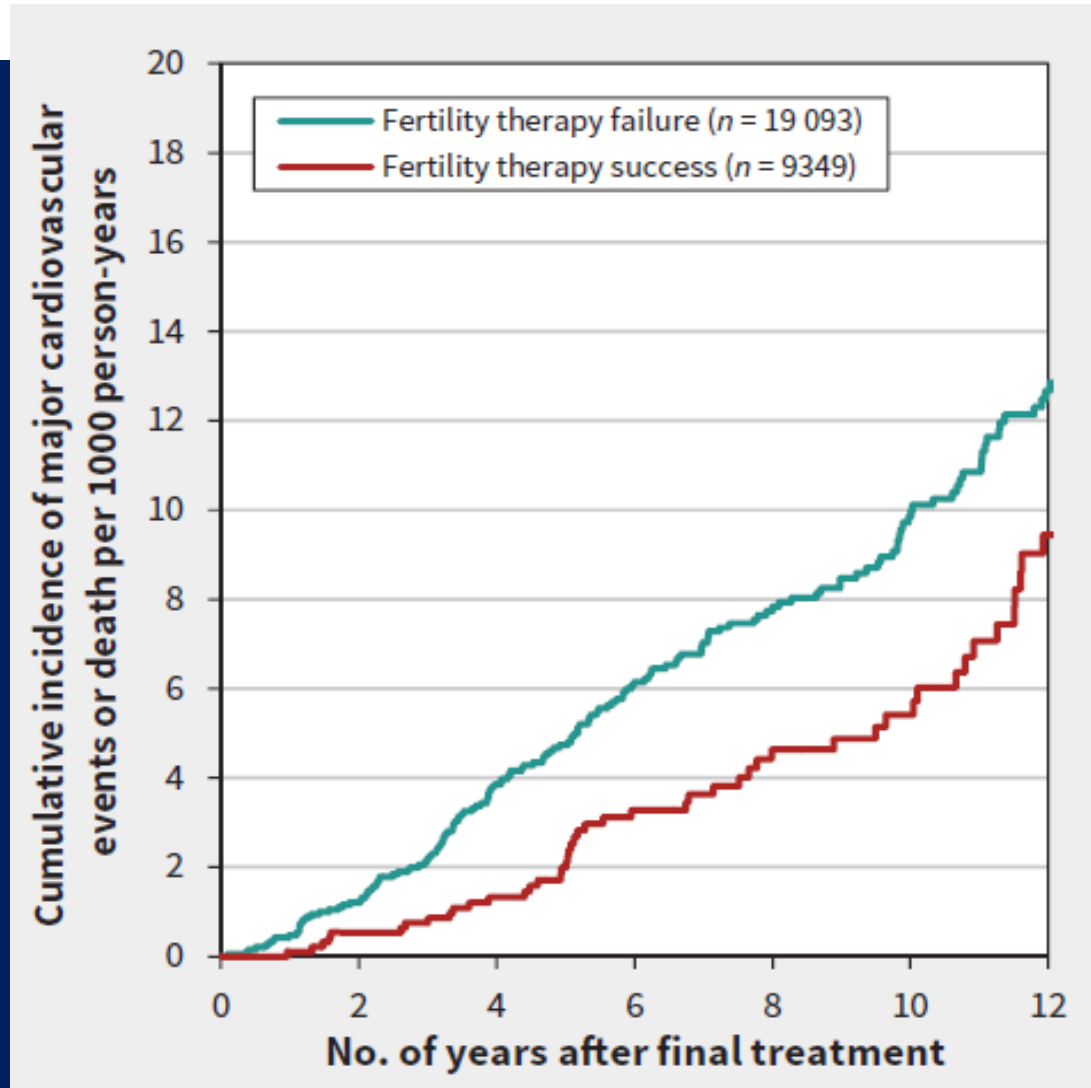
RISKS: LONG-TERM CV COMPLICATIONS AFTER FERTILITY THERAPY

Peripartum Events	No Fertility Therapy N = 1,179,774	Fertility Therapy N = 6,979
Gestational diabetes	3%	8%
Pre-eclampsia or eclampsia	3%	7%
Serious placental complications	3%	6%
Pre-term or threatened labor	8%	16%
Late pregnancy	11%	8%

RISKS: LONG-TERM CARDIOVASCULAR OUTCOMES AFTER FERTILITY THERAPY



RISKS: CV OUTCOMES AFTER FERTILITY THERAPY FAILURE AFTER FERTILITY THERAPY



Women conceiving with fertility therapy

Maternal cardiac complications

- Maternal death •
- Heart failure/volume overload •
- Arrhythmias
- Hypertensive disorders •

Fetal and neonatal complications

- Fetal death/neonatal deaths •
- Growth restriction •
- Preterm birth •
- Congenital birth defects •

Obstetric complications

- Multiple gestation •
- Antenatal bleeding •
- Postpartum bleeding
- Placenta complications •

	Women with heart disease	Women conceiving with fertility therapy
Maternal cardiac complications		
Maternal death	•	•
Heart failure/volume overload	•	•
Arrhythmias	•	
Hypertensive disorders	•	•
Fetal and neonatal complications		
Fetal death/neonatal deaths	•	•
Growth restriction	•	•
Preterm birth	•	•
Congenital birth defects	•	•
Obstetric complications		
Multiple gestation		•
Antenatal bleeding	•	•
Postpartum bleeding	•	
Placenta complications		•

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OUTCOMES IN WOMEN WITH CARDIAC DISEASE CONCEIVING WITH FERTILITY THERAPY

Baseline Characteristic	N=22 pregnancies
Age, years	37 +/- 4
Multiple gestation	9%

OUTCOMES IN WOMEN WITH CARDIAC DISEASE CONCEIVING WITH FERTILITY THERAPY

Cardiac Diagnosis

Congenital

- Repaired ASD
- Repaired aortic coarctation
- Bicuspid aortic valve
- Pulmonary stenosis (valvuloplasty)
- Tetralogy of Fallot (repaired)
- Hypertrophic Cardiomyopathy (HOCM)
- Mitral Valve Prolapse/MR
- Situs inversus/Kartagener syndrome

Acquired

- Dilated cardiomyopathy
- Pulmonary hypertension
- Coronary artery disease
- Arrhythmic

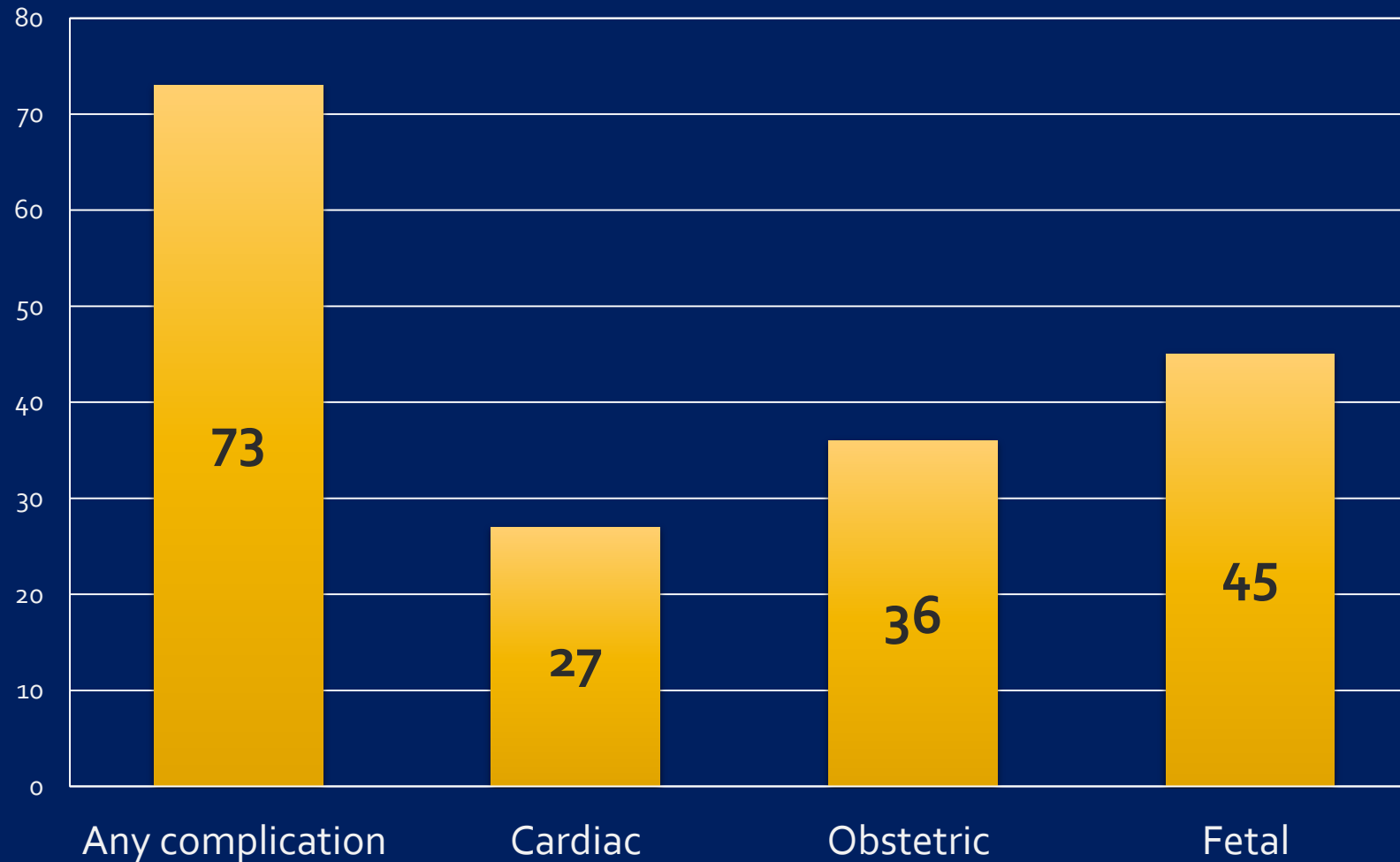
OUTCOMES IN WOMEN WITH CARDIAC DISEASE CONCEIVING WITH FERTILITY THERAPY

Type of assisted reproductive therapy	N=22 pregnancies
Ovarian stimulation only	1
Intra-uterine insemination	4
In vitro fertilization	17 (74%)
ICSI	4
Donor oocyte	4
With superovulation protocol	13
Natural cycle or low stimulation protocol	4

OUTCOMES IN WOMEN WITH CARDIAC DISEASE CONCEIVING WITH FERTILITY THERAPY

ART Outcome	All pregnancies N=22
Any ART outcome	4 (18%)
OHSS	4
Thrombosis	0
Bleeding during ovum retrieval	0

OUTCOMES IN WOMEN WITH CARDIAC DISEASE CONCEIVING WITH FERTILITY THERAPY



Dayan et al JACC 2014

SUMMARY

1. Use of assisted reproductive technologies is growing
2. When considering ART therapy in women with cardiac disease it is important to consider:
 - i. Risks associated with the medical condition causing infertility
 - ii. Risks of fertility drugs
 - iii. Risks of ART procedures
 - iv. Consequences of multifetal gestation
 - v. Other options may need to be considered such as surrogacy and adoption
3. Many more studies are required to understand risk in this population

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