



סוגיות בניהול הריונות בגיל המבוגר

פרופ' מיכל שמחן
מנהלת מחלקות יולדות א' וב'
אגף נשים ויולדות
מרכז רפואי 'שיבא' תל השומר

מקרה 1 ...

■ בת 52 ללא ילדים

■ משקל 95 קג, מעשנת

■ COPD קל

■ יתר ל"ד

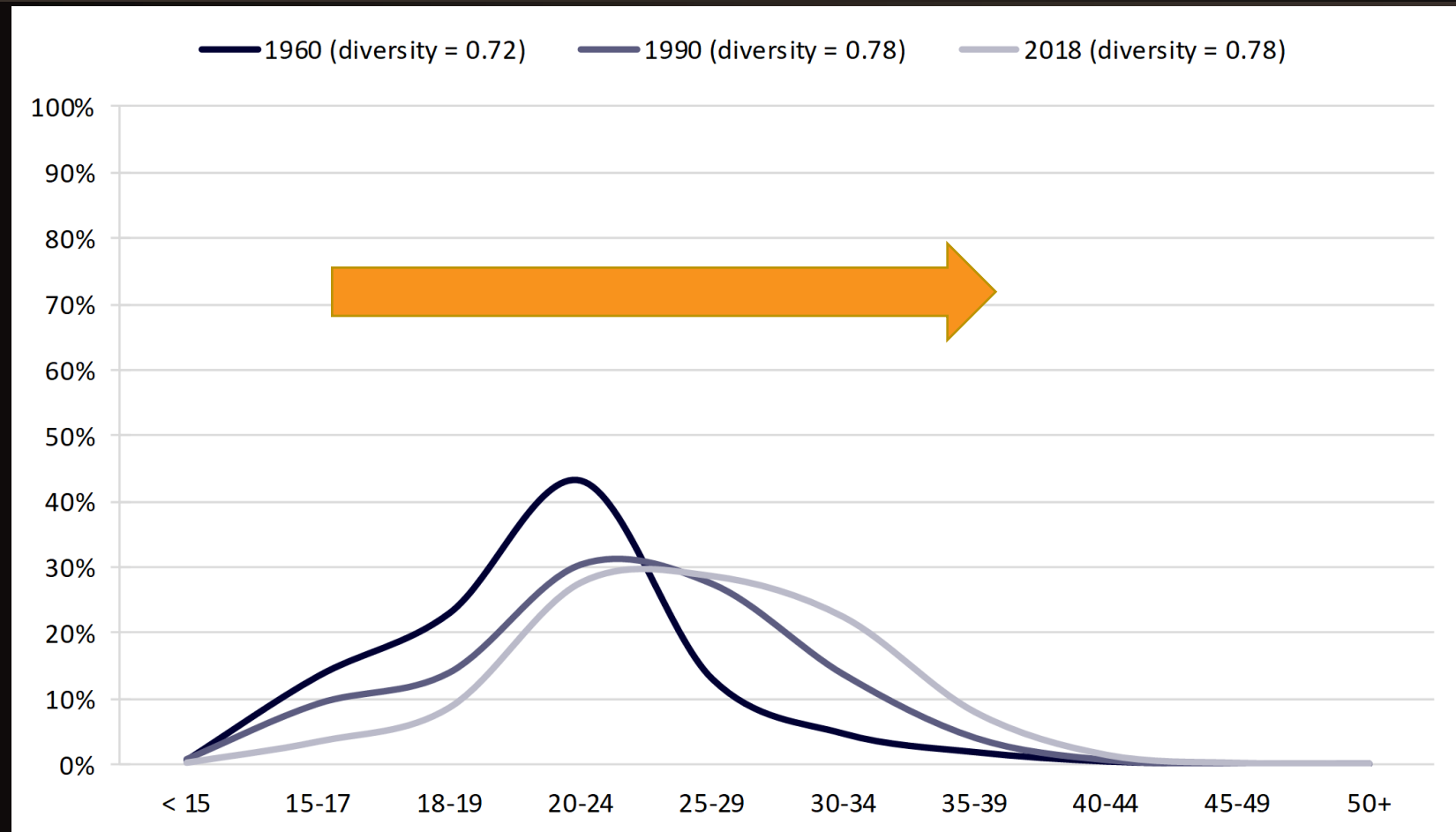
– קנדור, מאוזנת

■ סכרת

– מטפורמין

– HbA1C 7.8%

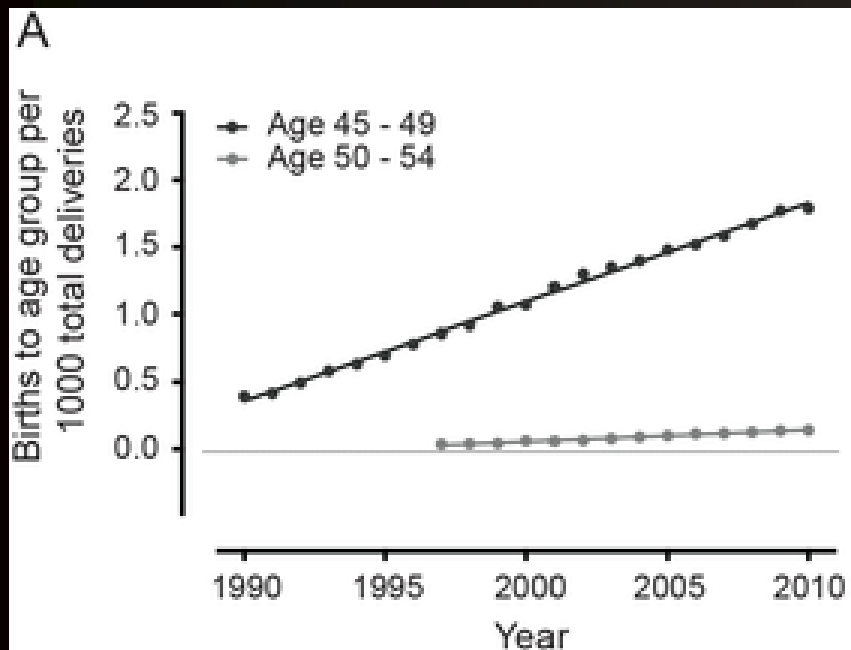
A gradual increase in maternal age at first pregnancy 1960-2018 (US)



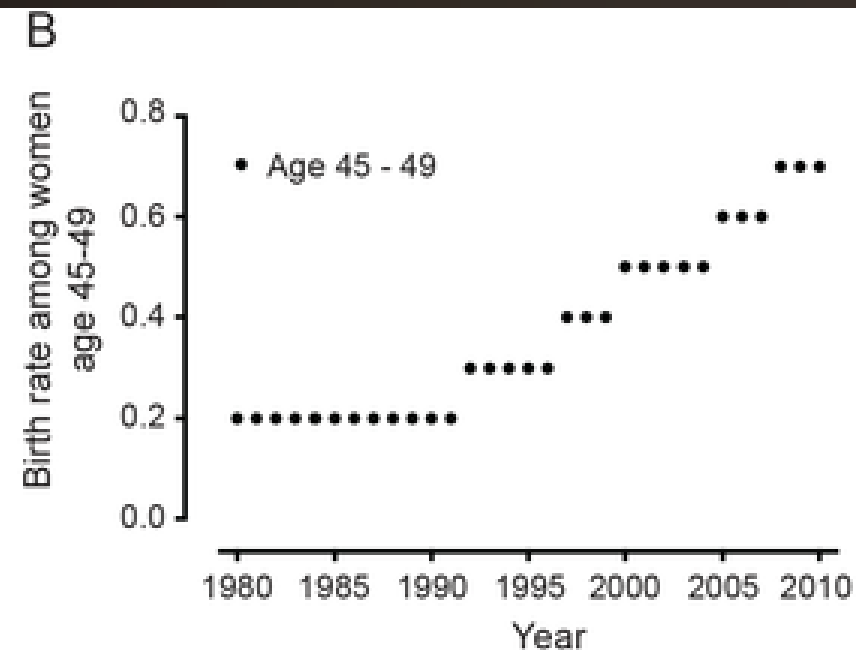
Total number of births and birth rates among women aged 45 and older

US data

Births to 1000 total deliveries



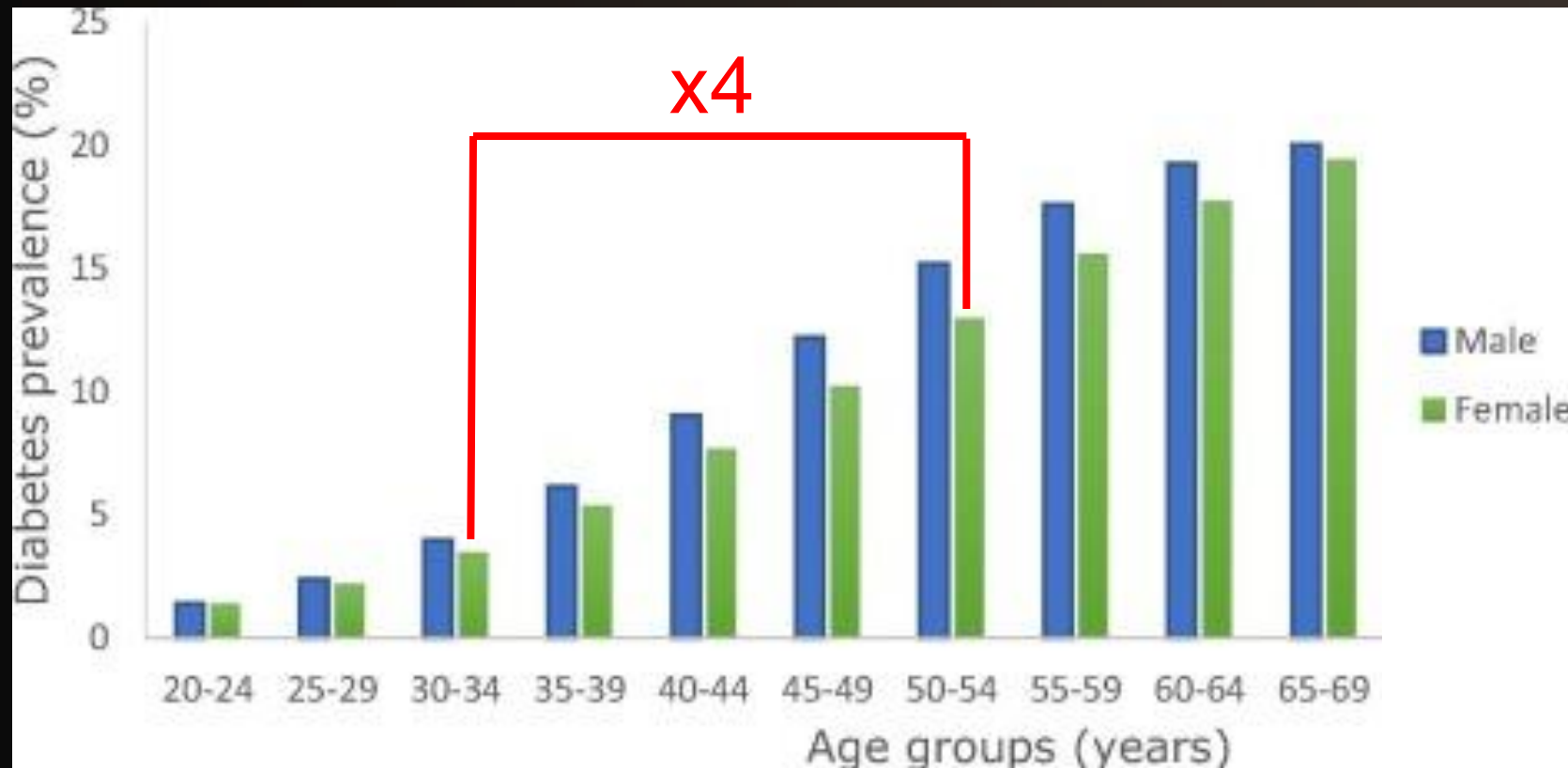
Birth rates



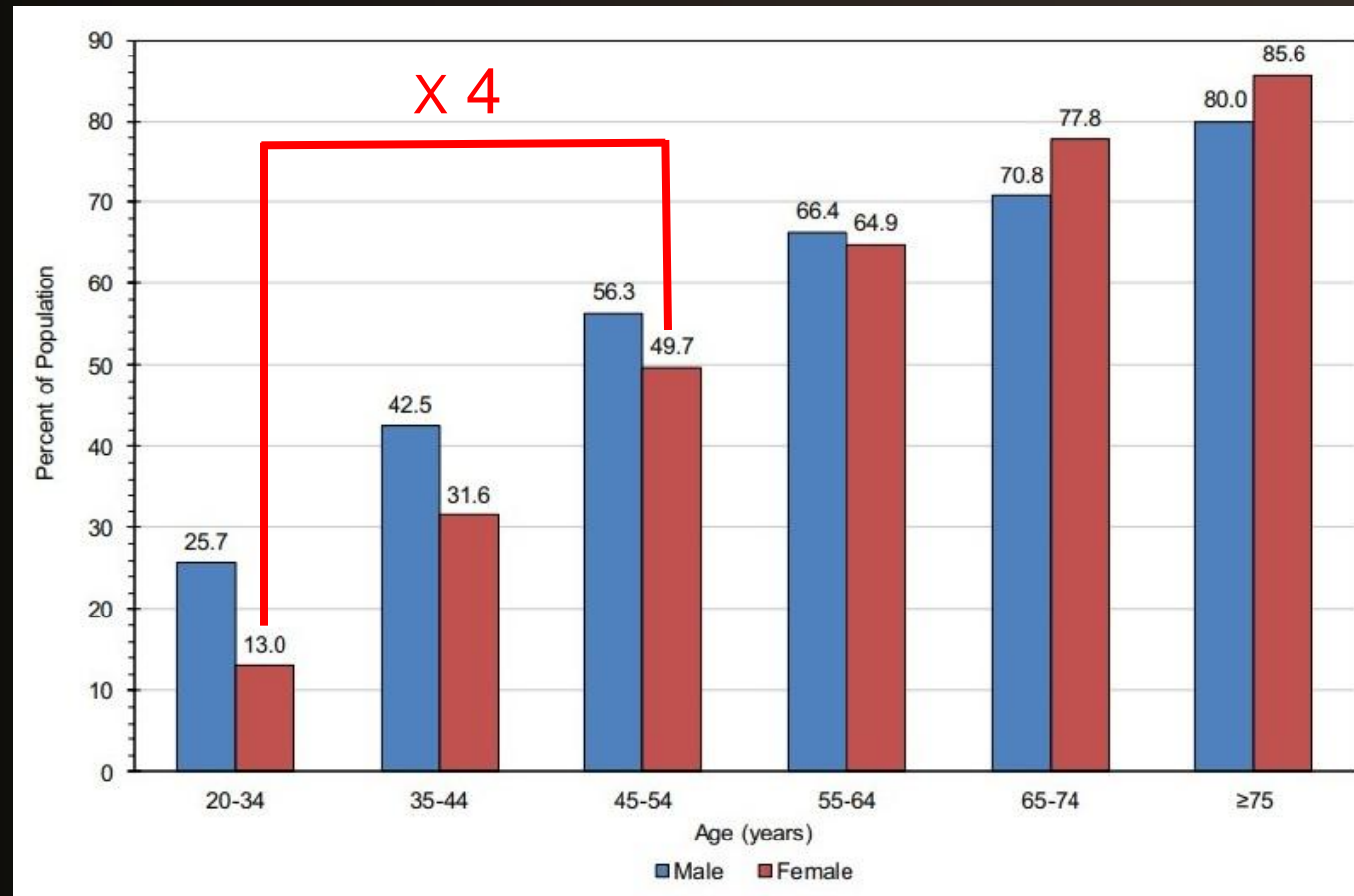
Pregnancy in older women –

what are the implications?

Background risk factors: Diabetes Mellitus



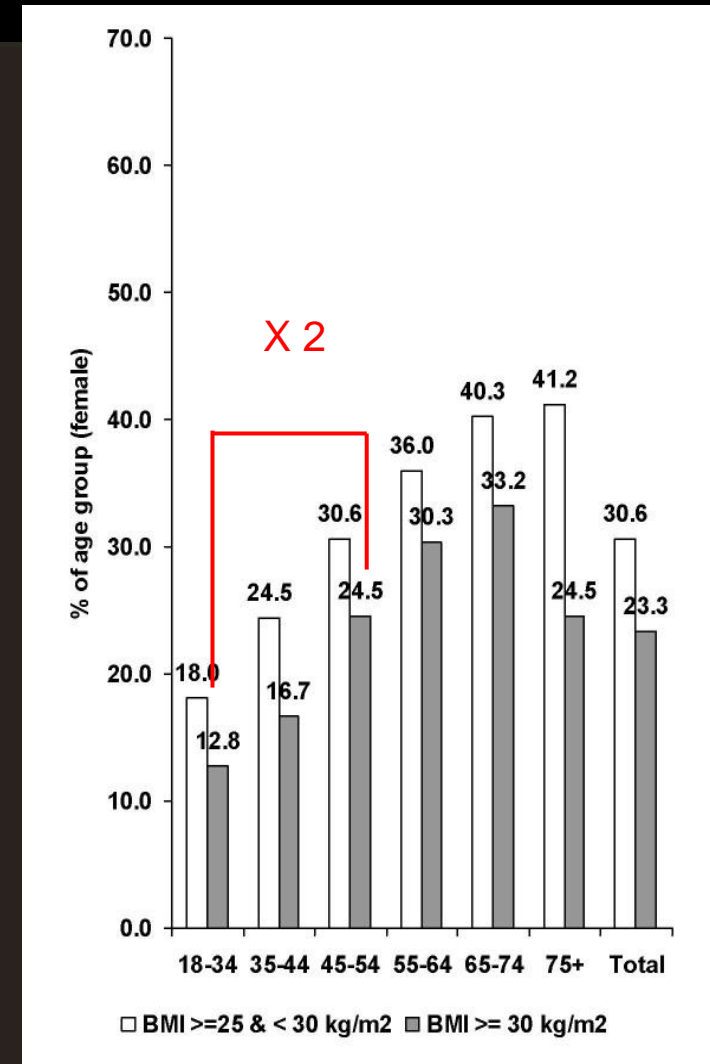
Background risk factors: Hypertension



Background risk factors: Prevalence of obesity

- BMI increase with age

All independent risk factors for adverse perinatal outcome



Advanced maternal age and adverse perinatal outcome

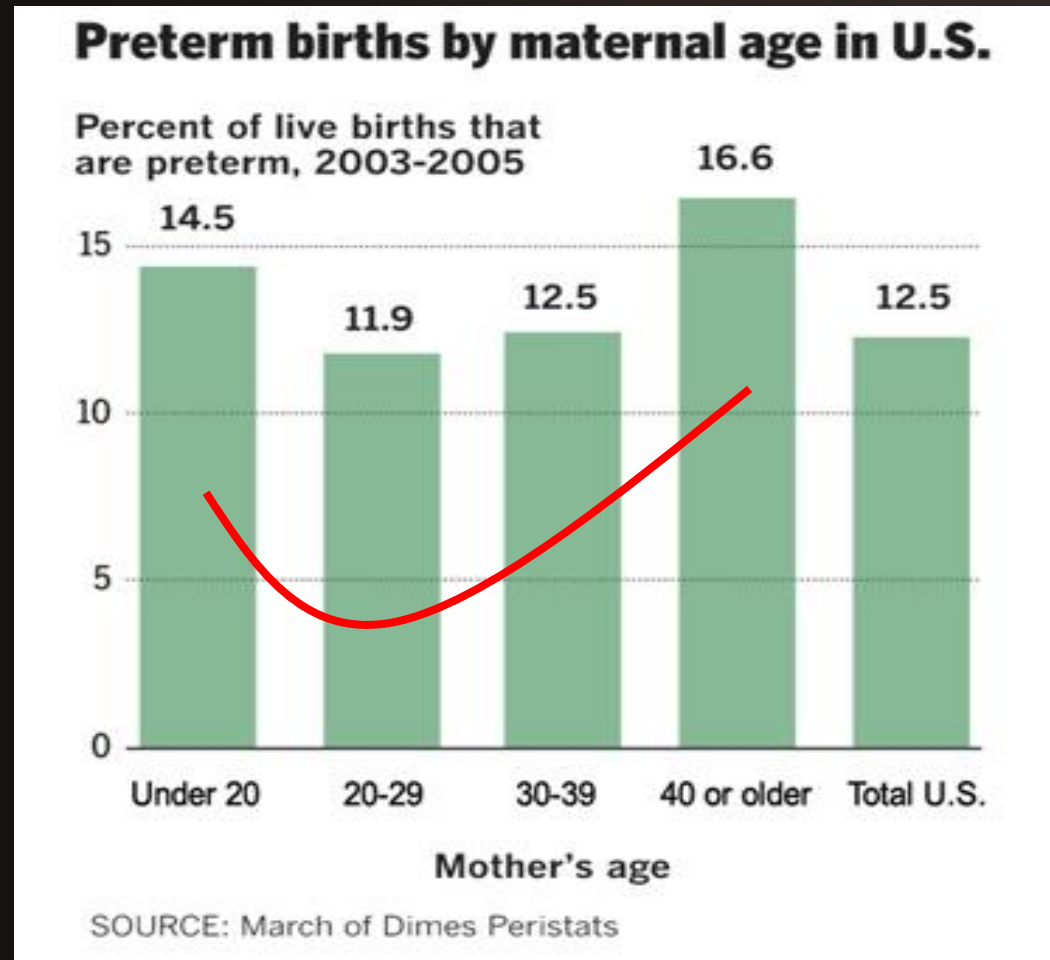
Swedish population registry n=900,000

<i>Adjusted Odds Ratio</i>	20-29 yrs	40-44 yrs	45 yrs &more
C-section	1	2.66	3.77
Preterm delivery <34 wks	1	1.57	1.68
SGA	1	1.94	2.67
Perinatal mortality	1	1.67	2.45

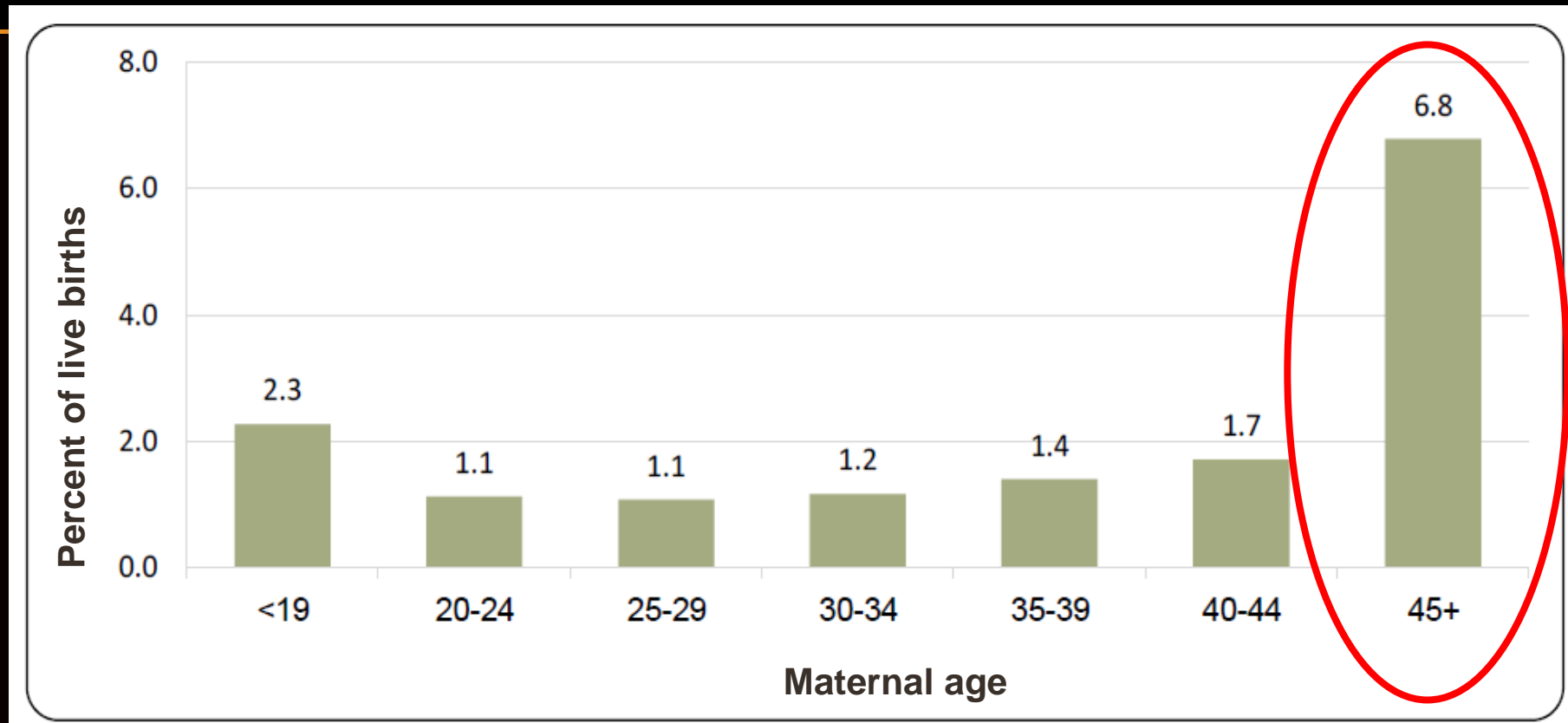
Increasing maternal age associated with

- Increasing background risk factors
- Also **independently** associated with adverse pregnancy outcome
- Age is a continuum, not a threshold effect

Preterm deliveries by maternal age

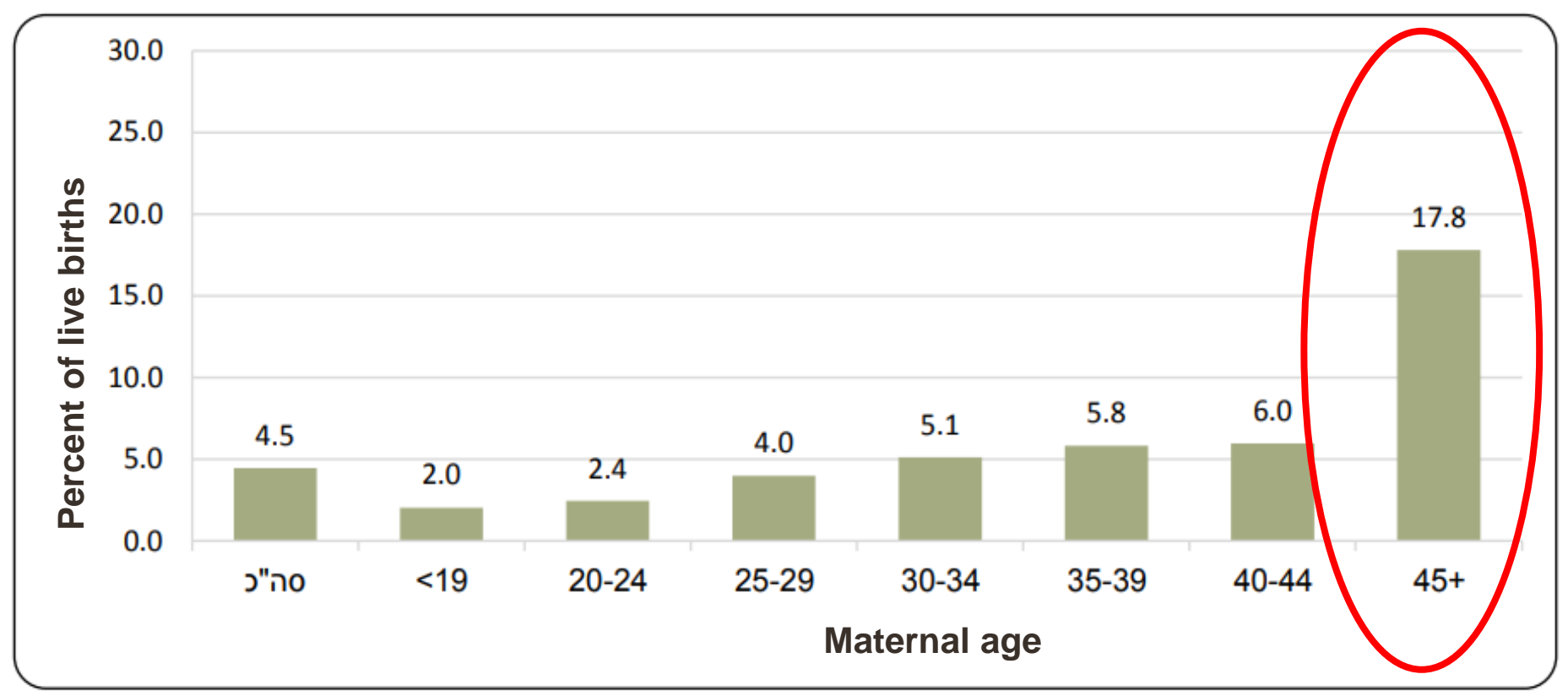


Preterm birth <33wks



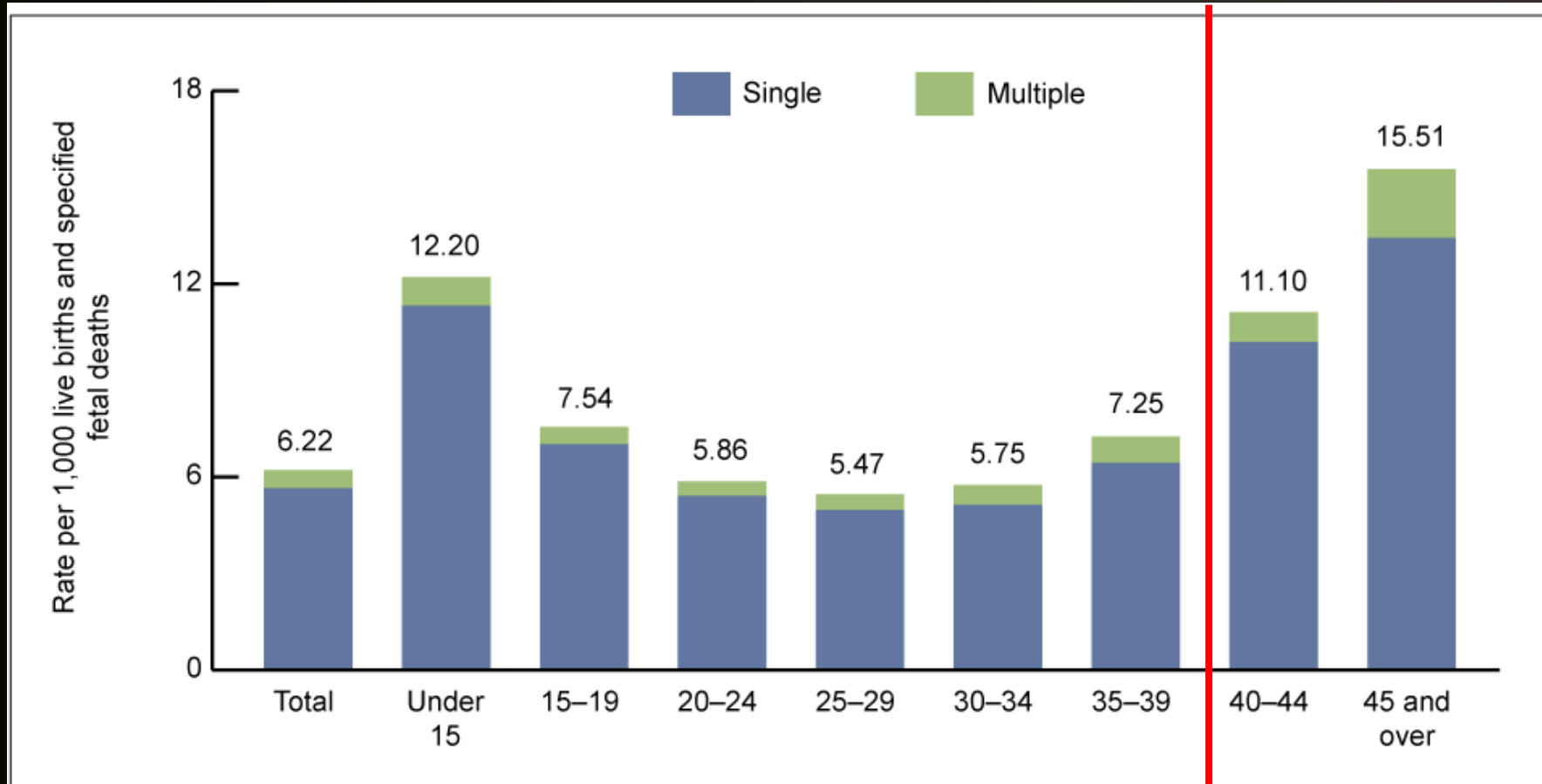
adapted from Israel Health ministry data
Presented in Annual meeting of the Israeli Maternal Fetal Medicine association 2017

Multifetal pregnancies



adapted from Israel Health ministry data
Presented in Annual meeting of the Israeli Maternal Fetal Medicine association 2017

Fetal mortality rates by maternal age, USA 2005



SOURCE: CDC/NCHS, National Vital Statistics System, fetal mortality data, 2005.

Age and fertility

- IVF
- Oocyte donation
- Oocyte cryopreservation
- Allow overcoming of age-related decline

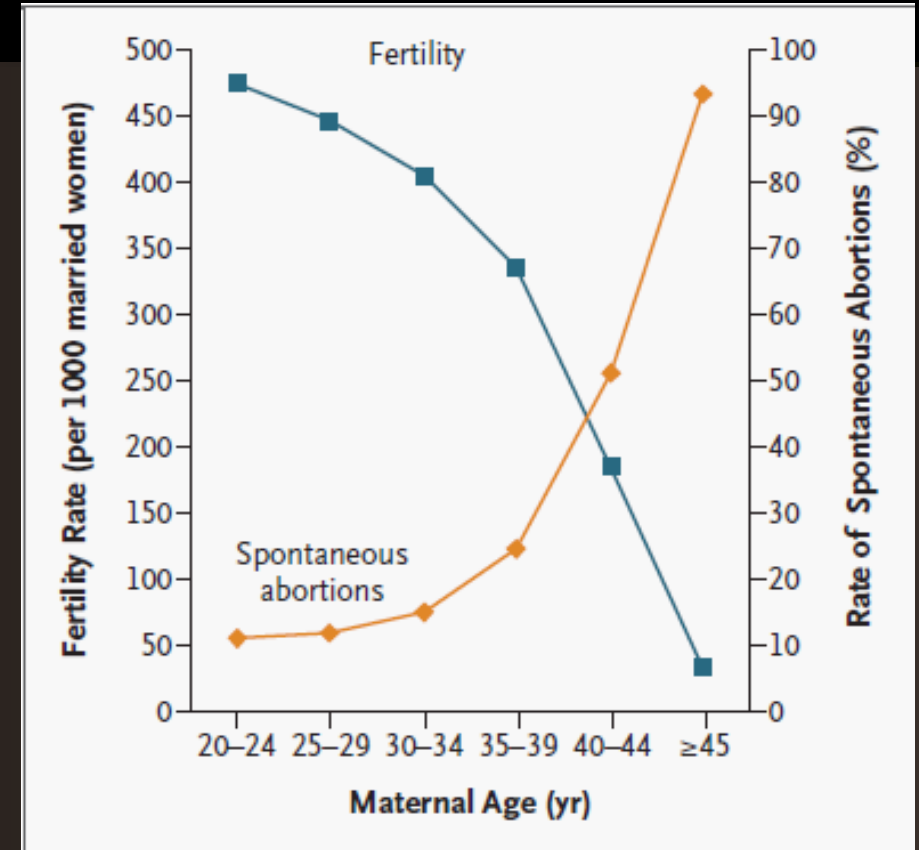


Figure. Fertility and Miscarriage Rates as a Function of Maternal Age.

Adapted from Menken et al.¹ and Anderson et al.²

Older-age pregnancy with ovum donation

- With young donor oocytes “the sky is the limit”
- 35-45% clinical pregnancy rates
- Increased risk of complications:
 - Age
 - Donated oocytes

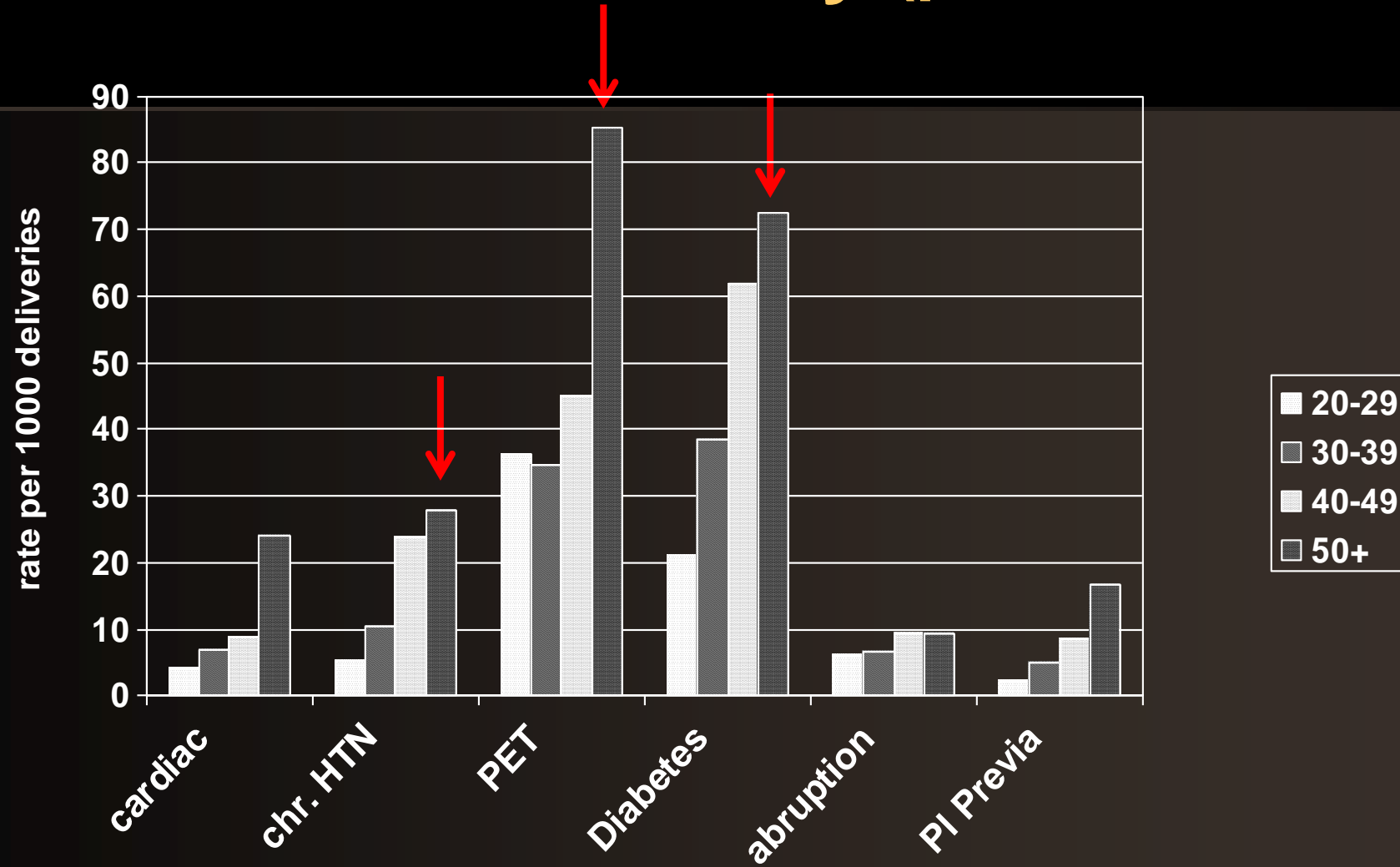


Pregnancy beyond age 50

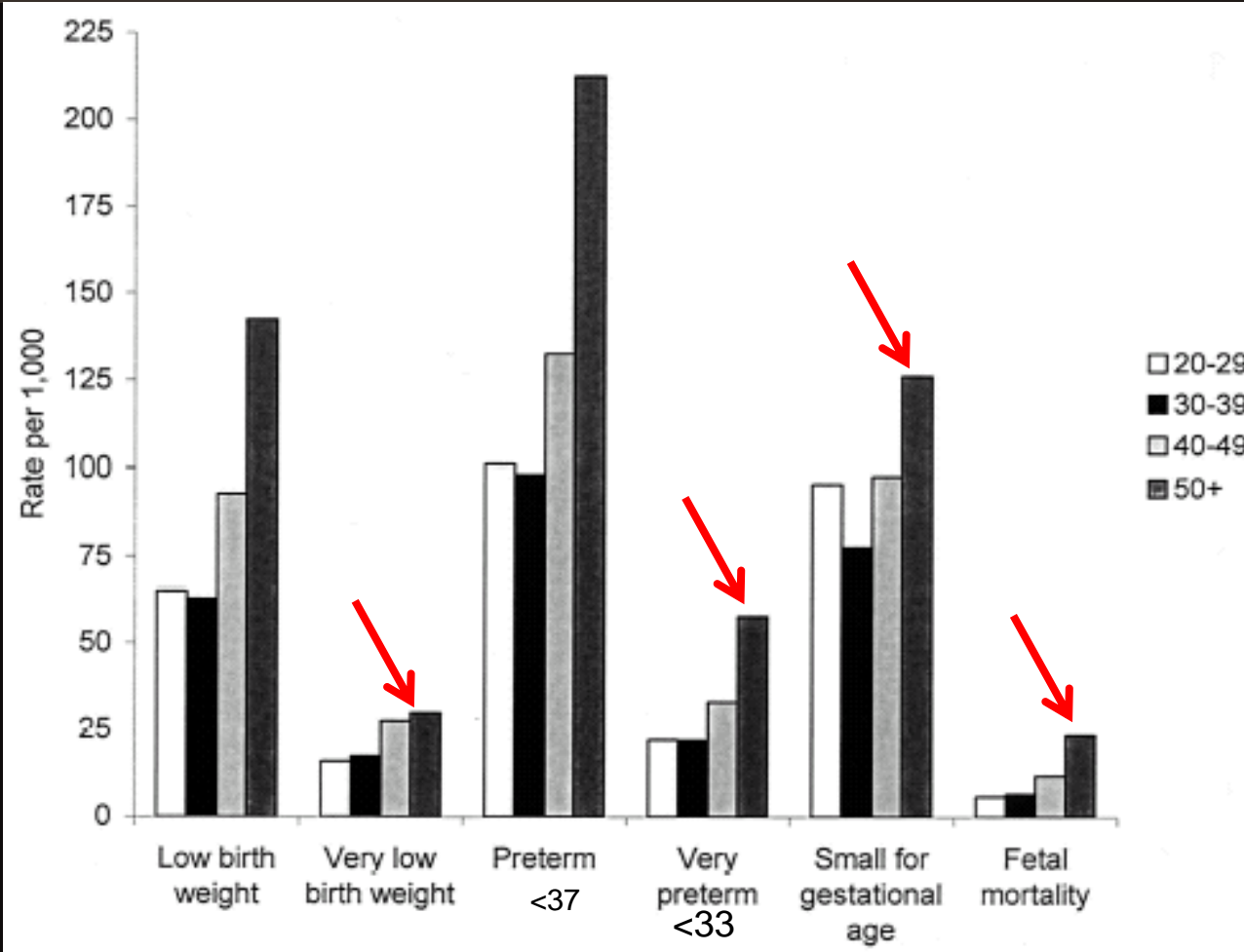
Salihu et al Obstet Gynecol 2003

- All deliveries in US 1997-1999 (n~12,000,000)
- Population registry
- 4 age groups: 20-29 30-39 40-49 50-54
- 50-54 yrs:
 - N=539
 - 29% primips
 - 37% multiples

Maternal morbidity (per 1000 deliveries)



Fetal morbidity (per 1000 deliveries)



Singletons

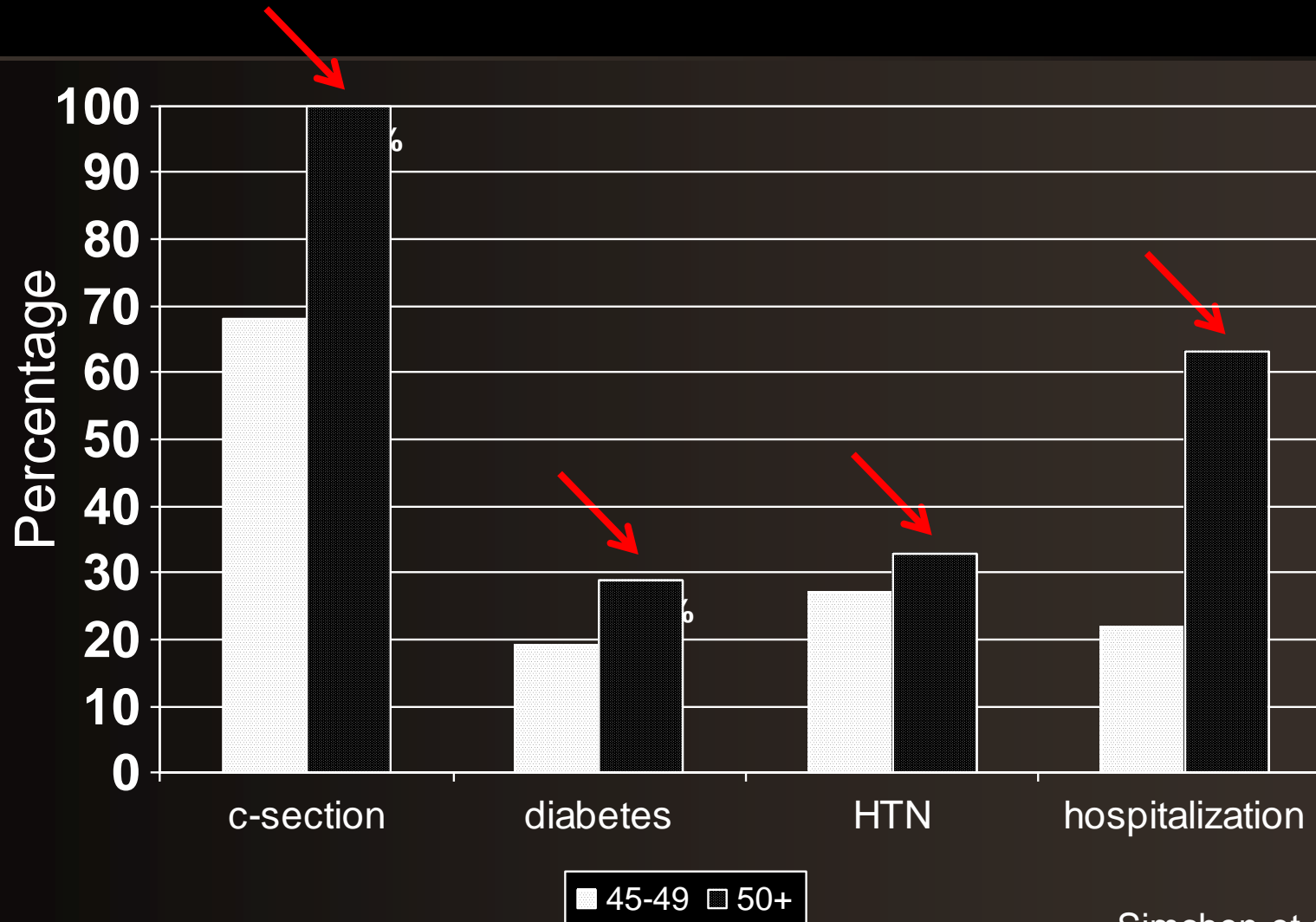
Pregnancy in the 6th decade of life

Paulson et al. *JAMA* 2002

	Singleton	Twins	Triplets
Gestational age	38.4 wks	35.8 wks	32.2 wks
Birth weight	3039 gr	2254 gr	1913 gr

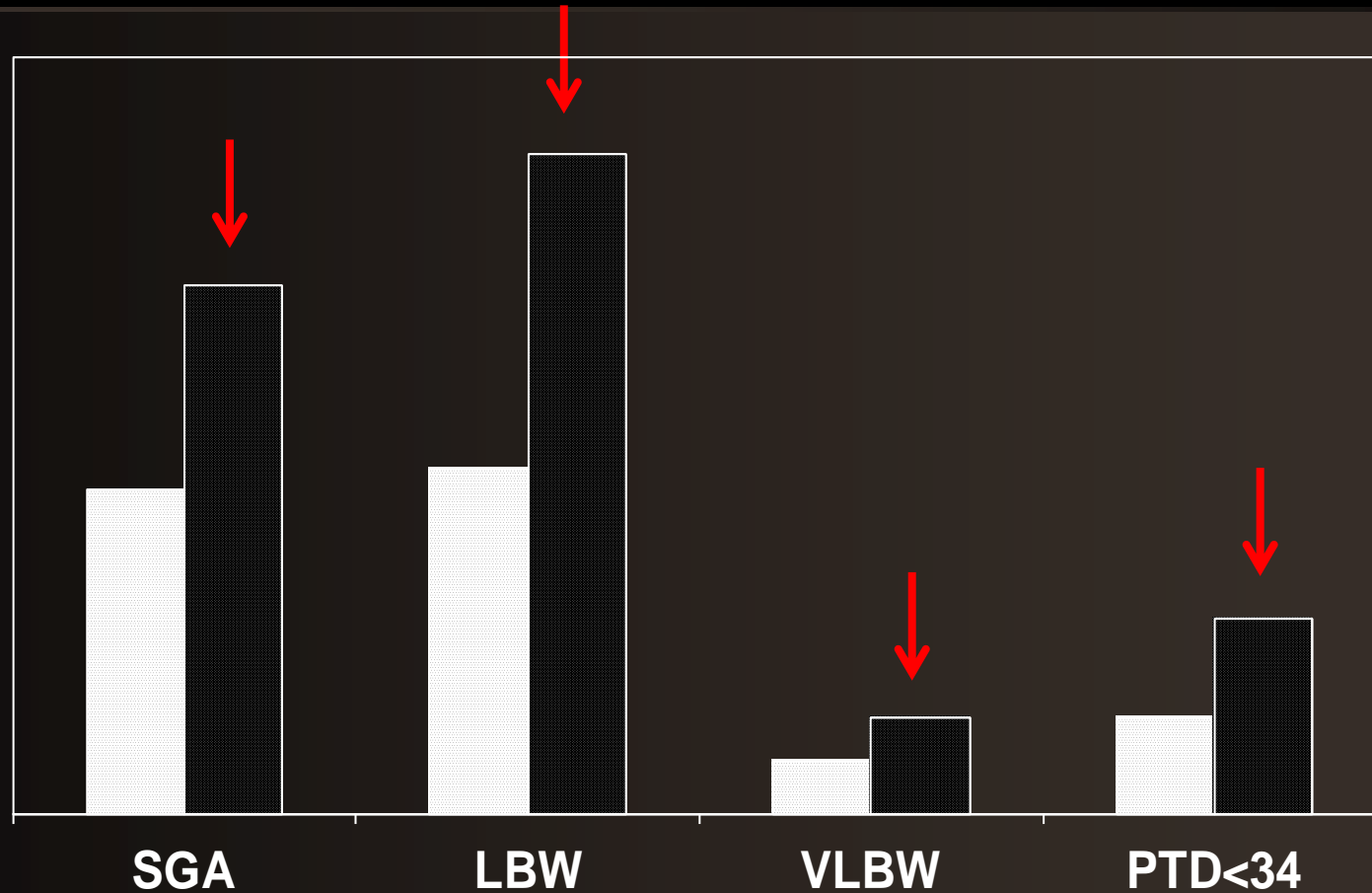
- 25% preeclampsia
- 10% severe preeclampsia

Pregnancy after age 50



Fetal outcome 45-49 vs 50+

SGA < 10th percentile; LBW < 2500gr; VLBW < 1500gr; PTD preterm delivery



Very advanced maternal age > 50 yrs

- In this older ED group - high rates of complications
- High rates of multifetal pregnancies, mostly twins
–25-35%

So –

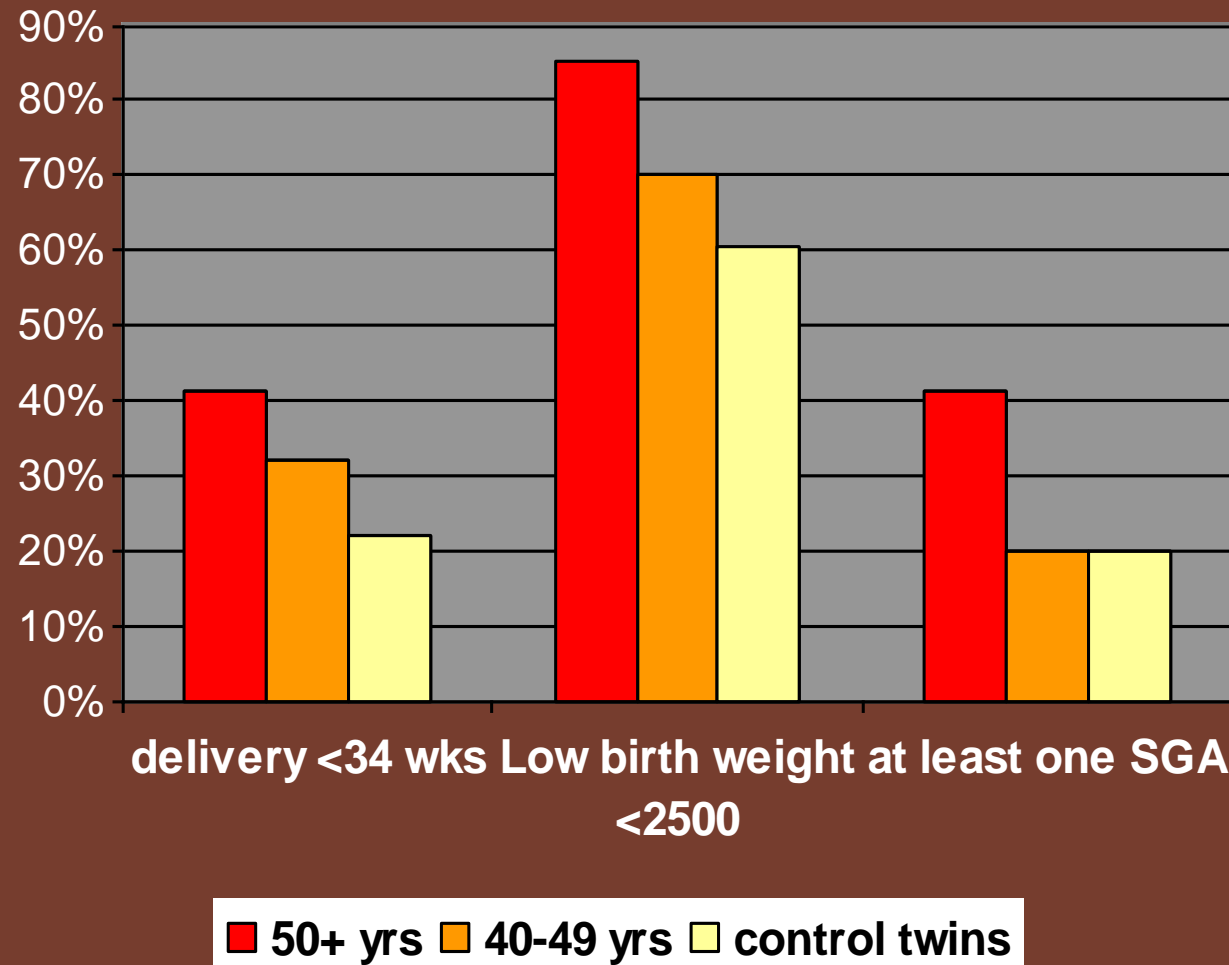
- What are the combined effects of age, oocyte donation and twins?

Age and plurality – synergistic effect?

Complications of pregnancy, delivery, and infant mortality by maternal age and plurality, all women.

Factor	Age	Singletons				Twins				Triplets			
		Percent	AOR ^a	95% CI	P value	Percent	AOR ^a	95% CI	P value	Percent	AOR ^a	95% CI	P value
Diabetes	<20	0.87	0.30	0.20-0.30	<.0001	1.02	0.31	0.26-0.36	<.0001	3.36	0.60	0.25-1.43	.26
	20-24	1.70	0.61	0.61-0.62	<.0001	2.02	0.62	0.58-0.67	<.0001	3.81	0.69	0.45-1.06	.09
	25-29	2.68	1.00	—	—	3.23	1.00	—	—	5.56	1.00	—	—
	30-34	3.57	1.37	1.26-1.38	<.0001	4.34	1.37	1.29-1.44	<.0001	6.22	1.13	0.91-1.40	.27
	35-39	4.87	1.89	1.7-1.91	<.0001	5.19	1.64	1.54-1.75	<.0001	7.81	1.42	1.13-1.80	.003
	≥40	6.69	2.64	2.53-2.68	<.0001	7.03	2.24	2.03-2.46	<.0001	7.28	1.32	0.91-1.92	.14
Chronic hypertension (<20 weeks)	<20	0.26	0.33	0.32-0.34	<.0001	0.48	0.46	0.36-0.59	<.0001	2.65	2.16	0.69-6.82	.21
	20-24	0.45	0.62	0.62-0.64	<.0001	0.72	0.76	0.67-0.87	<.0001	0.50	0.24	0.06-0.97	.045
	25-29	0.67	1.00	—	—	0.89	1.00	—	—	1.22	1.00	—	—
	30-34	0.94	1.48	1.44-1.48	<.0001	1.16	1.39	1.25-1.54	<.0001	1.17	0.66	0.61-1.51	.85
	35-39	1.54	2.43	2.39-2.47	<.0001	1.62	1.94	1.73-2.17	<.0001	1.65	1.36	0.84-2.20	.21
	≥40	2.71	4.27	4.17-4.37	<.0001	2.67	3.24	2.77-3.80	<.0001	3.36	2.73	1.24-6.00	.01
Pregnancy-associated hypertension	<20	4.35	0.89	0.89-0.90	<.0001	9.37	1.00	0.94-1.07	.916	6.04	0.68	0.35-1.32	.26
	20-24	3.82	0.98	0.97-0.98	<.0001	7.72	0.98	0.94-1.03	.408	7.46	0.78	0.57-1.09	.15
	25-29	3.69	1.00	—	—	7.97	1.00	—	—	10.24	1.00	—	—
	30-34	3.37	0.98	0.98-0.99	<.0001	7.86	0.99	0.95-1.03	.707	11.79	1.16	0.99-1.37	.07
	35-39	3.69	1.15	1.14-1.16	<.0001	8.19	1.07	1.02-1.12	.006	11.58	1.16	0.78-1.43	.07
	≥40	4.55	1.44	1.42-1.47	<.0001	11.35	1.45	1.34-1.56	<.0001	14.74	1.52	1.16-2.01	.003

Neonatal outcome – older OD women – twins vs. twin controls



Outcome of twins vs singleton pregnancies in the 5th and 6th decades of life

Outcome	Adjusted OR	p-value
Composite placental complications (preeclampsia, gestational hypertension, IUGR, placental abruption) OR 3.19 (1.93-5.28) twins vs singletons		
Preeclampsia	4.36 (2.37-8.02)	<0.001
IUGR	2.96 (1.47-5.96)	0.002
GDM	1.73 (1.05-2.86)	0.032

492 IVF women \geq 45 yrs
60 \geq 50 yrs

“Elderly” twins compared with “young” twins

	Study twins >45yrs (n=97)	Control twins <35yrs (n=406)	p-value
Cesarean delivery	91.8%	56.4%	<0.001
Gestational hypertension	10.3%	4.2%	0.016
Preeclampsia	32%	6.3%	<0.001
Gestational diabetes mellitus	35.1%	8.1%	<0.001

Pregnancy after ED in older women

- 40-50% Hypertensive complications
- 30% Diabetes in pregnancy
- 50-70% Hospitalization in pregnancy
- 90-100% C-section rate
- Increased risks
 - Preterm delivery
 - Small for gestational age
 - LBW < 2500

Especially in twins

בחזרה למקרה שלנו...

■ בת 52 יתר ל"ד וסכרת type2

■ מועמדת ל ED

ייעוץ טרום הריוני

■ הריון אפשרי, דיון על סיכונים נלווים

■ סכרת – איזון טרום הריוני!!!

– להמתין ל HbA1c מתחת ל6 לפני החזרת עוברים

■ עובר יחיד!!!!

מקרה 2...2



■ בת 49

■ נשואה בשנית

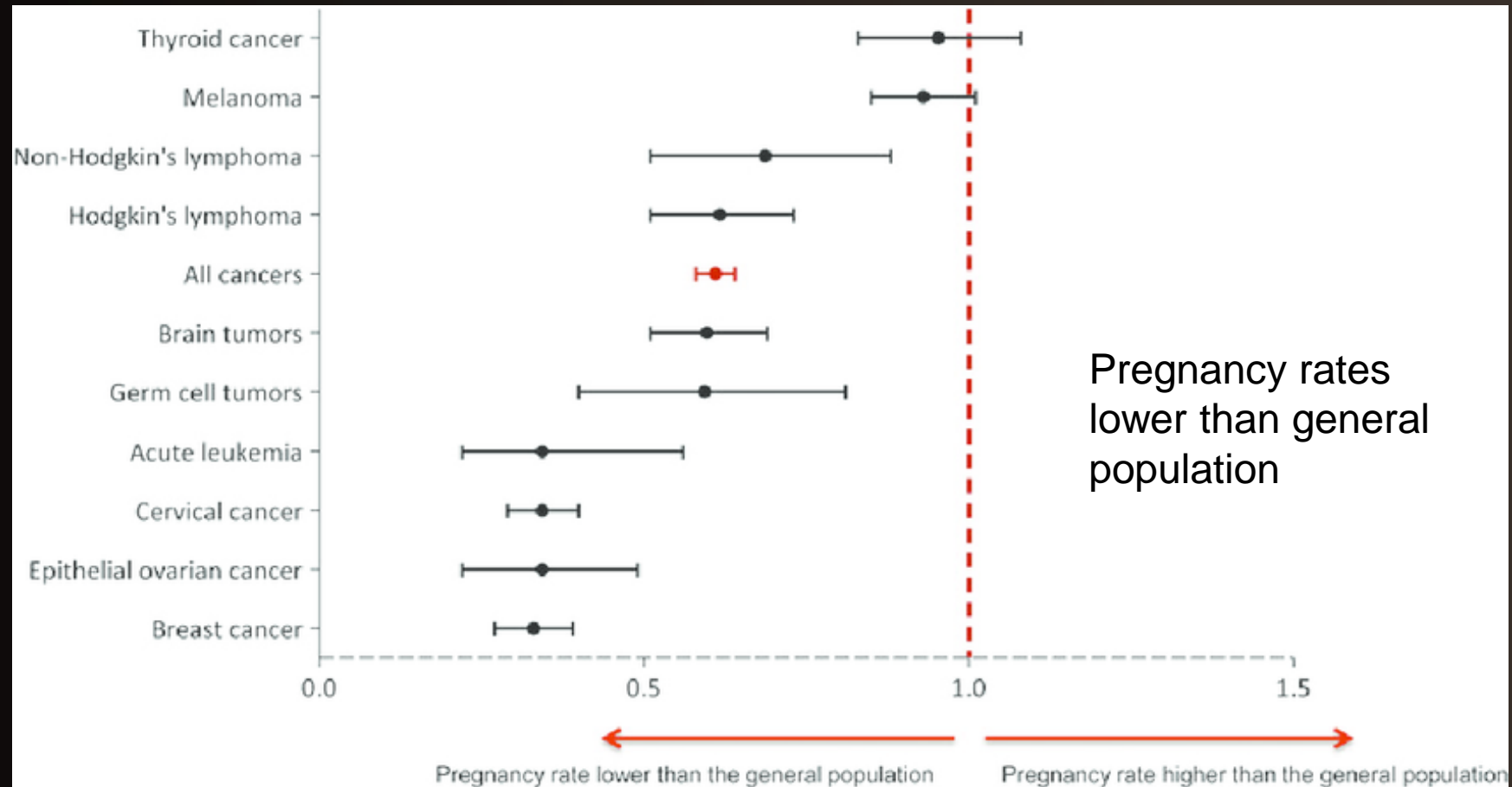
■ אם לילד בן 27

■ בעבר לידה רגילה

■ לפני שנתיים וחצי – סרטן שד עם בלוטות תפוסות

–סיימה כימותרפיה, הקרנות

Cancer, pregnancy and fertility



Adverse perinatal outcomes among females diagnosed with cancer

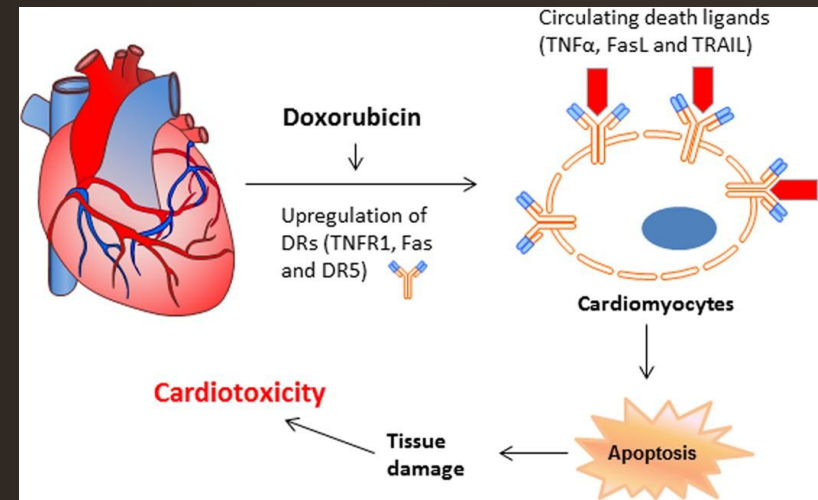
	AYA cancer	Comparison	ARR (95% CI) ^a
Maternal complications			
Threatened abortion (<20 weeks)	76(4%)	83 (2%)	2.09 (1.51–2.74)
Threatened preterm labor (20–36 weeks)	54 (3%)	91 (2%)	1.28 (0.88–1.88)
Pre-eclampsia	69 (4%)	111 (3%)	1.44 (1.13–1.87)
Maternal anemia	21(1%)	39 (1%)	1.31 (0.71–2.19)
Gestational diabetes	101 (5%)	83 (2%)	1.38 (1.09–2.98)
Postpartum hemorrhage	95 (5%)	199 (5%)	1.08 (0.82–1.56)
Antepartum hemorrhage	17 (1%)	41 (1%)	0.92 (0.59–1.78)
PRoM	99 (5%)	207 (5%)	0.99 (0.83–1.31)
Failure to progress	32 (2%)	47 (1%)	1.51 (0.97–2.37)
Retained placenta	57 (3%)	128 (3%)	0.98 (0.73–1.34)
Cesarean delivery	342 (18%)	288 (7%)	2.62 (2.22–3.04)
Postpartum LOS>5 days	227 (12%)	189 (5%)	3.01 (1.72–5.58)
Use of fertility treatment	57 (3%)	42 (1%)	1.94 (1.36–2.69)
Perinatal complications			
Sex ratio (reference: male)	948 (50%)	2029 (49%)	1.05 (0.98–1.10)
Gestational age at birth			
20–36 weeks	284 (15%)	412 (10%)	1.68 (1.21–2.08)
37–40 weeks	1458 (77%)	3310 (80%)	Reference
41–43 weeks	152 (8%)	416(10%)	1.04 (0.94–1.56)
Birth weight			
<2500 g	246 (13%)	331 (8%)	1.51 (1.23–2.12)
2500–4000 g	1439 (76%)	3435(83%)	Reference
>4000 g	208 (11%)	372 (9%)	1.33 (0.99–1.71)
Intrauterine growth restriction	119 (6%)	94 (2%)	1.21 (0.97–2.06)

Cancer survivors: Birth Outcomes

Characteristic	Adjusted Prevalence Ratio (95% CI) vs Noncancer Comparison Group (n = 1299) ^{a,b}					
	Preterm Birth, wk					
	<37	<34	Low Birth Weight	SGA	Cesarean Delivery	Apgar <7
Overall	1.52 (1.34-1.71)	2.03 (1.62-2.55)	1.59 (1.38-1.83)	0.97 (0.85-1.11)	1.08 (1.01-1.14)	1.18 (0.87-1.61)
Site group						
Breast	1.98 (1.56-2.51)	1.56 (0.92-2.63)	1.59 (1.18-2.15)	1.00 (0.73-1.36)	1.17 (1.04-1.33)	0.90 (0.40-2.02)
Hodgkin lymphoma	1.59 (1.06-2.37)	1.27 (0.48-3.37)	1.44 (0.89-2.33)	1.08 (0.71-1.64)	1.08 (0.88-1.34)	0.92 (0.30-2.79)
Non-Hodgkin lymphoma	2.11 (1.42-3.13)	3.42 (1.88-6.21)	2.41 (1.58-3.67)	1.09 (0.66-1.81)	1.18 (0.94-1.49)	2.07 (0.89-4.86)
Melanoma/skin carcinoma	1.12 (0.82-1.52)	1.67 (0.93-3.01)	0.99 (0.67-1.47)	0.65 (0.44-0.95)	1.04 (0.91-1.17)	0.88 (0.41-1.87)
Thyroid	0.97 (0.69-1.36)	0.92 (0.44-1.94)	1.23 (0.86-1.75)	0.94 (0.69-1.29)	0.97 (0.85-1.12)	1.10 (0.55-2.21)
Gynecologic	2.58 (1.83-3.63)	4.29 (2.43-7.58)	2.74 (1.86-4.05)	0.67 (0.36-1.26)	1.48 (1.21-1.79)	2.34 (0.99-5.56)
Time between diagnosis and birth						
Diagnosed during pregnancy	2.97 (2.47-3.58)	3.44 (2.34-5.05)	2.82 (2.25-3.53)	1.05 (0.77-1.42)	1.21 (1.06-1.38)	1.90 (1.04-3.46)
Diagnosed before pregnancy, y						
<2	1.35 (1.07-1.70)	2.19 (1.48-3.25)	1.47 (1.13-1.91)	0.86 (0.65-1.12)	1.02 (0.91-1.15)	0.99 (0.53-1.84)
2 to <3	1.32 (1.00-1.74)	1.49 (0.86-2.59)	1.40 (1.02-1.92)	0.88 (0.64-1.20)	1.01 (0.88-1.15)	1.13 (0.56-2.26)
3 to <5	0.98 (0.73-1.32)	1.48 (0.90-2.46)	1.20 (0.88-1.63)	0.89 (0.67-1.18)	1.11 (0.99-1.24)	0.83 (0.41-1.66)
>5	1.27 (0.95-1.69)	1.80 (1.11-2.90)	1.34 (0.98-1.83)	1.23 (0.96-1.58)	1.07 (0.94-1.21)	1.31 (0.75-2.30)
Treatment						
Surgery only	1.21 (1.01-1.45)	1.84 (1.33-2.55)	1.29 (1.05-1.59)	0.85 (0.70-1.04)	1.04 (0.96-1.13)	1.07 (0.70-1.64)
Radiation, no chemotherapy	1.21 (0.85-1.72)	0.52 (0.17-1.62)	1.34 (0.91-1.98)	0.92 (0.64-1.34)	1.08 (0.92-1.26)	1.52 (0.76-3.06)
Chemotherapy, no radiation	2.11 (1.68-2.66)	2.93 (1.97-4.36)	2.36 (1.84-3.03)	1.14 (0.85-1.52)	1.16 (1.01-1.32)	1.20 (0.62-2.30)
Chemotherapy and radiation	2.28 (1.77-2.93)	2.90 (1.83-4.60)	2.01 (1.48-2.72)	1.17 (0.86-1.60)	1.15 (0.98-1.35)	0.43 (0.11-1.72)

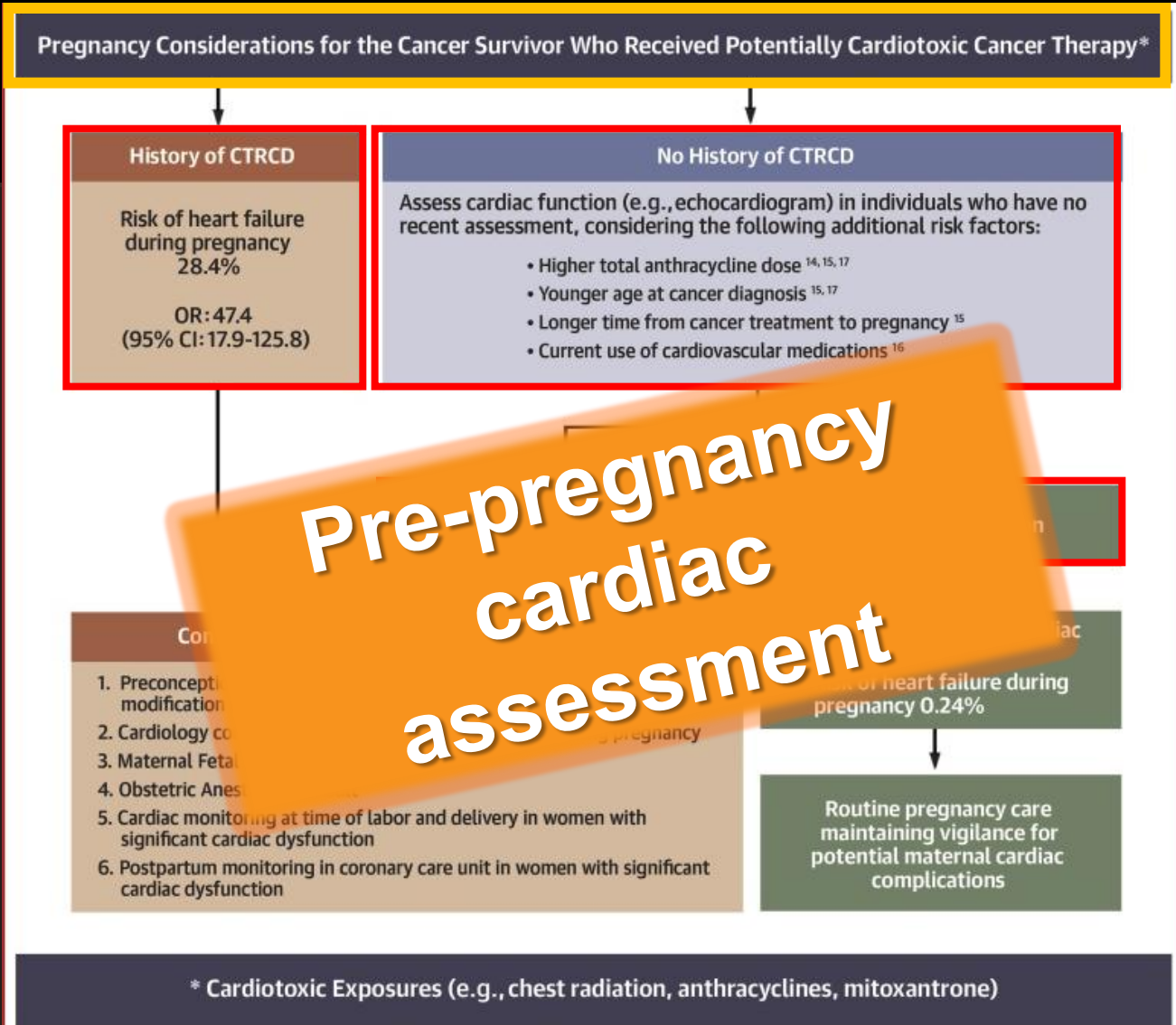
Anthracyclines and cardiotoxicity

- Potential for cardiac damage
- Acute – 2.2%-to 5% of patients
- Dose-dependent



- Chronic cardiotoxicity – *progressive*
 - Early onset - up to 1 year after completion of treatment
 - Late onset - many years after

What about the heart??



בחזרה למקרה שלנו...

- ייעוץ טרום הריוני – דיון על סיכונים

- אישור אונקולוגי להריון

- הערכה קרדיאלית

- מעקב הריון בסיכון גבוה

מקרה 3....

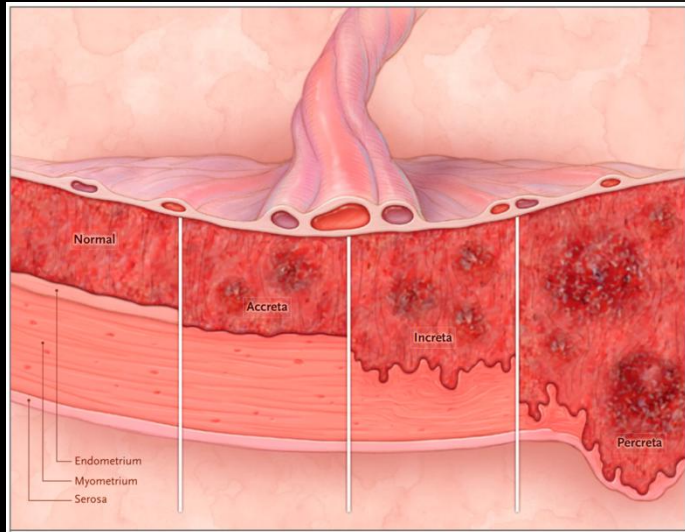


- בת 48 אם ל-5 ילדים
- s/p CS*5
- G1 – PPROM 29wk, לילד CP קל, CS
- G2-G5 – לידות במועד, ניתוחים קיסריים
- ניתוח אחרון עם שלית פתח אקרטה, קיבלה 6 מנות דם
- כעת בן זוג חדש

Risk factors for placenta previa/accreta

- Previous placenta previa
- Previous cesarean delivery
- Multiple gestation
- Multiparity
- Advanced maternal age
- Previous intrauterine surgical procedure
- Smoking
-

Risk of placenta accrete after previous CS



No. of previous cesarean deliveries

Risk of placenta accreta (%)

0

1.9

1

15.6

2

23.5

3

29.4

4

33.3

5

50.0

ייעוץ טרום הריוני:

■ סיכון ללידה מוקדמת

– מעקב אורך צואר הרחם, כן/לא פרוגסטרון

■ סיכון לקרע רחמי והצורך להמנע מצירים מוקדמים

– ניתוח מוקדם? אישפוז מקדים?

■ סיכון לארוע חוזר של שליה נעוצה

– עשרות אחוזים, עד 50% סיכון

■ אתגר ניתוחי – הידבקות, דימום, עיוות אנטומי

– קושי ניתוחי עד צורך בכריתת הרחם

– דימום ופגיעה באיברים חיוניים



הריון בגיל המבוגר

■ סיכוני מחלות רקע – יתר ל"ד, סכרת, סרטן, CVD...

■ סיכוני הריון בגיל מבוגר (מעל 45)

■ סיכוני הריון עם תרומת ביצית

■ Singleton vs twins

■ מעקב הריון בסיכון גבוה

■ מולטידיסיפלינרי



