פריון באשה המבוגרת –
מהו המחיר הבריאותי לאשה?

פרופ' אבי בן הרוש
מנהל השירות לשימור פוריות
היחידה לפוריות והפריה חוץ גופית
ביה"ח בילינסון

RABIN MEDICAL CENTER
BEILINSON • HASHARON

Outline

- Definition
- Guidelines/ opinions
- Statistics
- Complications
  - Obstetrical/neonatal
  - maternal

Advanced maternal age

- The age cut-off ? not uniformly defined
- Historically, AMA was defined as maternal age **≥ 35 years**
  - risk of fetal Down syndrome and the risk of amniocentesis
- Other studies:
  - AMA- age **≥ 40** or greater
  - "very advanced maternal age" – age **≥45** years or **≥50** years, depending on the study

- Fitzpatrick KE, Tuffnell D, Kurinczuk JJ, Knight M. Pregnancy at very advanced maternal age: a UK population-based cohort study. BJOG 2016.
- Waldenström U, Cnattingius S, Vixner L, Norman M. Advanced maternal age increases the risk of very preterm birth, irrespective of parity: a population-based register study. BJOG 2016.

- גיל מקסימלי של אישה לקבלת תרומת ביציות הוא **51** שהוא גיל החציון של הפסקת מחזורי הוסת .
יש לציין כי הסיכון לאישה במהלך ההריון והלידה בגיל מתקדם מעבר לגיל 50 גבוה יותר, וידוע גם על מקרי תמותה במהלך ההריון.

- **<u>למרות האמור</u>** -אפשרי לטפל בנשים מבוגרות יותר תוך מידע על סיכויי הצלחת הטיפול והסיכונים הכרוכים בטיפול ובהריון ולידה וכל זאת לא על חשבון המערכת הציבורית.

- משהוחלט על מתן טיפול לאישה מעל גיל 45 יש להקפיד על ברור מקיף של מצבה הבריאותי לשלילת הסיכונים במהלך הטיפול וההיריון.

חוק תרומת ביציות- 2010

- **בקשה לתרומה למטרת הולדה**
- "מצא רופא מטפל כי מטופלת שהיא תושבת ישראל, **שמלאו לה 18 שנים וטרם מלאו לה 54 שנים**,.....

ASRM PAGES

Oocyte or embryo donation to women of advanced reproductive age: an Ethics Committee opinion

Ethics Committee of the American Society for Reproductive Medicine
American Society for Reproductive Medicine, Birmingham, Alabama

2016

- Physicians should perform a thorough medical evaluation designed to assess the physical fitness of a patient for pregnancy before deciding to attempt transfer of embryos to any woman of **advanced reproductive age (>45 years).**

- Embryo transfer should be strongly discouraged or denied to women of ARA with underlying conditions that increase or exacerbate obstetrical risks.

- Because of concerns related to the high-risk nature of pregnancy, as well as longevity, **treatment of women over the age of 55 should generally be discouraged.**

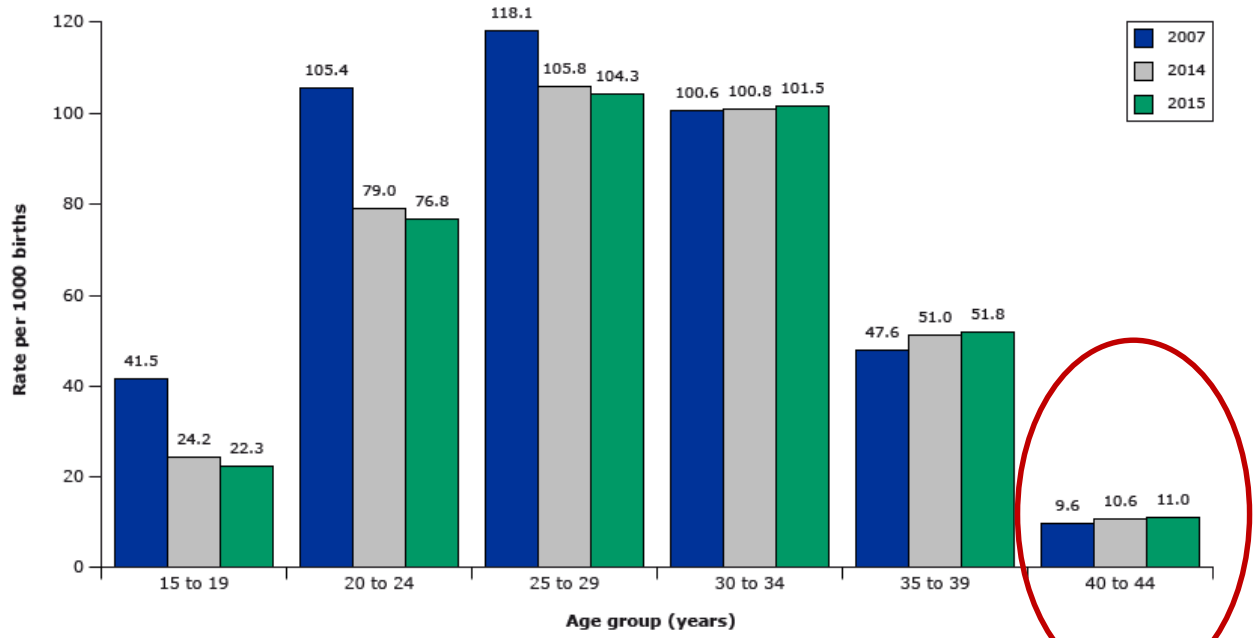
Change in birth rate per 1000 women from 1990 to 2014 by age cohort

	15 to 19	20 to 24	25 to 29	30 to 34	35 to 39	40 to 44	45 to 49
1990	59.9	116.5	120.2	80.8	31.9	5.5	0.2
2014	24.2	79.0	105.8	100.8	51.0	10.6	0.8

Reproduced from: Hamilton BE, Martin JA, Osterman MJ, Curtin SC, Matthews TJ. Births: Final data for 2014. Natl Vital Stat Rep 2015; 64:1.

Graphic 110497 Version 1.0

Birth rates by maternal age cohort from 2007 to 2015 in the United States

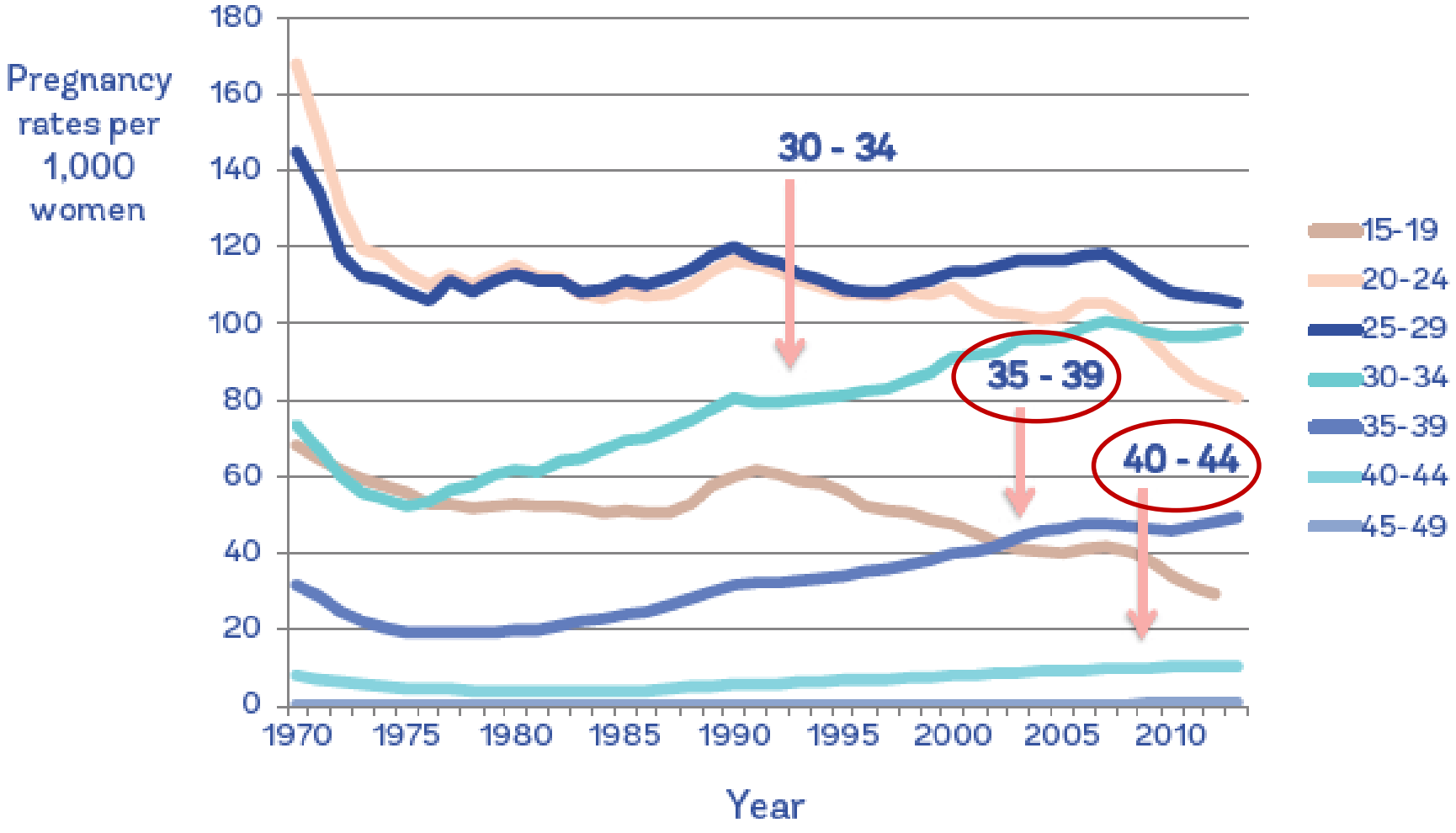


NOTE: For each age group, differences are significant from 2007 to 2014, 2007 to 2015, and 2014 to 2015 (p <0.05).

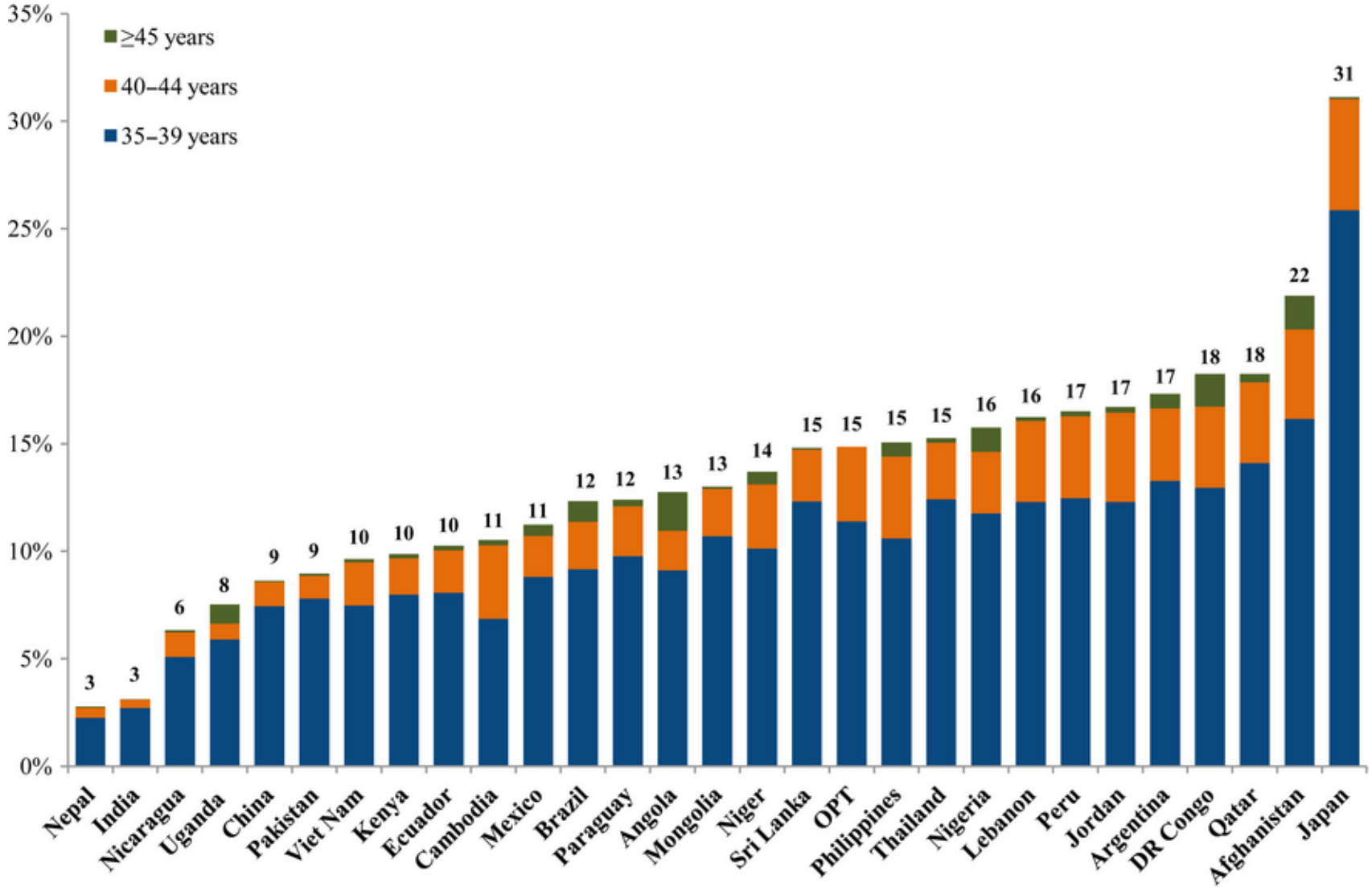
Reproduced from: Martin JA, Hamilton BE, Osterman MJ. Births in the United States, 2015. NCHS Data Brief 2016; 258:1.

Graphic 110511 Version 1.0

Figure 1: Increase in Pregnancy Rates among Women Age 30 and Older



Prevalence of women with advanced maternal age by country



Advanced maternal age and pregnancy outcomes: a multicountry assessment, Volume: 121, Issue: s1, Pages: 49-56, First published: 18 March 2014,

הלשכה המרכזית לסטטיסטיקה
Central Bureau of Statistics
دائرة الإحصاء المركزية

מדינת ישראל

הודעה לתקשורת

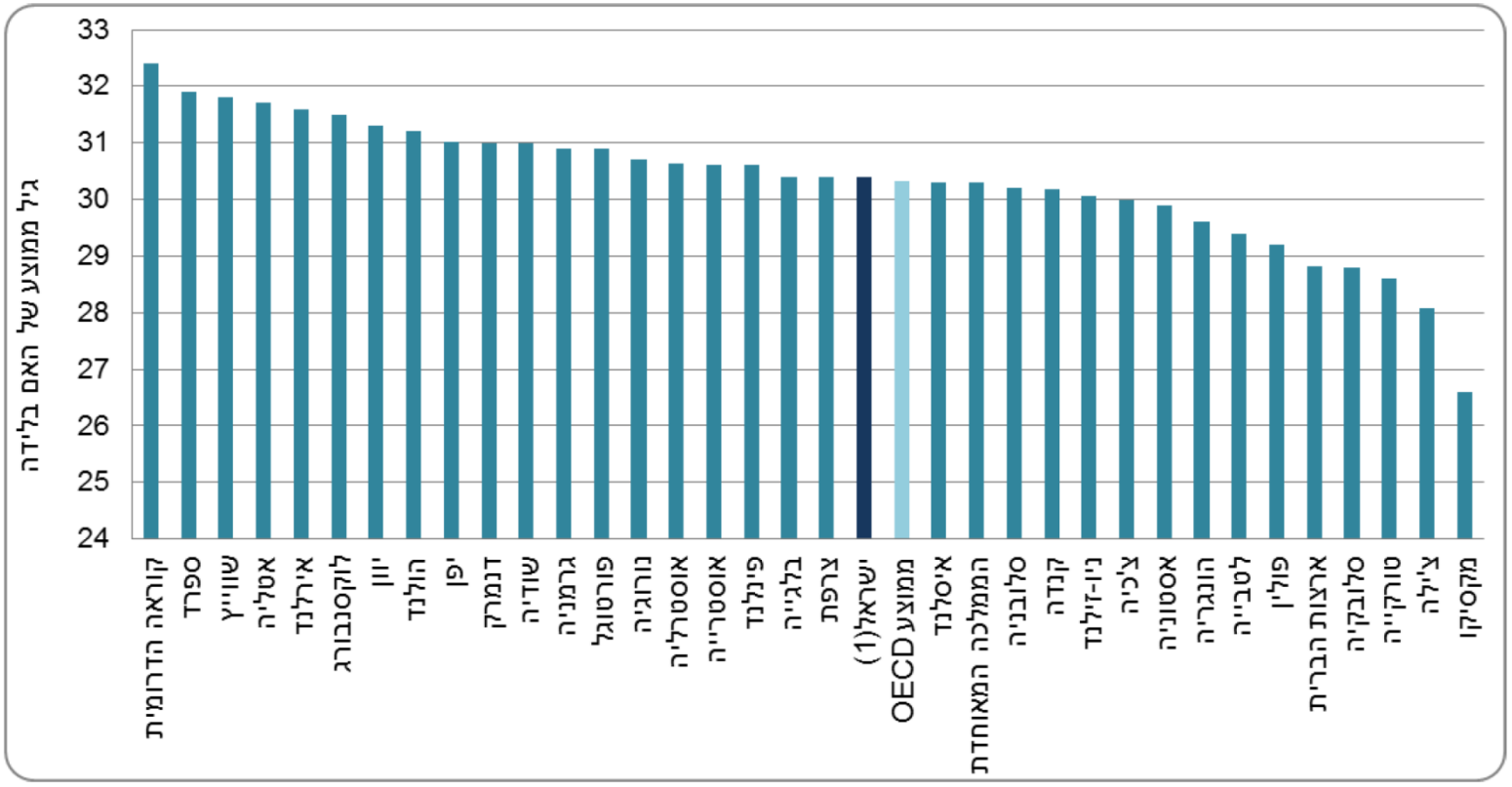
אתר: www.cbs.gov.il דוא"ל: info@cbs.gov.il פקס: 02-6521340

ירושלים, כ"ו באדר, תשע"ח
13 במרץ, 2017
073/2018

ילודה ופריון בישראל 2016

Births and Fertility in Israel, 2016

תרשים 3 - גיל ממוצע של האם בלידה במדינות ה-OECD, 2015



(1) נתון לשנת 2016

ישראל- למ"ס

משנת 2000 הייתה עלייה חדה יחסית בגיל האם הממוצע בלידה, והוא עלה בשנה וחמישה חודשים והגיע ל- **30.4** בשנת 2016 .

לידה הראשונה : גיל 25.7 ב- 2000 ל- 27.6 ב- 2016

נשים בגיל 30 :40.2% בשנת 2000, 51.5% בשנת 2016 .

נשים בגילים 30-34 :מ- 161.8 ילודים לכל 1,000 נשים ל- 183.4

3.15

לידות חי, לפי גיל האם ולפי תכונות נבחרות של האם

LIVE BIRTHS, BY MOTHER'S AGE AND BY SELECTED CHARACTERISTICS OF THE MOTHER

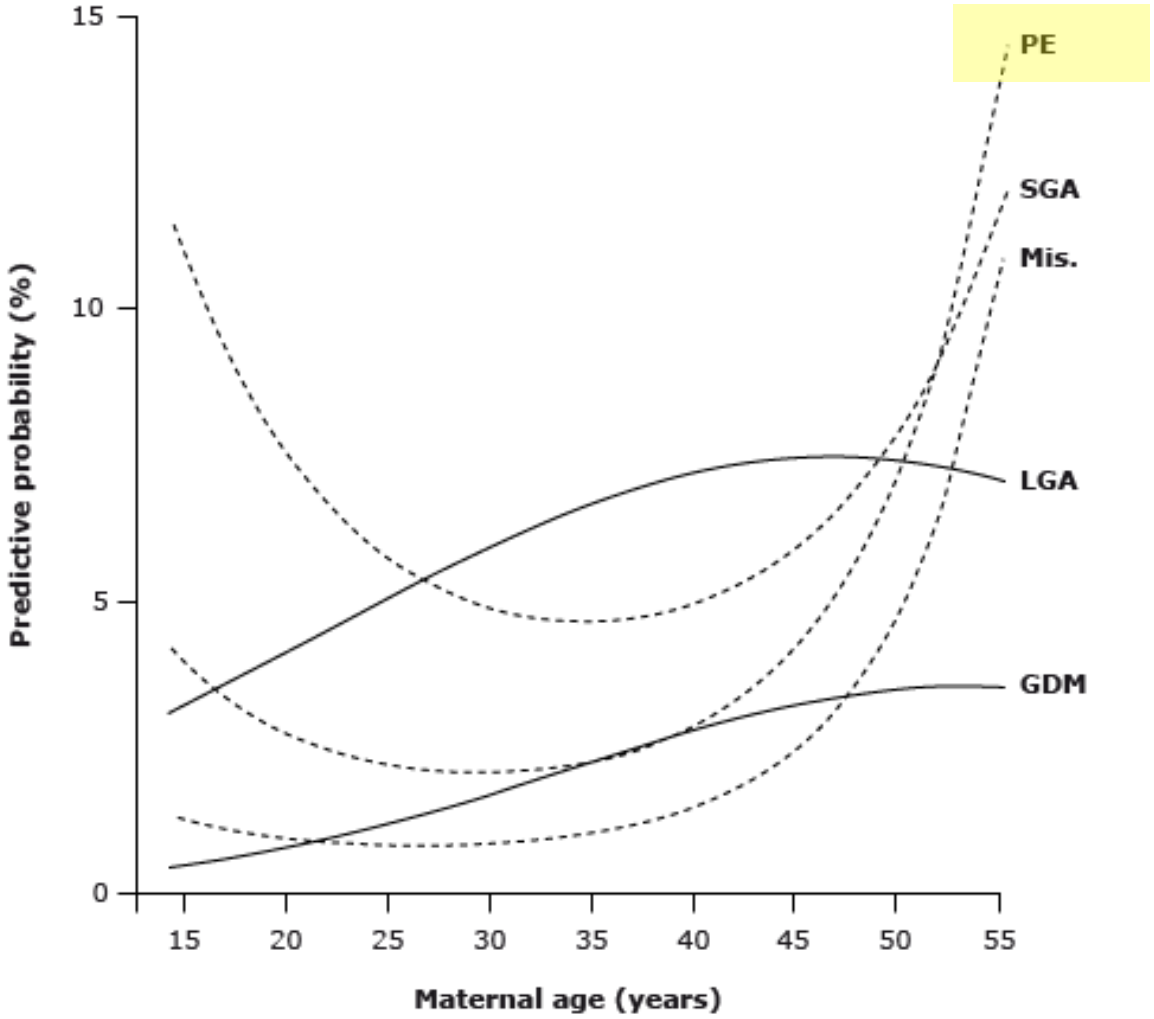
2016

Population group, religion, continent of birth and district	Mother's age								סך הכל Total	קבוצת אוכלוסייה, דת, יבשת לידה ומחוז
	לא ידוע Not known	45+	40-44	35-39	30-34	25-29	20-24	גיל האם עד 19 Up to 19		
GRAND TOTAL(1)(2)	**185**	**826**	**8,444**	**30,505**	**53,559**	**52,930**	**32,003**	**2,953**	**181,405**	**סך כולל(1)(2)**
		0.5%	**4.6%**	**16.8%**						
POPULATION GROUP										**קבוצת אוכלוסייה**
Jews and others - total(2)	*82*	*773*	*7,424*	*26,550*	*45,347*	*39,231*	*19,033*	*960*	*139,400*	*יהודיות ואחרות - סך הכל(2)*
Israeli born	24	608	5,831	20,843	35,269	31,069	16,745	838	111,227	ילידות ישראל
Born abroad - total	28	165	1,593	*5,707*	10,078	8,162	2,288	122	28,143	ילידות חו"ל - סך הכל
Asia	1	13	70	*185*	258	168	59	7	761	אסיה
Africa	4	35	202	*809*	1,243	980	260	24	3,557	אפריקה
Europe	19	84	1,027	*3,720*	7,109	5,767	1,425	70	19,221	אירופה
America	4	33	294	*993*	1,468	1,247	544	21	4,604	אמריקה
Arabs(1)	*103*	*53*	*1,020*	*3,955*	*8,212*	*13,699*	*12,970*	*1,993*	*42,005*	*ערביות(1)*

The Israeli National IVF Registry-2017

	Own Oocyte		
Age	**Total**	**Fresh**	**Thawed**
	%	**%**	**%**
< 35	40.7	36.0	49.9
35 – 39	25.6	26.6	23.8
40 – 42	20.8	23.7	15.1
43+	12.9	13.8	11.2

Maternal age and adverse pregnancy outcome

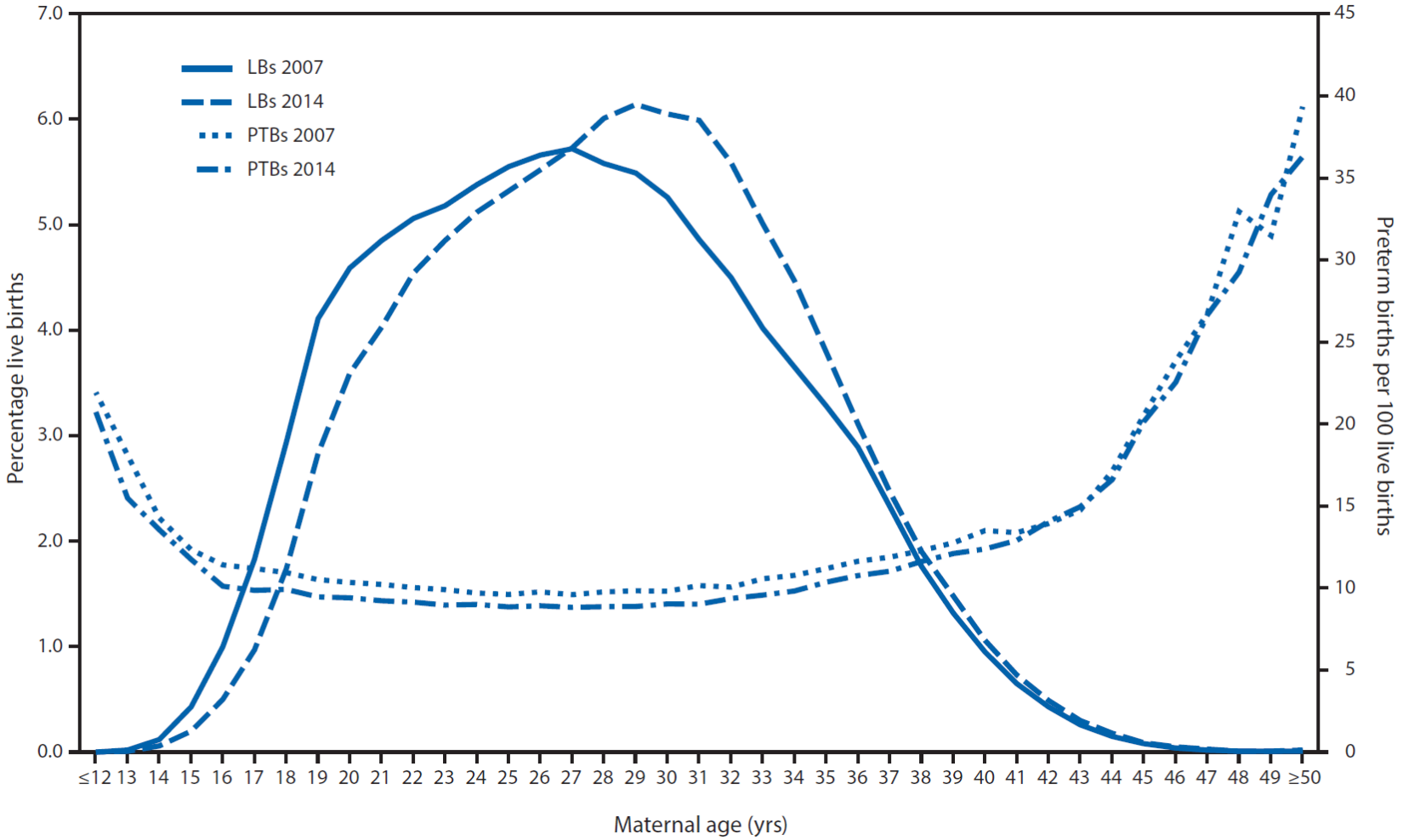


Predictive probability of miscarriage >11 weeks (Mis), preeclampsia (PE), small for gestational age (SGA) fetus, gestational diabetes mellitus (GDM), and large for gestational age (LGA) fetus plotted against maternal age.

From: Khalil A, Syngelaki A, Maiz N, et al. Maternal age and adverse pregnancy outcome: a cohort study. Ultrasound Obstet Gynecol 2013; 42:634.

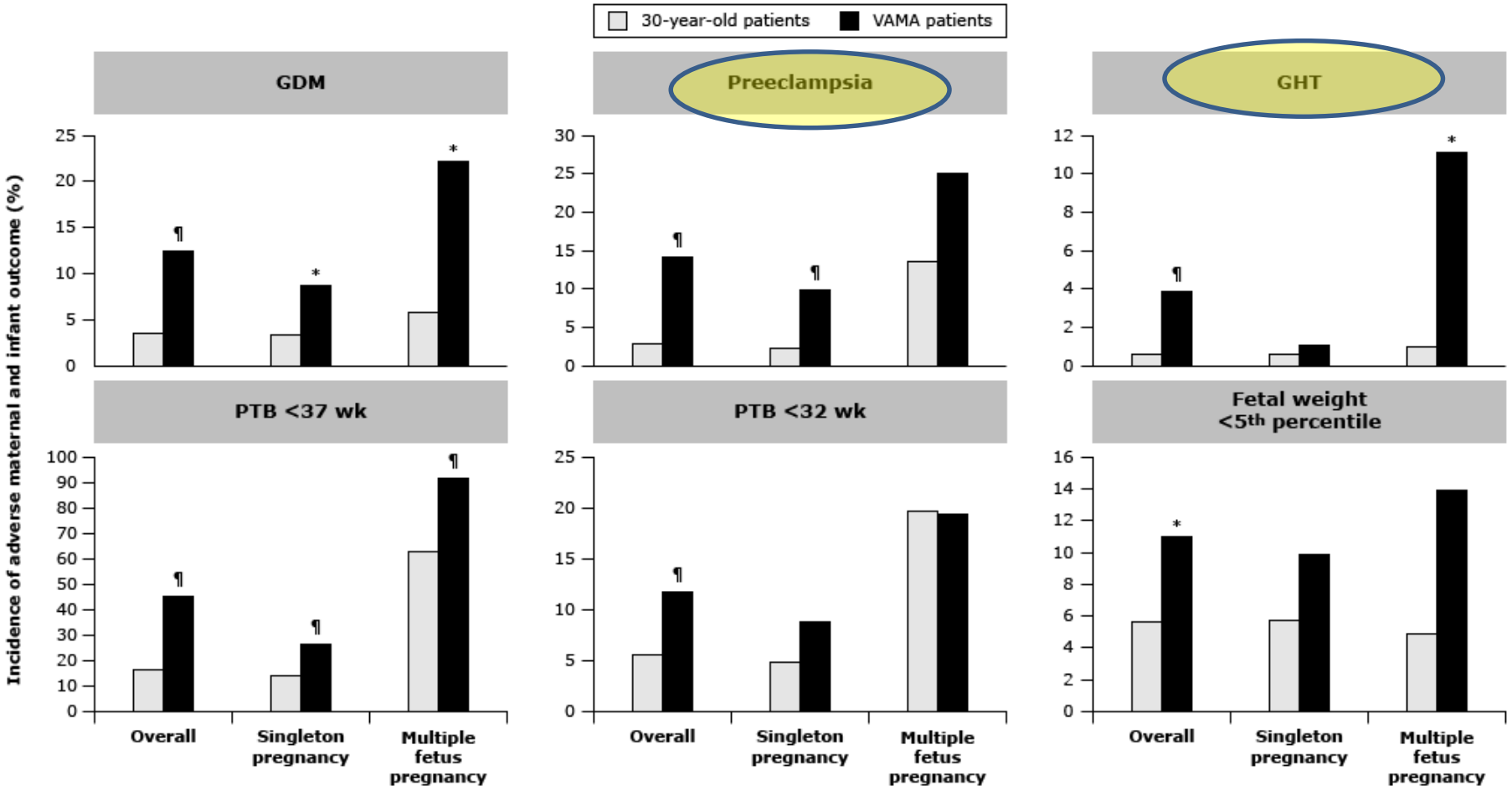
Preterm births

FIGURE. Percentages of live births (LBs) and preterm births (PTBs), by maternal age — United States, 2007 and 2014



Obstetrical complications (cont)

Risks of very advanced maternal age pregnancies



Incidence of adverse maternal and infant outcome in very advanced maternal age patients and 30-year-old patients within the overall group and within subgroups (singleton and multiple-fetus pregnancies).

Congenital malformations

Multivariable analysis

Age (years)	OR (95%CI)	P-Value
<35	Reference	
35-<40	0.95 (0.7, 1.3)	NS
40-<43	0.98 (0.6, 1.6)	NS
43+	1.13 (0.6, 2.3)	NS
Cycle type	**OR (95%CI)**	**P-Value**
Fresh	Reference	
Thawed	1.12 (0.8, 1.5)	NS
Birth weight (Gram)	**OR (95%CI)**	**P-Value**
+2500	Reference	
1500-2499	1.2 (0.9, 1.8)	NS
<1500	5.6 (3.6, 8.7)	<.0001
Plurality	**OR (95%CI)**	**P-Value**
Singletons birth	Reference	
Multiple birth	0.9 (0.6, 1.2)	NS

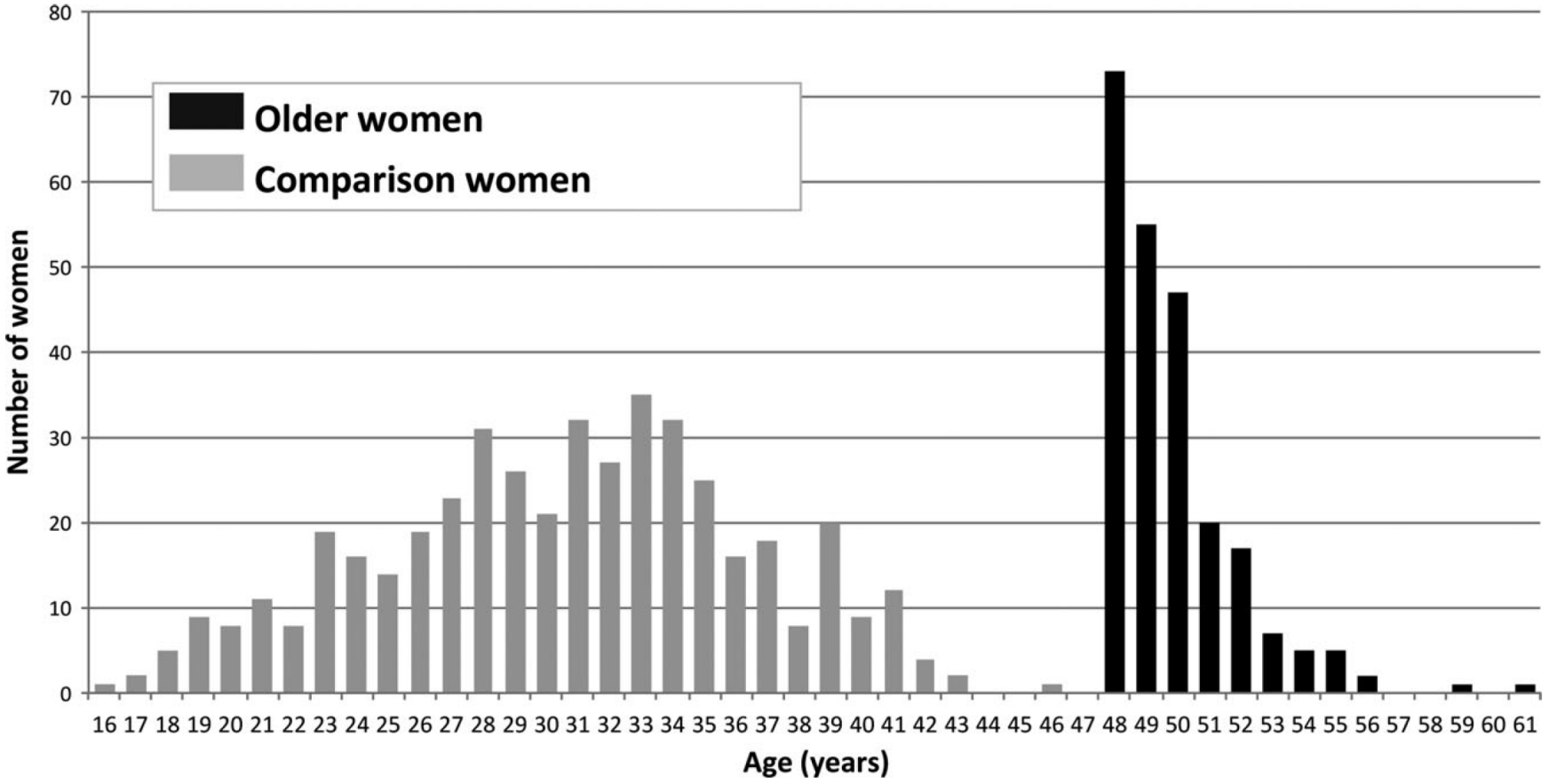
Confounders?

- Women of advanced maternal age have higher
  - **multiple gestation rates**……
  - other confounders

Pregnancy at very advanced maternal age: a UK population-based cohort study

KE Fitzpatrick,[a] D Tuffnell,[b] JJ Kurinczuk,[a] M Knight[a]

BJOG 2016



- Older women were more likely than comparison women:
  - **overweight** (33% versus 23%, P = 0.0011)
  - **obese** (23% versus 19%, P = 0.0318),
  - **nulliparous** (53% versus 44%, P = 0.0299),
  - **pre-existing medical conditions** (44% versus 28%, P < 0.0001),
  - **multiple pregnancy** (18% versus 2%, P < 0.0001),
  - **ART** (78% versus 4%, P < 0.0001).

- **Univariable analysis** and after **adjustment for demographic and medical factors**

- Higher rate of complications:
  - hypertensive disorders, gestational diabetes, postpartum haemorrhage, caesarean delivery, iatrogenic and spontaneous preterm delivery

	Number (%)* of older women (n = 233)	Number (%)* of comparison women (n = 454)	Unadjusted OR (95% CI)	P-value
Any gestational hypertensive disorder				
No	196 (85)	430 (95)	1	
Yes	34 (15)	24 (5)	**3.11 (1.79–5.38)**	**<0.0001**
Any gestational hypertensive disorder managed by early delivery				
No	219 (95)	442 (97)	1	
Yes	11 (5)	12 (3)	1.85 (0.80–4.26)	0.1482
Pregnancy induced hypertension				
No	209 (91)	440 (97)	1	
Yes	21 (9)	14 (3)	**3.16 (1.57–6.33)**	**0.0012**
Preeclampsia				
No	217 (94)	444 (98)	1	
Yes	13 (6)	10 (2)	**2.66 (1.15–6.16)**	**0.0225**
Gestational diabetes				
No	188 (82)	436 (96)	1	
Yes	42 (18)	18 (4)	**5.41 (3.04–9.65)**	**<0.0001**
Gestational diabetes requiring insulin				
No	221 (96)	452 (100)	1	
Yes	9 (4)	2 (0)	**9.2 (1.97–42.96)**	**0.0047**
Placenta praevia				
No	222 (97)	453 (100)		
Yes	8 (3)	0 (0)		
Placental abruption				
No	226 (99)	451 (100)	1	
Yes	3 (1)	2 (0)	2.99 (0.50–18.04)	0.2316
Diagnosed postpartum haemorrhage				
No	169 (74)	385 (85)	1	
Yes	59 (26)	69 (15)	**1.95 (1.32–2.88)**	**0.0009**
Diagnosed postpartum haemorrhage requring blood transfusion				
No	210 (94)	441 (98)	**1**	
Yes	14 (6)	8 (2)	**3.67 (1.52–8.90)**	**0.0039**
Thrombotic event				
No	229 (100)	453 (100)		
Yes	0 (0)	1 (0)		
Labour induced				
No	156 (69)	321 (71)	1	
Yes	71 (31)	133 (29)	1.1 (0.78–1.55)	0.5945
Caesarean delivery				
No	50 (22)	305 (67)	1	
Yes	178 (78)	149 (33)	**7.29 (5.03–10.55)**	**<0.0001**
Gestational age at delivery (weeks)				
Term (37+ weeks)	176 (78)	420 (93)	1	
Iatrogenic preterm (<37 weeks)	32 (14)	17 (4)	**4.49 (2.43–8.30)**	**<0.0001**
Spontaneous preterm (<37 weeks)	18 (8)	17 (4)	**2.53 (1.27–5.02)**	**0.0081**
Admitted to ITU				
No	224 (97)	453 (100)	1	
Yes	6 (3)	1 (0)	**12.13 (1.45–101.40)**	**0.0212**
In nulliparous women				
Caesarean delivery				
No				
Yes				
In women parity 1+				
Caesarean delivery				
No				
Yes				

- However,
  - adjustment for **multiple pregnancy** or
  - **use of assisted conception**
  - attenuated most effects
  - with significant associations remaining only with
    - **gestational diabetes** (aOR 4.81, 95% CI 1.93–12.00),
    - **caesarean delivery** (aOR 2.78, 95% CI 1.44–5.37)
    - **admission to an intensive care unit** (aOR 33.53, 95% CI 2.73–412.24).

Hypertension and early menopause after the use of assisted reproductive technologies in women aged 43 years or older: Long-term follow-up study

Rosato et al, 2016

- Healthy women who conceived by ART (72) and controls (80)
- women ≥ 43 years, who delivered
- In the ART group, SBP, DBP and hypertension were higher at three days, six months, and three years after delivery
- Menopausal age was significantly lower

OBSTETRICS

Pregnancy outcome at extremely advanced maternal age

Yariv Yogev, MD; Nir Melamed, MD; Ron Bardin, MD; Kinneret Tenenbaum-Gavish, MD; Gadi Ben-Shitrit, MD; Avi Ben-Haroush, MD

AJOG 2010

TABLE 1

Demographic and obstetric characteristics for the study and control groups

Variable	Overall (n = 5487)	Group 1: 20-29 y (n = 1770)	Group 2: 30-39 y (n = 1770)	Group 3: 40-44 y (n = 1770)	Group 4: ≥45 y (n = 177)	*P* value
Maternal age, y[a]	34.2 ± 7.0	26.1 ± 2.5	33.7 ± 2.6	41.5 ± 1.2	47.4 ± 2.6	< .001 (4≠3≠2≠1)
Gravidity[a]	3.6 ± 2.7	2.0 ± 1.3	3.4 ± 1.9	5.1 ± 3.2	4.3 ± 3.4	< .001 (3≠4≠2≠1)
Parity[a]	1.3 ± 1.1	0.4 ± 0.8	1.0 ± 0.9	2.4 ± 1.6	2.2 ± 2.0	< .001 (3,4≠2≠1)
Nulliparity, n (%)	2895 (52.8)	1287 (72.7)	954 (53.9)	585 (33.1)	69 (39)	< .001
Maternal obesity, n (%)	1139 (21)	336 (19)	354 (20)	407 (23)	42 (24)	.07
Multifetal gestations, n (%)	169 (3.1)	41 (2.3)	64 (3.6)	52 (2.9)	12 (6.8)	.004
Oocyte donation, n (%)	NA	NA	NA	NA	141 (79)	
Previous cesarean delivery, n (%)	752 (13.8)	91 (5.1)	246 (13.9)	375 (21.2)	40 (22.6)	< .001
Chronic hypertension, n (%)	76 (1.4)	2 (0.1)	14 (0.8)	48 (2.7)	12 (6.8)	< .001
Pregestational diabetes mellitus, n (%)	66 (1.2)	14 (0.8)	19 (1.1)	25 (1.4)	8 (4.5)	< .001
Gestational diabetes mellitus, n (%)	309 (5.6)	25 (1.4)	74 (4.2)	180 (10.2)	30 (17.0)	< .001
Gestational hypertension, n (%)	149 (2.7)	36 (2.0)	41 (2.3)	56 (3.2)	16 (9.0)	< .001
Preeclampsia toxemia, n (%)	99 (1.8)	12 (0.7)	26 (1.5)	42 (2.4)	19 (10.7)	< .001
Oligohydramnios, n (%)	145 (2.6)	43 (2.4)	39 (2.2)	55 (3.1)	8 (4.5)	.04

TABLE 2

Delivery outcome for the study and comparison groups

Variable	Overall (n = 5487)	Group 1: 20-29 y (n = 1770)	Group 2: 30-39 y (n = 1770)	Group 3: 40-44 y (n = 1770)	Group 4: ≥45 y (n = 177)	*P* value
Gestational age, wk[a]	38.8 ± 2.2	39.2 ± 2.0	38.9 ± 2.2	38.5 ± 2.4[b]	37.6 ± 2.5	< .001 (4≠3≠2,1)
<37, n (%)	541 (10.3)	130 (7.7)	152 (9.1)	221 (12.8)	38 (21.5)	< .001
<34, n (%)	149 (2.8)	27 (1.6)	49 (2.9)	62 (3.6)	11 (6.2)	< .001
<32, n (%)	76 (1.4)	15 (0.9)	23 (1.4)	34 (2.0)	4 (2.3)	.04
Spontaneous preterm delivery (<37 wk), n (%)	255 (47)	75 (58)	82 (54)	92 (42)	6 (15)	.01
Delivery mode, n (%)						
Normal vaginal delivery	3655 (66.6)	1384 (78.2)	1275 (72.0)	965 (54.5)	31 (17.5)	< .001
Instrumental delivery[b]	255 (4.6)	113 (6.4)	87 (4.9)	49 (2.8)	6 (3.4)	< .001
Cesarean delivery	1587 (28.9)	277 (15.7)	412 (23.3)	759 (42.9)	139 (78.5)	< .001
Elective cesarean delivery	551 (37.5)	55 (21.6)	131 (35.5)	293 (41.5)	72 (51.8)	< .001
Indication for cesarean delivery, n (%)						
Breech	265 (16.7)	55 (19.9)	79 (19.2)	101 (13.3)	30 (21.6)	.006
Multifetal gestation	75 (4.7)	13 (4.7)	28 (6.8)	26 (3.4)	8 (5.8)	.07
Dystocia	56 (3.5)	23 (8.3)	11 (2.7)	16 (2.1)	6 (4.3)	< .001
Nonreassuring fetal heart rate	79 (5.0)	14 (5.1)	13 (3.2)	40 (5.3)	12 (8.6)	.04
Placenta previa	35 (2.2)	2 (0.7)	10 (2.4)	20 (2.6)	3 (2.2)	.3
Previous cesarean delivery	461 (29.0)	43 (15.5)	127 (30.8)	268 (35.3)	23 (16.5)	< .001
Macrosomia	114 (7.2)	29 (10.5)	28 (6.8)	49 (6.5)	8 (7.0)	.13
Maternal request	NA	NA	NA	NA	20 (14.4)	
Preeclampsia	38 (2.4)	3 (1.1)	12 (2.9)	17 (2.2)	6 (4.3)	.18
Other	444 (28.0)	95 (34.3)	104 (25.2)	222 (29.2)	23 (16.5)	.001
Placenta previa	49 (0.9)	3 (0.2)	11 (0.6)	25 (1.4)	10 (5.6)	< .001
Placental abruption	37 (0.7)	6 (0.3)	12 (0.7)	17 (1.0)	2 (1.1)	.13
3rd-4th degree vaginal tears	26 (0.7)	9 (0.6)	15 (1.1)	2 (0.2)	0	.054
Postpartum hemorrhage	76 (1.4)	18 (1.0)	21 (1.2)	30 (1.7)	7 (4.0)	.007
Blood transfusions	24 (0.4)	3 (0.2)	5 (0.3)	14 (0.8)	2 (1.1)	.012
Postpartum fever	183 (3.3)	83 (4.7)	43 (2.4)	27 (1.5)	22 (12.5)	< .001
Prolonged hospitalization[c]	111 (2.0)	23 (1.3)	36 (2.0)	40 (2.3)	12 (7.2)	< .001
Intensive care unit admission	53 (0.96)	17 (1.0)	14 (0.8)	19 (1.1)	3 (1.7)	.1

TABLE 5

Pregnancy outcome in the study group: subgroup analysis

Variable	Group 4		*P* value
	45-49 y (n = 150)	≥50 y (n = 27)	
Oocyte donation, n (%)	114 (76)	27 (100)	.01
Chronic hypertension, n (%)	8 (5.3)	4 (14.8)	.07
Pregestational diabetes mellitus, n (%)	8 (5.3)	0	.47
Gestational diabetes mellitus, n (%)	22 (14.7)	8 (29.6)	.01
Preeclampsia/pregnancy-induced hypertension, n (%)	25 (16.7)	9 (33.3)	.04
Gestational age, wks[a]	37.8 ± 2.3	36.3 ± 3.1	.006
<37, n (%)	28 (18.7)	10 (37.0)	.03
<34, n (%)	7 (4.7)	4 (14.8)	.04
<32, n (%)	2 (1.3)	2 (7.4)	.04
Cesarean delivery, n (%)	116 (77.3)	23 (85.2)	.36
Placenta previa, n (%)	9 (6.0)	1 (3.7)	.6
Postpartum hemorrhage, n (%)	7 (4.7)	0	.25
Blood transfusions, n (%)	2 (1.3)	0	.54
Postpartum fever, n (%)	23 (15.3)	7 (25.9)	.17
Prolonged hospitalization, n (%)[b]	9 (6.4)	3 (11.5)	.35
Birthweight, g[a]	3001 ± 625	2737 ± 697	.04
<2500, n (%)	23 (15.3)	7 (25.9)	.17
<1500, n (%)	2 (1.3)	1 (3.7)	.38
Neonatal intensive care unit admission, n (%)	16 (10.1)	3 (11.1)	.10
Metabolic complications, n (%)[c]	7 (4.7)	1 (3.7)	.8

Examining the EVIDENCE

Are women of advanced maternal age at increased risk for severe maternal morbidity?

Yes. Severe maternal morbidities, including renal failure, shock, amniotic fluid embolism, and cardiac morbidity, **were significantly increased for women older than 39 years,** according to results of a study that included more than 800,000 singleton births over 10 years. The observed increases in maternal morbidity persisted after controlling for assisted conception and comorbid medical conditions.

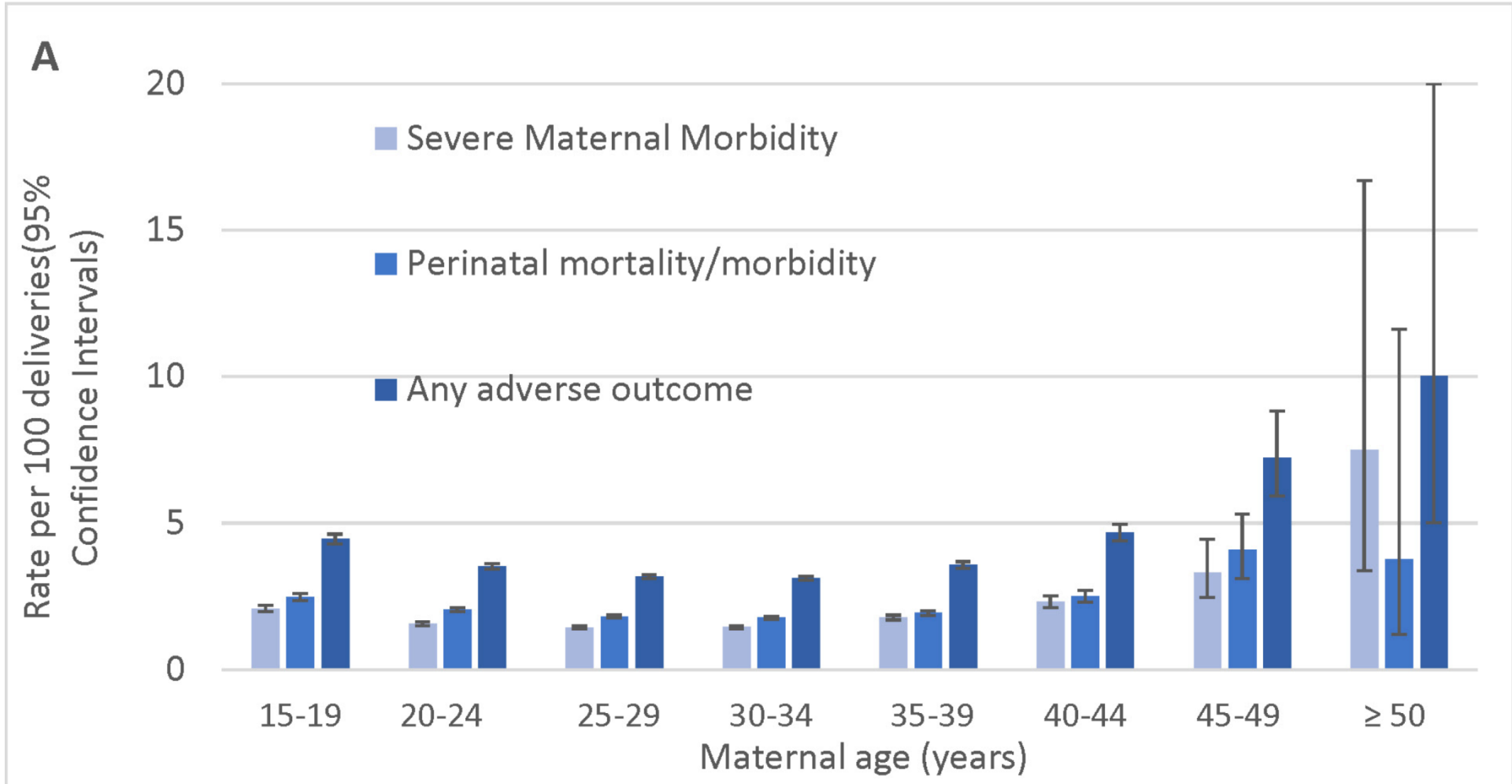
- ***Lisonkova S, Potts J, Muraca GM, et al. Maternal age and severe maternal morbidity: a population-based retrospective cohort study. PLoS Med. 2017;14(5):e1002307.***

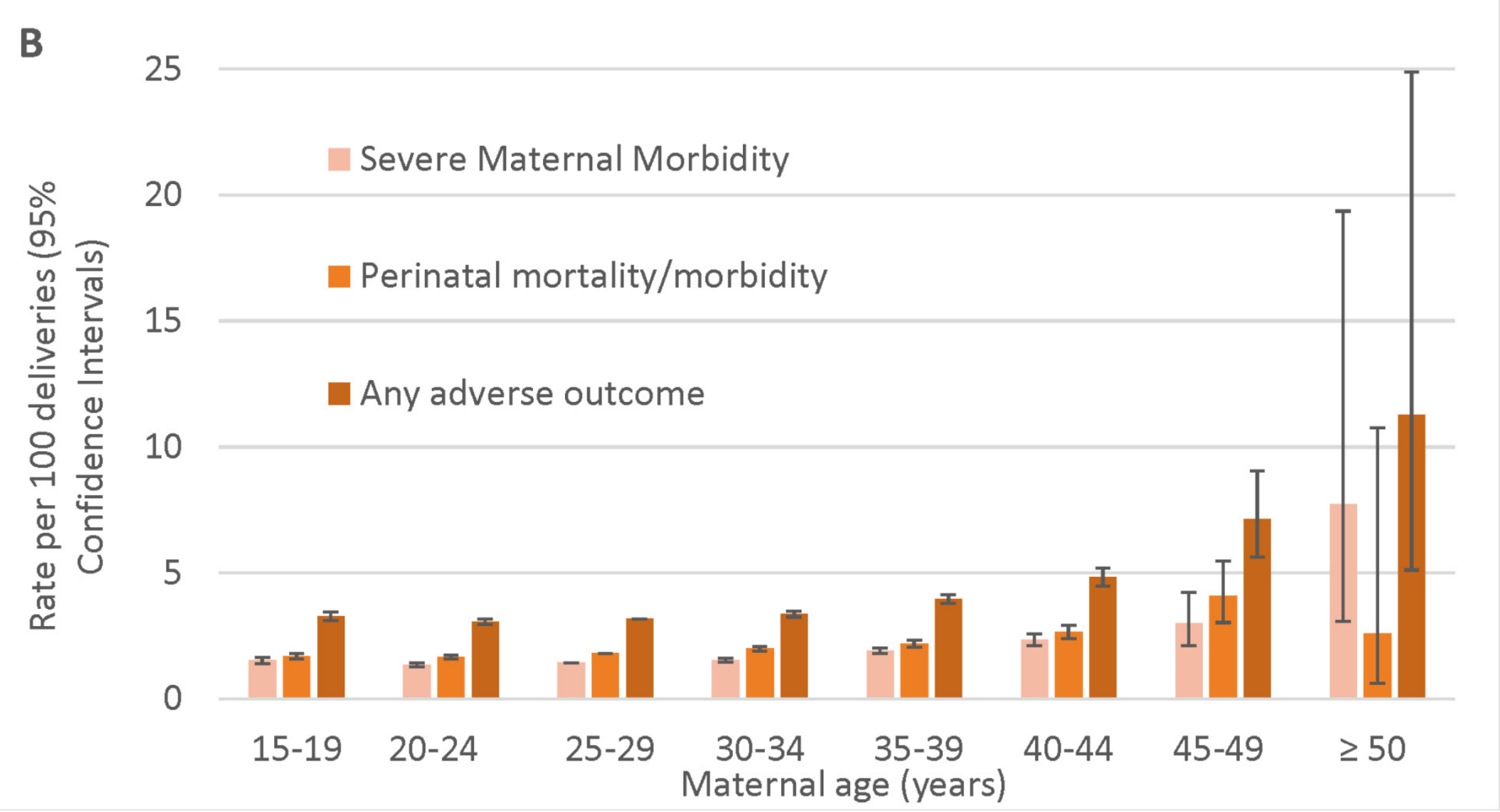
PLOS | MEDICINE

RESEARCH ARTICLE

Maternal age and severe maternal morbidity: A population-based retrospective cohort study

Sarka Lisonkova[1,2]*, Jayson Potts[3], Giulia M. Muraca[2], Neda Razaz[4], Yasser Sabr[5], Wee-Shian Chan[3], Michael S. Kramer[6,7]





- Adjusted for demographic and pre-pregnancy factors; singleton births, Washington State, US, 2003±2013.

Table 4. The association between maternal age and severe maternal morbidity and adverse birth outcomes among singleton births, Washington State, US, 2003–2013.

Outcome	Measure	OR[a] by maternal age						AOR[b] by maternal age					
		15–19 y	20–24 y	30–34 y	35–39 y	40–44 y	45–49 y	15–19 y	20–24 y	30–34 y	35–39 y	40–44 y	45–49 y
Severe maternal morbidity													
Antepartum hemorrhage[c]	OR or AOR	0.7	0.8	0.9	1.4	2.1	3.5	0.8	0.7	0.8	1.2	1.5	1.6
	95% CI	0.4–0.9	0.6–0.9	0.7–1.1	1.1–1.7	1.5–2.9	1.3–9.4	0.5–1.1	0.6–0.9	0.7–1.1	1.0–1.6	1.0–2.2	0.4–6.6
Respiratory morbidity	OR or AOR	1.1	1.0	1.0	1.4	2.2		0.7	0.8	1.1	1.4	2.5	
	95% CI	0.8–1.4	0.9–1.2	0.9–1.2	1.1–1.7	1.73.0		0.5–1.0	0.7–1.0	0.9–1.4	1.1–1.8	1.8–3.4	
AFE	OR or AOR	1.0	1.0	1.7	2.6	9.0		0.8	0.7	1.6	2.3	8.0	
	95% CI	0.2–4.5	0.3–2.8	0.7–4.2	1.0–6.6	3.3–25		0.1–4.0	0.2–2.4	0.6–4.0	0.8–6.2	2.7–23.7	
Thromboembolism/DVT	OR or AOR	0.9	0.8	1.0	1.1	1.6		0.8	0.7	1.0	1.2	1.6	
	95% CI	0.6–1.3	0.6–1.0	0.7–1.2	0.8–1.5	1.0–2.5		0.5–1.2	0.6–1.0	0.8–1.3	0.9–1.6	1.0–2.6	
Cerebrovascular morbidity	OR or AOR	0.8	1.0	1.1	1.2	2.3	3.1	0.3	0.7	1.4	1.6	3.2	4.8
	95% CI	0.4–1.5	0.6–1.4	0.8–1.6	0.8–1.8	1.3–4.2	0.4–22	0.2–0.7	0.4–1.0	0.9–2.0	1.0–2.5	1.7–6.0	0.7–34.6
All acute cardiac morbidity	OR or AOR	0.6	0.9	1.2	1.7	3.3		0.5	0.8	1.3	1.8	3.8	
	95% CI	0.3–1.0	0.7–1.2	0.9–1.5	1.3–2.2	2.3–4.8		0.3–0.9	0.6–1.0	1.0–1.7	1.3–2.5	2.5–5.7	
Cardiomyopathy	OR or AOR	0.8	1.0	1.7	1.1	3.6		0.6	0.7	2.0	1.0	4.7	
	95% CI	0.3–2.2	0.5–2.0	1.0–3.0	0.5–2.4	1.5–8.6		0.2–2.0	0.3–1.5	1.1–3.6	0.4–3.6	1.9–11.4	

- Adjusted for race, marital status, body mass index, drug use, smoking, parity, maternal education, type of health insurance, year of childbirth, and fetal sex.

Table 4. The association between maternal age and severe maternal morbidity and adverse birth outcomes among singleton births, Washington State, US, 2003–2013.

Outcome	Measure	OR[a] by maternal age						AOR[b] by maternal age					
		15–19 y	20–24 y	30–34 y	35–39 y	40–44 y	45–49 y	15–19 y	20–24 y	30–34 y	35–39 y	40–44 y	45–49 y
Severe maternal morbidity													
Severe PPH[c]	OR or AOR	1.5	1.1	1.0	1.2	1.3	2.5	1.2	1.0	1.0	1.2	1.2	1.9
	95% CI	1.3–1.7	1.0–1.2	0.9–1.1	1.1–1.3	1.1–1.6	1.4–4.5	1.0–1.4	0.9–1.1	0.9–1.1	1.1–1.4	0.9–1.5	0.9–3.8
Maternal sepsis	OR or AOR	2.2	1.4	0.9	0.9	1.0		1.2	1.1	1.0	1.1	1.2	
	95% CI	1.9–2.5	1.3–1.6	0.8–1.0	0.8–1.1	0.8–1.3		1.1–1.4	1.0–1.3	0.8–1.1	0.9–1.2	0.9–1.6	
Renal failure	OR or AOR	1.2	0.8	1.0	1.6	2.5	13.2	1.1	0.7	1.1	1.7	2.7	15.9
	95% CI	0.6–2.3	0.5–1.3	0.7–1.6	1.0–2.6	1.3–5.0	4.1–42.7	0.5–2.2	0.4–1.3	0.7–1.7	1.0–2.8	1.3–5.6	4.8–52
Obstetric shock	OR or AOR	1.1	0.7	1.7	2.9	3.7		0.8	0.8	1.6	2.6	2.9	
	95% CI	0.5–2.4	0.4–1.4	1.1–2.8	1.7–4.7	1.8–7.6		0.3–2.1	0.4–1.4	1.0–2.7	1.5–4.5	1.3–6.6	
Complications[d]	OR or AOR	0.8	0.8	1.2	1.5	1.7	4.2	0.6	0.7	1.3	1.7	1.6	4.7
	95% CI	0.6–1.0	0.6–0.9	1.0–1.4	1.3–1.8	1.3–2.2	2.2–8.2	0.5–0.8	0.5–0.8	1.1–1.5	1.4–2.0	1.2–2.2	2.3–9.5
DIC	OR or AOR	0.7	0.7	1.4	1.7	2.8		0.9	0.7	1.3	1.3	1.7	
	95% CI	0.4–1.4	0.4–1.1	1.0–2.0	1.1–2.5	1.5–5.0		0.4–1.9	0.4–1.2	0.91.9	0.8–2.1	0.8–3.5	
Potentially life-saving procedures	OR or AOR	1.4	1.1	1.0	1.3	1.8	3.1	1.1	0.9	1.0	1.3	1.6	2.2
	95% CI	1.3–1.5	1.0–1.1	0.9–1.1	1.2–1.4	1.6–2.0	2.1–4.4	1.0–1.2	0.9–1.0	1.0–1.1	1.2–1.4	1.4–1.9	1.4–3.5
ICU admission	OR or AOR	1.2	0.9	1.0	1.4	2.0	8.4	0.9	0.7	1.0	1.5	1.7	4.8
	95% CI	0.9–1.6	0.7–1.1	0.8–1.3	1.1–1.8	1.4–2.8	4.3–16.5	0.6–1.2	0.6–0.9	0.8–1.3	1.1–1.9	1.2–2.6	2.0–11.9
Maternal death/severe morbidity	OR or AOR	1.5	1.1	1.0	1.2	1.6	2.3	1.1	0.9	1.1	1.3	1.6	2.0
	95% CI	1.4–1.6	1.0–1.1	1.0–1.0	1.2–1.3	1.5–1.8	1.7–3.1	1.0–1.1	0.9–1.0	1.0–1.1	1.3–1.4	1.5–1.8	1.4–2.9

Factors associated with maternal mortality at advanced maternal age: a population-based case–control study

BJOG 2016

SJ McCall, M Nair, M Knight

- Age was associated with maternal mortality even after adjusting for other known risk factors

- Association between **maternal mortality** and **smoking** among women aged 35 years or older

Maternal death

- Between 2009 and 2012
  - **105** cases of maternal deaths aged ≥35 years
  - extracted from the surveillance Database
- 766 controls

- Five significant factors among women aged ≥35 years:
  - **Smoking** during pregnancy (adjusted odds ratio (aOR) 2.06, 95% CI 1.13–3.75),
  - inadequate use of **antenatal care** (aOR 23.62, 95% CI 8.79– 63.45),
  - **medical co-morbidities** (aOR 5.92, 95% CI 3.56–9.86)
  - **previous pregnancy problems** (aOR 2.06, 95% CI 1.23–3.45).

- The odds associated with death **increased by 12% per year increase in age** (aOR 1.12, 95% CI 1.02–1.22)

Journal of Human Hypertension (2010) 24, 104–110

www.nature.com/jhh

ORIGINAL ARTICLE

Maternal risk factors for hypertensive disorders in pregnancy: a multivariate approach

LCY Poon, NA Kametas, T Chelemen, A Leal and KH Nicolaides
Harris Birthright Research Centre for Fetal Medicine, King's College Hospital, London, UK

- 37 cases with early-PE
- 128 with late-PE
- 140 with GH

- 8061 cases that were unaffected by PE or GH

- Predictors of late-PE and GH were increased maternal age and BMI

Table 2 Multiple regression analysis in predicting early preeclampsia, late preeclampsia and gestational hypertension

Independent variable	*Early preeclampsia*		*Late preeclampsia*		*Gestational hypertension*	
	Adjusted OR (95% CI)	P	*Adjusted OR (95% CI)*	P	*Adjusted OR (95% CI)*	P
Maternal age in years	—	—	1.04 (1.00–1.07)	0.03	1.04 (1.01–1.07)	0.01
Body mass index in kg m^{-2}	—	—	1.10 (1.07–1.13)	<0.0001	1.10 (1.07–1.13)	<0.0001
Racial origin						
Black	3.64 (1.84–7.21)	<0.0001	2.97 (1.98–4.46)	<0.0001	—	—
Indian or Pakistani	—	—	2.66 (1.29–5.48)	0.008	—	—
Mixed	—	—	3.31 (1.55–7.06)	0.002	—	—
Parous						
No previous preeclampsia	0.31 (0.14–0.71)	0.006	0.24 (0.15–0.38)	<0.0001	0.29 (0.20–0.43)	<0.0001
Previous preeclampsia	4.02 (1.58–10.24)	0.004	2.18 (1.24–3.83)	0.007	—	—
Maternal history of preeclampsia	—	—	2.91 (1.63–5.21)	0.0003	2.64 (1.51–4.62)	0.0007
History of hypertension	8.70 (2.77–27.33)	<0.0001	—	—	—	—
Use of ovulation induction	4.75 (1.55–14.53)	0.006	—	—	—	—

Advanced Maternal Age Worsens Postpartum Vascular Function

frontiers in Physiology

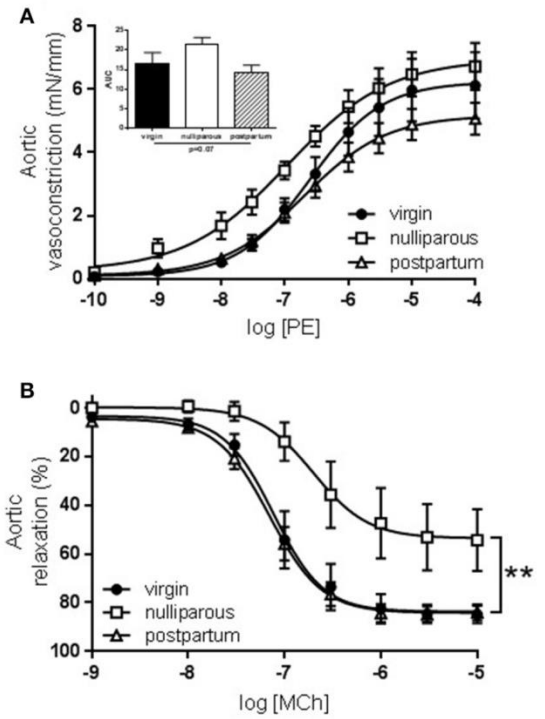
*Jude S. Morton[1,2], Alison S. Care[1,2], Raven Kirschenman[1,2], Christy-Lynn Cooke[1,2] and Sandra T. Davidge[1,2,3]**

- Pregnancy at an AMA increases maternal risk of gestational diabetes, preeclampsia, placenta previa and caesarian delivery;
  - complications which predict worsened cardiovascular health in later years

- hypothesized that pregnancy at AMA would lead to **postpartum vascular dysfunction**

Rat model

- Aged postpartum rats exhibited vascular dysfunction



CONCLUSIONS

- Higher prevalence of AMA (ART)
- AMA=higher risk of obstetrical and maternal complications
- Absolute risks? >35, >40, >45, >50
- Preconception evaluation and counseling
- Avoid multiple pregnancies!