

IU Death :Prediction and Prevention Gestational and Pregestational Diabetes

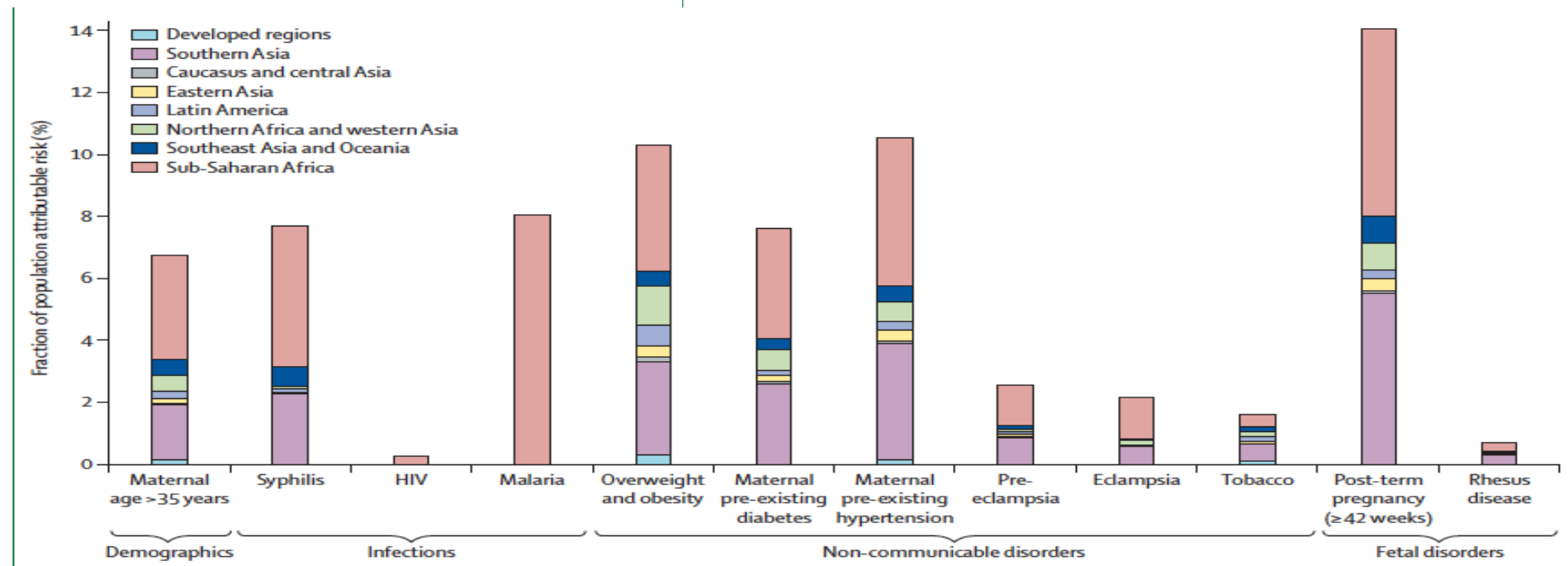
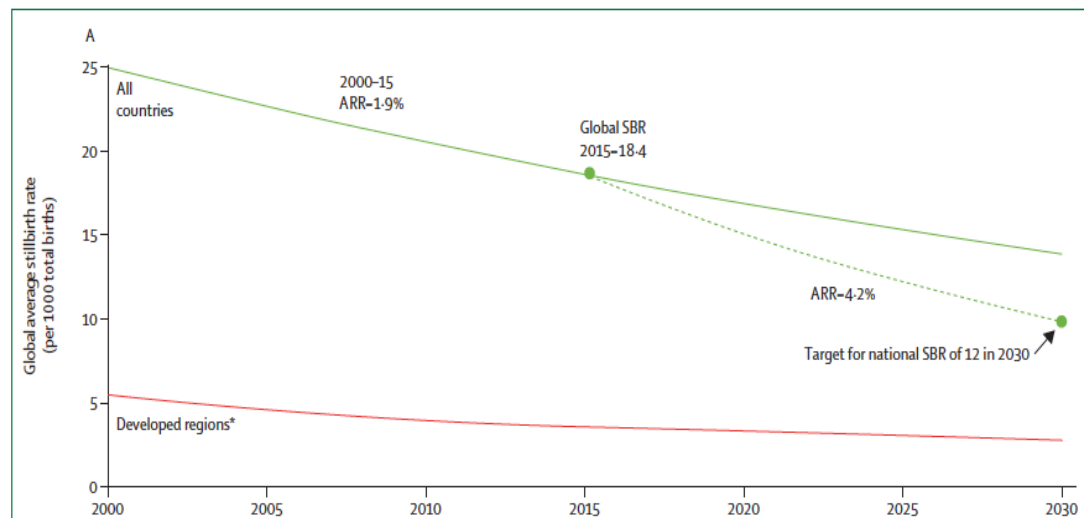
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Hastalıkları ve Doğum Anabilim Dalı

Stillbirths: rates, risk factors, and acceleration towards 2030

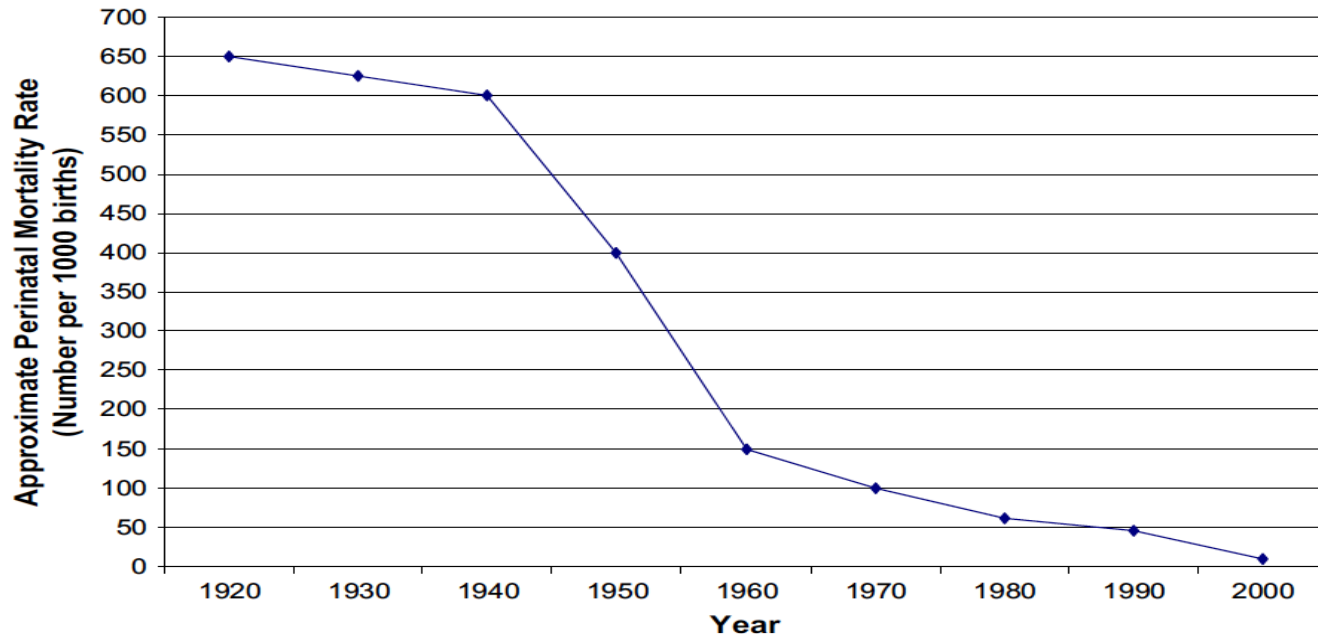
International Classification of Diseases 10th revision (ICD 10) definitions
(note birthweight was given priority over gestational age)

- Late fetal death 1000 g or more or 28 weeks or more or 35 cm or more
- Early fetal death 500 g or more or 22 weeks or more or 25 cm or more
- Miscarriage as a pregnancy loss before 22 completed weeks of gestational age



Gestasyonel ve Pregastasyonel Diabet İnsidansı

- Pre-gestational Diabetes % 0.5-2
- GDM % 7-17
- Pregestational diabette ölü doğum 25-29.2/1000 doğum
- Gestational diabetes 16/1000 doğum



IU ölüm-risk faktörleri

- **Diabet tipi**
 - Pre-gastational DM**
 - Gestational DM**
- **Obezite**
- **Gestasyonel yaş**
- **Kötü glisemik kontrol**
- **Fetal malformasyonlar**
- **FGR, preeklampsi**
- **Eşlik eden hastalıklar**

Pre-gestasyonel Diabet

Epidemiology of stillbirth in type 1 diabetics

Country	Years of study	Sample size	Rate/1000 births	Relative risk
Denmark	1990–2000	1361	18	—
Denmark	1993–1999	1218	21	6.2
Scotland	1979–1995	1112	25	4.7
Scotland	1998–1999	273	18.5	3.6
UK	1990–1994	462	25	5.0
UK	2002–2003	1707	25.8	4.5
USA	1995–1997	271,691	5.9	1.5

Epidemiology of stillbirth in type 2 diabetics

Country	Years of study	Sample size	Rate/1000 births	Relative risk
UK	1990–2002	182	12.2	2.3
UK	2002–2003	652	29.2	5.1
New Zealand	1985–1997	434	34 ^a	2.8 ^a

GDM

- Beischer et al., 1996 16/1000, OR: 1.53
- Aberg et al, 15/1000, OR 1.56
- Girz et al, 7.7/1000, OR: 1.5

The joint effects of obesity and pregestational diabetes on the risk of stillbirth

Table 2. Rate of stillbirth.^a

	Overall	<i>p</i> Value	24–33 weeks	<i>p</i> Value	34–36 weeks	<i>p</i> Value	37–39 weeks	<i>p</i> Value	40–42 weeks	<i>p</i> Value
Nondiabetic		<.001		<.001		<.001		<.001		<.001
Underweight	15.3		7.8		4.0		3.6		– ^b	
Normal weight nondiabetic	15.0		7.2		3.8		3.5		3.2	
Overweight	21.4		10.7		5.1		4.9		4.6	
Obese	25.1		11.3		6.0		6.9		6.2	
Morbidly obese	26.7		10.9		6.7		7.7		11.1	
Pregestational diabetic										
Underweight	48.5		–		–		–		–	
Normal weight	119.9		40.7		44.3		41.1		–	
Overweight	138.3		57.2		41.9		46.6		–	
Obese	155.8		30.1		53.1		88.5		–	
Morbidly obese	209.8		62.9		49.2		118.7		–	

^aResults reported as: rate per 10,000 pregnancies.

^bIncidence too low to report.

Non-diabetik normal BMI olan kadınlara göre;

Morbid obezlerde aHR 1.57

Normal kiloda PGDM aHR: 6.67

Morbid obezite ve PGDM aHR: 12.86

IU ex. riski 37-39 gebelik haft

Women with pre-gestational diabetes have a higher risk of stillbirth at all gestations after 32 weeks

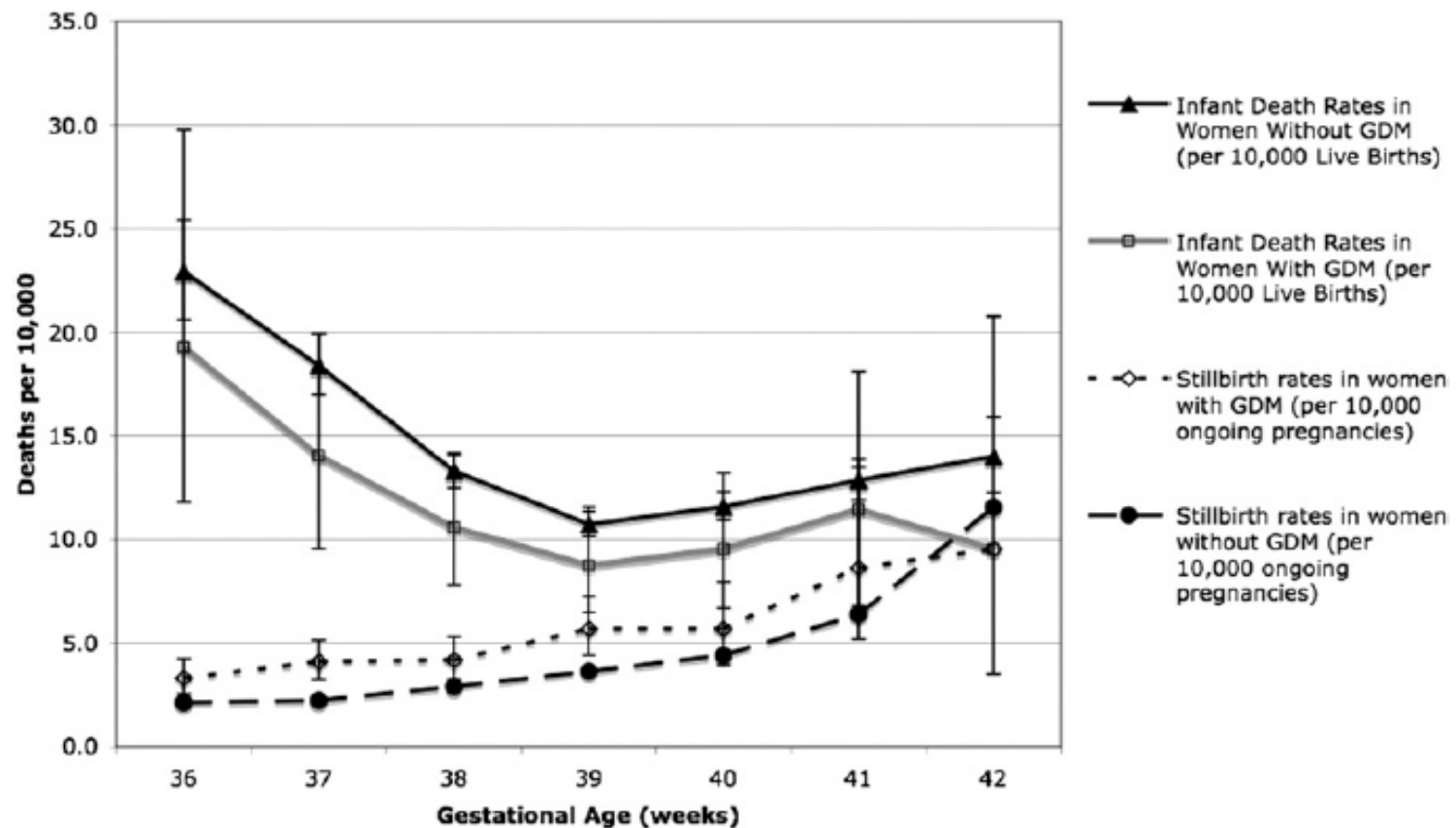
Table 1 Distribution and relative risk of stillbirth in women with pre-gestational diabetes (singleton pregnancies only) compared with all pregnancies in England and Wales

Gestation in weeks	Singleton pregnancies in women with pre-gestational diabetes				All pregnancies in England and Wales				Relative risk for women with diabetes compared with all pregnancies in England and Wales
	Stillbirths	Total births	Rate per 1000 total births	Rate per 1000 ongoing pregnancies	Stillbirths	Total births	Rate per 1000 total births	Rate per 1000 ongoing pregnancies	Per 1000 ongoing pregnancies (95% CI)
24–27	5	20	250.0 (89.8–490.8)	2.4 (1.0–5.6)	4483	16927	264.8 (257.2–272.6)	1.3 (1.2–1.3)	1.88 (1.21–2.92)
28–31	4	49	81.6 (29.5–194.6)	1.9 (0.8–5.0)	2981	31894	93.5 (90.2–96.9)	0.9 (0.8–0.9)	2.28 (1.72–3.01)
32–34	7	161	43.5 (20.6–87.7)	3.5 (1.7–7.2)	2436	69930	34.8 (33.5–36.2)	0.7 (0.7–0.7)	4.95 (4.24–5.78)
35–36	4	392	10.2 (3.9–26.0)	2.2 (0.8–5.5)	1946	143 609	13.6 (13.0–14.2)	0.6 (0.5–0.6)	3.77 (3.42–4.16)
37–38	6	1185	5.1 (2.3–11.0)	4.1 (1.9–8.9)	2325	670 426	3.5 (3.3–3.6)	0.7 (0.7–0.7)	5.75 (5.43–6.09)
≥ 39	3	278	10.8 (3.6–31.3)	10.8 (3.6–31.8)	3807	2 590 083	1.5 (1.4–1.6)	1.5 (1.4–1.5)	7.34 (6.52–8.25)
All	29	2085	13.9 (9.7–19.9)	13.9 (9.7–19.9)	17 978	2 522 869	5.1 (5.0–5.2)	5.1 (5.0–5.2)	2.73 (2.61–2.84)

The risk of stillbirth and infant death stratified by gestational age in women with gestational diabetes

FIGURE 1

Infant death and stillbirth rates in women with and without GDM



Patofizyoloji

- % 50 Kronik fetal hipoksi (Pedersen hipotezi)
Kardiak disfonksiyon
- % 50 IUGR, preeklampsi, umbilikal kord,
plasental abrupsiyo, konjenital
malformasyonlar

Ölü doğumların önlenmesi

- **Glisemik kontrol**
- **Antenatal testler**

FMC

NST

BPP

Ultrason- Doppler :

Fetal anomaliler

FGR (nefropati, preeklampsi)

- **Doğum zamanlaması**

Glisemik Kontrol ve Farmakolojik tedaviler

Glisemik Kontrol

- **Multidisipliner**

perinatoloji, endokrin, oftalmoloji, diyetisyen
Nutrisyonel terapi ve ekzersiz

- **Bireysel monitorizasyon**

Ekstrem kan glukoz düzeylerinin azaltılması

Sıklık?

Hedef glukoz düzeyleri ?

Hangi medikasyon kullanılmalı? İnsulin ?

Oral

antidiyabetikler?

Gestational Diabetes Mellitus and Frequency of Blood Glucose Monitoring

A Randomized Controlled Trial

Characteristic	Every Day Group (n=149)	Every-Other-Day Group (n=144)	RR (95% CI)	P
Required medical treatment	28 (18.9)	39 (27.3)	1.47 (0.96–2.24)	
Gestational age at start treatment (wk)	34.0 (32.6–35.0)	34.0 (32.1–35.0)		.87
Treatment required				
Glyburide	10 (6.8)	13 (9.1)	1.35 (0.61–2.97)	
Metformin	11 (7.4)	15 (10.5)	1.41 (0.67–2.97)	
Insulin	7 (4.8)	12 (8.4)	1.99 (0.92–4.31)	
Maternal hypoglycemia recorded on blood glucose log (less than 60 mg/dL)	4 (2.7)	2 (1.4)	0.51 (0.10–2.76)	
Average weekly blood glucose testing compliance (%)	88.8 (77.7–93.5)	91.8 (85.0–96.5)		<.01
Blood glucose testing compliance from diagnosis to delivery (%)	90.0 (79.2–96.2)	91.3 (85.2–96.2)		.01
Antenatal steroid administration	1 (0.7)	5 (3.5)	5.10 (0.60–43.2)	
Induced	70 (49.0)	69 (48.3)	0.99 (0.78–1.25)	
Gestational age at delivery (wk)	39.0 (38.1–39.5)	39.0 (38.1–39.4)		.47
Mode of delivery				
Vaginal delivery	89 (61.8)	92 (64.3)	1.04 (0.87–1.24)	
Cesarean delivery	49 (34.0)	47 (32.9)	0.97 (0.70–1.34)	
Assisted vaginal delivery	6 (4.2)	4 (2.8)	0.67 (0.19–2.33)	
Required delivery for uncontrolled GDM	9 (6.3)	6 (4.2)	0.68 (0.25–1.85)	
Obstetric complications				
Preeclampsia	23 (17.1)	15 (11.2)	0.63 (0.35–1.15)	
Chorioamnionitis	5 (3.7)	1 (0.8)	0.21 (0.02–1.85)	
Preterm labor	1 (0.8)	2 (1.5)	2.12 (0.19–23.9)	
Preterm PROM	17 (12.7)	18 (13.4)	1.06 (0.57–1.96)	
Postpartum hemorrhage	3 (2.2)	2 (1.5)	0.68 (0.11–4.33)	
Shoulder dystocia	8 (5.6)	11 (7.7)	1.39 (0.58–3.30)	
Fasting value PPD 1 (mg/dL)	82.5±18.5	88.7±24.5		.31
Wound infection*	0	0	—	
Days spent postpartum in hospital	3 (2–4)	3 (2–4)		.47

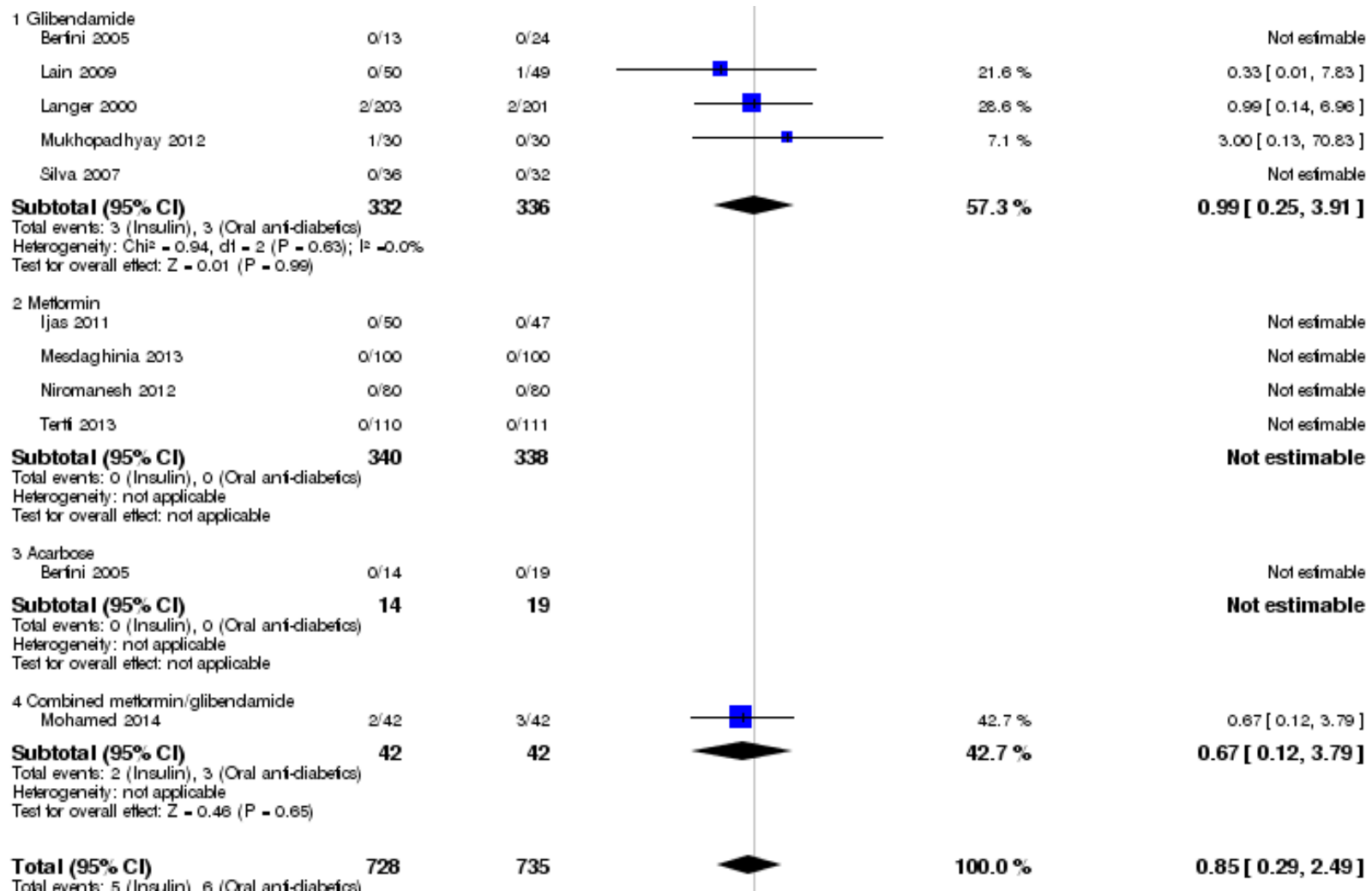
Continuous Glucose Monitoring Effects on Maternal Glycemic Control and Pregnancy Outcomes in Patients With Gestational Diabetes Mellitus: A Prospective Cohort Study

Pregnancy outcomes	All			Women With Insulin Treatment			Women Without Insulin Treatment		
	CGM Group	Routine Care Group	P Value	CGM Group	Routine Care Group	P Value	CGM Group	Routine Care Group	P Value
Maternal outcomes									
n	147	189		41	23		106	166	
Miscarriages, n	1	1		0	0		1	1	
Intrauterine fetal deaths, n	0	2		0	0		0	2	
Preeclampsia, n (%)	5 (3.4)	19 (10.1)	.019	1 (2.4)	2 (8.7)	.256	4 (3.8)	17 (10.2)	.051
Primary cesarean delivery, n (%)	51 (34.7)	88 (46.6)	.028	13 (31.7)	7 (30.4)	.916	38 (35.5)	81 (48.8)	.036
Repeat cesarean delivery, n (%)	29 (19.7)	36 (19)	.876	8 (20)	4 (17.4)	.8	21 (19.8)	32 (19.3)	.914
Neonatal outcomes									
n	146 ^b	186 ^b		41	23		105 ^b	163 ^b	
Gestational age at delivery, wk	38 (37–39)	39 (38–39)	.065	39 (38–39)	38 (38–39)	.123	38 (37–39)	39 (38–39)	.015
Premature delivery, n (%)	7 (4.8)	22 (11.8)	.024	2 (4.9)	2 (8.7)	.545	5 (4.8)	20 (12.3)	.039
Birth weight, g	3138 ± 484	3345 ± 508	<.001	3142 ± 461	3167 ± 587	.852	3136 ± 495	3370 ± 493	<.001
Birth weight percentile	66 (35–82)	82 (64–91)	<.001	65 (33–82)	75 (60–89)	.056	67 (38–82)	82 (66–91)	<.001
Macrosomia, n (%)	6 (4.1)	20 (10.8)	.025	2 (4.9)	2 (8.7)	.545	4 (3.8)	18 (11)	.035
LGA, n (%)	20 (13.7)	48 (25.8)	.01	6 (14.6)	5 (21.7)	.47	14 (13.3)	43 (26.4)	.011
SGA, n (%)	9 (6.2)	5 (2.7)	.202	3 (7.3)	1 (4.3)	.638	6 (5.7)	4 (2.5)	.169
Obstetric trauma, n	0	1		0	0		0	1	
Intensive neonatal care, ^c n (%)	138 (94.5)	177 (95.2)	.793	39 (95.1)	22 (95.7)	.923	99 (94.3)	155 (95.1)	.772
Hypoglycemia, n (%)	8 (5.5)	26 (14)	.011	2 (4.9)	3 (13)	.243	6 (5.7)	23 (14.1)	.031
Hyperbilirubinemia, n (%)	4 (2.7)	18 (9.7)	.012	1 (2.4)	2 (8.7)	.256	3 (2.9)	16 (9.8)	.03
RDS, n (%)	2 (1.4)	11 (5.9)	.034	0	1 (4.3)	.178	2 (1.9)	10 (6.1)	.102
Composite neonatal outcome, ^d n (%)	40 (27.4)	92 (49.5)	<.001	12 (29.3)	11 (47.8)	.138	28 (26.7)	81 (49.7)	<.001

Hedef glukoz düzeyleri

- **ADA ve ACOG glukoz hedefleri**
 - Açlık glukoz düzeyi: <95 mg/dL
 - Postprandial 1. saat: <140 mg/dL
 - Postprandial 2.saat: <120 mg/dL

Insulin for the treatment of women with gestational diabetes (Review)



Antenatal Fetal İzlem

Fetal hareketlerin sayılması

- Düşük risk grubu hastalarda 2 hft önce fetal hareketler azalma (aOR :14)(Heazell AEP, 2017)
- Ölü doğum açısından fark yok (Cochrane, 2017)

NST-AFI-BPP

- NST ve AFI / haftada 2 kez 1.4/1000 (Kjos, 1997)
- BPP/haftada iki 0-1.4/1000 (Jonhson, 1988)

Table 1 Evidence for antepartum fetal surveillance methods

Fetal evaluation method	Review	Selection criteria	Size	Conclusions	Limitations	False negative
Kick counts	Mangesi et al. 2015 [45]	RCTs cluster RCTs	5 trials 71,458 women	Insufficient evidence to influence practice	No comparison of fetal movement counting to no fetal movement counting Small studies (aside from cluster RCT) using different comparisons, nature of the intervention measured did not allow blinding Low quality evidence due to imprecise results and concerns regarding unclear risk of bias	
Non-stress test (NST)	Grivel et al. 2015 [56]	RCTs quasi-RCTs	4 trials 1636 women	No clear evidence that antenatal NST improves perinatal outcome	Data are not of high quality Lacked power to detect possible important differences in either benefit or harm	0.2–0.65%
Biophysical profile (BPP)	Lalor et al. 2008 [57]	RCTs quasi-RCTs	5 trials 2974 women	Insufficient evidence to support the use of BPPs in high risk pregnancies	Total number of women included in the meta-analysis remains small Some of the studies carry a high risk of bias	0.07–0.08%
Fetal and umbilical Doppler ultrasound	Alfirevic et al. 2017 [58]	RCTs Quasi-RCTs Cluster RCTs	19 trials 10,667 women	Use of umbilical artery dopplers in high risk pregnancies reduced the risk of perinatal deaths and results in fewer obstetric interventions Inconclusive evidence for serial monitoring of ductus venous doppler changes	Missing information on trial methods imprecision in risk estimates and heterogeneity No comparative long-term follow-up	6%

Fetal takip önerileri

Table 2 Society recommendations for antepartum fetal surveillance and delivery timing

	ACOG	SMFM	Fifth International Workshop on GDM
Antenatal fetal surveillance schedule			
A1GDM ^a	May not be necessary prior to 40 weeks		Kick counts, initiate at 30–32 weeks
A2GDM ^b	Initiate at 32 weeks		(insufficient data for more intensive monitoring)
Pregestational DM	Initiate at 32–34 weeks, twice weekly	Initiate at 32–34 weeks	–

Doppler

Randomize çalışma yok

Pregastational diabete bağlı vaskulopati, FGR ve Preeklampsi gelişen gebelikler takibinde faydalı olabilir (maulik ,2009

Table 1 Diagnostic efficacy of umbilical arterial Doppler in diabetic pregnancy

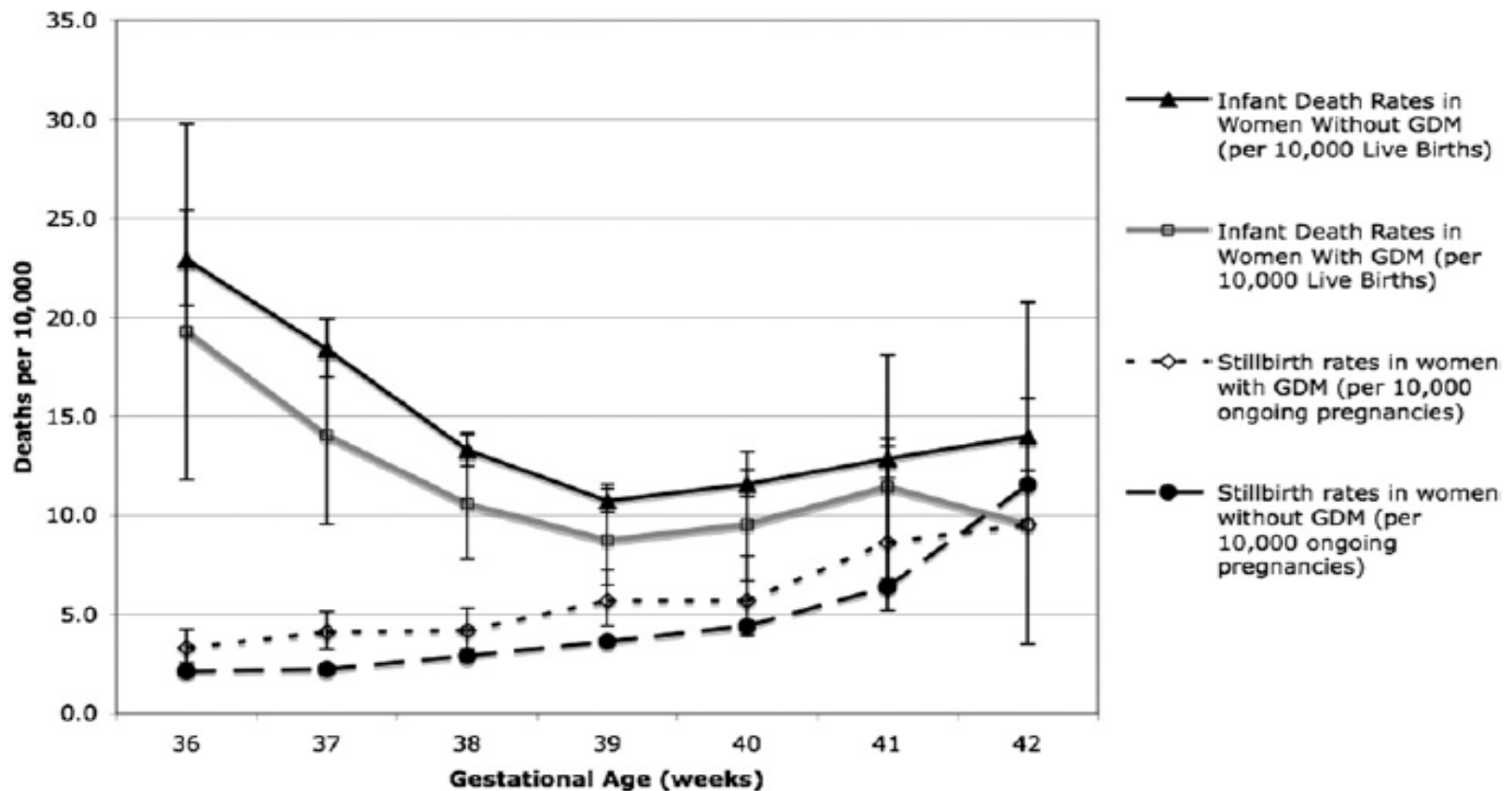
First author	Population (PGDM/GDM)	Outcome	Prevalence	Sensitivity	Specificity	PPV	NPV	LR+	LR-	Accuracy
Bracero ¹⁵	25/18	stillbirth	0.04	1	0.83	0.22	1	7.6	0	0.85
Landon ¹⁷	35/0	IUGR, FD	0.09	1	0.89	0.51	1	9.7	0	0.90
Johnstone ¹⁸	107/21	FD	0.05	0.42	0.95	0.33	0.96	8.6	0.6	0.92
Grunewald ²¹	24/0	C/S for FD	0.30	0.93	0.93	0.75	0.75	6.0	0.7	0.75
Bracero ¹⁶	93/114	composite	0.23	0.32	0.92	0.57	0.81	4.2	0.7	0.78
Fadda ²²	67/0	C/S for FD	0.27	0.61	0.75	0.48	0.84	2.5	0.5	0.71

Doğum Zamanlaması

The risk of stillbirth and infant death stratified by gestational age in women with gestational diabetes

FIGURE 1

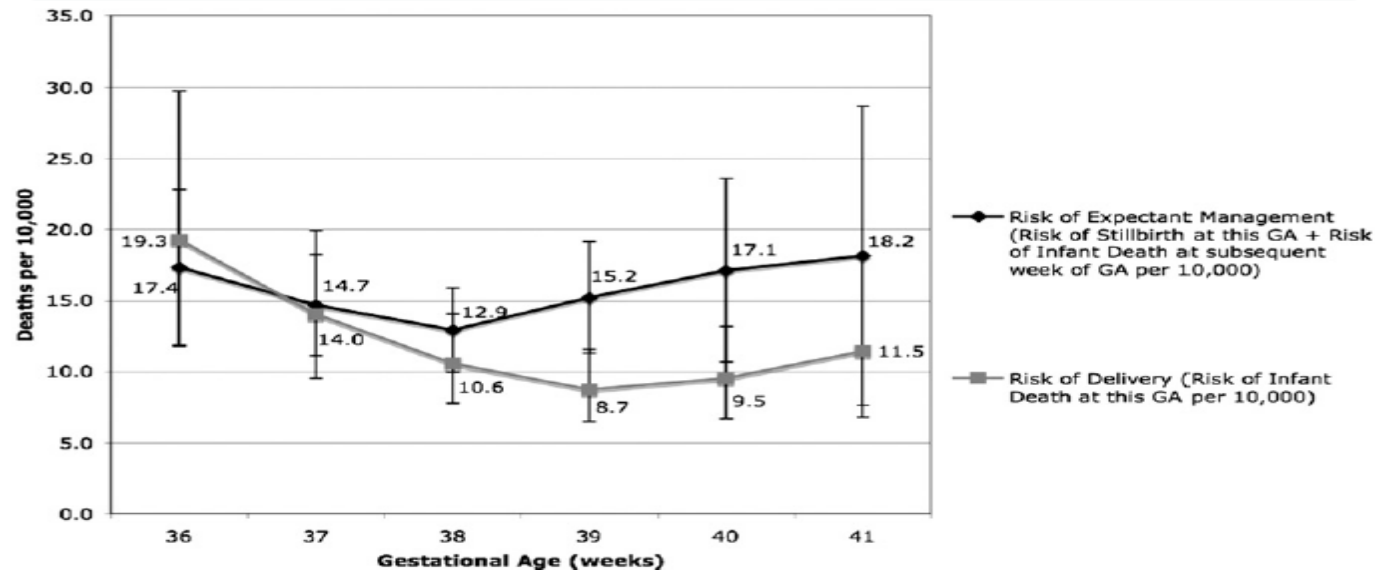
Infant death and stillbirth rates in women with and without GDM



Doğum Zamanı

FIGURE 2

Mortality risk of expectant management compared with delivery in women with gestational diabetes mellitus



Delivery timing

A1GDM 39 0/7 to 40 6/7 weeks

A2GDM 39 0/7 to 39 6/7 weeks^b

Late preterm, early term not indicated^c

No earlier than 38 weeks^a

(Up to 40 weeks with intensified fetal surveillance)

Pregestational DM Expectant management beyond the delivery date not recommended^b 39 0/7 to 39 6/7 weeks^d

—

Sonuç

- IU fetal kayıp açısından en fazla risk pregestasyonel DM
- IU fetal kaybın azaltılmasında en önemli faktör normogliseminin sağlanması
- Gebelikte normoglisemik hedefler ve farmakojik tedavi zamanı belirlenmeli
- Antenatal fetal takipte daha fazla randomize çalışmaya ihtiyaç var