

## OBSTETRICS

# The impact of maternal age on fetal death: does length of gestation matter?

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**OBJECTIVE:** The objective of the investigation was to study the association of fetal death with maternal age by length of gestation.

**STUDY DESIGN:** This was a population study including all ongoing pregnancies after 16 weeks of gestation in Norway during the period 1967-2006 ( $n = 2,182,756$ ).

**RESULTS:** The risk of fetal death was 1.4 times higher in women 40-44 years old than in women aged 20-24 years in midpregnancy but 2.8 times higher at term. In term pregnancies the relative importance of maternal age increased by additional pregnancy weeks. In gestational

weeks 42-43, the crude risk was 5.1 times higher in mothers 40 years old or older. In the recent period, the elevated risk of fetal death in elderly mothers at term has been attenuated.

**CONCLUSION:** Women 40 years old or older had the highest risk of fetal death throughout pregnancy, particularly in term and postterm pregnancies. Improved obstetric care may explain the attenuation of risk associated with age in recent time.

**Key words:** fetal death, gestational length, maternal age

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In the Western world, it has become increasingly common to postpone child-bearing. The mean age of primiparous women has increased during the last decades.<sup>1-4</sup> According to the Medical Birth Registry of Norway, more than 19% of child-bearing women were 35 years old or older in 2008. For comparison, only 8% were 35 years old or older 20 years ago. The mean age of all women giving birth was 29.8 years in 2006, more

than 4 years older than women delivering 30 years earlier.

The negative impact of high maternal age on fetal death risk is well known.<sup>5</sup> Recent knowledge suggests that the risk of fetal death varies considerably according to length of gestation. The fetal death rate seems to be high at 20-22 weeks of gestation and lowest at 27-33 weeks, before it increases rapidly from 37 through 43 gestational weeks.<sup>6,7</sup> The knowledge of the impact of maternal age on fetal death at different gestational ages is limited. Such knowledge, however, may be important in understanding causes of fetal death. It has been suggested that infectious causes play a greater role in midpregnancy than in fetal death at term,<sup>8-12</sup> whereas pregnancy-related maternal disease and placenta insufficiency seem to be increasingly important as the pregnancy proceeds.<sup>13</sup>

In a study comprising births from 36 states in the United States during 2001-2002, women of advanced maternal age had a higher risk of stillbirth across all gestational ages, with a peak risk postterm.<sup>14</sup> This study is essential; however, the lack of follow-up after the 41st gestational week and the high level of obstetrical interventions<sup>15,16</sup> may have caused an underestimation of the fetal death risk in term and postterm pregnancies.

Obstetrical ultrasonographic examination was gradually introduced in the public obstetric health in Norway by the mid-1980s, and since then almost all pregnancies have been examined at pregnancy weeks 17-19. This may have improved the term prediction in pregnancy and also the diagnosis of fetal failure to thrive when used later in pregnancy. Because elderly mothers are at increased risk of fetal death, they may in particular have gained from improved obstetrical diagnostic tools, if such tools are advantageous.

In all ongoing pregnancies after 16 weeks of gestation in Norway during the years 1967-2006, we estimated the risk of fetal death according to maternal age at different lengths of gestation. We also studied whether the fetal death risk at term in elderly mothers has changed after ultrasonographic examinations were introduced in obstetrical care.

## MATERIALS AND METHODS

Data were obtained from the Medical Birth Registry of Norway.<sup>17</sup> This registry contains information on all births after 16 weeks of gestation. Compulsory notification of birth is made on standardized forms by the midwife or attending physician at the delivery, and the data elements in the notification form have been almost

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**TABLE 1**  
**Characteristics of the study population, 2,182,756 pregnancies during 1967–2006 in Norway**

Characteristic	Total births	Percent	Fetal deaths, n	Fetal deaths per 1000 births, n
<b>Parity</b>				
0	901,171	41.3	9508	10.6
1	758,413	34.7	6456	8.5
2	356,952	16.4	3965	11.1
≥3	166,220	7.6	2825	17.0
<b>Plurality</b>				
1	2,125,470	97.4	20,633	9.7
≥2	57,286	2.6	2121	37.0
<b>Paternal age, y</b>				
<30	1,058,341	48.5	8661	8.2
30–39	932,983	42.7	8261	8.9
≥40	169,195	7.8	2252	13.3
Missing	22,237	1.0	3580	161.0
<b>Preeclampsia</b>				
Yes	67,200	3.1	1242	18.5
No	2,115,556	96.9	21,512	10.2
<b>Total</b>	<b>2,182,756</b>		<b>22,754</b>	<b>10.4</b>

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unchanged since the start of the registration in 1967 (<http://www.mfr.no>).<sup>17</sup>

The study population comprised deliveries after 16 weeks of gestation in Norway during the period 1967–2006, a total of 2,337,392 births. A total of 28,595 pregnancies were recorded to last longer than 43 weeks. A proportion of these were miscoded, and we could not with certainty determine whom, and we therefore decided to exclude all pregnancies recorded to last longer than 43 weeks. Information on length of gestation at birth was missing for 125,997 offspring, leaving 2,182,800 births for the crude data analyses. An additional 44 births lacked information on potentially confounding variables; hence, 2,182,756 births were included in the multivariable data analyses.

We defined fetal death as birth of a dead fetus after 16 weeks of gestation. We studied fetal death risk at the following gestational lengths; 16–22, 23–29, 30–36, and 37 or more weeks of gestation. Pregnancies lasting 38 weeks or longer

were in addition subdivided in groups of 2 week intervals: 38–39, 40–41, and 42–43 weeks of gestation.

Information on length of gestation at delivery was based on women's reporting of first day of the last menstrual period in standardized antenatal care forms or date of term estimated from ultrasonographic examination if available.

Maternal age at delivery was our main explanatory variable and coded as less than 20, 20–24 (reference), 25–29, 30–34, 35–39, 40–44, and 45 years and older. As potential confounders we included parity, plurality, year of delivery, paternal age, and preeclampsia (Table 1). Parity was defined as the number of previous births after the 16th week of gestation coded as 0, 1, 2, 3, and 4 or greater. Plurality was divided into 2 categories: 1 and 2 or more offspring. Year of delivery (period) was coded as 1967–1971, 1972–1976, 1977–1981, 1982–1986, 1987–1991, 1992–1996, 1997–2001, and 2002–2006. Paternal age was categorized as younger than 30, 30–39, 40 years old or older, and

missing. Preeclampsia was defined as maternal blood pressure above 140/90 mm Hg and proteinuria.

To calculate the absolute risk of fetal death (in percent) according to maternal age, the denominator was all women with a fetus still in utero at the gestational period being studied, and the numerator was women with stillbirths at that same period of gestation.<sup>18</sup> For instance, in weeks 30–36, only pregnant women who delivered after week 30 were included.

Cox regression models were applied to estimate the relative risk of fetal death.<sup>19</sup> The outcome variables was time (days) to fetal death. Births of live infants or live fetuses in utero at the end of a gestational length interval were treated as censored observations. In the adjusted analysis, the confounders were included as categorical variables with categorization as given in earlier text. Separate analyses were carried out for the different gestational length intervals. For term and postterm pregnancies, we also estimated the association of fetal death with maternal age in 2 different time periods: 1967–1986 and 1987–2006. We used the Statistical Package for the Social Sciences for statistical analyses (version 16.0; SPSS, Chicago, IL).

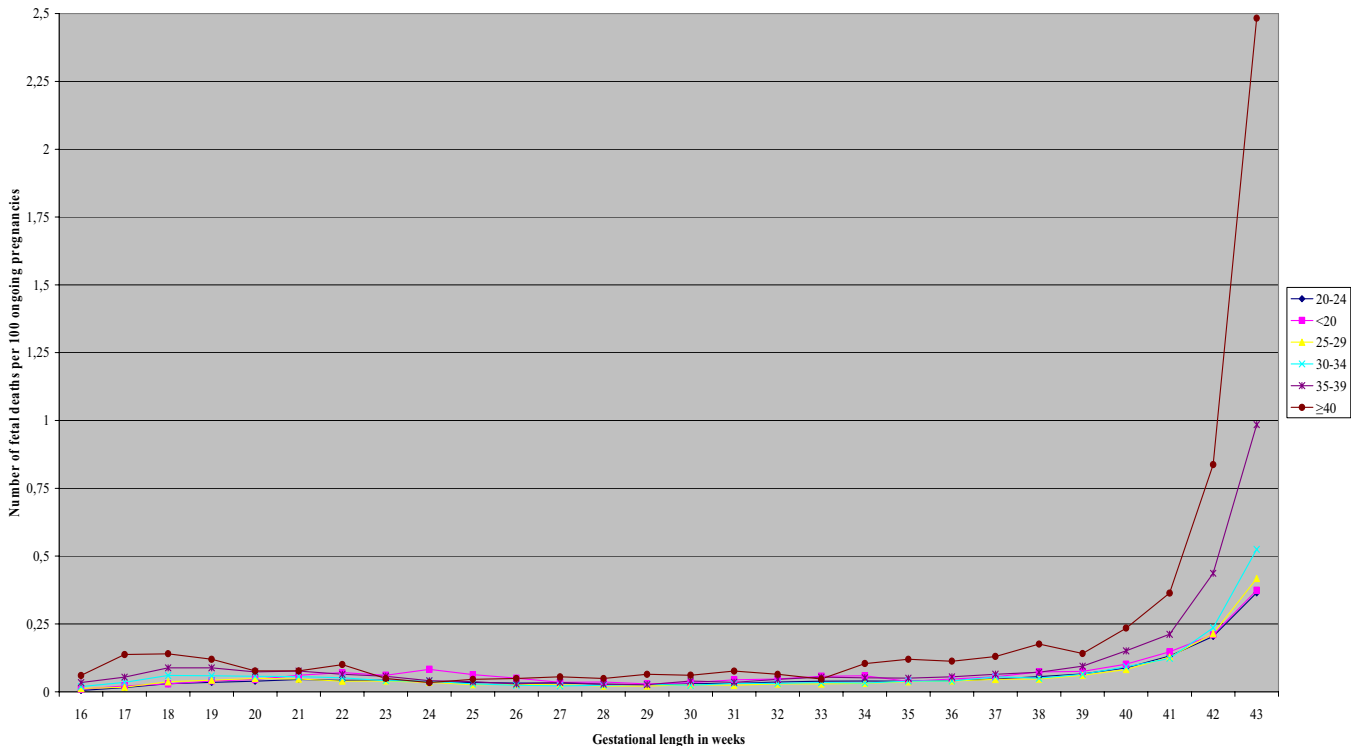
The study was approved by the Norwegian Data Inspectorate and the Publishing Committee for the Medical Birth Registry of Norway.

## RESULTS

A total of 22,754 fetal deaths occurred in 2,182,756 births during the study period, representing 1.04% of all births after 16 weeks of gestation. Of all pregnancies, 10.3% were in women 35 years old or older and 93.2% of the births were at the 37th gestational week or later.

The absolute risk of fetal death varied according to length of gestation (Figure 1). Women aged 40 years or older had the highest risk of fetal death at all gestational ages, but their increased risk was most pronounced in early gestation and at term. After gestational week 36, the risk of fetal death increased rapidly in all age groups. However, the increase in risk seemed to be highest in women 40 years old or older.

FIGURE 1

**Fetal deaths according to gestational length and maternal age during 1967-2006**

Number of fetal deaths per 100 ongoing pregnancies according to gestational length and maternal age, during 1967-2006.

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The relative importance of high maternal age on fetal death risk was confirmed to be elevated at term and in early gestation by Cox regression analyses (Table 2). The crude relative risk of fetal death in gestational weeks 16-22 was 3.45 (95% confidence interval [CI], 3.00–3.96) in women 40-44 years old as compared with women aged 20-24 years (reference), and it was 1.95 (95% CI, 1.66–2.28) after adjustment for period of delivery, parity, plurality, and paternal age.

In gestational weeks 23-29, the crude relative risk of fetal death in mothers 40-44 years old was 1.43 (95% CI, 1.18–1.74) as compared with women 20-24 years old. The corresponding crude relative risk in pregnancies lasting 37 weeks or longer was 2.80 (95% CI, 2.43–3.23). Women younger than 35 years of age had no increasing relative risk of fetal death throughout pregnancy as compared with younger women.

In a separate analysis of pregnancies lasting 38 weeks or longer, the relative

importance of high maternal age further increased. In the gestational weeks 38-39, the crude relative risk in mothers aged 40 years or older was 2.74 (95% CI, 2.19–3.43) as compared with the reference group. In gestational weeks 42-43, the corresponding risk was 5.09 (95% CI, 3.55–7.31) (Table 3). These increased relative risks for elderly mothers remained essentially unchanged after adjustment for the other study factors and were significantly higher in gestational weeks 42-43 as compared with weeks 38-39. Women 45 years old or older were not studied separately because of the lack of statistical power in postterm pregnancies.

In term and postterm pregnancies, we also studied the association of fetal death risk with maternal age in the years before and after 1986 (Table 4 and Figure 2). In the years 1967-1986, the crude relative risk of fetal death in the gestational weeks 42-43 was 7.31 (95% CI, 4.96–10.76) for women 40 years or older, as compared with women 20-24 years old. In compar-

ison, the corresponding risk was 1.94 (95% CI, 0.70–5.41) during 1987-2006.

### COMMENT

In this population-based study, including more than 2 million births from 1967 through 2006, women 40 years old or older had an overall higher risk of fetal death compared with younger mothers throughout pregnancy. The fetal death risk increased after 36 weeks of pregnancy and the increase was highest in the oldest women. Interestingly, there was a higher impact of maternal age on fetal death risk at term during the period 1967-1986 as compared with 1987-2006.

The association between high maternal age and risk of fetal death is well known. In a review of 37 studies examining the association of high maternal age with stillbirth risk,<sup>5</sup> most studies demonstrated a significant increased risk of stillbirth in women of advanced age.

In accordance with other studies, our results suggest the risk of fetal death to

TABLE 2

## Relative risk of fetal death in the gestational weeks 16–22, 23–29, 30–36 and &gt;37, according to maternal age

Gestational length	Maternal age, y	Fetal deaths, n	Number at risk	Crude RR	95% CI	Adjusted RR <sup>a</sup>	95% CI
Gestational wks 16–22 (d 112–160)	<20	345	125,009	1.31	1.17–1.48	1.09	0.96–1.23
	20–24	1211	576,584	1.00		1.00	
	25–29	1826	753,530	1.15	1.07–1.24	1.03	0.95–1.11
	30–34	1691	503,648	1.60	1.49–1.72	1.15	1.05–1.26
	35–39	897	188,760	2.27	2.08–2.47	1.37	1.23–1.53
	40–44	242	33,597	3.45	3.00–3.96	1.95	1.66–2.28
	≥45	7	1628	2.06	0.98–4.32	1.13	0.53–2.38
	Total	6219	2,182,756				
Gestational wks 23–29 (d 161–209)	<20	443	124,581	1.54	1.38–1.72	1.09	0.98–1.22
	20–24	1329	574,978	1.00		1.00	
	25–29	1469	751,093	0.85	0.79–0.91	0.99	0.91–1.07
	30–34	1026	501,387	0.89	0.82–0.96	1.05	0.94–1.16
	35–39	474	187,538	1.09	0.99–1.22	1.14	1.00–1.30
	40–44	110	33,254	1.43	1.18–1.74	1.25	1.01–1.56
	≥45	10	1615	2.68	1.44–5.00	1.91	1.01–3.60
	Total	4861	2,174,446				
Gestational wks 30–36 (d 210–258)	<20	391	123,108	1.27	1.14–1.42	0.87	0.78–0.98
	20–24	1433	570,728	1.00		1.00	
	25–29	1593	746,149	0.85	0.79–0.91	1.11	1.02–1.19
	30–34	1136	497,662	0.91	0.84–0.98	1.31	1.19–1.45
	35–39	604	185,788	1.30	1.18–1.43	1.66	1.47–1.87
	40–44	182	32,859	2.22	1.90–2.59	2.19	1.82–2.63
	≥45	15	1590	3.80	2.29–6.32	2.80	1.66–4.72
	Total	5354	2,157,884				
Gestational wks ≥37 (d 259–307)	<20	414	113,924	1.15	1.03–1.28	0.79	0.71–0.88
	20–24	1656	539,563	1.00		1.00	
	25–29	1956	707,049	0.94	0.88–1.01	1.23	1.14–1.31
	30–34	1344	468,660	1.03	0.96–1.11	1.44	1.31–1.57
	35–39	717	172,830	1.56	1.43–1.70	1.89	1.69–2.12
	40–44	216	30,245	2.80	2.43–3.23	2.66	2.24–3.15
	≥45	17	1418	4.75	2.95–7.66	3.54	2.17–5.78
	Total	6320	2,033,689				

CI, confidence interval; RR, relative risk.

<sup>a</sup> Adjusted for period of delivery, parity, plurality, paternal age, and preeclampsia. In gestational weeks 16–22, preeclampsia is not adjusted for.

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vary according to gestational length.<sup>6,7</sup> To our knowledge, only 1 previous study has explored the association between fetal death and maternal age at different gestational ages.<sup>14</sup> This study included more than 5 million births of singletons without malformations in the United

States from 2001 through 2002. Births from 20 through 41 weeks of gestation were included. Their limitations include the reliability of fetal death and birth certificate data and the exclusion of births with congenital anomalies.<sup>20</sup> Also, their cesarean section rate was high, around

25%.<sup>15,16</sup> Despite the difference in study sample, the absolute and relative impact of maternal age on fetal death were similar to our estimates for term pregnancies in recent years. However, our data obtained during a 40 years period show a large decrease in fetal risk at term, and

TABLE 3

Relative risk of fetal death in the gestational weeks 38–39, 40–41, and 42–43, according to maternal age during 1967–2006

Gestational length	Maternal age, y	Fetal deaths, n	Number at risk	Crude RR	95% CI	Adjusted RR <sup>a</sup>	95% CI
Gestational wks 38–39 (d 266–279)	<20	152	108,540	1.21	1.01–1.45	0.87	0.73–1.05
	20–24	598	517,220	1.00		1.00	
	25–29	686	677,188	0.88	0.79–0.99	1.10	0.97–1.23
	30–34	474	446,432	0.95	0.84–1.07	1.24	1.06–1.44
	35–39	249	162,765	1.39	1.20–1.61	1.60	1.33–1.94
	≥40	87	29,635	2.74	2.19–3.43	2.53	1.93–3.34
	Total	2246	1,941,780				
Gestational wks 40–41 (d 280–293)	<20	144	76,204	1.12	0.93–1.35	0.76	0.63–0.91
	20–24	582	358,804	1.00		1.00	
	25–29	691	457,024	0.97	0.87–1.09	1.24	1.10–1.40
	30–34	450	287,599	1.04	0.92–1.18	1.39	1.19–1.62
	35–39	259	100,137	1.76	1.52–2.03	2.07	1.72–2.51
	≥40	71	17,039	2.88	2.25–3.68	2.66	1.98–3.57
	Total	2197	1,296,807				
Gestational wks 42–43 (d 294–307)	<20	55	18,602	0.99	0.74–1.33	0.66	0.49–0.88
	20–24	221	78,458	1.00		1.00	
	25–29	256	87,799	1.13	0.94–1.35	1.65	1.36–2.00
	30–34	161	50,390	1.35	1.10–1.65	2.26	1.75–2.91
	35–39	97	16,716	2.54	2.00–3.23	3.57	2.60–4.89
	≥40	34	2749	5.09	3.55–7.31	4.85	3.07–7.65
	Total	824	254,714				

CI, confidence interval; RR, relative risk.

<sup>a</sup> Adjusted for period of delivery, parity, plurality, paternal age, and preeclampsia.

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this decrease has been most prominent in mothers older than 40 years.

Almost all deliveries in Norway during our study period have been at public hospitals, and reporting of births after 16 weeks of gestation to the Medical Birth Registry is compulsory by law; hence, we do not believe significant underreporting of fetal deaths has occurred. However, for fetal deaths in 16–22 weeks of gestation, the routines of reporting to the Medical Birth Registry are less established than at higher gestational lengths. Despite possible underreporting of early fetal deaths, we have no reason to believe that there has been a differential underreporting according to maternal age.

Before the introduction of ultrasonographic examinations in the 1980s, infor-

mation on length of gestation at delivery was based on women's reporting of the first day of her last menstrual period. This may be an unreliable measurement and could cause an inaccurate determination of the gestational length in women with irregular cycles or uncertain of the first day of the last menstrual period.<sup>21</sup> It is possible that pregnancy length was overestimated for some women before the introduction of ultrasound,<sup>22,23</sup> and consequently, fewer women have been classified as post-term after the introduction of ultrasound. Hence, the reduced risk of fetal death in elderly mothers from 1967–1986 to 1987–2006 may be an underestimate.

In our study, women 40 years old or older had an increased risk of fetal death at all gestational ages. Before the 20th gesta-

tional week, the absolute fetal death risk was moderately elevated in older as compared with younger mothers (Figure 1). A possible misclassification of induced abortions after 16 weeks of pregnancy as fetal death in the Medical Birth Registry could have resulted in increased risk of fetal death in early gestation. Such misclassification bias would probably have affected older women in particular because of their overrepresentation to induced abortions as a consequence of detected malformations or anomalies by prenatal screening. However, the number of induced abortions after the 16th week of pregnancy because of malformations was almost nonexistent before 1986, and these cases were reported separately after 1999 and could thereby be excluded from our study.

TABLE 4

Relative risks of fetal death in the gestational weeks 38–39, 40–41, and 42–43, according to maternal age during 1967–1986 and 1987–2006

Gestational length	Maternal age, y	1986 or earlier				1987 or later			
		Fetal deaths, n	Number at risk	Crude RR	95% CI	Fetal deaths, n	Number at risk	Crude RR	95% CI
Gestational wks 38–39 (d 266–279)	<20	119	79,780	1.04	0.85–1.27	33	28,760	1.77	1.20–2.60
	20–24	478	332,560	1.00		120	184,660	1.00	
	25–29	419	326,430	0.90	0.79–1.02	267	350,758	1.18	0.95–1.46
	30–34	255	159,806	1.14	0.98–1.32	219	286,626	1.20	0.96–1.50
	35–39	131	56,100	1.70	1.40–2.06	118	106,665	1.77	1.37–2.28
	≥40	64	13,092	3.65	2.81–4.73	23	16,543	2.30	1.47–3.59
	Total	1466	967,768			780	974,012		
Gestational wks 40–41 (d 280–293)	<20	119	57,184	0.99	0.81–1.21	25	19,020	1.52	0.98–2.36
	20–24	479	236,653	1.00		103	122,151	1.00	
	25–29	485	227,766	1.10	0.97–1.24	206	229,258	1.10	0.87–1.39
	30–34	237	106,209	1.20	1.02–1.40	213	181,390	1.46	1.16–1.85
	35–39	135	35,274	2.14	1.77–2.59	124	64,863	2.40	1.85–3.12
	≥40	56	7727	4.15	3.15–5.48	15	9312	2.04	1.19–3.51
	Total	1511	670,813			686	625,994		
Gestational wks 42–43 (d 294–307)	<20	47	14,436	0.94	0.68–1.29	8	4166	1.03	0.48–2.19
	20–24	177	53,532	1.00		44	24,926	1.00	
	25–29	195	45,847	1.37	1.12–1.67	61	41,952	0.90	0.61–1.33
	30–34	106	19,273	1.80	1.41–2.29	55	31,117	1.22	0.82–1.81
	35–39	56	5900	3.06	2.27–4.14	41	10,816	2.78	1.81–4.26
	≥40	30	1232	7.31	4.96–10.76	4	1517	1.94	0.70–5.41
	Total	611	140,220			213	114,494		

CI, confidence interval; RR, relative risk.

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Another explanation of the increased risk in early gestation could be related to a higher cumulative incidence of being treated with cervical cone excisions in older rather than younger women. The relative risk of preterm delivery, associated with cone excision, increases with decreasing duration in pregnancy.<sup>24</sup> In preterm deliveries, fetal deaths are likely to happen during labor and are caused by immaturity.

After 36 weeks of gestation, an increasing difference in risk of fetal death between younger and older mothers was observed. A failure of the uterine vasculature to adapt adequately to the increased hemodynamic demands of pregnancy, most pronounced in the oldest

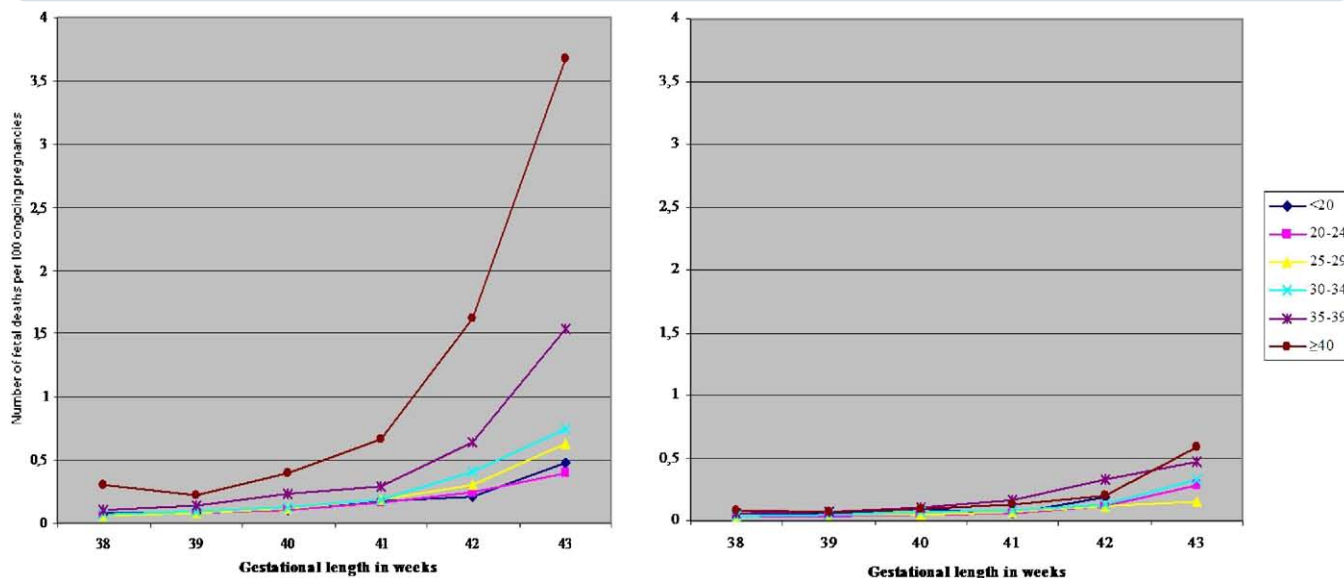
women, has been discussed.<sup>25,26</sup> However, fetal growth restriction has not been shown to have a stronger association with increased fetal death risk in the third trimester in older as compared with younger mothers.<sup>27</sup>

Obstetric practice in Norway has gone through major changes since the mid-1980s. This change may be attributed to the introduction of ultrasonographic examinations and extensive use of cardiotocography. The intervention rate has increased and the share of postterm pregnancies has decreased. The cesarean section rate has increased from 1.8% in 1967 to 16.3% in 2006. A total of 9.3% of the women delivered in gestational week 42 in 1967, as compared with 6.9% in

2006. The proportion of mothers delivering in gestational weeks 43 or after was 4.4% in 1967 and 0.3% in 2006.

Term predicted by ultrasonographic examination may, for many obstetricians, be more trustworthy than term predicted by last menstrual period. Hence, induction of labor may have been more common in pregnancies estimated to be postterm by ultrasonographic examination, than by the last menstrual period. Also, the treatment used for the induction of labor may have improved during our study period. It is likely that older women have been overrepresented to induction of labor in recent time because the tools used in pregnancy to diagnose fe-

FIGURE 2

**Fetal deaths according to gestational length and maternal age during 1967-2006 and 1987-2006**

Number of fetal deaths per 100 ongoing pregnancies according to gestational length and maternal age in term and post term pregnancies, during the periods 1967-1986 and 1987-2006.

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tal pathology have become more sensitive, and age is associated with such pathology.

The decreased fetal death risk at term in older women after 1986 may, however, also be a result of changes in selection of women child-bearing at higher age to better-educated and healthier women. There has, however, been an increase in Norwegian women's body mass index during the last 2 decades.<sup>28,29</sup> Because high body mass index is related to increased risk of fetal death, an increase rather than a decrease in fetal death rate would have been expected.

More women are having their first or second child above the age of 35 years. Reliable knowledge on the risk of fetal death associated with maternal age and length of gestation is therefore important for establishing appropriate antenatal care and clinical decisions on delivery timing. In this study, including ongoing pregnancies in Norway during 1967-2006, the impact of high maternal age on fetal death risk was highest at term and the relative importance of high age increased in post term pregnancies. This increased risk of fetal death in older women was more pronounced in the pe-

riod 1967-1986, suggesting that in the absence of modern obstetric care, the risk of fetal death in elderly mothers with postterm pregnancies is high. ■

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