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Trends in the Incidence of Venous Thromboembolism during Pregnancy or Postpartum: A 30-Year Population-Based Study

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Background: **The risk for venous thromboembolism during pregnancy or postpartum is uncertain.**

Objectives: **To estimate the relative and absolute risk for deep venous thrombosis and pulmonary embolism during pregnancy and postpartum and to describe trends in incidence.**

Design: **Population-based inception cohort study using the resources of the Rochester Epidemiology Project.**

Setting: **Olmsted County, Minnesota.**

Patients: **Women with deep venous thrombosis or pulmonary embolism first diagnosed between 1966 and 1995, including women with venous thromboembolism during pregnancy or the postpartum period (defined as delivery of a newborn no more than 3 months before the deep venous thrombosis or pulmonary embolism event date, including delivery of a stillborn infant after the first trimester).**

Measurements: **The authors obtained yearly counts of live births in Olmsted County between 1966 and 1995 from the Minnesota Department of Health.**

Results: **The relative risk (standardized incidence ratio) for venous thromboembolism among pregnant or postpartum women was 4.29 (95% CI, 3.49 to 5.22; $P < 0.001$), and the overall incidence of venous thromboembolism (absolute risk) was 199.7 per 100 000 woman-years. The annual incidence was 5 times higher among postpartum women than pregnant women (511.2 vs. 95.8 per 100 000), and the incidence of deep venous thrombosis was 3 times higher than that of pulmonary embolism (151.8 vs. 47.9 per 100 000). Pulmonary embolism was relatively uncommon during pregnancy versus the postpartum period (10.6 vs. 159.7 per 100 000). Over the 30-year study period, the incidence of venous thromboembolism during pregnancy remained relatively constant whereas the postpartum incidence of pulmonary embolism decreased more than 2-fold.**

Limitations: **Because the Olmsted County population was 98% white and of non-Hispanic ethnicity, the results may not be generalizable to other ethnicities.**

Conclusions: **Among pregnant women, the highest risk period for venous thromboembolism and pulmonary embolism in particular is during the postpartum period. Any prophylaxis against these events should be particularly targeted to postpartum women. Although the incidence of pulmonary embolism has decreased over time, the incidence of deep venous thrombosis remains unchanged, indicating the need to better identify pregnant women at increased risk.**

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Knowledge of the relative risk and incidence (absolute risk) of venous thromboembolism among pregnant and postpartum women is important for identifying patients who would benefit from prophylaxis. However, there are few data regarding the relative risk for venous thromboembolism during pregnancy (1), and the reported incidence of venous thromboembolism among pregnant or postpartum women varies widely. Previous studies reported incidence rates ranging from 18 to 95 events per 100 000 woman-years during pregnancy and from 199 to greater than 1900 per 100 000 woman-years during the postpartum period (2–7). Substantial variation also exists in the reported incidence of venous thromboembolism by trimester and by time after delivery (8–14). Given the markedly worse survival rate after pulmonary embolism compared with that after deep venous thrombosis alone (15), identification of those pregnant or postpartum women at high risk for pulmonary embolism is especially important. However, the incidence by type of venous thromboembolic event during pregnancy and during the postpartum period is uncertain (8, 10, 13, 14, 16–21).

The wide variability in reported rates probably reflects differences in study design. For example, published studies identified cases from a variety of sources, including hospital inpatient databases (2, 3, 16, 22), the United Kingdom's National Health Service (4, 23), and hospital discharge and maternity registries (5, 6). Because of diagnostic uncertainty or misclassification, data from these sources possibly underestimated or overestimated the actual incidence rate. Incidence rates derived from hospital inpatient databases potentially missed venous thromboembolism events that occurred after discharge (2, 3, 5, 7, 22), and rates possibly varied when data were reported by selected strata (23) or when only patients referred to tertiary care centers were included (7). Moreover, most studies did not separate incident from recurrent events or include autopsy-discovered events (13, 24, 25). Finally, only a few studies reported trends in pregnancy-associated venous thromboembolism incidence over time (5, 6, 23).

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Context

The risk for venous thromboembolism during pregnancy and in the postpartum period has not been well defined by previous studies.

Contribution

Using 30 years of data, these investigators found that the risk for a first episode of venous thromboembolism is 5 times higher in the postpartum period than during pregnancy. The risk for pulmonary embolism is 15 times greater during the postpartum period than during pregnancy.

Implications

Women at high risk for venous thromboembolism may require special consideration for anticoagulation in the postpartum period.

Cautions

The ethnicity of the study population was 98% white. The findings may not be generalizable to other ethnic groups.

—The Editors

Because of these limitations, we performed a population-based study to estimate the relative risk and incidence of venous thromboembolism during pregnancy and the postpartum period within a well-defined geographic area, and we sought to describe trends in incidence over time. We examined the incidence of pregnancy-associated deep venous thrombosis and pulmonary embolism in women living in Olmsted County, Minnesota, between 1966 and 1995. We calculated incidence during pregnancy, incidence during the first 3 postpartum months, and total incidence.

METHODS

Study Setting and Design

Using the data resources of the Rochester Epidemiology Project (26), we identified the inception cohort of Olmsted County residents with a first lifetime deep venous thrombosis or pulmonary embolism diagnosed between 1966 and 1995. We included all female residents of Olmsted County who had a venous thromboembolism during pregnancy or the postpartum period; the postpartum period was defined as delivery of a newborn within 3 months before the deep venous thrombosis or pulmonary embolism event date, including delivery of a stillborn infant after the first trimester (27). The institutional review board of the Mayo Clinic approved the study.

Definition of Deep Venous Thrombosis and Pulmonary Embolism

A diagnosis of deep venous thrombosis was confirmed by venography, computed tomography, magnetic resonance imaging, impedance plethysmography, continuous-wave Doppler ultrasonography (performed in the Mayo Clinic Vascular Laboratory), compression venous duplex ultrasonography, radionuclide venography, radiolabeled fibrinogen leg scan, or pathologic examination of a thrombus removed at surgery or autopsy. A patient was also included when 1) the medical record indicated that a physician diagnosed deep venous thrombosis (or possible deep venous thrombosis); 2) signs and symptoms consistent with deep venous thrombosis were present; and 3) the patient received a course of anticoagulant therapy with heparin, warfarin, or a similar agent or underwent a surgical procedure for treatment of deep venous thrombosis (27). A diagnosis of pulmonary embolism was confirmed by pulmonary angiography, computed tomography, magnetic resonance imaging, a perfusion or ventilation–perfusion lung scan indicating high probability for pulmonary embolism, or pathologic examination of a thrombus removed at surgery or autopsy. A patient was also included when 1) the medical record indicated that a physician made a diagnosis of pulmonary embolism; 2) signs and symptoms consistent with pulmonary embolism were present; and 3) the patient received a course of anticoagulant therapy with heparin, warfarin, or a similar agent or underwent a surgical procedure for treatment of pulmonary embolism, such as placement of an inferior vena cava filter. We did not include patients who received only short-term anticoagulation while awaiting results of diagnostic evaluation for suspected deep venous thrombosis or pulmonary embolism.

Statistical Analysis

We also used the resources of the Rochester Epidemiology Project to calculate Olmsted County pregnancy rates. We determined the denominator by using Olmsted County census data from 1970, 1980, 1990, and 2000 for the population estimates, with linear interpolation for the years between censuses. Yearly counts of live births, fetal deaths, and neonatal deaths in Olmsted County from 1966 to 1995 were obtained from published documents from the Minnesota Department of Health (Minnesota Health Statistics Annual Summary). Counts were derived from the residence of the mother rather than the place of birth. We were able to obtain maternal ages for live births in Olmsted County but not for fetal or neonatal deaths. We restricted our study to pregnant women who did not have spontaneous or therapeutic abortions, but we did include stillbirths. We calculated age-specific rates of live births by using the number of live births as the numerator; for the denominator, we used age-specific census estimates of the female population of Olmsted County to estimate person-years at risk.

Each mother who gave birth was assumed to have a single year of time within which to have a venous thromboembolism event (9 months during gestation and 3 months postpartum). Although the standard duration of the postpartum period is 6 weeks, we used a duration of 3 months for this analysis because we wished to include all

venous thromboembolism events that could possibly be related to pregnancy. We were able to calculate age-specific woman-years for each year (for example, number of live births in Olmsted County); therefore, woman-years could be summed over the relevant time interval to calculate the correct denominator for the estimates of venous thromboembolism incidence. To calculate the incidence of venous thromboembolism during pregnancy and postpartum separately, we separated the denominator data by multiplying the total number of woman-years by 0.75 for pregnancies and by 0.25 for postpartum women. When determining incidence by trimester, half-trimester, and week, we multiplied by 0.25, 0.125, and 0.019, respectively (13 of 52 weeks, 6.5 of 52 weeks, and 1 of 52 weeks). We also calculated age-specific incidence rates for deep venous thrombosis alone and for pulmonary embolism (with or without deep venous thrombosis) among pregnant and postpartum women. Age-specific incidence rates were calculated overall (1966 to 1995) and for 3 time periods: 1966 to 1975, 1976 to 1985, and 1986 to 1995. Overall incidence rates over time were directly adjusted to the age distribution of total woman-years during the entire time period (1966 to 1995).

Finally, we estimated the incidence of venous thromboembolism in Olmsted women of child-bearing years (age 15 to 45 years) that was not associated with pregnancy by subtracting pregnancy-related and postpartum-related venous thromboembolism cases from the total number of cases (numerator) and by subtracting the number of live births between 1966 and 1995 from the total person-years at risk for all Olmsted County women between the ages of 15 and 45 years (denominator). We estimated the relative risk (standardized incidence ratio) for venous thromboembolism among pregnant/postpartum Olmsted County women by dividing the observed number of venous thromboembolism events by the expected number of venous thromboembolism events determined using the incidence among nonpregnant Olmsted County women. We estimated the relative risk for venous thromboembolism during pregnancy or in the 3-month postpartum period by dividing the observed number of patients with venous thromboembolism during pregnancy or the postpartum period by the expected number with venous thromboembolism. The latter number was estimated by multiplying the age-specific incidence of venous thromboembolism attributable to other causes by the age-specific woman-years observed among the pregnant and postpartum women in Olmsted County between 1966 and 1995. We calculated exact 95% confidence intervals for all venous thromboembolism rates by assuming that the observed number of venous thromboembolism events followed a Poisson distribution.

We modeled the overall venous thromboembolism incidence, the incidence of deep venous thrombosis, and the incidence of pulmonary embolism among pregnant women and among postpartum women. To assess the relationships of crude incidence rates to year of diagnosis, to age at diagnosis, and to postpartum status, we used generalized linear models that assumed a Poisson error structure with a log-link function and a log(woman-years) offset (28). We modeled a categorical version and a functional (usually linear) version of each variable. When modeling functional forms of calendar year at diagnosis and age at diagnosis, we used the midpoint of the categorical interval. If the linear version of age or calendar year fit as well as the categorical version, we used the linear version, fitting higher-order terms (quadratic or interactions) if the model-scaled deviance suggested that they might explain the data better.

Model goodness-of-fit was assessed by model-scaled deviance, which has a limiting chi-square distribution with degrees of freedom equal to the number of cells minus the number of model parameterized. We also used Pearson chi-square residuals from the models with the most parameterized models (overall and within each postpartum subgroup) divided by the degrees of freedom to estimate dispersion parameters (φ). We had no biological reason to think there was overdispersion, and φ was less than 1.3 for all saturated models assessed; therefore, we decided that inflation of the model variance estimates was unnecessary. Among the models that fit, we assessed a variable's contribution by examining the change in deviance between the 2 nested models. The change in deviance has a chi-square distribution with degrees of freedom equal to the difference between the number of parameters in each of the 2 models. A P value of less than 0.05 was considered significant.

Role of the Funding Sources

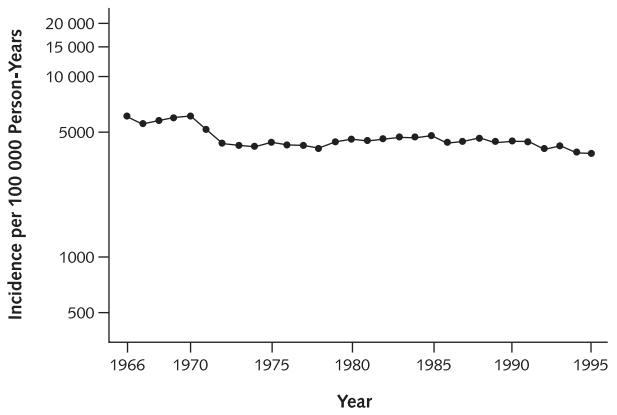
The funding sources, the National Institutes of Health and the Mayo Foundation, had no role in the design, conduct, or analysis of this study or in the decision to submit the manuscript for publication.

RESULTS

Altogether, 50 080 births occurred among Olmsted County women who were 15 years of age or older during the 30-year study period, 1966 to 1995. Within this time frame, both the population of Olmsted County and the number of pregnancies increased. However, the pregnancy rate (births per female population) decreased in the early 1970s but remained stable thereafter (**Figure 1**). A shift toward older maternal age also occurred during the study period. Among women of childbearing age, the rate of live births ranged from a low of 590.6 per 100 000 for women 35 years of age or older to a high of 14280.3 per 100 000 for those 25 to 29 years of age.

During this same time period, 105 cases of deep venous thrombosis or pulmonary embolism were identified in women who were either pregnant or postpartum. Five events occurred among women with spontaneous or therapeutic abortions and were excluded from further analysis because maternal age was unavailable in the Minnesota State Department of Health tables. Of the remaining

Figure 1. **Pregnancy rate (births per female population) in Olmsted County, Minnesota, 1966–1995, by calendar year.**



events, 76 represented deep venous thrombosis alone and 24 were cases of pulmonary embolism with or without deep venous thrombosis. This was over 4 times higher than the expected number of 23.3 venous thromboembolism events for nonpregnant women of the same age (standardized incidence ratio, 4.29 [CI, 3.49 to 5.22]; $P < 0.001$). The overall median age of pregnant or postpartum women with a venous thromboembolism event was 27.6 years (range, 16.8 to 43.8 years); the median age at diagnosis was 27.6 years for deep venous thrombosis and 28.5 years for pulmonary embolism cases. Two of the 100 women with venous thromboembolism during the postpartum period had pregnancies that ended in stillbirths at 36 weeks' gestation or later.

When all pregnant and postpartum women were considered together, the unadjusted incidence rates for any venous thromboembolism event, deep venous thrombosis alone, and pulmonary embolism with or without deep venous thrombosis were 199.7, 151.8 and 47.9 per 100 000 woman-years, respectively (**Table 1**); incidence rates were 292.8, 167.0 and 125.8 per 100 000 woman-years directly adjusted to the age distribution of the population of white women in the United States in the year 2000. The overall incidence of venous thromboembolism was higher in the postpartum period than during pregnancy (511.2 vs. 95.8 per 100 000). Not only was the overall incidence of deep venous thrombosis higher in the postpartum period than during pregnancy (351.4 vs. 85.2 per 100 000), but the observed incidence of pulmonary embolism was more than 15 times higher in the first 3 postpartum months (159.7 vs. 10.6 per 100 000).

The highest incidence of venous thromboembolism during pregnancy occurred within the youngest age group (15 to 19 years) (**Table 1**), and most events were cases of deep venous thrombosis alone. In contrast, the incidence of venous thromboembolism during the postpartum period increased with advancing maternal age and was highest in women in the oldest age group (35 years of age or older). Moreover, the incidence of pulmonary embolism was strikingly increased for postpartum women within the oldest age group. Of the postpartum women with pulmonary embolism, one 38-year-old woman died suddenly and pulmonary embolism was discovered at autopsy.

Only 4 venous thromboembolism events occurred during the first trimester. The overall incidence and the incidence of deep venous thrombosis and pulmonary embolism individually were nonsignificantly higher during the third trimester compared with the second trimester for all maternal age groups except for women from age 25 to 29 years ($P > 0.30$ univariately, $P > 0.60$ for interactions) (**Table 2**). Fourteen of 36 events occurred during the second trimester (weeks 13 to 26; incidence rate, 111.8 per 100 000 woman-years), whereas 18 of 36 events occurred during the third trimester (week 27 or later; incidence rate, 143.8 per 100 000 woman-years). However, the incidence rates were relatively constant for the last 20 weeks of pregnancy (incidence rate, 143.8 per 100 000 woman-years). The overall incidence and the incidence of deep venous thrombosis and pulmonary embolism individually were highest during the first postpartum week (25-fold higher in the first postpartum week than in the last trimester of pregnancy) and progressively decreased thereafter (**Table 2**).

Table 1. **Incidence of Deep Venous Thrombosis and Pulmonary Embolism among Pregnant, Postpartum, and Nonpregnant Women in Olmsted County, Minnesota, 1966–1995**

Age Group, y	Deep Venous Thrombosis						Pulmonary Embolism			
	Pregnancy		Postpartum		Total		Pregnancy		Postpartum	
	Women, *n*	Rate (95% CI)*	Women, *n*	Rate (95% CI)*	Women, *n*	Rate (95% CI)*	Women, *n*	Rate (95% CI)*	Women, *n*	Rate (95% CI)*
15–19	5	200.6	2	240.7	7	210.6	1	40.1	0	0.0
20–24	7	71.5	11	337.0	18	137.8	0	0.0	5	153.2
25–29	8	56.2	19	400.6	27	142.3	0	0.0	7	147.6
30–34	8	95.5	10	358.2	18	161.2	3	35.8	2	71.6
≥35	4	149.8	2	224.7	6	168.5	0	0.0	6	674.2
All ages†	32	85.2 (58.3–120.3)	44	351.4 (255.4–471.8)	76	151.8 (119.6–190.0)	4	10.6 (2.9–27.3)	20	159.7 (97.6–246.7)

* Incidence per 100 000 woman-years.
† Incidence per 100 000 woman-years unadjusted.

Sixty-two of 64 events occurred during the first 6.5 postpartum weeks (incidence rate, 990.4 per 100 000 woman-years), whereas only 2 events (at postpartum weeks 8 and 10) occurred in the second 6.5 postpartum weeks (incidence rate, 31.9 per 100 000 woman-years). In general, the incidence by week after delivery was highest among mothers who were 35 years of age or older.

Over the 30-year study period, the overall incidence of venous thromboembolism decreased by half, with most of the observed decrease occurring during the 1970s (**Table 3** and **Figure 2**). This decline was noted in all age groups except in patients 15 to 19 years of age, where the incidence more than doubled from the first to last decades (data not shown). The greatest decrease occurred among postpartum women, whereas the incidence among pregnant women remained essentially constant over the last 2 study decades. The overall incidence of deep venous thrombosis decreased from the earliest study decade to the last (from 223.8 to 148.9 per 100 000 woman-years), mainly because of a reduced incidence during the postpartum period. The incidence of deep venous thrombosis during pregnancy remained essentially unchanged for the entire period. The incidence of pulmonary embolism during pregnancy, postpartum, and overall was constant for the first 2 decades of study, but of particular note, there were no pulmonary embolism events among pregnant or postpartum women in the last study decade.

In the univariate analyses, the relative risk for venous thromboembolism was more than 5 times higher during the first 3 postpartum months versus during pregnancy (5.33 [CI, 3.55 to 8.02]; $P < 0.001$). The best fitting model included interactions between postpartum status (pregnancy vs. postpartum) and age, and between postpartum status and calendar year (**Figure 3**). During pregnancy, the risk for venous thromboembolism was significantly related to maternal age, with a higher risk for both younger and older mothers ($P = 0.044$) (**Table 4**). The risk for postpartum venous thromboembolism decreased significantly by calendar year ($P < 0.001$) and increased nonsignificantly with increasing maternal age ($P = 0.068$). The relative risk for deep venous thrombosis alone was more than 4 times higher during the first 3 postpartum months versus during pregnancy ($P < 0.001$). The relative risk for pulmonary embolism was significantly and directly related to the postpartum period and increasing maternal age and inversely related to calendar year.

DISCUSSION

We have described the incidence of deep venous thrombosis and pulmonary embolism among pregnant and postpartum women in a well-defined geographic population from 1966 to 1995. Previously, we estimated that the incidence of venous thromboembolism among Olmsted County women from 1966 to 1990 ranged from 27 to 84 per 100 000 woman-years for women 15 to 19 years of age and 40 to 44 years of age, respectively (27). Of the women in these age groups, 25% had venous thromboembolism during or immediately following pregnancy. The incidence of venous thromboembolism in women of childbearing age (15 to 45 years of age) attributable to other causes was 17.1, 35.0, 46.5, 57.4, and 62.6 per 100 000 woman-years, unadjusted, for women 15 to 19, 20 to 24, 25 to 29, 30 to 34, and 35 years of age or older, respectively. The overall incidence was 48.1 (directly adjusted to the age distribution of the population of white women in the United States in the year 2000). In the current study, which captures an additional 5 years of data and specifically addresses the frequency of venous thromboembolism among pregnant or postpartum women, the true incidence is much higher than previously published estimates: 240.7 per 100 000 woman-years for women between the ages of 15 and 19 years and 337.1 per 100 000 for women 35 years of age and older.

Previous reports of the incidence of deep venous thrombosis and pulmonary embolism during pregnancy versus postpartum are inconsistent (2–4, 6–8, 11, 13, 18, 21, 25). Most studies of pregnancy-associated venous thromboembolism used the number of deliveries (or maternities) as the denominator, which does not adjust for the different duration of risk for pregnancy versus the postpartum period (2–7). Furthermore, the definition of the post-

Table 1—**Continued**

Pulmonary Embolism		All Venous Thromboembolism							
Total		Pregnancy		Postpartum		Total		Not Pregnant or Postpartum	
Women, *n*	Rate (95% CI)*	Women, *n*	Rate (95% CI)*	Women, *n*	Rate (95% CI)*	Women, *n*	Rate (95% CI)*	Women, *n*	Rate (95% CI)*
1	30.1	6	240.7	2	240.7	8	240.7	19	17.1
5	38.3	7	71.5	16	490.1	23	176.1	40	35.0
7	36.9	8	56.2	26	548.2	34	179.2	53	46.5
5	44.8	11	131.3	12	429.8	23	206.0	64	57.4
6	168.5	4	149.8	8	898.9	12	337.1	117	62.6
24	47.9 (30.7–71.3)	36	95.8 (67.1–132.7)	64	511.2 (393.7–652.8)	100	199.7 (162.5–242.9)	293	46.0 (40.9–51.5)

Table 2. **Incidence of Venous Thromboembolism among Pregnant or Postpartum Women in Olmsted County, Minnesota, by Trimester and by Week for First 6 Postpartum Weeks, 1966–1995**

Age Group, y	Pregnancy				Postpartum			
	2nd Trimester		3rd Trimester		Week 1		Week 2	
	Women, *n*	Rate (95% CI)*	Women, *n*	Rate (95% CI)*	Women, *n*	Rate (95% CI)†	Women, *n*	Rate (95% CI)†
15–19	2	240.7	3	361.0	2	3166.8	0	0
20–24	3	91.9	4	122.5	4	1612.2	7	2821.4
25–29	4	84.3	2	42.2	16	4438.9	4	1109.7
30–34	4	143.3	6	214.9	8	3770.5	1	471.3
≥35	1	112.4	3	337.1	4	5913.7	2	2956.8
All ages‡	14	111 (61.1–187.6)	18	143.8 (85.2–227.2)	34	3573.2 (2474.6–4993.2)	14	1471.3 (804.4–2468.6)

* Incidence per 100 000 woman-years where the denominator is the number of live births divided by 4 (trimester set to 0.25 year).
† Incidence per 100 000 woman-years where the denominator is the number of live births divided by 52 (52 weeks per year).
‡ Incidence per 100 000 woman-years unadjusted.

partum period differed among studies. In general, our overall venous thromboembolism incidence rates, as well as the rates for deep venous thrombosis and pulmonary embolism per se, were 1.6 to 2.6 times higher than previously reported (2–7). We believe our community-wide medical records linkage system, which offered a more thorough case ascertainment, probably accounts for this difference. Because the Olmsted County population was 98% white and of non-Hispanic ethnicity, the results may not be generalizable to other ethnicities.

Although the incidence of venous thromboembolism is higher among pregnant or postpartum women than among women of similar age in the general population, our study cannot address whether prophylaxis during pregnancy or the postpartum period is indicated. However, our data can provide guidance to physicians who are considering prophylaxis for women who are believed to be at high risk for pregnancy-related venous thromboembolism. For example, the incidence of venous thromboembolism overall, and of pulmonary embolism in particular, was significantly higher among postpartum women, especially older postpartum women. Therefore, physicians who are contemplating venous thromboembolism prophylaxis should give strongest consideration to patients who fall into this category. For example, the overall venous thromboembolism incidences of 3.6% and 1.5% for the first and second postpartum weeks, respectively (**Table 2**), are at least comparable to the 2% to 5% incidence of symptomatic venous thromboembolism after elective total hip replacement in patients who did not receive prophylaxis (29). Our findings suggest that prophylaxis for a minimum of the first 2 postpartum weeks (ideally, for the first 6 weeks) will protect women during the highest period of risk. These suggestions are supported by a recent study showing that, of events occurring in the first 6 postpartum weeks, 50% occurred in the first 2 weeks and 50% occurred in the next 4 weeks; only 2 events occurred within postpartum weeks 7 through 12 (30).

In contrast, the incidence of venous thromboembolism in pregnant women was higher among the youngest (15 to 19 years) and the oldest (35 years of age or older) women. We could not estimate the incidence of venous thromboembolism during the first trimester because pregnancies of less than 13 weeks' duration are not uniformly captured by the Minnesota Department of Health. However, only 4 events occurred during the first trimester, suggesting that the incidence is low compared with that during the second and third trimesters. Because many women are unaware of a pregnancy until relatively late into the first trimester, one could consider providing prophylaxis during the period of conception for women considered at high risk for pregnancy-associated venous thromboembolism. However, our data suggest that such a practice is unnecessary. Although the incidence was higher in the third trimester than the second trimester, the incidence rates were relatively constant for the last 20 weeks of pregnancy, as sug-

Table 3. **Trends by Decade for Incidence of Venous Thromboembolism among Pregnant or Postpartum Women in Olmsted County, Minnesota, ≥15 Years of Age, 1966–1995**

Time Period	Deep Venous Thrombosis						Pulmonary Embolism			
	Pregnancy		Postpartum		Total		Pregnancy		Postpartum	
	Women, *n*	Rate (95% CI)*	Women, *n*	Rate (95% CI)*	Women, *n*	Rate (95% CI)*	Women, *n*	Rate (95% CI)*	Women, *n*	Rate (95% CI)*
1966–1975	11	103.8 (40.2–167.5)	21	583.5 (328.1–838.9)	32	223.8 (144.0–303.5)	2	19.1 (0–46.8)	10	245.1 (90.8–399.4)
1976–1985	9	76.5 (26.1–126.8)	10	243.2 (91.2–395.3)	19	118.2 (64.6–171.7)	2	18.1 (0.0–43.2)	10	278.8 (103.7–453.9)
1986–1995	12	94.0 (38.8–149.2)	13	313.8 (135.1–492.4)	25	148.9 (88.0–209.8)	0	0.0 (0.0–7.4)	0	0.0 (0.0–7.4)

* Incidence per 100 000 woman-years directly adjusted to the overall age distribution of pregnant and postpartum woman-years in Olmsted County, 1966–1995.

Table 2—**Continued**

Postpartum							
Week 3		Week 4		Week 5		Week 6	
Women, *n*	Rate (95% CI)†	Women, *n*	Rate (95% CI)†	Women, *n*	Rate (95% CI)†	Women, *n*	Rate (95% CI)†
0	0	0	0	0	0	0	0
1	403.1	1	403.1	2	806.1	0	0
3	832.3	1	277.4	0	0	2	554.9
1	471.3	0	0	0	0	1	471.3
1	1478.4	1	1478.4	0	0	0	0
6	630.6 (231.4–1372.5)	3	315.3 (65.0–921.4)	2	210.2 (25.4–759.3)	3	315.3 (65.0–921.4)

gested in a previous report (18). However, contrary to 1 previous report (21), we observed no spike in venous thromboembolism incidence in the last week of pregnancy (data not shown). Therefore, our data suggest that prophylaxis during pregnancy should be particularly directed to women in the youngest and oldest age groups and those in the second and third trimesters, particularly in the last 20 weeks of pregnancy.

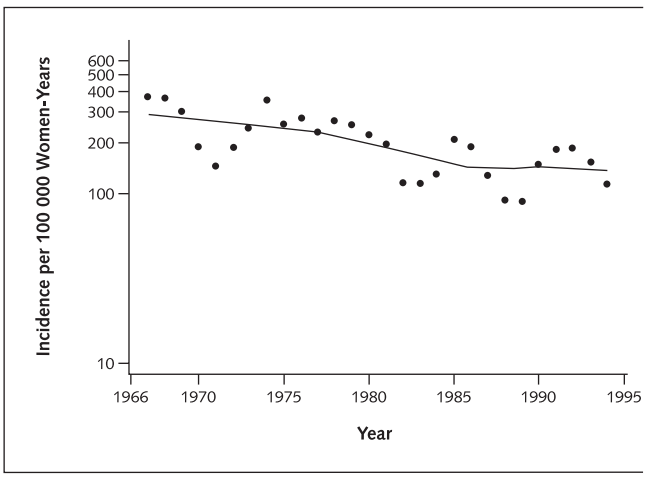
The incidence of venous thromboembolism in the general population is strongly and directly related to advancing patient age (27). Previous studies found a similar relationship between venous thromboembolism incidence and maternal age (23). Consequently, we were surprised to find that the youngest women had a significantly higher incidence of deep venous thrombosis and venous thromboembolism overall during pregnancy. Recent analyses of the Nationwide Inpatient Sample (Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality) reached a similar conclusion (James AH. Personal communication). In a previous population-based case–control study, we tested many baseline and pregnancy-related characteristics as potential risk factors for venous thromboembolism (20). In univariate analyses, smoking, previous superficial venous thrombosis, and varicose veins were associated with venous thromboembolism during pregnancy or the postpartum period, whereas maternal age, body mass index, parity, gravidity, preeclampsia, bed rest, surgery or anesthesia, anticoagulant prophylaxis, and hormone therapy were not. In multivariate analyses, only smoking (odds ratio, 2.4 [CI, 1.2 to 4.6]) and previous superficial venous thrombosis (odds ratio, 9.4 [CI, 1.2 to 75.4]) were independent risk factors for venous thromboembolism during pregnancy or postpartum. Within our cohort of women with venous thromboembolism during pregnancy, the proportion of the youngest women who were current or former smokers was similar to that of older women. Futhermore, none of the women within the youngest age group had previous superficial venous thrombosis, preeclampsia, hypertension, placenta previa, hyperemesis gravidarum, or a history of prolonged bed rest. Therefore, we could not identify any recognized provocation that might have caused a higher incidence of venous thromboembolism during pregnancy among the youngest age group.

The overall incidence of pregnancy-associated venous thromboembolism decreased over the 30-year study period, predominantly because of a decrease in the postpartum incidence of pulmonary embolism. Among pregnant women, there was little change in the overall rate of venous thromboembolism. When all women were considered, the incidence of deep venous thrombosis declined slightly and nonsignificantly, but the incidence of pulmonary embolism decreased dramatically during the last 10 years of the study. Indeed, no pregnancy-associated pulmonary embolism events occurred during this latter period. This observation is unlikely to have occurred by chance (assuming a Poisson distribution; $P < 0.02$). The observed decline in pulmonary embolism incidence was not attributable to a decrease in the number of pregnancies, loss of Olmsted County population, or a decrease in the pregnancy rate

Table 3—**Continued**

Pulmonary Embolism		All Venous Thromboembolism					
Total		Pregnancy		Postpartum		Total	
Women, *n*	Rate (95% CI)*	Women, *n*	Rate (95% CI)*	Women, *n*	Rate (95% CI)*	Women, *n*	Rate (95% CI)*
12	75.6 (31.8–119.4)	13	122.9 (53.5–192.3)	31	828.6 (530.2–1127.0)	44	299.3 (208.4–390.3)
12	83.3 (35.6–130.9)	11	94.6 (38.3–150.8)	20	522.0 (290.1–753.9)	31	201.4 (129.7–273.1)
0	0.0 (0.0–7.4)	12	94.0 (38.8–149.2)	13	313.8 (135.1–492.4)	25	148.9 (88.0–209.8)

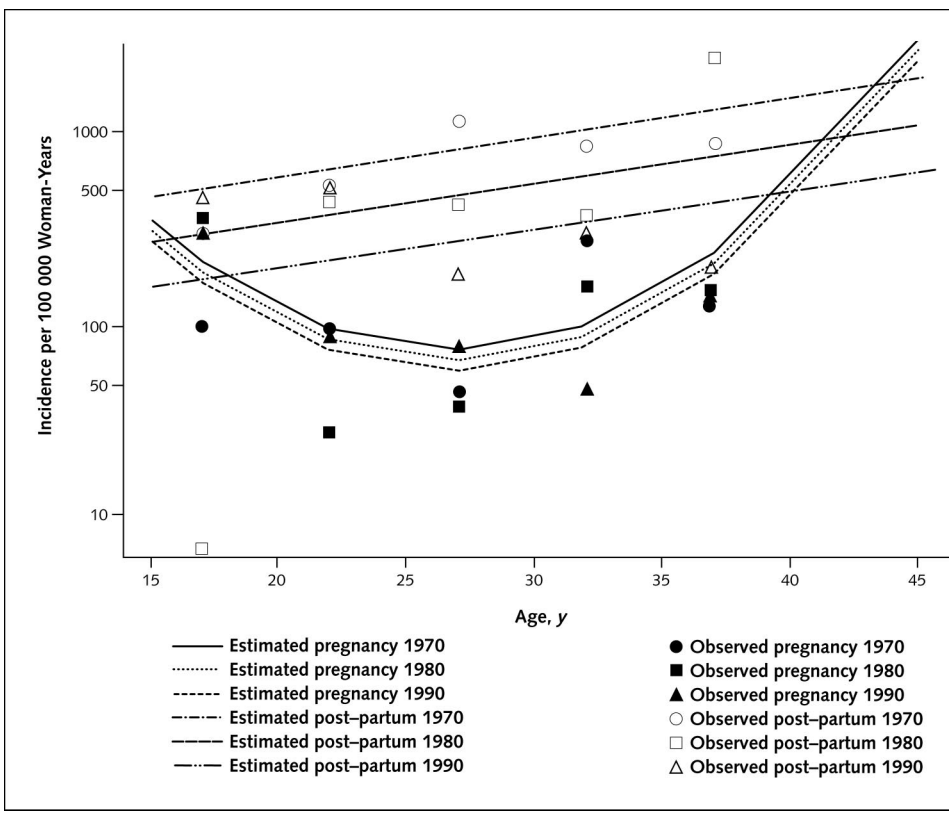
Figure 2. **Adjusted incidence per 100 000 woman-years of venous thromboembolism among pregnant or postpartum women in Olmsted County, Minnesota, adjusted to the overall age distribution of pregnancy and postpartum years from 1966–1995, by calendar year (3-year moving window of time).**



(**Figure 1**). Because most pulmonary embolism events occurring between 1976 and 1985 were objectively diagnosed, an improved ability to rule out pulmonary embolism is unlikely to account for the observed absence of pulmonary embolism events during the last study decade. Instead, we speculate that this observation may be related to earlier mobilization of the mother associated with progressively shorter hospitalizations after delivery in the recent decade. Further studies are required to test this hypothesis.

In summary, we have shown that the incidence of venous thromboembolism among pregnant or postpartum women exceeds the incidence among nonpregnant women of similar age after correctly accounting for the time at risk. The postpartum period is the highest-risk period for venous thromboembolism and pulmonary embolism in particular. This risk can be further stratified by maternal age and time since delivery. For uncertain reasons, the incidence of postpartum venous thromboembolism, particularly pulmonary embolism, appears to be declining over time. In contrast, the overall incidence of venous thromboembolism (and deep venous thrombosis in particular) during pregnancy appears unchanged over time. The incidence of venous thromboembolism during pregnancy is highest during the last 20 weeks of pregnancy, particularly among the youngest and the oldest mothers. Our study results have significant implications for prophylaxis consid-

Figure 3. **Poisson regression models of venous thromboembolism incidence rates by year of maternal age among pregnant or postpartum women in Olmsted County, Minnesota, 1966–1995.**



Actual age-specific and year-specific rates are shown as data points, and modeled age-specific and year-specific rates derived from the Poisson regression analyses are shown as lines.

Table 4. **Relative Risk for Venous Thromboembolism by Pregnancy Status, Calendar Year, and Maternal Age among Women from Olmsted County, Minnesota, 1966–1995**

Comparison	Model Estimates		Model Goodness of Fit	
	Relative Risk (95% CI)	*P* Value	Deviance Divided by Degrees of Freedom	*P* Value
Venous thromboembolism during pregnancy				
Age 15 y vs. 25 y	5.22 (1.34–20.36)	0.044*	0.995	0.45
Age 40 y vs. 25 y	5.46 (1.31–22.78)			
Age 40 y vs. 15 y	1.05 (0.29–3.80)			
Venous thromboembolism during postpartum period				
Risk per increasing calendar year	0.95 (0.92–0.98)	<0.001	1.185	0.29
Risk per 10 years of age	1.57 (0.97–2.55)	0.068		
Deep venous thrombosis				
Postpartum vs. pregnancy	4.12 (2.62–6.50)	<0.001	1.285	0.143
Pulmonary embolism				
Postpartum vs. pregnancy	15.00 (5.13–43.89)	<0.001	1.327	0.123
Risk per increasing calendar year	0.90 (0.85–0.96)	<0.001		
Risk per 10 years of age	2.99 (1.37–6.52)	0.006		

* Two degrees of freedom chi-square (quadratic form of age).

erations in pregnant and postpartum women. Whereas maternal mortality has declined dramatically in the past 70 years, pulmonary embolism remains 1 of the most common causes of maternal death in the United States and the United Kingdom (31–34). The rate of pulmonary embolism–related maternal death remains at about 2 to 3 per 100 000 live births in the United States (17, 33). By better directing prophylaxis to women considered at high risk for pregnancy-related venous thromboembolism, health care providers may be able to reduce the rate of maternal deaths resulting from pulmonary embolism. Additional studies are needed, however, to identify risk factors for venous thromboembolism during pregnancy.

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