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## Trends in venous thromboembolism among pregnancy-related hospitalizations, United States, 1994-2009

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### Abstract

**OBJECTIVE**—The purpose of this study was to evaluate national trends in the rate of pregnancy-related hospitalizations for venous thromboembolism (VTE) from 1994-2009 and to estimate the prevalence of comorbid conditions among these hospitalizations.

**STUDY DESIGN**—An estimated 64,413,973 pregnancy-related hospitalizations among women 15-44 years old were identified in the 1994-2009 Nationwide Inpatient Sample. Trends in VTE-associated pregnancy hospitalizations were evaluated with the use of variance-weighted least squares regression. Chi-square tests were used to assess changes in prevalence of demographics and comorbid conditions, and multivariable logistic regression was used to evaluate the likelihood of VTE during the study period after adjustment for comorbid conditions. Antepartum, delivery, and postpartum hospitalizations were evaluated separately and reported in 4-year increments.

**RESULTS**—From 1994-2009, there was a 14% increase in the rate of overall VTE-associated pregnancy hospitalizations; antepartum and postpartum hospitalizations with VTE increased by 17% and 47%, respectively. Between 1994-1997 and 2006-2009, the prevalence of hypertension and obesity doubled among all VTE-associated pregnancy hospitalizations; significant increases in diabetes mellitus and heart disease were also noted. A temporal increase in the likelihood of a VTE diagnosis in pregnancy was observed for antepartum hospitalizations from 2006-2009 when compared with 1994-1997 (adjusted odds ratio, 1.62; 95% confidence interval, 1.48–1.78).

**CONCLUSION**—There has been an upward trend in VTE-associated pregnancy hospitalizations from 1994-2009 with concomitant increases in comorbid conditions. Clinicians should have a heightened awareness of the risk of VTE among pregnant women, particularly among those with comorbid conditions, and should have a low threshold for evaluation in women with symptoms or signs of VTE.

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## Keywords

pregnancy; pulmonary embolism; venous thromboembolism; venous thrombosis

Venous thromboembolism (VTE), a disease characterized by deep vein thrombosis (DVT) and pulmonary embolism (PE), is an important cause of maternal morbidity and death in the United States and other developed countries. Although the rate of maternal mortality in developed countries has declined over the past few decades, PE remains one of the leading causes of maternal deaths in the United States.<sup>1-4</sup> The overall prevalence of thromboembolic events during pregnancy is estimated to be 2 per 1000 deliveries,<sup>2,4,5</sup> which represents a 4-fold increase in risk when compared with the nonpregnant population.<sup>1,2</sup> In the postpartum period, rates of 25-99 per 10,000 women-years have been reported with up to 21.5-fold to 84-fold increase in risk in the first 6 weeks after birth when compared with nonpregnant nonpostpartum women.<sup>6</sup> This increased risk may be due to physiologic changes such as hormonally induced decreased venous outflow,<sup>7,8</sup> mechanical obstruction by the uterus,<sup>9</sup> decreased mobility,<sup>10</sup> and vascular injury<sup>5</sup>; however, hypercoagulability that is associated with pregnancy may be the most important contributing factor.<sup>3,4,7</sup> Other factors that are associated with increased risk for pregnancy-related VTE include history of thrombosis, black race, heart disease, sickle cell disease, diabetes mellitus, lupus, advanced maternal age, obesity, hemorrhage, and cesarean delivery.<sup>1,4,7</sup>

Few studies have examined trends in the incidence of pregnancy-related VTE in the United States, and these studies have shown variable results.<sup>3,4,11</sup> For example, using data from a population-based cohort study in Olmsted County, MN, Heit et al<sup>4</sup> reported no change in the incidence of clinically validated VTE among pregnant and postpartum women from 1966-1995. In contrast, James<sup>2</sup> and Stein et al<sup>3</sup> analyzed data from the National Hospital Discharge Survey and documented a significantly increased trend in the rate of DVT diagnosis among pregnancy-associated hospitalizations in the United States between 1982 and 1999.

The main objective of this analysis was to describe recent national trends in pregnancy-related hospitalizations that were complicated by VTE. Furthermore, in light of recent data that suggest an increasing prevalence of factors that are associated with VTE (such as heart disease,<sup>12</sup> diabetes mellitus, obesity,<sup>13</sup> and postpartum hemorrhage<sup>14</sup>), we also evaluated the relationship between pregnancy-related VTE and concurrent medical conditions and pregnancy complications over the study period.

## Materials and Methods

The data that were used for this study were obtained from the 1994-2009 Nationwide Inpatient Sample (NIS) Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality.<sup>15</sup> The NIS is the largest nationwide all-payer inpatient database in the United States and contains information on hospital use, diagnoses, procedures, and charges for a 20% stratified sample of US community hospitals from participating states.<sup>15</sup> Each year of the NIS includes approximately 5-8 million inpatient stays from approximately 1000 hospitals. The number of hospitals that contributes data has increased over time; during

2009, the NIS was drawn from 44 states and encompassed approximately 96% of all US hospital discharges. Because discharge sample weights were calculated within each sampling stratum, estimates for a nationwide representative population can be computed. The data have no personal identifiers and therefore was exempt from review by the institutional review board of the Centers for Disease Control and Prevention.

Hospitalizations for women who were 15-44 years old with a pregnancy-related discharge diagnosis were included for each year. Pregnancy hospitalizations were identified with the use of the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic codes 630-677, V22, V23, V24, V28, and 792.3; ICD-9-CM procedure codes 72-75; and diagnosis-related group codes (DRG) 370-384 for DRG version 24 and earlier or 765-782 for DRG version 25 and later. These hospitalizations were classified further hierarchically into delivery, postpartum, and antepartum hospitalizations. Delivery hospitalizations were identified with a previously validated method<sup>16</sup>; postpartum hospitalizations were identified by the fifth digit of “4” in ICD-9-CM codes for primary or secondary diagnosis, ICD-9-CM code V24 for any diagnosis, and postpartum DRG codes (376-377 for DRG version 24 and earlier or 769 or 776 for DRG version 25 and later). Antepartum hospitalizations were identified by the fifth digit of “3” in ICD-9-CM codes for primary or secondary diagnosis; ICD-9-CM codes V22, V23, V28, and 792.3 for any diagnosis; and antepartum DRG codes (378-384 for DRG version 24 and earlier or 770, 777-782 for DRG version 25 and later).

VTE diagnoses were identified by the presence of ICD-9-CM codes for DVT (671.3x, 671.4x, 671.5x, 671.9x, 451.11, 453.9, 451.19, 451.2, 451.81, 453.2, 453.40-453.42, 453.8, and 453.9) or PE (673.2x, 673.8x, 415.11, and 415.19) in any of the 15 available discharge diagnostic fields. Medical conditions and pregnancy complications that were reported during the hospitalization were identified similarly by ICD-9-CM codes and included anemia (280-281, 285.9, and 648.2), chronic and gestational diabetes mellitus (250.0-250.9, 648.0, and 648.8), essential and secondary hypertension (401-405, 642.0-642.2, and 642.9), obesity (278.0 and 649.1), blood transfusion (99.00-99.09), cesarean delivery (74.0-74.2, 74.4, 74.99, and 669.7), antepartum or postpartum hemorrhage (641.1-641.3, 641.8-641.9, and 666.0-666.3), multiple gestation (651 and V27.2-V27.7), preeclampsia (642.4-642.5 and 642.7), and postpartum infection (670 and 672). The specific conditions and ICD-9-CM codes that were used to define chronic heart disease have been described in detail elsewhere.<sup>16</sup>

All statistical analyses were conducted with SUDAAN software (version 10; RTI International, Research Triangle Park, NC) to account for the complex sampling design of the NIS. The study period was divided into 4-year intervals (1994-1997, 1998-2001, 2002-2005, and 2006-2009), and the rate of DVT only, PE with or without DVT (PE with or without DVT), and VTE per 1000 deliveries was calculated during each 4-year interval for each hospitalization type (antepartum, delivery, and postpartum). Differences in the distribution of patient and hospital characteristics and concurrent conditions in 1994-1997, compared with 2006-2009, among VTE-associated pregnancy hospitalizations were assessed with the use of Rao-Scott  $\chi^2$ . A probability value of  $< .05$  was considered significant; estimates with relative standard errors of  $\geq 50\%$  were considered unstable and were omitted;

estimates with relative standard errors of 30-50% are statistically unreliable and were flagged, and the remaining estimates have a relative standard error of <30%.

Temporal trends were assessed by variance weighted regression. Because this method does not assume homogeneity of variance across the sample years, the computed probability values take into account differing sample variances for each year. Stata software (version 11; StataCorp, College Station, TX) was used for this component of the analysis.

Multivariable logistic-regression analysis was used to assess the likelihood of VTE diagnosis in the years 1998-2001, 2002-2005, and 2006-2009 compared with 1994-1997 after adjustment for maternal age, primary payer (public, private, self, or other), hospital region (northeast, midwest, south, west), hospital location (rural vs urban), and the aforementioned medical and pregnancy-related conditions.

## Results

In the period of 1994-2009, there were an estimated 64,413,973 pregnancy-related hospitalizations; of those, 118,982 hospitalizations (0.18%) had a VTE diagnosis reported. For all types of VTE-associated pregnancy hospitalizations between 1994-1997 and 2006-2009, approximately one-half occurred in women 25-34 years old (Table 1). Regardless of hospitalization type, the proportion of VTE hospitalizations among women 15-24 years old decreased between 1994-1997 and 2006-2009 (Table 1). VTE-associated pregnancy hospitalizations were more prevalent in hospitals that were located in urban areas, and this proportion increased over the study period among antepartum and postpartum hospitalizations (85.5-91.8% and 83.2-89.3%, respectively).

For all types of pregnancy hospitalizations, the rate of VTE-associated hospitalization increased 14% between 1994-1997 and 2006-2009 (1.74-1.99 per 1000 deliveries), and the rate of hospitalization associated with PE (with or without DVT) increased by 128% (0.32-0.73 per 1000 deliveries; Table 2). In contrast, the rate of DVT-associated hospitalization decreased from 1.42-1.26 per 1000 deliveries between 1994-1997 and 2006-2009. When stratified by hospitalization type, VTE-associated antepartum and postpartum hospitalizations increased by 17% and 47%, respectively; however, there was no significant change in the rate of VTE-associated delivery hospitalization. The rate of DVT remained constant or declined slightly for antepartum, delivery, and postpartum hospitalizations; the rate of PE (with or without DVT) increased regardless of hospitalization type.

Between 1994-1997 and 2006-2009, the proportion of VTE-associated antepartum and postpartum hospitalizations with a report of anemia increased (12.5-18.9% and 21.8-31.4%, respectively); no change was noted for delivery hospitalizations (Table 3). For all 3 types of VTE-associated pregnancy hospitalizations, the prevalence of comorbid heart disease, hypertension, and obesity increased significantly between 1994-1997 and 2006-2009. The prevalence of blood transfusions reports more than doubled among delivery and postpartum hospitalizations that were complicated by VTE between 1994-1997 and 2006-2009 (3.2-9.1% and 3.6-8.0%, respectively). Among VTE-associated delivery hospitalizations, the

frequency of cesarean delivery increased (47.1-54.3%); the frequency of postpartum infections declined (17.7-7.1%) over the study period. The proportion of VTE-associated delivery and postpartum hospitalizations with hemorrhage and preeclampsia also increased significantly between 1994-1997 and 2006-2009.

After adjustment for covariates, the likelihood of VTE diagnosis during an antepartum hospitalization was higher in the years 1998-2001, 2002-2005, and 2006-2009 compared with 1994-1997 (Table 4). Among delivery hospitalizations, the odds of VTE were lower during 1998-2001 and 2006-2009 compared with 1994-1997; no difference was noted for postpartum hospitalizations. For all types of VTE-associated pregnancy hospitalizations, the likelihood of VTE diagnosis increased with increasing age; the highest odds were noted among women 35-44 years old compared with those who were 15-24 years old. Pregnancy hospitalizations with anemia were approximately twice as likely to have VTE compared with those without anemia, regardless of type of hospitalization. For all hospitalizations, heart disease was associated with 1.4- to 3.6-fold increased odds of VTE diagnosis, and obesity was associated with 1.5- to 3.7-fold increased odds of VTE diagnosis. Delivery hospitalizations with postpartum infection were 7 times more likely to have a VTE diagnosis compared with those without a postpartum infection, and delivery hospitalizations with cesarean delivery were twice as likely to have a VTE diagnosis compared with those with vaginal delivery. Hemorrhage, multiple gestation, and preeclampsia were associated with an increased likelihood of VTE diagnosis for delivery hospitalizations, but not for other hospitalization types.

## Comment

Using a large nationwide sample, we found a 14% increase in the rate of VTE-associated hospitalization for all types of pregnancy hospitalizations between 1994-1997 and 2006-2009. Although the rate of VTE-associated hospitalization was highest among delivery hospitalizations, the rate among delivery hospitalizations remained relatively constant over the study period. In contrast, the rate of VTE among antepartum and postpartum hospitalizations increased by 17% and 47%, respectively. Consistent with findings from an analysis of Canadian pregnancy discharges,<sup>15</sup> the results of the present study suggest that the observed trend was largely due to increases in the rate of PE throughout the study period, in contrast to DVT rates alone, which remained fairly constant. Several reports have suggested increased clinician awareness and widespread adoption of computed tomographic pulmonary angiography to test for PE as possible explanations for significant increases in the incidence of PE that was noted in hospitalized patients.<sup>3,17</sup>

The prevalence of VTE-associated pregnancy hospitalizations (0.18%) in the present study is consistent with previous reports.<sup>4,11</sup> Although other studies have indicated that the prevalence of VTE is highest during the postpartum period,<sup>4</sup> we found that the rate of VTE-associated hospitalization was generally lower for postpartum hospitalizations than delivery hospitalizations. This was likely due to the fact that a certain proportion of postpartum VTEs were included in the delivery hospitalization group because the event occurred before discharge.

Although the likelihood of VTE diagnosis within the first few days after delivery has not been established, Salonen et al<sup>18</sup> reported a 100-fold increase in the incidence of venous thrombosis 2 days before and 1 day after delivery, compared with nonpregnancy and early pregnancy periods. In addition, during the study period, perioperative antibiotic prophylaxis for cesarean delivery became routine practice. Postpartum infection has been shown to increase the risk of VTE, and declining rates of postpartum infection may have contributed to decreasing rates of VTE-associated delivery hospitalizations.

VTE was noted to occur more frequently in urban hospitals, as opposed to rural hospitals, because urban hospitals are usually more specialized and manage more complications. Although we are unable to assess the reason for this from our analysis, it is possible that increasing risk factors in the general population of pregnant women (such as older age, obesity, more cesarean deliveries) have given rise to a similar increase in the proportion of pregnant patients with such risk factors who are being cared for at urban hospitals. Generally, increasing trends in the prevalence of hypertension, obesity, and diabetes mellitus in the United States have been reported.<sup>19-21</sup> Similarly, we found that the proportion of VTE-associated pregnancy hospitalizations with hypertension and obesity more than doubled over the 14-year study period, with a moderate increase in diabetes mellitus also noted. Consistent with other studies,<sup>10,11,22</sup> we found that blood transfusion was a significant risk factor for VTE. The pathophysiologic condition is thought to be due to the storage and preservation of red blood cells, which increase their aggregability.<sup>23,24</sup> However, this may also be due to the association of conditions for which blood transfusion is required, such as cesarean delivery and postpartum hemorrhage, both of which are known risk factors for VTE in pregnancy.

Regardless of the period of pregnancy, older women (35-44 years) were significantly more likely to be diagnosed with VTE. This is important to consider, given that there have been an increasing number of pregnancies in this age group over the last decade in the United States.<sup>25</sup> These women may also be more likely to have medical conditions that are associated with increased VTE risk and to have used assisted reproductive technology that may result in thromboembolic events because of hyperstimulation of the ovaries.<sup>26</sup>

Our results indicated that temporal increases in VTE-associated hospitalization were significant only for antepartum hospitalizations. Although this finding may be due to inaccuracies in the methods for the assignment of the type of pregnancy hospitalization, it may also provide some evidence that comorbid conditions interact differently during different periods of pregnancy and confer varying degrees of risk of VTE. As such, it may be hypothesized that increases in the prevalence of chronic conditions and in the proportion of pregnancies among women of advanced maternal ages may impact differentially the likelihood of the development of VTE during all pregnancy periods.

Our study has several limitations that should be considered in the interpretation of the results. First, all medical conditions that were ascertained for this analysis were derived solely from ICD-9-CM and DRG codes and may be subject to misclassification because of differences in the diagnostic criteria that are used by physicians, changes or improvement in coding practices over time, or inaccurate reporting. The predictive value of pregnancy-

specific VTE codes has been estimated to be 30%; however, the predictive value of standard codes to identify VTE during pregnancy is considerably higher (85%).<sup>27</sup> Although it is likely that some degree of misclassification of VTE occurred in our study, both types of codes were used to improve ascertainment.

Second, the use of inpatient discharge data limits generalizability of our results because we were unable to evaluate conditions that were diagnosed in an outpatient setting or those that were not reported during the pregnancy-related hospitalization. Given that outpatient diagnosis and the management of VTE is increasing,<sup>28</sup> we may have under estimated the frequency of pregnancy-related VTE. However, most pregnant and postpartum women likely initially receive inpatient treatment for VTE.

Third, it is possible that some postpartum hospitalizations, especially those that occurred towards the end of the postpartum period, may not have been coded properly and as such were not included in study. In addition, we were unable to determine the timing of the antepartum or postpartum hospitalization and therefore could not assess variations in VTE diagnosis in relation to the delivery.

Fourth, we were unable to include race and ethnicity in our analysis because up to 30% of hospitalizations are missing data on these variables in NIS.

Finally, because the NIS includes discharge level information, we were unable to account for multiple hospitalizations for the same woman. As such, our findings may overestimate rates of VTE-associated pregnancy hospitalizations, although likely only to a small degree.

In conclusion, this is one of very few nationwide studies that have focused on recent trends in VTE among pregnant women and the effect of certain comorbid medical conditions, which have been increasing among the US population as a whole. We found that the rate of VTE-associated pregnancy hospitalizations increased largely because of increases in PE diagnoses. Furthermore, we report increasing prevalence of comorbid medical conditions among pregnancy-related hospitalizations with VTE and their relative impact during different types of pregnancy hospitalizations. Clinicians should have heightened awareness of the risk of VTE among pregnant women, particularly those of older reproductive age and with medical conditions.

## REFERENCES

1. Berg CJ, Callaghan WM, Syverson C, Henderson Z. Pregnancy-related mortality in the United States, 1998 to 2005. *Obstet Gynecol.* 2010; 116:1302–9. [PubMed: 21099595]
2. James AH. Venous thromboembolism in pregnancy. *Arterioscler Thromb Vasc Biol.* 2009; 29:326–31. [PubMed: 19228606]
3. Stein PD, Hull RD, Kayali F, et al. Venous thromboembolism in pregnancy: 21-year trends. *Am J Med.* 2004; 117:121–5. [PubMed: 15234649]
4. Heit JA, Kobbervig CE, James AH, Petterson TM, Bailey KR, Melton LJ 3rd. Trends in the incidence of venous thromboembolism during pregnancy or postpartum: a 30-year population-based study. *Ann Intern Med.* 2005; 143:697–706. [PubMed: 16287790]
5. Marik PE, Plante LA. Venous thromboembolic disease and pregnancy. *N Engl J Med.* 2008; 359:2025–33. [PubMed: 18987370]

6. Jackson E, Curtis KM, Gaffield ME. Risk of venous thromboembolism during the postpartum period: a systematic review. *Obstet Gynecol.* 2011; 117:691–703. [PubMed: 21343773]
7. Macklon NS, Greer IA. The deep venous system in the puerperium: an ultrasound study. *BJOG.* 1997; 104:198–200.
8. James AH. Pregnancy-associated thrombosis. *Hematology Am Soc Hematol Educ Program.* 2009:277–85. [PubMed: 20008211]
9. Dombrowski, MP.; Whitty, JE. Respiratory diseases in pregnancy. In: Gabbe, SG.; Niebyl, JR.; Simpson, JL., editors. *Normal and problem pregnancies.* 4th ed. Churchill Livingstone; New York: 2002. p. 1033–64.
10. Danilenko-Dixon DR, Heit JA, Silverstein MD, et al. Risk factors for deep vein thrombosis and pulmonary embolism during pregnancy or post partum: a population-based, case-control study. *Am J Obstet Gynecol.* 2001; 184:104–10. [PubMed: 11174488]
11. James AH, Jamison MG, Brancazio LR, Myers ER. Venous thromboembolism during pregnancy and the postpartum period: incidence, risk factors, and mortality. *Am J Obstet Gynecol.* 2006; 194:1311–5. [PubMed: 16647915]
12. Kuklina EV, Tong X, Bansil P, George MG, Callaghan WM. Trends in pregnancy hospitalizations that included a stroke in the United States from 1994 to 2007: reasons for concern? *Stroke.* 2011; 42:2564–70. [PubMed: 21799174]
13. Albrecht SS, Kuklina EV, Bansil P, et al. Diabetes trends among delivery hospitalizations in the U.S., 1994–2004. *Diabetes Care.* 2010; 33:768–73. [PubMed: 20067968]
14. Callaghan WM, Kuklina EV, Berg CJ. Trends in postpartum hemorrhage: United States, 1994–2006. *Am J Obstet Gynecol.* 2010; 202:353.e1–6. [PubMed: 20350642]
15. Nationwide Inpatient Sample HCUP. Healthcare Cost and Utilization Project (HCUP). 1994–2009. Agency for Healthcare Research and Quality; Rockville, MD: 2011.
16. Kuklina E, Callaghan W. Chronic heart disease and severe obstetric morbidity among hospitalisations for pregnancy in the USA: 1995–2006. *BJOG.* 2011; 118:345–52. [PubMed: 21091604]
17. Wiener RS, Schwartz LM, Woloshin S. Time trends in pulmonary embolism in the United States: evidence of overdiagnosis. *Arch Intern Med.* 2011; 171:831–7. [PubMed: 21555660]
18. Salonen Ros H, Lichtenstein P, Belloc R, Petersson G, Cnattingius S. Increased risks of circulatory diseases in late pregnancy and puerperium. *Epidemiology.* 2001; 12:456–60. [PubMed: 11416782]
19. Cowie CC, Rust KF, Ford ES, et al. Full accounting of diabetes and pre-diabetes in the U. S. population in 1988–1994 and 2005–2006. *Diabetes Care.* 2009; 32:287–94. [PubMed: 19017771]
20. National Task Force on the Prevention and Treatment of Obesity. Overweight, obesity, and health risk. *Arch Intern Med.* 2000; 160:898–904. [PubMed: 10761953]
21. Egan BM, Zhao Y, Axon RN. US trends in prevalence, awareness, treatment, and control of hypertension, 1988–2008. *JAMA.* 2010; 303:2043–50. [PubMed: 20501926]
22. Liu S, Rouleau J, Joseph KS, et al. Epidemiology of pregnancy-associated venous thromboembolism: a population-based study in Canada. *J Obstet Gynaecol Can.* 2009; 31:611–20. [PubMed: 19761634]
23. Lelubre C, Vincent JL. Red blood cell transfusion in the critically ill patient. *Ann Intensive Care.* 2011; 1:43. [PubMed: 21970512]
24. Ho J, Sibbald WJ, Chin-Yee IH. Effects of storage on efficacy of red cell transfusion: when is it not safe? *Crit Care Med.* 2003; 31(suppl):S687–97. [PubMed: 14724467]
25. Martinez G, Daniels K, Chandra A. Fertility of men and women aged 15–44 years in the United States: National Survey of Family Growth, 2006–2010. *Natl Health Stat Rep.* 2012; 51:1–28.
26. Metwally M, Ledger WL. Long-term complications of assisted reproductive technologies. *Hum Fertil (Camb).* 2011; 14:77–87. [PubMed: 21631242]
27. White RH, Brickner LA, Scannell KA. ICD-9-CM codes poorly identified venous thromboembolism during pregnancy. *J Clin Epidemiol.* 2004; 57:985–8. [PubMed: 15504642]
28. Spencer FA, Lessard D, Emery C, Reed G, Goldberg RJ. Venous thromboembolism in the outpatient setting. *Arch Intern Med.* 2007; 167:1471–5. [PubMed: 17646600]

TABLE 1

Patient and hospital characteristics of VTE-associated pregnancy hospitalizations, Nationwide Inpatient Sample, 1994-2009

Variable	Hospitalization, %					
	Antenatal		Delivery		Postnatal	
	1994-1997 (n = 8597)	2006-2009 (n = 11,476)	1994-1997 (n = 11,607)	2006-2009 (n = 12,419)	1994-1997 (n = 6052)	2006-2009 (n = 10,047)
Age categories, y						
15-24	33.0	30.7 <sup>a</sup>	34.8	26.9 <sup>a</sup>	35.4	29.9 <sup>a</sup>
25-34	52.1	49.7	48.9	50.3	46.1	51.2
35-44	15.0	19.6	16.3	22.8	18.4	18.9
Primary payer						
Public	52.6	45.0 <sup>a</sup>	52.4	50.7	51.3	45.7
Private	38.8	45.4	40.4	42.5	41.1	46.6
Self-pay	5.1	5.6	3.2	3.0	3.2	3.9
Other	3.6	4.1	3.9	3.8	4.4	3.8
Region of hospital						
Northeast	20.9	18.6	23.1	20.2	19.3	15.3
Midwest	27.1	24.0	26.1	23.0	26.9	27.9
South	29.2	36.0	31.3	35.5	33.7	37.8
West	22.8	21.5	19.5	21.2	20.0	19.0
Hospital location						
Rural	14.5	8.3 <sup>a</sup>	11.5	10.1	16.8	10.7 <sup>a</sup>
Urban	85.5	91.8	88.5	89.9	83.2	89.3
Disposition of patient						
Routine discharge	79.6	85.2 <sup>a</sup>	91.4	90.7	87.8	80.5 <sup>a</sup>
Transfer to short term hospital	5.0	5.2	0.6	1.1	1.6	2.7
Other transfers <sup>b</sup>	1.3	0.5	0.7	0.7	1.6	1.9
Home health care	12.5	7.1	5.4	6.3	7.1	13.3
Death in hospital	—	0.5 <sup>d</sup>	0.9	0.8	0.7 <sup>d</sup>	0.7

Variable	Hospitalization, %					
	Antenatal		Delivery		Postnatal	
	1994-1997 (n = 8597)	2006-2009 (n = 11,476)	1994-1997 (n = 11,607)	2006-2009 (n = 12,419)	1994-1997 (n = 6052)	2006-2009 (n = 10,047)
Other <sup>c</sup>	1.6	1.4	1.0	0.4 <sup>d</sup>	1.2	0.8

Data for 1998-2005 are not shown.

VTE, venous thromboembolism.

<sup>a</sup> Rao-Scott  $\chi^2$  probability value < .05: distribution of variable from 1994-1997 vs distribution from 2006-2009;

<sup>b</sup> Included skilled nursing facility, intermediate care, and another type of facility;

<sup>c</sup> Included left against medical advice and discharged alive, destination unknown;

<sup>d</sup> Unreliable estimate; relative standard error, 30-50%.

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**TABLE 2**  
Trends in the rate of VTE-associated hospitalization among pregnancy hospitalizations, Nationwide Inpatient Sample, 1994-2009

Variable	Years of study						P value <sup>d</sup>	
	1994-1997		1998-2001		2002-2005			2006-2009
	Weighted, n	Rate per 1000 deliveries, %	Weighted, n	Rate per 1000 deliveries, %	Weighted, n	Rate per 1000 deliveries, %	Weighted, n	Rate per 1000 deliveries, %
All hospitalizations								
DVT only	21,459	1.42	19,990	1.28	22,953	1.39	21,571	1.26
PE with/without DVT	4797	0.32	5778	0.37	10,058	0.61	12,371	0.73
All VTE	26,256	1.74	25,768	1.65	33,011	1.99	33,942	1.99
Antenatal hospitalizations								
DVT only	6932	0.46	6659	0.43	7925	0.48	7425	0.44
PE with/without DVT	1665	0.11	2103	0.13	3477	0.21	4051	0.24
All VTE	8597	0.57	8762	0.56	11,402	0.69	11,476	0.67
Delivery hospitalizations								
DVT only	10,175	0.67	8550	0.55	9944	0.60	9437	0.55
PE with/without DVT	1432	0.09	1659	0.10	2577	0.16	2982	0.17
All VTE	11,607	0.77	10,209	0.65	12,521	0.76	12,419	0.73
Postnatal hospitalizations								
DVT only	4352	0.29	4781	0.31	5084	0.31	4709	0.28
PE with/without DVT	1700	0.11	2016	0.13	4004	0.24	5338	0.31
All VTE	6052	0.40	6797	0.44	9088	0.55	10,047	0.59

DVT, deep vein thrombosis; PE, pulmonary embolism; VTE, venous thromboembolism.

<sup>a</sup> P value for trend estimated using variance weighted regression.

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**TABLE 3**

Medical conditions and pregnancy complications among VTE-associated pregnancy hospitalizations, Nationwide Inpatient Sample, 1994-2009

Variable	Years of study, %					
	1994-1997 (n = 8597)	2006-2009 (n = 11,476)	1994-1997 (n = 11,607)	2006-2009 (n = 12,419)	1994-1997 (n = 6052)	2006-2009 (n = 10,047)
Medical condition						
Anemia	12.5	18.9 <sup>a</sup>	24.0	23.1	21.8	31.4 <sup>a</sup>
Diabetes mellitus	4.0	4.4	6.6	9.0 <sup>a</sup>	1.5 <sup>b</sup>	4.0 <sup>a</sup>
Heart disease	5.4	9.0 <sup>a</sup>	5.9	9.3 <sup>a</sup>	7.7	16.6 <sup>a</sup>
Hypertension	1.6	5.4 <sup>a</sup>	2.6	4.2 <sup>a</sup>	3.5	10.5 <sup>a</sup>
Obesity	3.1	7.5 <sup>a</sup>	1.4	5.0 <sup>a</sup>	3.9	8.2 <sup>a</sup>
Pregnancy-related conditions						
Blood transfusion	1.2	2.4	3.2	9.1 <sup>a</sup>	3.6	8.0 <sup>a</sup>
Cesarean delivery	N/A	N/A	47.1	54.3 <sup>a</sup>	N/A	N/A
Hemorrhage	1.5	1.7	10.2	12.8 <sup>a</sup>	4.7	6.1 <sup>a</sup>
Multiple gestation	2.6	3.5	3.5	4.4	N/A	N/A
Preeclampsia	1.0	0.8	7.8	9.7 <sup>a</sup>	1.8	3.8 <sup>a</sup>
Postnatal infection	N/A	N/A	17.7	7.1 <sup>a</sup>	12.2	11.5

Data for 1998-2005 are not shown.

N/A, not applicable; VTE, venous thromboembolism.

<sup>a</sup>Rao-Scott  $\chi^2$  probability value < .05; distribution of variable from 1994-1997 vs distribution from 2006-2009;

<sup>b</sup>Unreliable estimate; relative standard error, 30-50%.

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**TABLE 4**

Estimated ORs for VTE-associated pregnancy hospitalization, Nationwide Inpatient Sample, 1994-2009

Adjusted model (adjusted for all covariates)	<b>Hospitalization</b>					
	<b>Antenatal</b>		<b>Delivery</b>		<b>Postnatal</b>	
	<b>OR</b>	<b>95% CI</b>	<b>OR</b>	<b>95% CI</b>	<b>OR</b>	<b>95% CI</b>
Year of discharge						
1994-1997	Referent		Referent		Referent	
1998-2001	1.17	1.06–1.28	0.88	0.80–0.96	1.00	0.91–1.11
2002-005	1.50	1.37–1.65	0.93	0.83–1.04	1.06	0.96–1.16
2006-2009	1.53	1.40–1.69	0.84	0.77–0.93	0.99	0.90–1.08
Age, y						
15-24	Referent		Referent		Referent	
25-34	1.38	1.30–1.46	1.17	1.11–1.23	1.26	1.18–1.34
35-44	1.77	1.64–1.91	1.49	1.39–1.60	1.44	1.33–1.57
Primary payer						
Private	Referent		Referent		Referent	
Public	1.08	1.02–1.15	0.89	0.84–0.94	1.21	1.14–1.29
Self/other	0.85	0.77–0.93	0.91	0.82–1.02	0.82	0.73–0.91
Region of hospital						
Northeast	Referent		Referent		Referent	
Midwest	1.27	1.15–1.39	0.90	0.80–1.03	1.31	1.18–1.45
South	0.92	0.85–1.00	0.74	0.66–0.84	1.01	0.92–1.11
West	1.07	0.97–1.18	0.72	0.63–0.83	1.01	0.91–1.13
Location of hospital						
Urban	Referent		Referent		Referent	
Rural	0.92	0.83–1.01	0.92	0.84–1.02	1.33	1.22–1.45
Medical condition						
Anemia	2.14	1.99–2.32	1.79	1.69–1.91	2.18	2.04–2.33
Diabetes mellitus	0.43	0.38–0.49	1.19	1.09–1.29	0.86	0.73–1.02
Heart disease	2.54	2.31–2.79	3.59	3.27–3.92	1.42	1.30–1.56

Adjusted model (adjusted for all covariates)	Hospitalization					
	Antenatal		Delivery		Postnatal	
	OR	95% CI	OR	95% CI	OR	95% CI
Hypertension	0.78	0.68–0.89	1.30	1.15–1.46	0.77	0.69–0.86
Obesity	3.74	3.30–4.24	1.52	1.33–1.74	1.88	1.67–2.11
Pregnancy complication						
Blood transfusion	0.72	0.60–0.87	3.19	2.84–3.59	1.19	1.05–1.36
Cesarean delivery	N/A		2.07	1.97–2.18	N/A	
Hemorrhage	0.34	0.29–0.40	1.63	1.51–1.76	0.37	0.33–0.42
Multiple gestation	0.67	0.57–0.77	1.47	1.32–1.64	N/A	
Preeclampsia	0.23	0.17–0.31	1.45	1.34–1.58	0.34	0.29–0.39
Postnatal infection	N/A		7.30	6.70–7.95	0.56	0.51–0.60

*CI*, confidence interval; *N/A*, not applicable; *OR*, odds ratio; *VTE*, venous thromboembolism.

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