

VTE and pregnancy

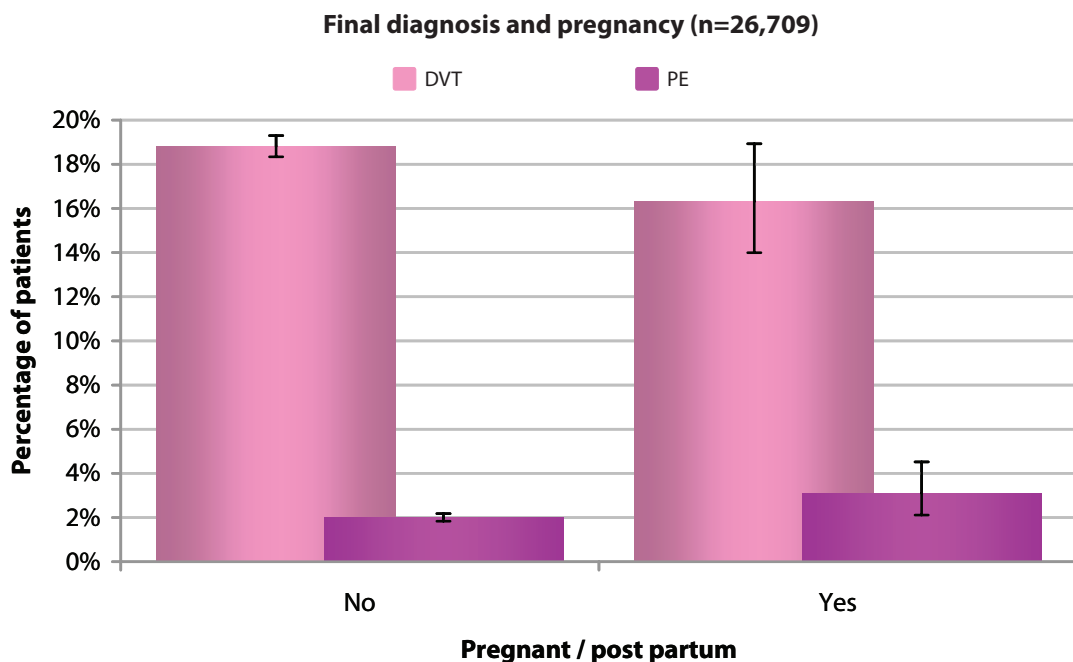
VTE and pregnancy

Overview

VTE is a rare but serious complication of pregnancy. The Confidential Enquiry into Maternal and Child Health (CEMACH; www.cemach.org.uk)¹ provides important figures for deaths caused by PE, but there remains a paucity of knowledge about the overall rate of VTE, risk factors for VTE and the extent of long-term morbidity from VTE in pregnant women. In addition, it is not completely clear to what extent risk factors for VTE among men and non-pregnant women can be generalized to pregnant and *puerperal* women as pregnancy and *puerperium* themselves are associated with an increased thrombotic risk. Recent data suggest that smoking and obesity are risk factors for VTE in pregnancy and the *puerperium* compared with non-pregnant age and sex-matched controls².

In this chapter, we review the risk factor profile of pregnant women with VTE and attempt to offer useful information based on the simple questions asked in VERITY about pregnant women. We attempt to establish more firmly the risk factors for pregnant women by comparing with the clinical characteristics of all non-pregnant women in the same age range in VERITY. In addition, we present the current guidelines on thromboprophylaxis for women at risk of VTE during pregnancy issued by the RCOG in 2004³.

		Final diagnosis					
		Non-VTE	DVT	PE	PE + DVT	Unspecified	All
Pregnancy status	Not pregnant / <i>post partum</i>	20,437	4,855	417	99	3,874	29,682
	Pregnant / <i>post partum</i>	726	147	23	5	139	1,040
	Unspecified	1,004	508	23	10	1,272	2,817
	All	22,167	5,510	463	114	5,285	33,539



Diagnosis of VTE in pregnancy and *post partum*

Overall, there are 1,040 women in the combined database recorded as pregnant or *post partum*. In the old database (n=633), there are 90 cases of VTE associated with pregnancy / *post partum*. In the new, on-line database (n=407), a distinction is made between pregnancy and *post partum*, with 30 pregnancy-associated VTE and 55 *post partum* VTE.

		Final diagnosis					All
		Non-VTE	DVT	PE	PE + DVT	Unspecified	
Pregnancy status	Pregnant	175	28	1	1	18	226
	<i>Post partum</i>	118	48	6	1	21	181

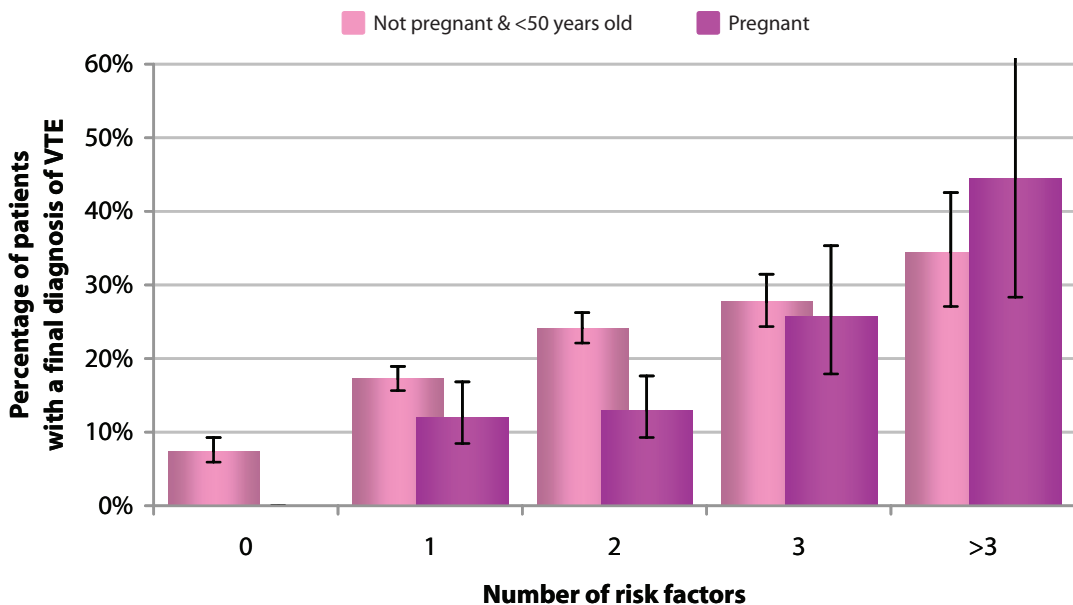
Risk factors and pregnancy

This comparison of number of risk figures for pregnant and non-pregnant women is interesting, suggesting that there is little difference between the two groups. Although the proportion of women with two risk factors is higher in the non-pregnant control population, this simply reflects the fact that pregnancy itself is included as a risk factor. The graph below shows that all pregnant women with VTE have at least one risk factor, again reflecting the pregnancy risk factor. It is notable that 31 women diagnosed with VTE had no risk factors other than their pregnancy. In the previous VERITY report, we reviewed the women with two risk factors (pregnancy plus one other) and found the most common second risk factor by far was a history of smoking (54% of this group) followed by family history, which was reported for 10% of the group. In the next graph on page 101 we review these and other risk factors for VTE in more detail.

			Final diagnosis			
			Non-VTE	VTE	Unspecified	All
Pregnancy status and number of risk factors	Not pregnant and <50 years	0	935	75	129	1,139
		1	1,730	360	316	2,406
		2	1,284	408	252	1,944
		3	458	176	102	736
		>3	101	53	27	181
		Unspecified	1,367	304	271	1,942
	Pregnant	0	0	0	0	0
		1	226	31	21	278
		2	236	35	38	309
		3	78	27	20	125
		>3	20	16	7	43
		Unspecified	166	66	53	285

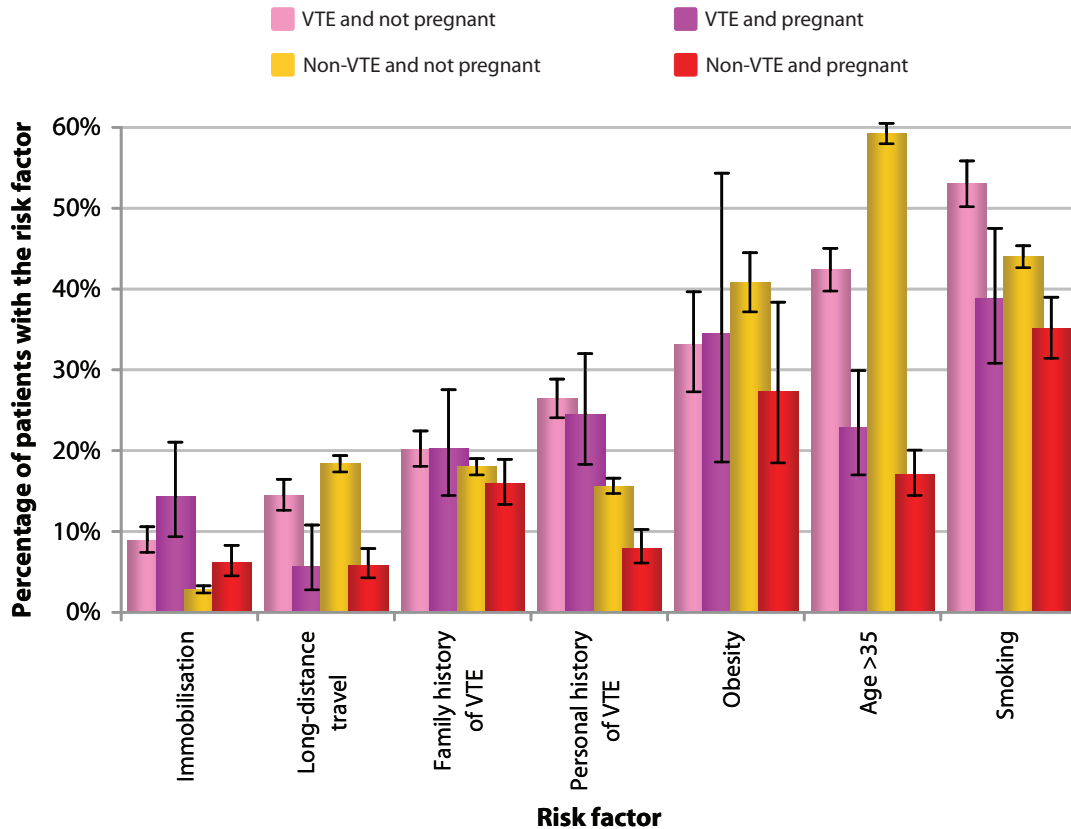
Pregnancy

Final diagnosis and pregnancy (n=6,249)



The graph below compares 4 different populations of women to investigate further the risk factors for VTE in pregnancy. The graph compares pregnant and non-pregnant women with and without a diagnosis of VTE. Comparing smoking rates in women with VTE, we can see that smoking is significantly under-represented as a positive risk factor for VTE in pregnant women. However, in women with VTE, there is no difference in a personal history of VTE or obesity in pregnant and non-pregnant women.

Risk factor presence according to the patient's final diagnosis and recorded pregnancy status; female patients only

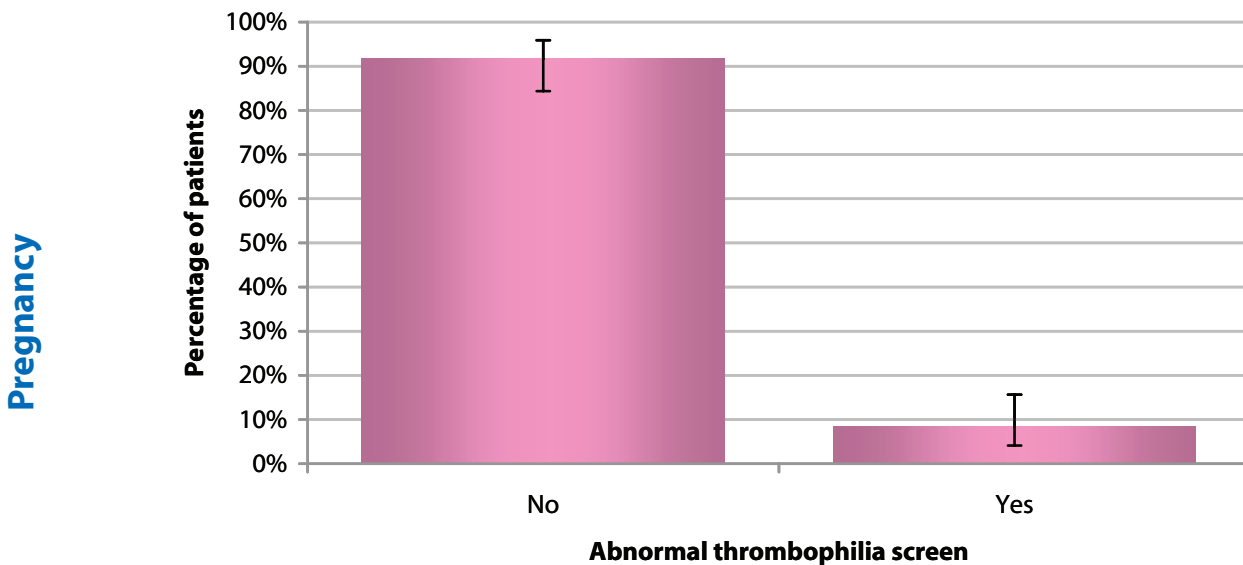


Pregnancy

Recurrence risk is increased in pregnant women who have already suffered from VTE^{4,5}, and is higher in women with thrombophilia or following idiopathic events^{5,6,7,8}. A higher prevalence of combined and homozygous thrombophilic defects has been found in women with VTE during pregnancy compared with age-matched women without previous VTE⁹. Very recently, the TREATS study found the highest risk in pregnancy was found for factor V Leiden (FVL) and VTE; in particular, homozygous carriers of this mutation are approximately 34 times more likely to develop VTE in pregnancy than non-carriers. Significant risks for individual thrombophilic defects were also established for early, recurrent and late pregnancy loss; pre-eclampsia; placental abruption; and intrauterine growth restriction¹⁰.

In the new database, of those pregnant women for whom we know their previous VTE status (n=170), 10 women have had a prior thromboembolic event in a previous pregnancy and of these women, 5 women have suffered a further VTE event in this pregnancy. Although these numbers are small, it helps us begin to form a picture of prior VTE in pregnancy as a risk factor. This graph shows that about 9% of pregnant women in VERITY for whom we know if the thrombophilia screen was completed have an abnormal finding. Reviewing these numbers in more detail, the pregnancy thrombophilia screen question was completed in 53 cases; 4 pregnant women had an abnormal screen and 3 were confirmed with VTE. It is difficult to interpret the meaning of these results further, but they do confirm that of those found to have thrombophilia, a high percentage were confirmed to have VTE.

Thrombophilia screen results for pregnant / post partum patients (n=108)



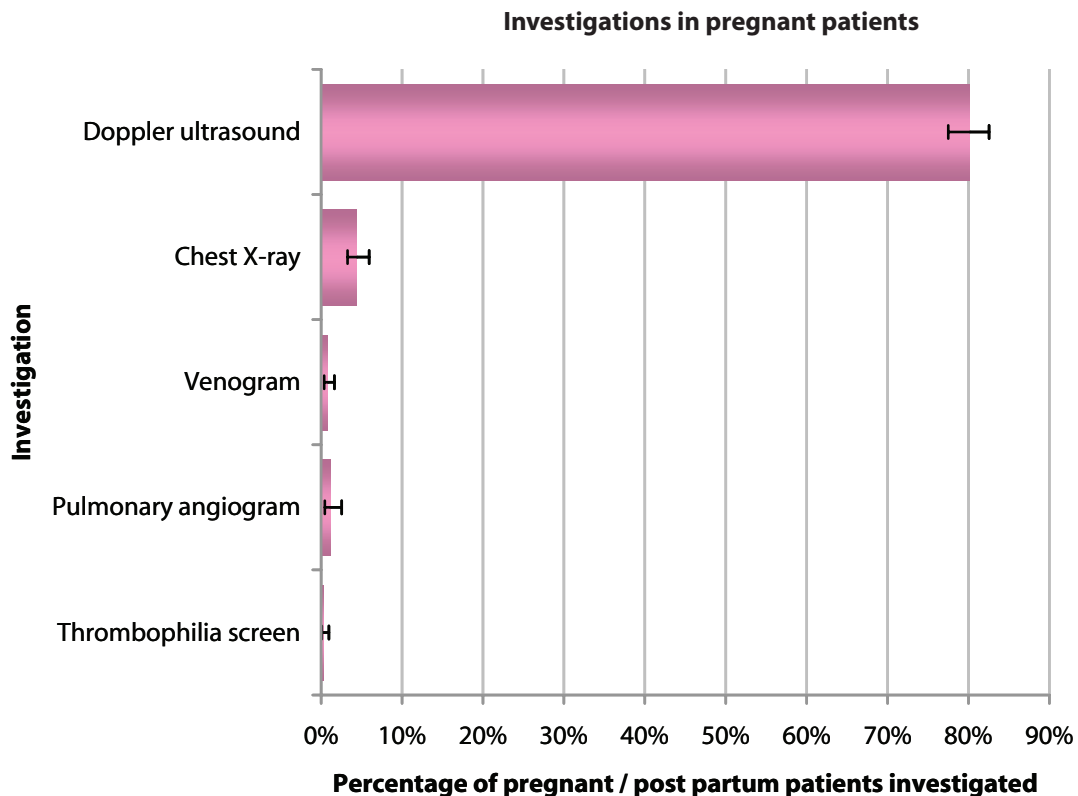
Diagnosis and pregnancy

As previously described and as expected, duplex ultrasound is the main diagnostic tool for VTE in pregnancy, and was performed in a very high proportion (80%) of pregnant women in the database.

Investigations and pregnancy

A key finding is the lack of additional diagnostic tests, particularly those used in the diagnosis of PE. These data show that only 6 pulmonary angiograms were performed, despite the fact that there are 28 cases of PE in pregnant women. Again we emphasise that it is important to fully investigate PE in pregnancy and not base the diagnosis on signs and symptoms and inference. PE diagnostic tests such as CTPA present a low risk of radiation exposure to the abdomen and therefore should not pose a significant threat to the foetus, and should not be avoided.

		Investigation performed			
		No	Yes	Unspecified	All
Investigation	Doppler ultrasound	198	799	43	1,040
	Chest X-ray	953	44	43	1,040
	Pulmonary angiogram	531	6	503	1,040
	Venogram	988	8	44	1,040
	Thrombophilia screen	993	3	44	1,040



Pregnancy

Use and doses of LMWH

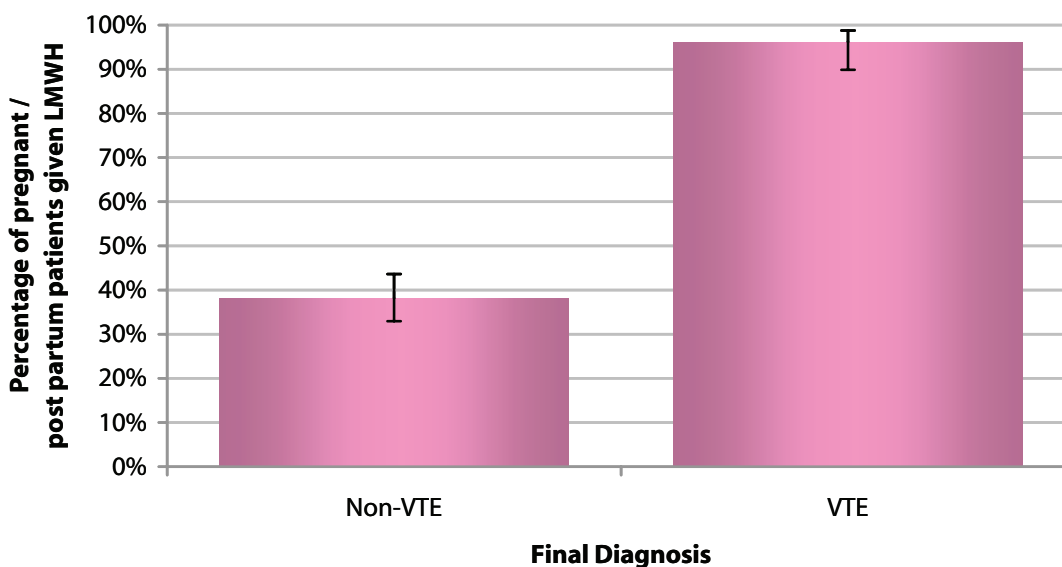
These data below confirm the previous VERITY finding that LMWH is being commenced in pregnant patients with suspected VTE while awaiting confirmation of diagnosis, with almost 40% of patients with suspected but unconfirmed VTE receiving treatment. In at least a proportion of patients, this heparin treatment will reflect heparin thromboprophylaxis because of the woman’s risk profile. LMWH was given to more than 95% of pregnant women with VTE.

Doses of LMWH

An interesting finding from the new database is that there has been a large increase in the proportion of patients receiving LMWH for longer duration compared with the findings presented in the last report. The average number of doses of LMWH was almost 50 in the new database. The patient numbers are small, but this change in practice will be investigated further and reported on the VERITY website.

		Final diagnosis			
		Non-VTE	VTE	Unspecified	All
LMWH used	No	206	4	30	240
	Yes	127	100	33	260
	Unspecified	393	71	76	540
	All	726	175	139	1,040

LMWH use and final diagnosis for pregnant patients (n=437)



Pregnancy

RCOG guideline 37 Thromboprophylaxis during pregnancy, labour and after vaginal delivery

All women should undergo an assessment of risk factors for VTE in early pregnancy or before pregnancy. This assessment should be repeated if the woman is admitted to hospital or develops other intercurrent problems. C

Women with previous VTE should be screened for inherited and acquired thrombophilia, ideally before pregnancy. B

Regardless of their risk of VTE, immobilisation of women during pregnancy, labour and the puerperium should be minimised and dehydration should be avoided. ✓

Women with previous VTE should be offered *post partum* thromboprophylaxis with LMWH. It may be reasonable not to use antenatal thromboprophylaxis with heparin in women with a single previous VTE associated with a temporary risk factor that has now resolved. C

Women with previous recurrent VTE or a previous VTE and a family history of VTE in a first-degree relative should be offered thromboprophylaxis with LMWH antenatally, and for at least six weeks *post partum*. B

Women with asymptomatic inherited or acquired thrombophilia may qualify for antenatal or postnatal thromboprophylaxis, depending on the specific thrombophilia and the presence of other risk factors. C

Women with three or more persisting risk factors should be considered for thromboprophylaxis with LMWH antenatally and for three to five days *post partum*. ✓

Women should be reassessed before or during labour for risk factors for VTE. Age over 35 years and BMI greater than 30 or body weight greater than 90 kg are important independent risk factors for *post partum* VTE even after vaginal delivery. The combination of either of these risk factors with any other risk factor for VTE (such as pre-eclampsia or immobility) or the presence of two other persisting risk factors should lead the clinician to consider the use of LMWH for three to five days *post partum*. ✓

Antenatal thromboprophylaxis should begin as early in pregnancy as practical. *Post partum* prophylaxis should begin as soon as possible after delivery (but see precautions after use of regional anaesthesia). B

LMWHs are the agents of choice for antenatal thromboprophylaxis. They are as effective as and safer than unfractionated heparin in pregnancy. B

Warfarin should usually be avoided during pregnancy. It is safe after delivery and during breast-feeding. B

Once the woman is in labour or thinks she is in labour, she should be advised not to inject any further heparin. She should be reassessed on admission to hospital and further doses should be prescribed by medical staff. ✓

Conclusions

Pregnancy-related VTE remains an emotive topic, with the feeling that any VTE event, but particularly death from VTE, could have been prevented with effective risk assessment and appropriate thromboprophylaxis. However, it is important to realise that the risk factor profile of pregnant patients with VTE is not fully characterised, the interaction between VTE risk factors not fully understood, and the optimal thromboprophylaxis strategy is not fully investigated and defined.

The VERITY data show that fewer pregnant patients with VTE smoke than non-pregnant patients with VTE, which suggests that smoking is not particularly associated with VTE in pregnant women. This contrasts with recent findings that smoking appeared to be an independent risk factor for VTE during pregnancy and the *puerperium*, and other studies, such as a large Swedish register study, found a tobacco consumption-dependent increase in the risk of VTE among pregnant smokers ¹¹, and a population based case-control study from North America among women with a first lifetime VTE during pregnancy or *post partum* found that smoking was an independent risk factor for VTE ¹².

There is controversy in the literature over the adequacy of testing for thrombophilia in pregnant patients with VTE. The number of cases with this risk factor recorded are quite low in VERITY and because of this, we were not able to confirm either an increased frequency of thrombophilia in VTE cases compared to non-pregnant patients in the same age range, or an increase in the frequency of VTE in cases of confirmed thrombophilia; nonetheless, of the 4 pregnant women with an abnormal thrombophilia screen, 3 were confirmed with VTE, in keeping with the view that thrombophilia is an important risk factor in pregnant women.

For the prevention of VTE in pregnant women, a management strategy of risk assessment, followed by heparin prophylaxis at an intensity and duration defined by the level of perceived venous thromboembolic risk, is the suggested approach.

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