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# Preventing venous thrombosis in critically ill children: What is the right approach?

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# Pediatric Anesthesia

## Preventing venous thrombosis in critically ill children: What is the right approach?

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7 **Preventing venous thrombosis in critically ill children: what is the right approach?.**  
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For Peer Review

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2  
3 Abstract  
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7 Background: The incidence of venous thromboembolic (VTE) events in children  
8  
9 has increased in recent years<sup>1,2</sup> yet there is currently no consensus as to what  
10  
11 VTE prophylaxis, if any, should be applied to the paediatric population.  
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15 Objectives/Aims: Our aim was to audit current practice in paediatric VTE  
16  
17 prophylaxis across England and Wales and to **advocate simple measures** for  
18  
19 prevention. We illustrate the importance of the condition with a series of cases  
20  
21 from the South West Paediatric Burns and Neurosurgical Services based in  
22  
23 Bristol.  
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26  
27  
28 Methods: Every paediatric intensive care unit (PICU) and burns centre admitting  
29  
30 children in England and Wales was invited to participate in a structured  
31  
32 telephone questionnaire designed to find out how **VTE in children** were being  
33  
34 prevented. **We performed a** literature review of specific risk factors and  
35  
36 management of these factors.  
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41  
42 Results: Only one of the 24 units surveyed had written guidelines specific for  
43  
44 children. Four other units used modified adult guidelines in older **children**. In  
45  
46 the remaining 19 units that had no written guidelines, decisions regarding  
47  
48 prophylaxis were based on individual cases and consultant-led.  
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51  
52  
53 Conclusion: There is no consensus in England and Wales as to which VTE  
54  
55 prophylactic measures should be applied in **patients of less than 18 years of**  
56  
57 **age**. The National Institute for Health and Clinical Excellence (NICE) guidelines  
58  
59 apply to adults only. Given the rarity of VTE events in children it is unlikely that  
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3 randomised controlled trials will provide the answer. We therefore propose **that**  
4  
5 simple empirical **measures be formally implemented** in critically ill children  
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8 **to reduce the risk of developing this important but under-recognised**  
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10 **condition.**  
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For Peer Review

## Introduction

The incidence of venous thromboembolic (VTE) events in children has increased in recent years, perhaps because of increased use of central venous catheters (CVCs) and the survival of children with previously fatal conditions<sup>1-3</sup>. However, VTE is still comparatively rare in children with frequencies estimated to be one tenth to one hundredth of that in the adult population<sup>1,2</sup>. Nevertheless, it is an important cause of potentially preventable mortality and morbidity in children. The Canadian VTE Registry, which is the largest published, comprises prospectively collected data from 15 tertiary care centres. In a report from this registry analysing 405 consecutive cases of VTE in children aged one month to 18 years over a six year period, the mortality attributed to thromboses was 2.2%<sup>3</sup>. Unlike adults, children often survive for sixty years or more following VTE, and post-thrombotic syndrome (PTS), a condition marked by limb swelling and pain aggravated by activity, may develop in 50% of children who have experienced VTE<sup>4</sup>.

Current clinical guidelines issued by the National Institute for Health and Clinical Excellence (NICE) in **January 2010** for reducing the risk of venous thromboembolism apply only to patients over the age of 18 years<sup>5</sup>. In view of the potential mortality, morbidity, increased length of hospital stay and associated increased health costs of VTE in children, the case for similar guidelines for the paediatric population particularly in the critical care setting, (paediatric intensive care and high dependency services), is compelling. However, given the rarity of paediatric VTE, the risk-to-benefit ratio for **formal** prophylaxis remains controversial. For more than 10 years there have been calls

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3 for prospective randomised trials to define an effective strategy for preventing  
4 deep vein thrombosis (DVT) in children judged to be at risk<sup>3</sup>. To date such trials  
5  
6 have not materialised.  
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11 The aims of this paper were to audit the current practice in paediatric VTE  
12 prophylaxis in critical care units across England and Wales, to **promote** daily  
13 VTE risk review and **propose simple preventative measures**. We illustrate the  
14 importance of the condition with a series of patients who developed DVT over  
15 the course of 24 months at the South West Paediatric Burns and Neurosurgical  
16 Services based in Bristol.  
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### 31 Methods

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34 A review of all diagnosed cases of **DVT** occurring in children in the South West  
35 Paediatric Burns and Neurosurgical Services over the last two years was carried  
36 out with particular attention to risk factors **present**. The hospital admits  
37 approximately 2900 paediatric surgical patients per year including  
38  
39 approximately 350 admitted with burns, 500 admitted for neurosurgery, 1200  
40 with plastic surgical conditions and 500 with orthopaedic trauma. **Roughly fifty**  
41  
42 **percent of these patients remain in hospital for at least one night and**  
43  
44 **approximately 180 CVCs are sited within this population per year.**  
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55 Every paediatric intensive care unit (PICU) listed on the 'Paediatric Intensive Care  
56 Audit Network' website<sup>6</sup> and every centre admitting critically ill children with  
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58 burns in England and Wales was contacted by telephone. A single senior member  
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3 of medical or nursing staff was invited to participate in a structured  
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5 questionnaire. The nature and purpose of the study were explained and  
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7 reassurance that the data collected would be anonymised such that no  
8  
9 healthcare professional or unit would be identifiable. If agreement to participate  
10  
11 was obtained, a short structured interview was conducted to determine the  
12  
13 following: whether a written protocol for VTE prophylaxis in children existed  
14  
15 and was in use; whether risk of deep vein thrombosis was specifically assessed  
16  
17 each day; which, if any, groups of patients wore graduated compression  
18  
19 stockings (Thrombo-Embolus Deterrent stockings or TEDs) or pneumatic  
20  
21 compression boots (Flowtron® DVT Prophylaxis Systems, Huntleigh Healthcare  
22  
23 Ltd); and if no written protocol existed, which grade of doctor made individual  
24  
25 decisions regarding thromboprophylaxis **in patients of less than 18 years of**  
26  
27 **age**. If no one was able to respond to the survey a single follow-up phone call  
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29 was made.  
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#### 38 Case Studies:

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40 Six cases of VTE were diagnosed in our own service between September 2007  
41  
42 and September 2009: that is, 6 out of **3070 inpatients** (0.2%) and 5 of the 360  
43  
44 patients with CVCs (1.4%).  
45  
46

47  
48 **Case 1: A 13 month old girl with a 70% scald required four PICU admissions**  
49  
50 **complicated by sepsis and hyponatremia. Facial swelling was noted one**  
51  
52 **month after presentation. CT scanning demonstrated a thrombus in the**  
53  
54 **right internal jugular (RIJ) vein and superior vena cava associated with a**  
55  
56 **RIJ catheter that had been in place for five days. After receiving a heparin**  
57  
58 **infusion for 6 days, she was given low molecular weight heparin (LMWH).**  
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3 **Given the large surface area of her burns, tinzaparin was used to minimize**  
4 **the number of injections. After a 72 day hospitalization she was discharged**  
5  
6 **home on LMWH for 3 months.**  
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13 Case 2: A 14 month old girl admitted with a 65% scald subsequently developed  
14  
15 *Staphylococcus aureus* septicaemia and hypernatraemia. **An ultrasound**  
16 **performed when leg swelling occurred** after 12 days **confirmed** a left femoral  
17  
18 DVT extending into the iliac vein. A CVC had been present in the vein for three  
19  
20 days and had been removed four days prior to diagnosis. She was treated with  
21  
22 heparin before completing a three-month course of enoxaparin. A persistent  
23  
24 thrombocytosis (platelet count up to  $1,299 \times 10^9/l$ ) attributed to iron deficiency  
25  
26 could have been a contributory factor to the development of the thrombus.  
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35 Case 3: An 18 month old boy was admitted for elective craniotomy with anterior  
36  
37 vault reconstruction and re-modelling for metopic synostosis. **During** seven  
38  
39 hours **of surgery** he received a total of 4240mls of fluid and blood products.  
40  
41 Swelling of the right leg was noted on the third post-operative day and  
42  
43 **ultrasound confirmed** the presence of a thrombus in the right femoral vein,  
44  
45 associated with the central venous catheter that had been inserted at time of  
46  
47 surgery. A decision had been made to keep the line *in situ* after surgery to allow  
48  
49 for daily blood sampling whilst avoiding the need for phlebotomy. He was  
50  
51 treated with three3 months of enoxaparin.  
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59 Case 4: An 18 month old boy was admitted for craniotomy and excision of an  
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atypical teratoid/rhabdoid tumour. Right femoral arterial and venous lines were

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sited at the time of surgery, 600 mls of blood loss were replaced with 600 mls of blood products. Surgical duration was 6.5 hours. On the second post-operative day his right leg was found to be swollen; ultrasonic examination confirmed the presence of a thrombus in the right common femoral vein. Intravenous heparin infusion was commenced in view of his recent extensive surgery and the need for a further craniotomy. Following a second procedure he was commenced on LMWH for 3 months. He died 8 months after diagnosis from recurrent disease.

Case 5: A 7 year old girl presented acutely with an extensive cerebral gliosarcoma. Two craniotomies a week apart lasted 11 and 7 hours. Three days after the second procedure the patient **developed pain and swelling in the left leg**. Ultrasound **demonstrated** an extensive left common femoral vein thrombus **despite no cannulation of this vessel**. A CVC was present in the right femoral vein. **The significant** risk of pulmonary embolism **prompted treatment with unfractionated heparin** despite relative risk of neurosurgical haemorrhage. After five days enoxaparin was substituted for heparin, whereupon she developed subdural and intraventricular haemorrhages and anticoagulation was stopped. The risk of inferior vena cava (IVC) rupture was considered too great for an IVC filter to be placed. She died six weeks after diagnosis after receiving palliative care.

Case 6: A 7 year old boy presented after falling from a tractor and being crushed by the trailer. He had multiple injuries comprising: fractures of the basal skull, temporal bone, ribs and clavicle as well as bilateral pneumothoraces and bilateral pelvic fractures. He spent seven days sedated and ventilated. In the

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3 second week *Staphylococcus aureus* was isolated from blood cultures. He was  
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5 treated with intravenous antibiotics. Nineteen days after presentation he  
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7 underwent open pelvic fixation lasting three hours. A decision was made to  
8  
9 avoid LMWH prophylaxis, although TED stockings and pneumatic compression  
10  
11 boots were employed. On the sixth post-operative day pain and swelling in the  
12  
13 left thigh prompted an ultrasound scan which confirmed the presence of  
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15 thrombus in the proximal superficial and common femoral veins. LMWH was  
16  
17 commenced and factor Xa levels were monitored as per the hospital protocol.  
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22 The patient made a good recovery.  
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## 28 Survey Results

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32 Twenty-eight centres in England and Wales were contacted between 10<sup>th</sup> August  
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34 2009 and 29<sup>th</sup> September 2009 by one of the authors (AB). A senior member of  
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36 staff was prepared to answer the structured questionnaire at 24 units (86%).  
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41 Only one of the 24 units surveyed had written guidelines designed specifically  
42  
43 for the prevention of VTE in children. Two units used adult guidelines in  
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45 adolescent patients aged over 12 years based on those issued by NICE. A fourth  
46  
47 unit admitting children with burns used adult guidelines for children 13 years  
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49 and over and modified guidelines for children under 13 years. A fifth unit had  
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51 hospital-wide guidelines for patients, including children, admitted with diabetic  
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53 ketoacidosis (DKA), which included LMWH prophylaxis.  
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59 In units with no written guidelines, individual case-based decisions regarding  
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VTE prophylaxis were *ad hoc* and usually consultant-led. Risk of VTE was

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3 assessed daily in a ward round proforma in only one unit. TEDs were used in  
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5 some larger children and adolescents in all but one unit (96%). No unit reported  
6  
7 using Flowtron boots routinely.  
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## 10 11 12 13 14 15 Discussion

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19 The case for thromboprophylaxis in children is less clear than in adults because  
20  
21 of the relative rarity of paediatric VTE. Why children should have a lower  
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23 incidence of DVT than adults is not clear but possible explanations include  
24  
25 reduced capacity for thrombin generation, increased capacity of  $\alpha_2$ -  
26  
27 macroglobulin to inhibit thrombin and enhanced antithrombotic potential by  
28  
29 vessel walls<sup>2</sup>. VTE prophylaxis itself is associated with complications and cost,  
30  
31 therefore it is important to ascertain which children might benefit.  
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37 The aetiology and risk factors associated with VTE in children are well known  
38  
39 and have been described in international registries<sup>3</sup>. More than ninety percent  
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41 of children who develop VTE will have more than one predisposing factor<sup>7</sup>. By  
42  
43 far the most common risk factor is the presence of a CVC<sup>2</sup>. More than ninety  
44  
45 percent of VTEs in neonates and greater than fifty percent of VTEs in older  
46  
47 children are secondary to CVCs<sup>7</sup>. CVCs, however, are an essential component of  
48  
49 the care of critically ill children in order to allow accurate fluid management,  
50  
51 haemodialysis or inotropic use. Venous thrombosis, usually undetected clinically,  
52  
53 has been shown by routine ultrasound examination to have an incidence as high  
54  
55 as 44% of children with CVCs in place for greater than 48 hours<sup>8</sup>. Risk is highest  
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57 during the first four days after insertion and decreases thereafter<sup>9</sup>. Peripherally-  
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3 inserted central catheters are also associated with the development of VTE  
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5 although the incidence is lower (up to 9%) than when the catheter is inserted  
6  
7 centrally<sup>10</sup>. Younger and smaller children are more likely to develop catheter-  
8  
9 related VTE<sup>11</sup> which suggests that vessel size may be important. In the upper  
10  
11 venous system the risk of VTE is increased significantly with a CVC in the  
12  
13 subclavian veins, suggesting that placement in the brachial or jugular veins may  
14  
15 be preferable<sup>12</sup>. Young children with diabetic ketoacidosis have an increased  
16  
17 incidence of clinical DVT associated with the placement of CVCs **which may be**  
18  
19 **related to dehydration**<sup>13</sup>. . **The literature therefore reflects that CVCs are a**  
20  
21 **major risk factor for childhood VTE particularly in those children that are**  
22  
23 **less than one year of age, those admitted following trauma or with**  
24  
25 **underlying malignancy. It is therefore important that CVCs should be**  
26  
27 **removed as soon as possible and a simple risk benefit analysis should be**  
28  
29 **undertaken at least daily**<sup>14</sup>.  
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38 Despite the documented increase in the incidence of paediatric VTE and calls for  
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40 the effects of prophylactic measures to be studied, our survey confirms that in  
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42 England and Wales only one PICU uses written guidelines devised specifically for  
43  
44 children and there is wide variation in clinical practice. Awareness of the risk of  
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46 VTE within units also appears to vary enormously, some units addressing such  
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48 risk daily and others not. When non-pharmaceutical measures were taken, the  
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50 age and patient groups deemed at risk varied between units.  
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57 In contrast to VTE prevention in adults, the options for non-pharmaceutical  
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59 prophylactic measures for smaller children are limited: TEDs are only available  
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for a calf circumference greater than 25cm and a toe to knee measurement

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4 greater than 32.5cm. **Pneumatic compression** boots come in only one size.  
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6 However, both TEDs and **pneumatic compression devices** can be used in  
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8 adolescents and larger younger children. Heparin bonded (HB) CVCs are  
9  
10 currently under evaluation. In a prospective randomized controlled trial of 209  
11  
12 patients HB CVCs were shown to reduce the incidence of CVC related thrombosis  
13  
14 significantly<sup>15</sup>, although there seems to be no advantage in using HB CVCs in  
15  
16 infants less than one year old<sup>16</sup>. The use of LMWH for primary prophylaxis in  
17  
18 children must not be undertaken lightly. In a review of the literature since 1980,  
19  
20 LMWHs were found to be associated with minor bleeding in 21% and major  
21  
22 bleeding in 3% of patients receiving primary prophylaxis<sup>17</sup>. There is one  
23  
24 previously published paediatric VTE guideline<sup>18</sup>.  
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31 **We propose the following based on our survey, case review within our**  
32 **regional childrens services and a formal literature review; that all**  
33 **paediatric critical care areas formally assess risk of VTE daily, that CVCs**  
34 **are removed as soon as possible particularly in children less than one year**  
35 **of age and that non-pharmacological prophylactic measures are used**  
36 **where appropriate and feasible. LMWHs should be used only in high-risk**  
37 **patients and at the discretion of the consultants responsible.**  
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49 **In our unit we have implemented a risk assessment table similar to that**  
50 **used in our adult population according to the new adult NICE guidelines<sup>5</sup>**  
51 **(Figure 1). Five of the six cases seen at our hospital occurred in association**  
52 **with a CVC and all six had a combination of other risk factors. In most**  
53 **instances the CVC could have been removed earlier, the patients identified**  
54 **as medium to high risk for the development of VTE, and additional**  
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4 **prophylactic measures considered. The reasons for failure to remove a**  
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6 **CVC within 24hrs is documented and reviewed.**  
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11 **This paper aims to raise the profile of VTE prevention in children. To**  
12  
13 **devise a protocol which would be applicable across all areas and ages is**  
14  
15 **difficult but we encourage units to develop their own guidelines in**  
16  
17 **collaboration with the specialties involved.**  
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22 Summary  
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26  
27 VTE is a recognised cause of preventable mortality and morbidity in children and  
28  
29 with the increasing use of CVCs the incidence of VTE is rising. Our case series  
30  
31 highlights the problem in a typical cohort of critically ill children **following**  
32  
33 **neurosurgery, trauma and major burn injuries.** The survey confirms that  
34  
35 there is no consensus in the England and Wales as to which prophylactic  
36  
37 measures against VTE should be applied **in patients of less than 18 years of**  
38  
39 **age.** Given the rarity of VTE events in children it is unlikely that randomised  
40  
41 controlled trials will clarify this. **We therefore propose that a risk assessment**  
42  
43 **tool and simple empirical measures are employed within critical care**  
44  
45 **areas.** Other potential areas of development include further clinical trials into  
46  
47 the use of **heparin bonded** CVCs, as well as the possible development and  
48  
49 evaluation of TEDs and Flowtron boots for use in younger children.  
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For Peer Review

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For Peer Review

Name:

Date of Birth:

Hospital No.:  
Or attach addressograph.

**Paediatric Thromboprophylaxis Risk Assessment Chart**

To be followed DAILY for the following:  
PACU patients  
HDU patients  
Patients with CVCs

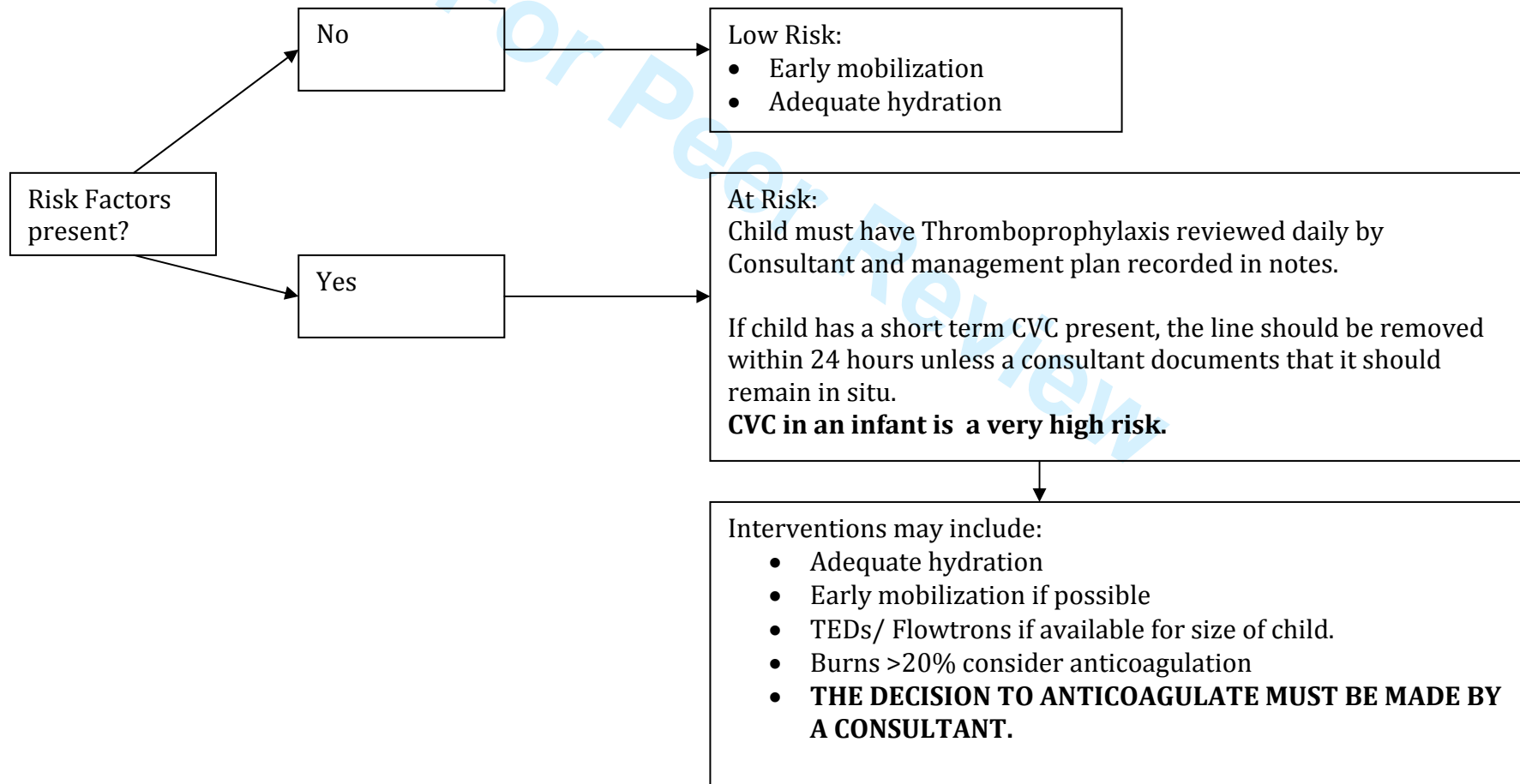
To be discontinued when child is fully mobilizing.

Date / Time					
Known Risk Factors (tick):					
Central Venous Catheter					
Pregnancy					
Congenital Heart Disease					
Obesity (BMI > 30)					
Malignancy					
Major Trauma – (Lower limb # or major organ)					
Burns >20%					
Oral Contraceptive Pill					
Surgery > 4 hrs					
Long term Steroids > 3 months					
Ventilated					
Assessed by: (name)					
Designation:					
Signature:					
Name of SpR or Consultant informed:					

**Decision to Anticoagulate can only be made by a Consultant.** NB. Any child with congenital pro-thrombotic disorder should be regarded as at risk.

## Paediatric Thromboprophylaxis Flow Chart

**NB. Daily Consultant Review Decisions must be documented in the Medical Notes**



Risk Factors  
present?

No

Low Risk:

- Early mobilization
- Adequate hydration

Yes

At Risk:

Child must have Thromboprophylaxis reviewed daily by  
Consultant and management plan recorded in notes.

If child has a short term CVC present, the line should be removed  
within 24 hours unless a consultant documents that it should  
remain in situ.

**CVC in an infant is a very high risk.**

Interventions may include:

- Adequate hydration
- Early mobilization if possible
- TEDs/ Flowtrons if available for size of child.
- Burns >20% consider anticoagulation
- **THE DECISION TO ANTICOAGULATE MUST BE MADE BY  
A CONSULTANT.**