Insufficient duration of venous thromboembolism prophylaxis after total hip or knee replacement when compared with the time course of thromboembolic events

FINDINGS FROM THE GLOBAL ORTHOPAEDIC REGISTRY

Patients who have undergone total hip or knee replacement (THR and TKR, respectively) are at high risk of venous thromboembolism. We aimed to determine the time courses of both the incidence of venous thromboembolism and effective prophylaxis. Patients with elective primary THR and TKR were enrolled in the multi-national Global Orthopaedic Registry. Data on the incidence of venous thromboembolism and prophylaxis were collected from 6639 THR and 8326 TKR patients.

The cumulative incidence of venous thromboembolism within three months of surgery was 1.7% in the THR and 2.3% in the TKR patients. The mean times to venous thromboembolism were 21.5 days (SD 22.5) for THR, and 9.7 days (SD 14.1) for TKR. It occurred after the median time to discharge in 75% of the THR and 57% of the TKA patients who developed venous thromboembolism. Of those who received recommended forms of prophylaxis, approximately one-quarter (26% of THR and 27% of TKR patients) were not receiving it seven days after surgery, the minimum duration recommended at the time of the study.

The risk of venous thromboembolism extends beyond the usual period of hospitalisation, while the duration of prophylaxis is often shorter than this. Practices should be re-assessed to ensure that patients receive appropriate durations of prophylaxis.

A high risk of venous thromboembolism after total hip replacement (THR) or total knee replacement (TKR) has long been appreciated. The reported incidence of asymptomatic deep-vein thrombosis (DVT) lies between 41% and 85%.1 For proximal DVT it is between 5% and 36% and for fatal pulmonary embolism, the reported incidence lies between 0.1% and 1.0% in the absence of effective prophylaxis.1

Previous studies have shown that the risk of venous thromboembolism continues for some time after surgery. In a study of 499 patients who had undergone THR the peak onset of thrombosis was on the fourth post-operative day, with the period of elevated risk extended to at least day 18 after surgery.2 In 19 586 THR and 24 059 TKR patients in California in whom the cumulative incidences of venous thromboembolism were 2.8% and 2.1%, respectively, the median time to diagnosis after surgery was 17 days for THR and seven days for TKR.3 Although ostensibly 88% of these patients received in-hospital prophylaxis, 76% and 47% of venous thromboembolism events in the THR patients and TKR patients respectively, were diagnosed after discharge from hospital, and only 32% of the patients received outpatient prophylaxis.3 An even longer duration of elevated risk was observed in a Norwegian study of THR and TKR patients who had received in-hospital prophylaxis for approximately ten days.4 Symptoms of DVT appeared at a mean of 27 days after THR and 16 days after TKR.4

Early studies have shown that prophylaxis between seven and 14 days reduces the risk of venous thromboembolism.5-10 This length of time was chosen for use in trials based on the trials based on the then-average length of hospital stay as opposed to on physiology. These trials led to their data being used as evidence for consensus guideline recommendations from the American College of Chest Physicians in 2001, stating that THR and TKR patients should receive prophylaxis for a minimum of seven to ten days.11 Furthermore, meta-analyses of studies on prophylaxis with low-molecular-weight heparin (LMWH) have shown that increasing the length of time to at least five weeks after THR and TKR further reduces the risk of venous thromboembolism, cutting clinical and asymptomatic event rates.
by more than a half, without an increase in the risk of major bleeding. While reports of the proportion of THR and TKR patients who receive any form of prophylaxis ranges from 88% to 100%, the pattern of use of recommended forms of prophylaxis in relation to the time course of an elevated risk of venous thromboembolism has not yet been concurrently determined or reported.

The Global Orthopaedic Registry records in-hospital treatment and clinical outcomes of consecutively-enrolled patients who have undergone elective THR or TKR. This multi-national registry reflects diverse, ‘real-world’, contemporary surgical practices and has, to date, collected data from 15,020 patients from 100 university-affiliated or community hospitals in 13 countries. In our study on data from this Registry, we aimed firstly to determine the time course of the occurrence of venous thromboembolic events in THR and TKR patients who had been operated on using contemporary surgical practices, and secondly, to ascertain whether these patients received prophylaxis, during the period in which they were at increased risk of venous thromboembolism, according to expert consensus group recommendations.

Patients and Methods

Design of the study. The study was designed and co-ordinated by the Center for Outcomes Research (University of Massachusetts, Worcester, Massachusetts) under the guidance of a Scientific Advisory Board. Participating surgeons enrolled consecutive patients who had undergone elective primary THR or TKR. Patients who underwent revision of previous surgery for a fracture of the hip or the knee were excluded. In-hospital data were collected for all patients. Data on selected aspects of out-patient management and post-discharge outcomes were collected after three and 12 months.

The scientific co-ordinating Centre ensured that the registry complied with scientific and ethical standards. Approval for the study was obtained from local ethics committees or institutional review boards, as required. When required by each hospital’s ethics review committee, signed informed consent was obtained from the patients before they participated in the registry.

Collection of data. Participating surgeons and trained study co-ordinators used standard case report forms to collect data, including details of the patient, primary diagnosis, pre-existing comorbid conditions, the length of stay in hospital, the type of anaesthesia, venous thromboembolism prophylaxis (type and duration), in-hospital complications, discharge disposition and patient self-reported quality of life.

Completed case report forms were sent to the scientific co-ordinating Centre for entry into the database and subsequent analysis. Data were double-key entered into a computer database and subsequently analysed using SAS-PC software version 9.1 (SAS Institute, Cary, North Carolina). The quality of the data was monitored using standardised query logic. Out-of-range or illogical responses were queried on a quarterly basis and corrections were faxed to the co-ordinating Centre.

A DVT or pulmonary embolism, collectively referred to as a venous thromboembolism, was defined as a symptomatic event, subsequently confirmed by diagnostic imaging techniques including venography, ultrasound, radio-isotope scanning and three-dimensional (3D) CT. The dates on which clinically diagnosed symptomatic DVT or pulmonary embolism occurred were recorded. Two TKR and no THR patients died in hospital of pulmonary embolism (confirmed by autopsy). Only 25 patients died in hospital in total (9 THR and 16 TKR). Of the THR patients, one died of pulmonary embolism within three months of discharge (23 patients died post-discharge in total - 16 THR and seven TKR). The three fatal pulmonary embolisms are included in our analysis.

Details of the patients and surgical practice. In total, 15,020 patients (6695 THR and 8325 TKR) were enrolled in the Global Orthopaedic Registry from 100 hospitals (156 surgeons) in 13 countries (Australia, Brazil, Bulgaria, Canada, Colombia, Germany, Italy, Japan, Poland, Spain, Turkey, United Kingdom and USA) between June 2001 and December 2004. Data on the timing of venous thromboembolic events, or data required to determine the period of follow-up, had not been recorded for 145 patients and these patients were excluded, leaving a total of 6639 THR and 8236 TKR patients for analysis. Overall, 74% (4912) of the THR and 67% (5526) of the TKR patients had follow-up data for at least three months. Of the 14,875 patients, 46% (3084) of THR and 62% (5135) of TKR patients were enrolled in the USA.

Details of the patients and surgery are shown in Table I. The table allows for the lack of some variables recorded on each patient’s case report form. Compared with the THR patients, the TKR patients were similar in age, but were more likely to be women and to have a body mass index (BMI) over 30 kg/m². The TKR patients were also more likely to have a previous history of venous thromboembolism and tended to have a slightly shorter stay in hospital. However, a higher proportion of TKR patients were discharged to a rehabilitation centre than the THR patients.

Statistical analysis. The Kaplan-Meier method was used to estimate the cumulative incidence rates of DVT and pulmonary embolism, and the median time to an event, starting from the day of surgery. The corresponding time course of the use of venous thromboembolism prophylaxis was determined by plotting the proportion of patients with data available on day t who were receiving prophylaxis, against time. This estimated the time course of prophylaxis, assuming that it was the same for patients with in-hospital only data and those with in-hospital and post-discharge data. In the follow-up period, the duration of prophylaxis was determined by assuming that prophylaxis started on the day of surgery and continued without interruption for the duration specified in a patient’s case report form. The median dura-
tion of the prophylaxis and the interquartile range (IQR) were calculated using data from only those patients who had been followed up at three months or more. For those who received intermittent pneumatic compression in combination with either LMWH or warfarin, the duration of prophylaxis was defined as the duration of either LMWH or warfarin or intermittent pneumatic compression, whichever was the longest. For this paper, the duration of individual forms of prophylaxis was only calculated for LMWH, warfarin, and intermittent pneumatic compression, since only these were recommended by the American College of Chest Physicians at the time of this study. Prophylaxis was defined as any use of LMWH, warfarin, fondaparinux, unfractionated heparin or intermittent pneumatic compression.

In order to relate the time course of thromboembolic events to the recommended duration of prophylaxis we took into account three time points. These included, the median length of hospital stay, the seventh day after surgery (the end of the minimum duration of prophylaxis recommended by the sixth American College of Chest Physicians guidelines for the prevention of venous thromboembolism in 2001) and the 28th day after surgery (the end of the minimum duration of prophylaxis recommended for THR patients by the seventh American College of Chest Physicians guidelines in 2004).

A univariate Cox regression was performed to identify factors associated with an increased incidence of thromboembolism after surgery. All patients in this analysis received some form of prophylaxis. The characteristics considered included the type of surgery (THR or TKR), the American Society of Anesthesiologists (ASA) physical status classification, gender, BMI above 30 kg/m², age (years in increasing intervals), type of anaesthesia, previous venous thromboembolism, ischaemic heart disease and venous stasis syndrome. Factors associated with an increased incidence of thromboembolism (significance at $p \leq 0.25$) were considered for inclusion in a Cox multiple-regression model. The model adjusts for the length of hospital stay and country. Factors which remained in the model and were statistically significant ($p \leq 0.05$) were considered to be independent predictors of venous thromboembolism after surgery.

### Results

#### Incidence and factors associated with venous thromboembolism.

The cumulative incidence of thromboembolism in the 14,875 patients with data on the timing of thromboembolic events was 2.0%.

Of the 6639 THR patients, 76 experienced a DVT within three months of surgery at a mean of 22.5 days (6 to 37, SD 23.3) after surgery, while 11 had a pulmonary embolism at a mean of 14.3 days (2 to 31, SD 14.2) after surgery (Table I).
The mean time to venous thromboembolism was 21.5 days (5 to 36, SD 22.5). The cumulative incidence of venous thromboembolism within the three months after THR was 1.7%. An additional seven patients experienced a thromboembolic event after THR, but the dates on which the events occurred had not been recorded. If we assume that they had occurred during the three months after surgery and they are included, the cumulative incidence would have been 1.8%.

Of the 8236 TKR patients, 134 experienced a DVT during the three months after surgery at a mean of 9.5 days (3 to 8, SD 13.6) after surgery, while 18 had a pulmonary embolism at a mean of 10.7 days (3 to 11, SD 17.9) after surgery (Table II). The mean time to venous thromboembolism was 9.7 days (3 to 9, SD 14.1). The cumulative incidence of thromboembolism within the three months after TKR was 2.3%. An additional 23 patients had a thromboembolic event after TKR, but were excluded because the dates of occurrence had not been recorded. If it is assumed that these events occurred during the three months after surgery and they are included, the cumulative incidence would have been 2.6%.

Factors which were associated with venous thromboembolism are shown in Table III. Consideration of these factors along with the patients’ country of origin in a multiple Cox regression model showed that previous venous thromboembolism (hazard ratio 4.92, 95% confidence interval (CI) 3.15 to 7.67) and BMI above 30 kg/m² (hazard ratio 1.68, CI 1.16 to 2.40) were significant predictors. Other factors that were associated with an increased risk of thromboembolism included post-surgery (%) ≤ 10 days (hazard ratio 2.38, CI 1.67 to 3.38, p < 0.0001), previous VTE (%) 7.1 (hazard ratio 4.46, CI 2.97 to 6.70, p < 0.0001), and women (%) 1.9 (hazard ratio 1.46, CI 1.10 to 1.94, p = 0.01).

Table II. Number of venous thromboembolism (VTE) events and timing after total hip replacement (THR) and total knee replacement (TKR)

<table>
<thead>
<tr>
<th>Thromboembolic event</th>
<th>Total number of thromboembolic events</th>
<th>Median time after surgery (IQR)</th>
<th>Total number of thromboembolic events</th>
<th>Median time after surgery (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVT</td>
<td>76</td>
<td>13 (6 to 37)</td>
<td>134</td>
<td>5 (3 to 8)</td>
</tr>
<tr>
<td>PE</td>
<td>11</td>
<td>5 (2 to 31)</td>
<td>18</td>
<td>4.5 (3 to 11)</td>
</tr>
<tr>
<td>VTE (DVT or PE)</td>
<td>87</td>
<td>12 (5 to 36)</td>
<td>152</td>
<td>5 (3 to 9)</td>
</tr>
</tbody>
</table>

* DVT, deep-vein thrombosis; PE, pulmonary embolism
† total number of symptomatic thromboembolic events that occurred after surgery and were later objectively confirmed
‡ IQR, interquartile range

Table III. Univariate Cox analysis of the incidence (%) of venous thromboembolism (VTE) in 14 565* total knee replacement (TKR)/total hip replacement (THR) patients

<table>
<thead>
<tr>
<th>Factor</th>
<th>VTE incidence</th>
<th>Hazard ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(TKR vs THR) (%)</td>
<td>In patients with factor</td>
<td>In patients without factor</td>
<td></td>
</tr>
<tr>
<td>Post-surgery (%)</td>
<td>1.9 (150/8026)</td>
<td>1.3 (87/6539)</td>
<td>1.50 (1.16 to 1.96)</td>
</tr>
<tr>
<td>≤ 10 days</td>
<td>4.9 (117/2402)</td>
<td>2.8 (42/1506)</td>
<td>2.38 (1.67 to 3.38)</td>
</tr>
<tr>
<td>&gt; 10 days</td>
<td>0.6 (33/624)</td>
<td>0.9 (45/5033)</td>
<td>0.67 (0.43 to 1.05)</td>
</tr>
<tr>
<td>ASA grade (severe or worse vs less than severe) (%)</td>
<td>1.4 (59/4136)</td>
<td>1.8 (171/9673)</td>
<td>0.90 (0.74 to 1.09)</td>
</tr>
<tr>
<td>Previous VTE (%)</td>
<td>7.1 (26/369)</td>
<td>1.5 (211/14 196)</td>
<td>4.46 (2.97 to 6.70)</td>
</tr>
<tr>
<td>Previous ischaemic heart disease (%)</td>
<td>2.1 (41/1950)</td>
<td>1.6 (196/12 615)</td>
<td>1.38 (0.99 to 1.93)</td>
</tr>
<tr>
<td>Previous venous stasis syndrome (%)</td>
<td>3.9 (23/590)</td>
<td>1.5 (214/13 974)</td>
<td>2.38 (1.55 to 3.66)</td>
</tr>
<tr>
<td>Women (%)</td>
<td>1.9 (186/8397)</td>
<td>1.3 (67/5321)</td>
<td>1.46 (1.10 to 1.94)</td>
</tr>
<tr>
<td>Body mass index &gt; 30 kg/m² (%)</td>
<td>1.9 (99/5343)</td>
<td>1.4 (95/7207)</td>
<td>1.47 (1.11 to 1.94)</td>
</tr>
<tr>
<td>Any hip/knee component cemented (%)</td>
<td>1.7 (180/10 377)</td>
<td>1.4 (57/4188)</td>
<td>1.27 (0.94 to 1.71)</td>
</tr>
</tbody>
</table>

* dates were not recorded for VTE occurrence in 30 patients and were missing for 115 patients. Of these left, 310 patients did not receive prophylaxis. The remaining 14 565 patients were included in the analyses
† denominations vary since not all the variables were recorded on each patient’s case report form
‡ CI, confidence interval
§ ASA, American Society of Anesthesiologists
¶ this was not recorded for 2015 patients
95% CI 1.25 to 2.26) were independently associated with an increased risk of venous thromboembolism. In the univariate analysis (Table III), TKR surgery was also significantly associated with an increased incidence of venous thromboembolism compared with THR surgery. In the multiple Cox regression model, an interaction with time after surgery and type of surgery were also observed (p < 0.0001), with a higher risk of thromboembolism after TKR during the early post-operative period and lower risk during the late post-operative period, compared with THR patients (hazard ratio 2.41, 95% CI 1.60 to 3.63 for TKR vs THR during the first ten days after surgery; hazard ratio 0.61, 95% CI 0.36 to 1.03 for TKR vs THR after ten days).

Methods of venous thromboembolism prophylaxis. In total, 14,565 of the 14,875 patients (98%) received a pharmacological or mechanical form of prophylaxis with LMWH, warfarin, unfractionated heparin, fondaparinux or intermittent pneumatic compression on the first day after surgery. No prophylaxis was given to 310 patients. The use of prophylaxis varied by region and the type of surgery (Fig. 1). Surgeons commonly used warfarin for both THR and TKR patients in the USA either alone or combined with intermittent pneumatic compression, while in other countries, LMWH (either alone or combined with intermittent pneumatic compression) was most frequently used as a form of prophylaxis on the first day after surgery. It was more common to use intermittent pneumatic compression combined with warfarin or LMWH in the USA than in other countries.

Patterns of prophylactic practice and incidence. In the THR patients, 65 of 87 (75%) thromboembolic events occurred after the median time to hospital discharge (five days after surgery, Fig. 2). Of the THR patients who received any form of prophylaxis on the day after surgery, 796 of 5308 (15%) were not receiving it five days after surgery (Fig. 3a). In the TKR patients, 86 of 152 (57%) thromboembolic events occurred after the median time to hospital discharge (four days after surgery, Fig. 2). Of the TKR patients who received any form of prophylaxis on the day after surgery, 682 of 6517 (10%) were not receiving it four days after surgery (Fig. 3b).

In the THR patients, 54 of 87 (62%) thromboembolic events occurred after seven days following surgery; prophylaxis had been discontinued in 26% (1329 of 5113) of those who had initially received any form of prophylaxis. At seven days after TKR surgery, 46 of 152 (30%) thromboembolic events were yet to occur while prophylaxis had been discontinued in 27% (1558 of 5763) of those who had initially received prophylaxis.

In the THR patients, 26 of 87 (30%) thromboembolic events occurred after 28 days following surgery, while prophylaxis had been discontinued in 54% (2484 of 4637) of those who had initially received prophylaxis. At the same time point after TKR surgery, only 11 of 152 (7%) thromboembolic events were yet to occur while 63% (3192 of 5096) of the TKR patients who initially received prophylaxis were no longer receiving it.
The patterns of prophylactic use varied depending on the method used. In the THR patients who received LMWH alone, the time course of use was characterised by a slow and linear decrease from the time of surgery to about ten weeks after surgery; all THR patients who received LMWH received it up to the median time of hospital discharge and more than one-third were not receiving it 28 days after surgery (Fig. 4a). By contrast, the use of warfarin alone in THR patients was characterised by a dramatic decrease around the time of hospital discharge. Prophylaxis with warfarin was discontinued in 4.5% (31 of 690) at day three, 66% (392 of 593) at day five, and 75% (427 of 571) at day seven. Of the THR patients who had received warfarin alone, 86% (443 of 518) were no longer receiving prophylaxis 28 days after surgery (Fig. 4a).

The patterns of prophylactic use in the TKR patients were similar to those in the THR patients. Of the TKR patients who received LMWH alone, all were receiving it at the median time to hospital discharge and 40% (672 of 1689) were no longer receiving it 28 days after surgery (Fig. 4b). Of those receiving warfarin alone, 40% (417 of 1048) and 74% (605 of 820) were no longer receiving prophylaxis at the median time to hospital discharge and 28 days after surgery, respectively (Fig. 4b).

Compared with patients who received prophylaxis with LMWH alone, patients who received a combination of intermittent pneumatic compression and LMWH were less likely to continue to receive prophylaxis up to 28 days after surgery. Of the THR and TKR patients who received both intermittent pneumatic compression and LMWH, 80% (595 of 750) and 83% (1075 of 1302), respectively, were not receiving prophylaxis 28 days after surgery. By contrast, those who received warfarin alone were less likely to be receiving prophylaxis 28 days after surgery than patients...
who had received the combination of intermittent pneumatic compression and warfarin. Of the THR and TKR patients who had received both intermittent pneumatic compression and warfarin, 36% (306 of 853) and 30% (234 of 772) were not receiving it at the median time to hospital discharge, and 48% (360 of 745) and 56% (340 of 604) were not receiving prophylaxis 28 days after surgery, respectively.

Discussion

Our analyses of data from the Global Orthopaedic Registry confirm previous reports that the duration of the elevated risk of venous thromboembolism extended beyond the usual period of hospitalisation.1,3,4,18,19 In our study, between one-third and one-half of thromboembolic events occurred after the median time to hospital discharge.

Our study was the first to report both the incidence of venous thromboembolism and the use of recommended forms of prophylaxis concurrently, allowing us to determine the time course of both thromboembolic events and prophylactic use in the same group of patients. The duration of prophylaxis was often shorter than that recommended by evidence-based practice guidelines current at the time of the patients’ enrolment1 and shorter than the period of risk of venous thromboembolism in THR and TKR patients. While nearly all patients received prophylaxis on the first day after surgery, more than a quarter were not receiving any form of prophylaxis seven days after surgery, which was the minimum duration specified by the American College of Chest Physicians guidelines published in 2001.11

Patients who received LMWH were most likely still to be receiving prophylaxis at any time during the course of the study. Nonetheless, approximately 37% of the THR patients initially receiving LMWH did not receive this form of prophylaxis up to 28 days after surgery, now recommended by the seventh American College of Chest Physicians guidelines.1 By contrast, the duration of prophylaxis was shortest in the patients who had received warfarin with or without intermittent pneumatic compression.

Our study suggested a higher cumulative incidence and an earlier occurrence of thromboembolism after TKR than THR as has been seen in some previous studies. By contrast, the study of 19 586 THR and 24 059 TKR patients by White et al.13 showed a three-month cumulative incidence of thromboembolism which was higher after THR than after TKR (2.8% vs 2.1%, p < 0.001). More recently, Bjørnara, Gudmundsen and Dahl20 have produced similar figures, and a meta-analysis of data from randomised, controlled trials has shown a higher incidence of symptomatic thromboembolism after THR (1.4% to 4.3%) than after TKR (1.0% to 1.4%).12 The differences in incidence may be explained in part by different methodologies, the different surgical treatments, and the variable prophylactic practices at the times of these studies as well as by the regional differences. In addition, we cannot exclude the possibility that the type and regimen of prophylaxis used in TKR patients enrolled in our registry were less optimal than in the enrolled THR patients, especially during the early post-operative phase.

Factors independently associated with an increased incidence of thromboembolism in our population were previous thromboembolism and a BMI of more than 30 kg/m². This accords well with other studies,21-23 some of which have additionally reported poor ASA classification, increasing age, chronic heart failure, the individual surgeons practice, varicose veins and a lack of prophylaxis, as independent predictors of the risk of thromboembolism in this population.22-24 We did not confirm this. Previous thromboembolism, obesity, and hospital stay with recent surgery have been shown to be risk factors in general, not only in orthopaedic patients.21,26

Although the duration of prophylaxis in our study appeared to follow more appropriately the time course of thromboembolic events in TKR compared with THR, we stopped prophylaxis in a significant proportion of TKR patients before the median time of occurrence of thromboembolism, the time point when 50% of all thromboembolism events had still not occurred. From this it is clear that prophylactic practices in these patients are still to be improved.

Clinical trial data support extended periods of prophylaxis in THR and TKR patients.3,12,14 The evidence-based practice guidelines of 2004 recommend prophylaxis for a minimum of ten days,4 as opposed to seven days recommended in 200111 in THR and TKR patients, and up to 28 to 35 days in THR patients.3 Given that recommendations suggest prophylaxis be given to patients after discharge and that clinical trials have failed to show an increase in the risk of major bleeding associated with this practice,12,14 post-discharge practices clearly need to be reviewed. This is particularly the case for surgeons using warfarin, to ensure that all patients receive the recommended forms of prophylaxis for a duration which will provide sufficient protection from thromboembolism.

The lack of compliance with the recommendations for the duration of prophylaxis which we observed is likely to be related, at least partially, to the length of hospitalisation. We observed a marked decrease in the rate of prophylaxis around the median time to discharge. This was particularly notable for patients who received prophylaxis with warfarin alone. Another possibility could be that surgeons may not have all been aware of the significant post-discharge risk of thromboembolism in THR and TKR patients and the importance of providing appropriate prophylaxis during this period.

Given that our study has demonstrated that the period of risk of thromboembolism extends well beyond the standard periods of hospitalisation presently, especially for THR patients, clinical practices should be changed to account for the need to protect patients with appropriate post-discharge prophylaxis. Eikelboom et al.12 demonstrated
that, extended-duration prophylaxis with LMWH reduced the risk of symptomatic thromboembolism, compared with a placebo or no prophylaxis, with the only cost being an increase in the incidence of minor bleeding. Changes in clinical practice could be achieved by educating surgeons whose responsibility it is to provide care during patient hospitalisation as well as to both physicians and nurses who may be involved in post-discharge care. For example, Durieux et al\textsuperscript{27} observed an increase in compliance with thromboembolism prophylaxis guidelines from 82.8\% to 94.9\% in an orthopaedic department of a French teaching hospital when a computer-based clinical-decision support system was introduced. Furthermore, the use of computerised electronic alerts almost doubled the use of pharmacological prophylaxis in a hospital in the USA and resulted in a reduction in the risk of thromboembolism of 41\% at 90 days.\textsuperscript{28}

Our data do not exclude the possibility that thromboembolism will occur in some patients despite the use of prophylaxis, either because of inappropriate doses, or as a result of delayed first dose. Notably, a previous analysis of this registry showed that two-thirds of surgeons aimed for a target international normalised ratio (INR) which was lower than that recommended as effective for venous thromboembolism prophylaxis (INR 2 to 3).\textsuperscript{29} Even in cases where surgeons aimed for an INR above 2, less than one-half achieved this target by day two after surgery.\textsuperscript{29} In other cases, patients may be at particularly high risk of thromboembolism because of a predisposing factor, such as thrombophilia or cancer.\textsuperscript{26} However, our data clearly demonstrate a need for the more effective use of prophylaxis.

With the possibility that the participating surgeons in our study had a particular interest in the prevention of thromboembolism, they may not have been completely representative of surgeons worldwide. This could have resulted in an overestimation of the compliance of orthopaedic surgeons with prevention guidelines. However, the three-month follow-up was 74\% for THR and 67\% for TKR patients. This is considered to be acceptable for observational studies such as the Global Orthopaedic Registry and does not limit the strength of our conclusions.

In conclusion, the risk of venous thromboembolism after THR or TKR extends well beyond the usual period of hospitalisation of patients. Current prophylactic practices do not often comply with evidence-based practice guidelines. Our study has shown that the duration of prophylaxis given to these patients is often much shorter than the period in which thromboembolic events occur after surgery. This worrying leaves many patients in danger of suffering a late occurring thromboembolic event which may have been prevented if effective prophylaxis had been used for a longer duration, most notably THR patients who have the longest duration of elevated risk of thromboembolism. Even the correct duration of prophylaxis may not give adequate protection from venous thromboembolism if an incorrect prophylactic method or incorrect dose regimen is used.

Our data are consistent with recommendations made by internationally accepted expert consensus guidelines, such as those from the American College of Chest Physicians\textsuperscript{1} and Nicolaides et al\textsuperscript{30} and organisations such as the House of Commons Select Committee on Health in the United Kingdom.\textsuperscript{31} Health-care decision-makers and surgeons should re-assess practices of prevention of venous thromboembolism to ensure that THR and TKR patients receive recommended forms of prophylaxis for an appropriate period of time, not only during hospitalisation but also after discharge.

**Supplementary Material**

Details of the Global Orthopaedic Registry advisory committee are available with the electronic version of this article on our website at www.bjs.org.uk

The Global Orthopaedic Registry is supported by an unrestricted educational grant from sanofi-aventis and is co-ordinated by the Center for Outcomes Research at the University of Massachusetts Medical School, Worcester, Massachusetts. The Registry is overseen by a Scientific Advisory Committee. Additional information about this registry, including a full list of the Advisory Committee members, is available on the website at www.outcomes.org.

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**References**


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