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RESEARCH ARTICLE

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# Preferences for thromboprophylaxis in the intensive care unit: An international survey

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## Abstract

**Background:** Venous thromboembolism (VTE) is a frequent complication in critically ill patients, who often have multiple risk factors. Pharmacological thromboprophylaxis is widely applied to lower this risk, but guidelines lack dosing recommendations.

**Objective:** This survey aims to assess current thromboprophylaxis preferences and willingness to participate in future randomized clinical trials (RCTs) on this topic.

For affiliations refer to page 9

**Method:** We conducted an international online survey between February and May 2023 among intensive care unit (ICU) physicians, including 16 questions about preferences in relation to thromboprophylaxis and preferences on topics for a future RCT. The survey was distributed through the network of the Collaboration for Research in Intensive Care.

**Results:** A total of 715 physicians from 170 ICUs in 23 countries contributed information, with a mean response rate of 36%. In most ICUs, both pharmacological ($n = 166$, 98%) and mechanical thromboprophylaxis ($n = 143$, 84%) were applied. A total of 36 pharmacological thromboprophylaxis regimens were reported. Use of low-molecular-weight heparin (LMWH) was most common ($n = 149$ ICUs, 87%), followed by subcutaneous unfractionated heparin ($n = 44$ ICUs, 26%). Seventy-five percent of physicians indicated that they used enoxaparin 40 mg (4000 IU), dalteparin 5000 IU, or tinzaparin 4500 IU once daily, whereas 25% reported the use of 16 other LMWH type and dose combinations. Dose adjustment according to weight was common (78 ICUs, 46%). Participants perceived high variation in the application of thromboprophylaxis and were willing to consider an alternative LMWH type ($n = 542$, 76%) or dose ($n = 538$, 75%) in the context of an RCT.

**Conclusion:** LMWH was the preferred agent for thromboprophylaxis in critically ill patients. There was considerable variation in the application of LMWH for prophylaxis, reflected by the use of different types, doses, and dosing strategies. Most physicians would be willing to participate in an RCT on thromboprophylaxis.

**Editorial comment:** This survey demonstrates current patterns in implementation preferences for critically ill patients. While there is one approach and drug that is commonly preferred, these findings show that there is some variation in practice.

KEYWORDS
ICU, survey, thromboprophylaxis

## 1 | INTRODUCTION

Venous thromboembolism (VTE), which encompasses deep vein thrombosis (DVT) and pulmonary embolism (PE), is a potentially severe complication of critical illness. Critically ill patients typically suffer a multitude of comorbidities and risk factors for VTE, placing them at a particularly high risk of thrombotic complications compared to non-critically ill patients.[1,2] Development of VTE is associated with short-term complications, such as hemodynamic deterioration or even death, as well as long-term complications, including post-thrombotic syndrome and chronic pulmonary hypertension.[1,3–6]

The American Society of Hematology, National Institute for Health and Care Excellence, and European Society of Anaesthesiology recommend the use of low-molecular-weight heparin (LMWH) over unfractionated heparin (UFH) as pharmacological thromboprophylaxis for critically ill patients.[7–9] Despite the widespread application of prophylaxis, the residual risk of VTE is estimated at 4% to 27%, depending on whether screening was performed.[1,6,10–13] Theoretically, the burden of VTE might be reduced by using higher doses of pharmacological thromboprophylaxis; however, data from trials including patients with COVID-19 have highlighted the potential increased risk of bleeding that can occur with higher doses of anticoagulants in patients who are critically ill.[14] While careful consideration of the balance of benefits and risks with anticoagulation is essential when choosing an appropriate dose of anticoagulant therapy, in general, there is insufficient evidence on the optimal LMWH dose for thromboprophylaxis.[8]

Accordingly, we hypothesized that there would be substantial variation in reported practice in relation to VTE prophylaxis in critically ill patients and undertook a survey to assess variation in the preferences for thromboprophylaxis in critically ill patients and to evaluate physicians' views on—and willingness to participate in—further research on this topic.

## 2 | METHODS

### 2.1 | Study design

We conducted an international survey to evaluate the practices of thromboprophylaxis in critically ill patients and to assess the

willingness of physicians to engage in randomized clinical trials (RCTs) on this topic.

The survey was carried out using the secure web application Research Electronic Data Capture (REDCap version 12.4.6), hosted by the University Medical Center Groningen. Ethical review was not required since no patient data were collected. Participation was anonymous. Participation was voluntary, and no financial compensation was provided. Informed consent of the participants was assumed upon activation and completion of the survey link. The survey was conducted between February 1, 2023 and May 31, 2023. We sent two reminders to all participating sites before closing the survey. The preparation of this manuscript adhered to the guidelines outlined in the Consensus-Based Checklist for Reporting of Survey Studies (CROSS) (Table S1).

## 2.2 | Survey description

The online survey consisted of four sections containing 16 questions, accompanied by a varying number of sub-questions. The first section (questions 1 through 5) aimed to collect information on the physician's level of training (e.g., specialist, trainee or researcher), type of Intensive Care Unit (ICU) (medical, surgical or mixed) and hospital (general or specialist (academic)) the participant was affiliated with, the country in which the hospital was located, and the hospital name. The survey was conducted in English.

The second part of the survey (questions 6 through 12) evaluated self-reported clinical practice with regard to thromboprophylaxis. Participants were asked about their views on practice variation within their country and department, the presence of a local protocol guiding thromboprophylaxis, the use and application of a risk assessment model to determine which patients should receive thromboprophylaxis, and on the use of compression stockings and pneumatic compression devices.

The third section (question 13) featured more in-depth questions on the use of pharmacological thromboprophylaxis. This section included multiple sub-questions inquiring about the type (LMWH, intravenous or subcutaneous UFH, direct oral anticoagulants (DOAC) and/or pentasaccharides), dose, duration, frequency (daily, twice a day or three times a day) and timing of administration (morning, afternoon and/or evening). We implemented branching logic functions to obtain more detailed information on different aspects of pharmacological thromboprophylaxis (e.g., dosing based on a risk assessment model, weight, or anti-factor Xa (anti-Xa) levels (by peak level, through level or both) based on the respondents' preceding answers).

The final section (questions 14 through 16) aimed to assess physicians' opinions on the importance of several topics for future research on thromboprophylaxis, by evaluating their willingness to participate in a variety of scenarios of RCTs assessing several theoretical research questions. Finally, we inquired whether participants collaborate with hematologists and pharmacologists when making decisions concerning thromboprophylaxis.

The target population for this survey was intensive care physicians. The survey underwent pilot testing among intensive care physicians in the departments of the coordinators in the Netherlands, Denmark, and Australia, and was revised accordingly. The full survey is included in Table S2.

## 2.3 | Survey distribution

The survey was distributed to participants through the Collaboration for Research in Intensive Care (CRIC) network, a collaborative network of academic partners engaged in clinical research in intensive care (www.cric.nu). For each country, a national coordinator from the CRIC network was invited and tasked with recruiting site coordinators. The site coordinators received a direct access link and were requested to disseminate the survey to ICU physicians within their respective hospitals and register the number of recipients and respondents. All types of ICUs were eligible for participation, and it was allowed to extend the invitation link to all physicians working at a particular ICU.

## 2.4 | Analysis

Depending on the content of the question, data are presented at the individual respondent, ICU, or country level. Accordingly, when data are presented on an ICU level, data of individual respondents were aggregated, resulting in one single response for each ICU. In case of conflicting responses between several respondents from a single ICU, responses were aggregated at the ICU level when 80% or more of the participants were in agreement or presented as 'mixed' when agreement among respondents within one ICU was below 80%. The decision to set the cutoff point at 80% was reached through deliberation within our research team. We collectively determined that if more than 80% of the physicians indicated the use of a particular method or intervention in their respective departments, we would regard this as accurate.

Categorical variables are presented as numbers with percentages. We report the proportion of missing data, and all analyses are based on complete-case analyses. The statistical analyses were carried out using R (version 4.0.2). Since we used a convenience sample, we did not conduct any sample size estimation.

# 3 | RESULTS

We received a total of 722 responses. Data from seven physicians were excluded: four submissions were completely empty, and three submissions lacked information on a large number (>75%) of questions. A total of 715 physicians from 170 ICUs across 23 countries were included in the analyses (Figure 1 and Table S3). The mean response rate for the countries with a known denominator (all of those who were invited to participate in the survey) was 36% (95% confidence interval (CI): 34.1–38.6). Detailed information about the response rates per country is available in Table S4.

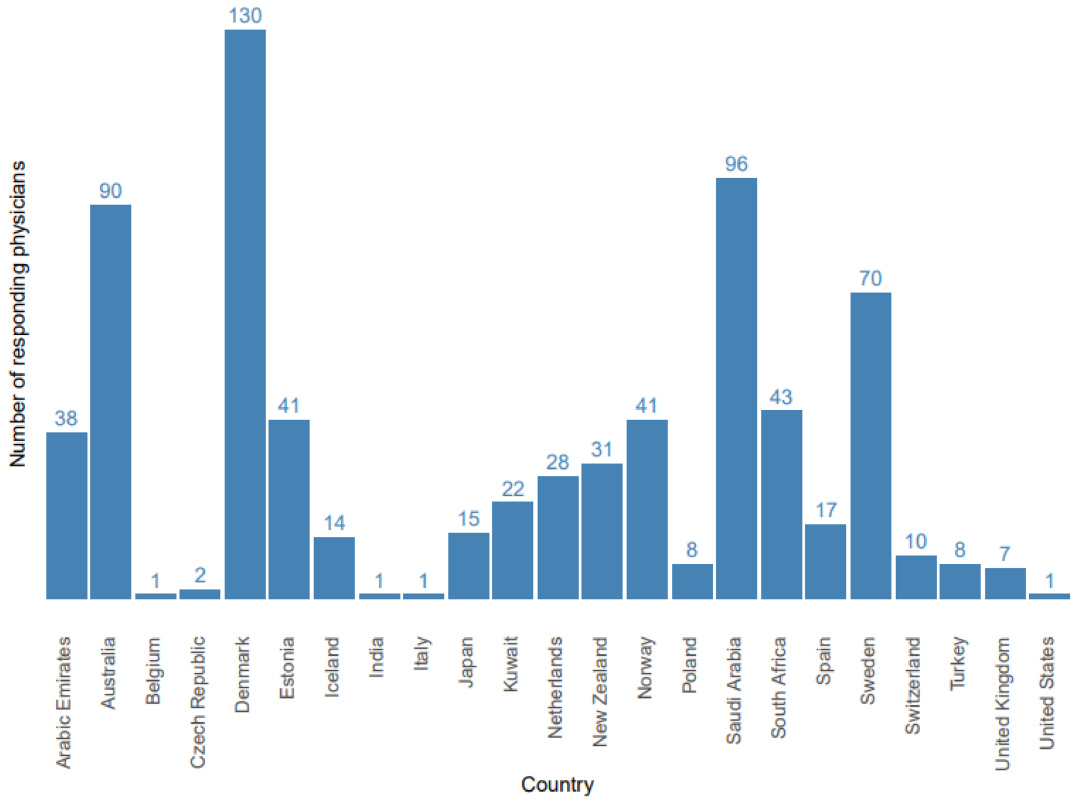


**FIGURE 1** Number of responding physicians per country.

**TABLE 1** Reported preferences for the use of thromboprophylaxis by number of ICUs.

| Variable | Participant responses aggregated at ICU level ($n = 170$)[a] | | |
|---|---|---|---|
| | Mostly yes[b] | Mixed[b] | Mostly no[b] |
| Use of any type of thromboprophylaxis[c] | 167 (98%) | 1 (1%) | 2 (1%) |
| Use of pharmacological prophylaxis | 166 (98%) | 2 (1%) | 2 (1%) |
| Use of a local guideline or protocol on the use of thromboprophylaxis | 99 (58%) | 42 (25%) | 29 (17%) |
| Use a risk assessment model to decide eligibility for thromboprophylaxis | 55 (32%) | 42 (25%) | 73 (43%) |
| Use of compression stockings | 99 (58%) | 37 (22%) | 34 (20%) |
| Use of pneumatic compression devices | 121 (71%) | 7 (4%) | 42 (25%) |
| Continuation of pharmacological prophylaxis during the entire ICU stay[d] | 167 (98%) | 0 | 0 |
| Recommendation on (dis)continuation of thromboprophylaxis in discharge letter | 51 (31%) | 45 (30%) | 71 (43%) |

Abbreviations: DOAC, direct oral anticoagulant; ICU, intensive care unit; LMWH, low-molecular-weight heparin.
[a]Values are numbers (percentages).
[b]Data of individual physicians were aggregated, resulting in one single response for each ICU. In the case of conflicting responses between several physicians from a single ICU, responses were aggregated at the ICU level when 80% or more of the participants were in agreement or presented as 'mixed' when agreement among physicians within one ICU was below 80%.
[c]Either mechanical or pharmacological in all adult patients, provided that there are no contraindications such as active bleeding.
[d]Answers from three ICUs were missing.

The majority of the participants worked in general hospitals ($n = 369$, 52%), followed closely by specialist hospitals ($n = 338$, 47%) and a small group worked in 'other' hospitals ($n = 8$, 1.1%). The majority of the participants worked in mixed ICUs ($n = 600$, 84%), followed by medical ($n = 76$, 11%) and surgical ICUs ($n = 28$, 4%). The physicians were primarily ICU specialists ($n = 638$, 89%), while trainees ($n = 55$, 8%), individuals from other professions ($n = 16$, 2%) and researchers (n = 6, 1%) also participated.

## 3.1 | Preferences for thromboprophylaxis

A total of 284 out of 715 participants (40%) perceived variation in the application of thromboprophylaxis within their department, and 561 (78%) perceived variation within their country. In most ICUs ($n = 167$, 98%) thromboprophylaxis, either mechanical or pharmacological, was used in all adult patients, provided that there were no contraindications (Table 1). In nearly all of these ($n = 166$, 98%)

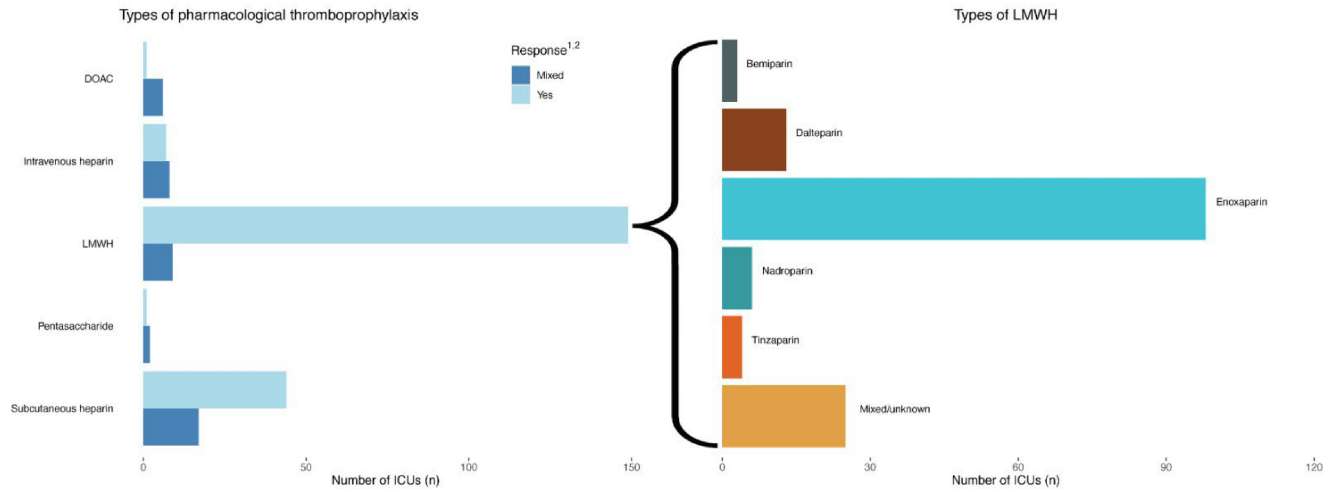


**FIGURE 2** Reported types of thromboprophylaxis (left) and reported subtypes of LMWH (right) by numbers of ICUs. LMWH, low-molecular-weight heparin; DOAC, direct oral anticoagulant; ICU, intensive care unit. N is higher than the total amount of ICUs (N=170) because physicians from multiple ICUs reported the use of more than one type of pharmacological prophylaxis. Data of individual physicians were aggregated resulting in one single response for each ICU. In case of conflicting responses between several physicians from a single ICU, responses were aggregated at ICU level when 80% or more of the participants were in agreement, or presented as 'mixed' when agreement among physicians within one ICU was below 80%.

pharmacological prophylaxis was applied. In the majority, some form of mechanical prophylaxis was also applied ($n = 143$, 86%). Participants reported the presence of a local protocol for thromboprophylaxis in more than half of the ICUs ($n = 99$, 58%), and the application of some form of risk assessment to guide prophylaxis in roughly a third of the ICUs ($n = 55$, 32%). Collaborations with hematologists and/or pharmacologists were reported on the basis of various reasons: 41 ICUs (24%) reported collaborations on taking decisions concerning thromboprophylaxis in complex cases, and within this subgroup, 22 ICUs (13%) also collaborated in the formulation of policies. Twelve ICUs (7%) solely collaborated in policy writing, and from 73 ICUs (43%) we received mixed responses. Nineteen ICUs (11%) did not report any form of collaboration.

## 3.2 | Pharmacological thromboprophylaxis

A total of 36 different pharmacological thromboprophylaxis regimens were reported in the 166 ICUs where pharmacological thromboprophylaxis was used. LMWH was the most frequently reported type of thromboprophylaxis in all countries and in most ICUs ($n = 149$, 90%). Enoxaparin was the most frequently reported LMWH ($n = 96$ ICUs, 64%; Figure 2). The use of subcutaneous UFH was reported by physicians in 44 ICUs (27%) in 12 out of 23 countries. Alternative types of thromboprophylaxis (intravenous UFH, DOACs, or pentasaccharides) were less frequently reported, and if reported, consensus among physicians within ICUs was limited (Figure 2). Types of thromboprophylaxis reported by country are detailed in Tables S5 and S6.

There was a clear preference for specific doses and frequencies of administration. A total of 75% of the participants reported the use of either enoxaparin 40 mg (4000 IU) once daily, dalteparin 5000 IU once daily, or tinzaparin 4500 IU once daily, whereas 25% reported a total of 16 other LMWH type and dose combinations (Table 2). In the case of subcutaneous UFH use, a dose of 5000 IU administered twice or three times daily was predominantly reported.

Timing of administration of pharmacological thromboprophylaxis varied: the evening ($n = 64$, 39%) was most frequently reported, followed by the morning ($n = 27$, 16%), the afternoon ($n = 11$, 7%), and various time points ($n = 8$, 5%); from the remaining ICUs ($n = 56$, 34%) we received mixed answers. Participants from all ICUs reported that they continued administration of pharmacological prophylaxis throughout the entire ICU stay.

## 3.3 | Dosing strategies

In ICUs where pharmacological prophylaxis was used ($n = 166$), different dosing strategies were employed. Dose adjustments based on weight were reported by participants of 78 ICUs (47%), with mixed responses in 60 ICUs (36%), and no or infrequent adjustments in 27 ICUs (16%).

Among all ICUs where at least one participant reported the use of LMWH ($n = 158$, 93%), dosing was guided by anti-Xa levels in 14 ICUs (9%); while this was rarely or never performed in 92 ICUs (58%) and mixed answers were received from participants in 52 ICUs (33%). If anti-Xa levels were used for dose adjustments, dosing was most commonly guided by anti-Xa peak levels ($n = 5$, 36%), followed by trough levels ($n = 4$; 29%) and both peak and through levels ($n = 2$, 14%). Mixed answers were reported in two ICUs (14%).

In ICUs, where UFH (subcutaneous or intravenous) was administered for pharmacological thromboprophylaxis ($n = 78$), dosing was guided by activated partial thromboplastin time in 13 (17%), while in

**TABLE 2** Type, subtype, dose, and administration frequency of pharmacological thromboprophylaxis in ICUs.

| Anticoagulant class (*n* [%]) | Anticoagulant type | Dose and frequency | *n* (% of anticoagulant class) |
|---|---|---|---|
| DOAC, *n* = 21 (2%) | Apixaban | 2.5 mg QD | 1 (5%) |
| | | 2.5 mg BID | 2 (10%) |
| | | 5 mg BID | 5 (24%) |
| | | Not reported | 4 (19%) |
| | Edoxaban | 30 mg QD | 1 (5%) |
| | Rivaroxaban | 10 mg QD | 1 (5%) |
| | | 15 mg QD | 1 (5%) |
| | | Not reported | 1 (5%) |
| | Not reported | – | 5 (24%) |
| UFH i.v., *n* = 56 (6%) | | Not reported | 56 (100%) |
| UFH s.c., *n* = 227 (23%) | | 1000 IU QD | 3 (13%) |
| | | 2500 IU QD | 1 (0.4%) |
| | | 2500 IU TID | 1 (0.4%) |
| | | 4500 IU QD | 1 (0.4%) |
| | | 5000 IU QD | 4 (2%) |
| | | 5000 IU BID | 137 (60%) |
| | | 5000 IU TID | 63 (28%) |
| | | Not reported | 17 (7%) |
| LMWH, *n* = 655 (68%) | Bemiparin | 2500 IU QD | 1 (0.2%) |
| | | 3500 IU QD | 2 (0.3%) |
| | Dalteparin | 2500 IU QD | 9 (1%) |
| | | 2500 IU BID | 1 (0.2%) |
| | | 4500 IU QD | 2 (0.3%) |
| | | 5000 IU QD | 84 (13%) |
| | | Not reported | 5 (1%) |
| | Enoxaparin | 2000 IU QD | 2 (0.3%) |
| | | 3000 IU QD | 1 (0.2%) |
| | | 4000 IU QD | 323 (49%) |
| | | 4000 IU BID | 7 (1%) |
| | | 4000 IU TID | 1 (0.2%) |
| | | 5000 IU QD | 3 (0.5%) |
| | | 6000 IU QD | 12 (2%) |
| | | Not reported | 22 (3%) |
| | Nadroparin | 2850 IU QD | 14 (2%) |
| | | 3800 IU QD | 4 (1%) |
| | | Not reported | 4 (1%) |
| | Tinzaparin | 2500 IU QD | 1 (0.2%) |
| | | 3500 IU QD | 8 (2%) |
| | | 4000 IU QD | 2 (0.3%) |
| | | 4500 IU QD | 83 (13%) |
| | | Not reported | 2 (0.3%) |
| | Not reported | – | 62 (9%) |
| Pentasaccharide, *n* = 10 (1%) | Fondaparinux | 2.5 mg QD | 6 (60%) |
| | | 5 mg QD | 1 (10%) |
| | | 7.5 mg QD | 1 (10%) |
| | | Not reported | 2 (20%) |

Abbreviations: BID, twice daily; DOAC, direct oral anticoagulant; i.v., intravenous; LMWH, low-molecular-weight heparin; n, number of physicians; QD, once daily; s.c., subcutaneous; TID, three times a day; UFH, unfractionated heparin.

34 (44%) this was rarely or never done, and in 31 (40%) participants provided mixed responses.

### 3.4 | Research priorities and knowledge gaps

The willingness to participate in any theoretical future RCT was generally high (Table 3). The majority of participants were willing to consider adopting an alternative type ($n = 542$, 76%) or dose ($n = 538$, 75%) of thromboprophylaxis in such an RCT. The main reasons for unwillingness or uncertainty included the unavailability of a certain type of anticoagulation, a preference for an intermediate dose, views that external authorities (e.g., heads of departments or hospital administration) should make the determination, logistical constraints (impeding their participation in any trials), and preferences to exclude specific categories of patients from participation in a trial. In addition, most participants would agree to participate in an RCT evaluating different approaches to dosing of thromboprophylaxis: low versus intermediate dose LMWH ($n = 606$, 85%); respective dosing of LMWH based on weight ($n = 636$, 89%), anti-Xa peak ($n = 535$, 75%) or through levels ($n = 512$, 72%); once versus twice daily LMWH dosing ($n = 561$, 79%); dosing based on individual risk assessment ($n = 502$, 70%); and ultrasound screening versus no screening ($n = 514$, 72%). Finally, willingness to participate in an RCT that included placebo as a comparator was low ($n = 261$, 37%).

## 4 | DISCUSSION

This international survey distributed through collaborators of the CRIC network aimed to evaluate the preferences for thromboprophylaxis in critically ill patients, as well as ICU physicians' attitudes towards several theoretical research questions that could be assessed in a future RCT. Our findings suggest that there is considerable practice variation, reflected by the use of different types, doses, and dosing strategies of pharmacological thromboprophylaxis in critically ill patients. A total of 36 different pharmacological thromboprophylaxis regimens were reported, including 19 different regimens of different LMWH subtypes. In addition, there was variation in the use of risk stratification and the use of dosing strategies based on weight or anti-Xa levels to guide thromboprophylaxis. These results align with the variation in clinical practice perceived by most physicians and willingness to participate in multiple possible research questions for an RCT on thromboprophylaxis.

### 4.1 | Comparison with literature

International guidelines provide no recommendations on specific LMWH types or doses for use in critically ill patients, most likely because of a lack of direct evidence.[7–9] Eck et al. recently conducted a Bayesian network meta-analysis, synthesizing data on thromboprophylaxis of over 90.000 hospitalized patients, and concluded that an intermediate dose of LMWH, as compared to a lower dose, may provide the best balance between benefits and harms for the prevention of VTE.[15] However, it is unclear to what extent these results are generalizable to critically ill patients. Three previous trials directly evaluated various dosing regimens of LMWH in critically ill patients. One trial compared different doses of enoxaparin, and two trials compared intermediate doses of different types of LMWH. All trials were relatively small (60 to 100 patients), focused on surrogate outcome measures, and used screening strategies rather than symptomatic patient-relevant outcomes.[16–18] Other trials have examined different LMWH and/or UFH doses specifically in critically ill patients with COVID-19.[14,19–21] These studies concluded that increasing doses of thromboprophylaxis did not decrease mortality and venous thrombosis, while potentially increasing the risk of bleeding. Moreover, these studies concentrated on a specific subgroup of critically ill patients, so generalizing these conclusions to the general critically ill population may be inappropriate. Any recommendations on the optimal dose of LMWH for thromboprophylaxis in critically ill patients would rely on indirect evidence and therefore an RCT evaluating different doses of LMWH in critically ill patients is needed.[8]

While individualized thromboprophylaxis regimes based on weight, anti-Xa levels, or individualized risk assessment were frequently reported, there is a lack of evidence for these practices. Previous studies that assessed weight-based dosing were generally small, focused on subgroups of critically ill patients, and often used anti-Xa levels as surrogate outcomes, limiting the application of their findings in clinical practice.[16,22–25] Similarly, no large randomized trials have assessed the value of anti-Xa guided prophylaxis, and consequently, its use is not recommended in two guidelines,[8,9] whereas one guideline recommends considering anti-Xa levels in critically ill patients with renal insufficiency.[7] Finally, VTE risk assessment models—those developed for general hospital settings and also those specifically designed for critical care patients—were all found to have either weak predictive performance or a lack of external validation, implying they are thus not suitable for clinical implementation.[26–28]

Although guidelines suggest the use of LMWH over UFH in all critically ill patients without contraindications, a substantial number of physicians reported that they used alternative agents or prophylaxis strategies.[7–9] We did not enquire about motivations for choosing UFH over LMWH and cannot exclude the possibility that there are national guidelines recommending UFH over LMWH, or other reasons such as costs or the application of UFH in patients with renal failure or perceived high bleeding risk.

### 4.2 | Strengths and limitations

This survey was designed with unambiguous closed questions targeting intensive care physicians caring for a broad population of critically ill patients. It was intended to be sufficiently concise and detailed, but at the same time as minimally time-consuming as possible, to increase the likelihood of participation. The manuscript was prepared and reported according to the Consensus-Based Checklist for Reporting the Survey Studies. Despite some missing data on the invited participants in some countries, we obtained an acceptable response rate of

**TABLE 3** Questions and answers about characteristics of thromboprophylaxis applied in ICU patients according to responses.

| Questions | *n* (%) |
|---|---|
| *Would you be willing to use a different type of thromboprophylaxis in the interest of a trial?* | |
| Probably yes | 542 (76%) |
| Probably no | 61 (8.5%) |
| I don't know | 100 (14%) |
| Other | 12 (1.7%) |
| *Would you be willing to use a different dose of thromboprophylaxis in the interest of a trial?*[a] | |
| Probably yes | 537 (75%) |
| Probably no | 64 (9.0%) |
| I don't know | 103 (14%) |
| Other | 10 (1.4%) |
| **Would you be willing to participate in a RCT evaluating the following:** | ***n* (%)** |
| *Low versus intermediate dose LMWH for thromboprophylaxis in (selected high-risk) critically ill patients* | |
| Probably yes | 606 (85%) |
| Probably no | 63 (8.8%) |
| I don't know | 46 (6.4%) |
| *Placebo versus low dose LMWH in critically ill patients (at low risk of VTE)?*[a] | |
| Probably yes | 261 (37%) |
| Probably no | 363 (51%) |
| I don't know | 90 (13%) |
| *Dosing of LMWH guided by weight versus standard dosing?* | |
| Probably yes | 636 (89%) |
| Probably no | 45 (6.3%) |
| I don't know | 34 (4.8%) |
| *Dosing of interventions guided by anti-Xa peak levels versus standard dose?* | |
| Probably yes | 535 (75%) |
| Probably no | 112 (16%) |
| I don't know | 68 (9.5%) |
| *Dosing of interventions guided by anti-Xa trough level (anti-Xa level measured just before the next gift of thromboprophylaxis) versus standard dose?*[a] | |
| Probably yes | 512 (72%) |
| Probably no | 120 (17%) |
| I don't know | 82 (11%) |
| *Once versus twice daily LMWH dosing for thrombosis prophylaxis?*[b] | |
| Probably yes | 561 (79%) |
| Probably no | 89 (12%) |
| I don't know | 63 (8.8%) |
| *Systematic venous thromboembolism screening versus no screening while all receiving thromboprophylaxis?* | |
| Probably yes | 514 (72%) |
| Probably no | 132 (18%) |
| I don't know | 69 (9.7%) |
| *Different interventions based on individual risk assessment (e.g., LMWH vs. stockings)?* | |
| Probably yes | 502 (70%) |
| Probably no | 128 (18%) |
| I don't know | 85 (12%) |

Abbreviations: DOAC, direct oral anticoagulant; LMWH, low-molecular-weight heparin; *n*, number of physicians.
[a]Data from one survey was missing.
[b]Data from two surveys was missing.

approximately 36%. Prior to distribution, the survey underwent pilot testing within the departments of the study coordinators.

We should acknowledge several limitations. First, this survey was distributed through our network of collaborators of the CRIC, and there was substantial variability in physician participation both within ICUs and across countries, which inherently results in selection bias. This distribution was chosen deliberately with a possible future RCT in mind that may be conducted within the CRIC network. However, this selection precludes generalization, and our results should not be viewed as a reliable sample of the current practice in each participating country. Second, we only distributed the survey in the English language, which may have been a barrier for participation. Third, tracking the number of invited participants in certain countries proved challenging, resulting in unknown response rates in some countries. Therefore, the overall response rate of the survey could only be calculated based on the countries with known denominators. Fourth, although we took care to extensively inform the respondents that this survey was designed to study thromboprophylaxis (ie, not therapeutic use of anticoagulants), a few of the reported doses are quite high, which has caused some ambiguity, implying either high-dose prophylaxis or a mistake. Fifth, our study did not anticipate the prevalent practice of using a risk assessment model to ascertain eligibility for thromboprophylaxis, nor the frequent use of anti-Xa or weight-directed dosing. As a result, we did not explore these specific approaches in more detail. Sixth, we should also acknowledge that several specialties collaborate on decision-making on thromboprophylaxis, and our question on this topic (which was limited to hematologists or pharmacologists) was probably framed too narrowly. Seventh, participants were queried about their preferences and perceptions of clinical practices in their respective departments, sometimes leading to divergent responses within a single ICU. This diversity presented challenges in the aggregation of data on the ICU or country level, further emphasizing the broader issue of variability of clinical practice.

## 5 | CONCLUSIONS

LMWH was the preferred agent for thromboprophylaxis in critically ill patients. There was considerable variation in the application of

LMWH for prophylaxis, reflected by the use of different types, doses, and dosing strategies. Most physicians would be willing to participate in an RCT on thromboprophylaxis.

## AUTHORS CONTRIBUTIONS

ERHH, FK, MHM, AP, MM, KM and RJE designed the survey. ERHH coordinated the distribution of the survey worldwide. All authors contributed as national or site coordinators by distributing the survey and assisting data collection. All authors critically reviewed the manuscript and agreed with the final version and findings. All authors read and approved the final manuscript.

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## CONFLICT OF INTEREST STATEMENT

Anders Perner reported research grants from the Novo Nordisk Foundation and Sygeforsikringen Danmark and honorarium from Novartis; Antony George Attokaran is chair for a working group (Stop The Clots) aiming to improve VTE prophylaxis in health service. Annika Reintam Blaser is holding a grant from Estonian Research Council (PRG1255) and has received consultancy fee from VIPUN Medical and speaker fee from Nutricia. None of them is related to this manuscript; Ricard Ferrer reported consulting fees from Inotrem, Pfizer and Citosorbent. Payments or honoraria for lectures, presentations, speaker bureaus, manuscript writing or educational events from Shionogi, MSD, Gilead, Menerini and Thermofisher; Massimiliano Greco reported a small speaking fee from Baxter; Kwok M. Ho reported consulting fee paid by Cardinal Health to present on the 2023 Asia Pacific World Thrombosis Day as an expert in thromboembolism; Peter Kruger reported 2024 Metro South Health Research Support Scheme (MSH RSS) Novice Researcher Grant application for the study entitled "BIOFluid-induced Lung injury: appraising a nOvel pathOgenic mechanism in acute respiratory Distress syndrome (The BIO-FLOOD study)" has been successful. $24,990.00 over 2 years, commencing January 1, 2024 and ending December 31, 2025. Llyod, Faser, Labassi, McGiffin, Kruger, Redmond. Individualized blood pressure targets versus standard care among critically ill patients with shock—a multicenter randomized controlled trial—REACT SHOCK. 2023—Panwar et al. (Kruger CI-G), MRFF $2,823,845.94. The effect of modifying nutritional support on glucose metabolism and clinical outcomes during critical illness Research Team: Dr. Ra'eesa Doola, A/Prof Peter Kruger, A/Prof Adam Deane, Dr. Kyle White, Prof Josephine Forbes Dr. James Walsham, Jason Meyer. 2023. SERTA PAH $ 100,000. Physiotherapy management for hypoxaemia following abdominal surgery: walk + talk + breathe + noninvasive ventilation. A pilot feasibility randomised controlled trial (PHYSIO+++) 2022. Ms. Claire Hackett, A/Prof Peter Kruger, Prof Mark Smithers, Dr. Rachel Walker, Nina Gray, Prof Linda Denehy, Dr. Ianthe Boden, Louise Hope. SERTA PAH $ 100,000. MLNGM is Professor of Critical Care Research at the 1st Department of Anaesthesiology and Intensive Therapy, Medical University of Lublin, Poland. He is co-founder, past-President and current Treasurer of WSACS (The Abdominal Compartment Society, http://www.wsacs.org). He is member of the medical advisory Board of Pulsion Medical Systems (now fully part of Getinge group), Serenno Medical, Potrero Medical, Sentinel Medical and Baxter. He consults for BBraun, Becton Dickinson, ConvaTec, Spiegelberg, Medtronic, MedCaptain, and Holtech Medical, and received speaker's fees from PeerVoice. He holds stock options for Serenno and Potrero. He is co-founder and President of the International Fluid Academy (IFA). The

IFA (http://www.fluidacademy.org) is integrated within the not-for-profit charitable organization iMERiT, International Medical Education and Research Initiative, under Belgian law; Marlies Ostermann reported research funding from Baxter, Biomerieux, LaJolla Pharma; Bodil Steen Rasmussen reported a grant from the Novo Nordisk Foundation and from the Danish Ministry of Research and Education for the HOT-ICU and the HOT-COVID trials; Karina Meijer reported speaker fees from Alexion, Bayer and CSL Behring, participation in trial steering committees for Bayer and Astra Zeneca, consulting fees from Uniqure and Therini, participation in data monitoring and endpoint adjudication committee for Octapharma (all fees paid to her institution).

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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