



COMMENTARY

A known unknown? Pharmacological prevention of venous thromboembolism in nursing home residents

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Venous thromboembolisms (VTEs), including pulmonary embolism (PE) and deep vein thrombosis (DVT) are a growing healthcare problem strongly associated with mortality and functional deterioration, with a rising prevalence due to aging of the population and age-associated risk-factors.¹ Preventing VTE lowers the incidence of morbidity and mortality and improves health-related quality of life.² Therefore, primary pharmacological prophylaxis is generally recommended in surgical and medical in-hospital wards.³ However, in nursing homes, where residents frequently are at similar or even higher VTE risk than hospitalized medical patients, it is still unknown whether primary pharmacological prophylaxis is an effective and safe approach to prevent VTE.^{4,5}

On top of the increasing VTE incidence with age,⁶ nursing home residents are known to be at an additional high risk of first-time VTE compared with community dwelling older persons due to distinct risk factors, such

as immobility, ischemic stroke, congestive heart failure, malignancy, and (recurrent) episodes of infection.^{7,8} The incidence of acute VTE among nursing home residents varies between 0.7 and 1.3 events per 100 person-years, increasing even further to 2.4 events per 100 person-years when also asymptomatic VTEs are taken into account.⁹ In an autopsy study of institutionalized older individuals, PE was found to be the clinical cause of death with the lowest rate of detection and highest diagnostic error rate.¹⁰ As such, these data suggest that there is a serious underestimation of this potentially lethal, yet preventable condition as most nursing home residents do not show typical signs of VTE due to their diminished mobility, nor will they routinely undergo diagnostic imaging. Furthermore, little is known about the safety and efficacy of thromboprophylaxis to prevent VTE in this population. Indeed, current guidelines provide no specific recommendations for thromboprophylaxis in the nursing home setting.³ This is likely the case because in-hospital studies

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cannot be readily used to extrapolate to the nursing home population, due to distinct risk factors for VTE in the nursing home population such as dependency in activities of daily living (ADL), wheelchair use, and frequent/prolonged immobilization.^{5,8} Alternatively, there exists an incremental increase of bleeding risk in this vulnerable population based on individual risk factors such as falls, dementia, use of non-steroidal anti-inflammatory drugs, and/or renal failure to make a balanced decision on the use of thromboprophylaxis.

When we systematically assessed the currently available literature on primary VTE-prevention in nursing home residents (see Appendix S1 for methods [Tables S1–S3] and results [Figure S1]), we identified a vital discrepancy between the high prevalence of VTE in nursing home residents and a complete lack of clinical trials investigating whether pharmacological interventions can safely mitigate this risk. To the best of our abilities, we could not identify any study that formally evaluated the efficacy and safety of thromboprophylaxis in this large, high-risk, often overlooked, population. Nevertheless, critically reviewing the currently available evidence surrounding thromboprophylaxis in nursing home residents may help to expose the exact knowledge gaps and serve as a guide for future research.

A summary of the current literature (Table 1) shows that most available evidence primarily addressed the prescribing pattern of primary thromboprophylaxis in a nursing home population, serving at best as circumstantial evidence for the use of pharmacological VTE prevention. In multiple studies^{11,12} evaluation of the adequacy of thromboprophylaxis prescription decisions was based on consensus or clinical practice guidelines aimed at hospitalized patients at risk for VTE.¹³ This highlights the problem at hand; lack of awareness concerning the fact that nursing home residents cannot simply be compared to hospitalized patients in general. In two other studies,^{14,15} questionnaires were sent out to geriatricians to survey the rate and duration of thromboprophylaxis in long-term care patients, while two additional studies evaluated thromboprophylaxis prescription in hospice inpatients.^{16,17} Unfortunately, none of these studies addressed the safety and efficacy of thromboprophylaxis. Nevertheless, all these studies highlight the fact that thromboprophylaxis is deemed important in clinical practice even though evidence supporting its use is lacking. One prospective study in older post-acute care patients did address the efficacy of thromboprophylaxis as well as the lack of an applicable guideline in this specific population of hospitalized older patients.¹⁸ A practice guideline (developed using group consensus of expert panelists and a systematic review of literature) for the prescription of thromboprophylaxis was developed after which a preintervention–postintervention

study was conducted. The prophylactic intervention resulted in a significant decrease in the rate of any DVT within the study population. Although promising, these results cannot be extrapolated to the nursing home population since it does not account for risk factors specific to the high-risk nursing home population even though the population studied shows great resemblance to the high-risk nursing home population. To provide a uniform prescription guideline specifically for high-risk nursing home residents an American study group developed an assessment tool to assess the risk for VTE among long-term care residents.¹⁹ This model also included recommendations on the use of thromboprophylaxis. Although this model could be used to select patients at high risk of thrombosis in the nursing home population, this model has yet to be validated in a prospective clinical trial whether its use is safe and effective.

Altogether, the key issue at hand seems to be that data on VTE prophylaxis from in-hospital or post-acute care settings cannot be extrapolated to the nursing home population, as these populations differ in several key areas. First, compared with hospitalized community dwelling individuals, nursing home residents may carry an increased risk of VTE due to advanced age, higher proportion of comorbidities, ADL-dependency, and immobility. Furthermore, while hospitalized patients only experience a transiently increased risk of VTE, nursing home residents experience a persistently elevated risk of VTE, which may increase even further when common (recurrent) acute medical illnesses occur in this population. Second, while the benefit of preventing fatal VTE may be obvious in both settings, preventing post-VTE morbidity (such as post-thrombotic syndrome or chronic thromboembolic pulmonary hypertension) may be less beneficial in the nursing home population that already experiences a severely reduced exercise intolerance. Third, the nursing home population consists of a clinically heterogeneous group of individuals, while institutional characteristics may further contribute to heterogeneity of potential benefit from VTE prophylaxis. It is likely that traits, such as reason for admission, cognitive status and life expectancy play an important role in whether physicians consider diagnostic investigations to diagnose VTE, let alone to initiate thromboprophylaxis.

The main issue to be addressed remains whether primary pharmacological prophylaxis is safe and efficacious in the nursing home population. Therefore, a trial comparing thromboprophylaxis to usual care (or placebo) among high-risk nursing home patients has the main priority. Primary outcomes of interest are in our view the incidence of symptomatic VTE and (major) bleeding. Nevertheless, such a trial alone would not be sufficient to write evidence-based guidelines for the NH population,

TABLE 1 Summary of the current literature

References	Population (sample size)	Study type/design	Age (years)	Aim of study	Outcome measure	Results
12	2962 patients (1426 preintervention and 1536 postintervention) admitted to acute care, post-acute care (or rehabilitation) and long-term care wards in 12 geriatric departments	RCT with multifaceted intervention consisting of two groups; one receiving educational material on guidelines for VTE prophylaxis and the other group with usual care	Median 85 [IQR 79;90]	To evaluate the efficacy of an intervention on the practice of venous thromboembolism prevention	Overall adequacy of VTE-P prescription at the patient level, defined as a composite endpoint consisting of indication, regimen, and duration of treatment	For the overall 18.9% rate of inadequate VTE-P, 11.1% was attributable to underuse and 7.9% overuse. No improvement in VTE-P prescription adequacy with intervention
13	376 (re)admissions from 17 long term care facilities following acute care hospitalization	Descriptive cohort study Phase 1 of a 3-phase educational intervention study. It describes current VTE-P practices	Mean 77 ± 12 (SD)	Examines VTE-P practices in LTC facilities before and after an educational intervention to bring practice patterns consistent with guidelines	Data summary consists of a description of VTE-P, indications and contraindications for VTE-P	Indications for VTE-P were evident in 85%. VTE-P was initiated in two thirds. 24% of those receiving VTE-P had absolute or relative contraindications to it. Logistic regression predicted no relationship between the presence of any indication or contraindication for VTE-P and the initiation of VTE-P
15	2912 patients were present on the day of the study: 857 patients in acute care, 367 in rehabilitation care, 1568 in long-term care, and 141 in day hospital	A questionnaire was sent to 94 geriatricians to be filled out for each patient older than 65 years of their institutions who received LMWH during 1 day of December 2000	Mean 82.2 ± 7.6 (SD)	To assess the rate and duration of medical utilization of LMWH for VTE-P by European geriatricians	Rate and duration of VTE-P. Incidence of risk factors for VTE in the study population	Prophylaxis by LMWH was given to 284 medical patients (9.75%, mean age 82.2 years). Use of LMWH was more frequent in acute and rehabilitation care (22.4% and 9.8%) than in long-term care (3.1%). The duration VTE-P exceeded 30 days in 51 patients (12%) and 1 year in 15 patients (3.3%)
16	96 participating centers, including 7762 long-term care patients	A questionnaire among 150 geriatricians for each patient who received	Mean 84.4 ± 9.1 (SD)	To assess the use and the duration of LMWH for VTE-P in French long-term care settings	Rate of use and duration of VTE-P were reported	Among 7762 patients 4.9% received VTE-P using LMWH. The mean duration of the treatment

TABLE 1 (Continued)

References	Population (sample size)	Study type/design	Age (years)	Aim of study	Outcome measure	Results
		LMWH during 1 day of December 1997				for VTE-P at the day of the study was 298 days, ranging from 5 to 4915 days
17	Retrospective review of case notes on 750 admissions to three UK hospices. 300 patients before implementation of a prevention policy and 350 patients after implementation of a prevention policy	Retrospective preintervention-postintervention study	70 years (range 22–96) for patients included before and after the VTE prevention guideline and 69.6 (range 18–98) by Pan Birmingham Cancer Network Flowchart	To assess primary VTE-P prescribing in hospices	Information was extracted on level of risk for VTE, prescription of VTE-P, demographics and diagnosis	The percentage of hospice inpatients who may benefit from VTE-P, and who have no clear contra indication, is low (6%). The number of patients receiving VTE-P increased slightly from 1% to 3.6% after implementation of a new VTE prevention guideline
18	317 individuals with advanced non-cancer disease admitted to a dedicated geriatric palliative care unit (PCU)	Single-center retrospective chart review	78.8 for patients with a non-cancer diagnosis and 86.7 for patients with a cancer diagnosis	To compare VTE-P in older adults with advanced non-cancer diagnoses to those with advanced cancer on a dedicated PCU	Information was extracted from the electronic medical records on VTE-P, demographics and admission diagnosis	VTE prophylaxis was administered at similar rates in participants with (31.9%) and without (26.8%) cancer on admission. The rate of VTE-P in participants who were bedbound (29.8%) was similar to that of those who were ambulatory (32.2%)
19	1373 patients aged 65 years or older (preintervention phase, <i>n</i> = 709; postintervention phase, <i>n</i> = 664) were enrolled in 33 hospital-based post-acute care facilities in France	Prospective pre-/postintervention study by multifaceted intervention (educational program to prescribers)	Median 82 [IQR, 77–88]	To determine whether a multifaceted intervention was followed by a decrease in DVT	Any DVT diagnosed at routine comprehensive ultrasonography on the day of a cross-sectional study	A DVT was found in 12.8% of patients in the preintervention phase and in 7.8% of patients in the postintervention phase (<i>p</i> = 0.002). The decrease in DVT remained significant after adjusting for risk factors

as additional studies are needed to address (i) the epidemiology and risk factors for VTE in the nursing home, to achieve a validated risk stratification between low-risk and high-risk nursing home residents; (ii) the development of a reliable screening test and subsequent diagnostic trajectory in the nursing home; (iii) implementation strategies of VTE prophylaxis in the nursing homes; and (iv) feasibility, acceptability, and costs of the proposed diagnostic trajectories and treatments. Finally, also health-related quality of life should be integrated as outcome.

In conclusion, as Western societies show a demography of more and more older people, the percentage of older individuals residing in long-term care facilities is also increasing. Moreover, this unique, but overall frail population with multiple comorbidities, may not only become severely affected by VTE, but is also underrepresented in the current literature about prevention of VTE. It is therefore of vital importance to determine the impact of thromboprophylaxis in this population. We have identified several important knowledge gaps concerning thromboprophylaxis that cannot be filled in by simply extrapolating hospital practices to the nursing home setting. Therefore, additional studies are needed and we suggest a randomized clinical trial that includes clear risk stratification between low risk and high risk nursing home residents to address whether thromboprophylaxis is safe and efficacious in this population.

CONFLICT OF INTEREST

The authors have declared no conflicts of interest.

AUTHOR CONTRIBUTIONS

Study conception and design: Brüggemann, Alnima, ten Cate, Spaetgens, ten Cate-Hoek. *Acquisition of data:* Brüggemann, Alnima, Spaetgens. *Analysis and interpretation of data:* Brüggemann, Alnima, Brouns, Spaetgens, ten Cate-Hoek. *Drafting of the manuscript:* Brüggemann, Alnima, Spaetgens, ten Cate-Hoek. *Critical revision of the manuscript for important intellectual content:* Brüggemann, Alnima, Brouns, Hanssen, Schols, ten Cate, Spaetgens, ten Cate-Hoek. All authors approved the final version to be submitted for publication.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

Appendix S1. Supporting information.

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