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Venous Thromboembolism (VTE) Incidence and VTE-associated Survival among Olmsted County Residents of Local Nursing Homes

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Abstract

Nursing home (NH) residency is an independent risk factor for venous thromboembolism (VTE), but the VTE burden within the NH population is uncertain. This study estimates VTE incidence and VTE-associated mortality among NH residents. We identified all NH residents in any NH in Olmsted County, MN, 10/1/1998–12/31/2005 and all first lifetime VTE among County residents to estimate VTE incidence while resident of local nursing homes (NHVTE), using Centers for Medicare and Medicaid Services Minimum Data Set and Rochester Epidemiology Project resources. We tested associations between NHVTE and age, sex, and time since each NH

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AUTHORSHIP

All authors have seen the final submitted version of the manuscript. All authors had full access to the data in the study and take responsibility for the data integrity and accuracy of the data analyses.

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admission using Poisson modelling. Additionally, we tested incident NHVTE as a potential predictor of survival using Cox-proportional-hazards, adjusting for age, sex, and NH residency. Between 10/1/1998–12/31/2005 3,465 Olmsted County residents with 1 admission to a local NH, contributed 4,762 NH stays. Of the 3,465 NH residents, 111 experienced incident NHVTE (2.3% of all eligible stays), for an overall rate of 3,653/100,000 NH person-years (**NH-PY**). VTE incidence was inversely associated with time since each NH admission, and was highest in the first 7 days after each NH admission (18,764/100,000 NH-PY). The adjusted hazard of death for incident NHVTE was 1.90 (95% CI: 1.38–2.62). In conclusion, VTE incidence among NH residents was nearly 30-fold higher than published incidence rates for the general Olmsted County population. VTE incidence was highest within 7 days after NH admission, and NHVTE was associated with significantly reduced survival. These data can inform future research and construction of clinical trials regarding short-term prophylaxis.

Keywords

epidemiology; venous thromboembolism; nursing home; incidence; survival

INTRODUCTION

Venous thromboembolism (**VTE**), consisting of deep vein thrombosis (**DVT**) and pulmonary embolism (**PE**), is a relatively common condition with potentially debilitating, life-threatening, and costly outcomes.[1–4] Studies of VTE risk factors reveal that nursing home (**NH**) residents are at substantially increased risk.[5–7] Using Rochester Epidemiology Project (**REP**) population-based longitudinal medical-records-linkage resources, we previously identified and characterized all Olmsted County, MN, residents with incident and recurrent VTE from 1/1/1966–12/31/2010.[3] We showed that the risk of VTE among NH residents was >5-fold higher than that for non-NH residents, even after adjusting for other established VTE risk factors.[7] VTE among NH residents (**NHVTE**) accounted for 13% of incident VTE in the population generally.[8]

Reductions in VTE incidence and its consequences within the NH population could reduce the burden on the individual and on society as a whole. However, despite long-standing recognition of the need for additional data,[5,9–15] there remains a serious shortage of reliable estimates of the burden of VTE among NH residents. This study attempts to address the shortage with a cohort study that combines unique REP resources with Centers for Medicare and Medicaid Minimum Data Set (**CMS-MDS**) 2.0 (first available for research use as of 10/1/1998).[16] Using CMS-MDS, we identified all NH residents admitted to local nursing homes 10/1/1998–12/31/2005. Employing individual identifiers contained in both CMS-MDS and REP, we merged the list of NH residents with the list of all Olmsted County residents ever seen at any REP provider since 1/1/1965 and enumerated their CMS-MDS NH stays/days as an Olmsted County resident. We then used labour-intensive review of REP resources to identify those individuals who experienced a first lifetime VTE while a NH resident to estimate incident NHVTE/100,000 NH person-years-at-risk. These combined resources also afforded a rare opportunity to estimate VTE-associated risk of death among all NH residents (including whether death occurred in NH, hospital, or elsewhere).

MATERIALS AND METHODS

Study design/setting.

This population-based historical cohort study was conducted among Olmsted County, MN, residents (2010 census=144,248) with admission to a NH from 10/01/1998–12/31/2005 located within or on Olmsted County borders (subsequently referred to as ‘local nursing homes’).

Data sources.

REP: Rochester, the county seat, is approximately 80 miles from the nearest major metropolitan area and home to Mayo Clinic, a large tertiary-care medical centre. Mayo Clinic and Olmsted Medical Center (OMC), a second group practice, and their affiliated hospitals, provide essentially all medical care received by local residents.[17] Since 1907, every Mayo Clinic patient is assigned a unique identifier. Detailed information from every contact (office/NH/emergency department/hospital inpatient/hospital outpatient) is contained within a unit record for each patient. Information includes medical history/clinical assessments/consultations/surgical procedures/dismissal summaries/laboratory and radiology results/correspondence/death certificates/autopsy reports. Diagnoses assigned at each visit are coded and entered into continuously updated files. Under auspices of the REP, the unique identifiers, diagnostic index, and records-linkage were expanded to other medical providers, including OMC and the few private practitioners in the area.[17] REP also affords an essential census of all Olmsted County residents on any given date from 1965 through present (Supplement).[17,18] The REP has been continuously funded by National Institutes of Health for >50 years.

CMS-MDS: We used MN CMS-MDS to establish NH residency and determine NH person-years-at-risk.[16] For this study, the designation ‘NH’ includes both Skilled Nursing Facilities and Nursing Facilities and is limited to facilities certified by CMS and thus required to submit MDS forms. MDS was developed in response to the Omnibus Budget Reconciliation Act requirement that all Medicare- and Medicaid-certified long-term-care facilities assess each resident (regardless of payer status) at multiple specified times throughout their stay: admission/re-entry/discharge/annual review/quarterly review/significant change in health status.[19] Each individual is assigned an anonymous identifier that is maintained for all admissions across all MN nursing homes. Resident and NH identifiers, assessment dates, and reason for assessment are recorded. Admission date and source are recorded on admission or re-entry assessments. Discharge date and disposition, and anticipated return to NH are recorded on discharge assessments, thus affording NH residency status on each day and making it possible to tally days in and out of the NH for every Olmsted County resident.

Study sample.: This study was approved by Mayo Clinic and OMC Institutional Review Boards and was limited to individuals who had not refused authorization for use of medical records in research.[20] Typically, <5% of individuals refuse authorization at all providers in REP studies.[17] We used CMS-MDS to first identify each unique NH resident with any MDS assessments 10/1/1998–12/31/2005 conducted by any local nursing homes. This list of

NH residents was then linked to the list of all Olmsted County residents contained within REP (Supplement; Figure S1). Linkage was performed by merging individuals in CMS-MDS with Mayo and REP resources on Social Security number, Medicare Health Insurance Claim number, sex, and birth date employing an algorithm of exact matches, followed by manual review of inexact matches (Supplement). Using the unique CMS-MDS identifier, all NH assessments were compiled for each individual. All NH stays for each individual were assigned by aligning NH admission and corresponding discharge dates (Supplement).

Identifying VTE.: Using REP resources, the complete provider-linked medical records of all Olmsted County residents in a local NH were reviewed from date first seen by a REP provider until earliest of death, emigration, or 12/31/2005 for first lifetime (incident) VTE and vital status. We used multiple sources, including all previously identified REP Olmsted County VTE cases (incident and recurrent) from 1966 forward[3,7,21,22] as well as additional screening of REP resources for Olmsted County residents admitted to nursing homes on the County border (Supplement). All incident VTE were confirmed by study-trained registered nurses. Criteria for establishing objectively-verified VTE and for determining when VTE occurred (i.e., symptom-onset date) were those previously described for REP studies of the entire Olmsted County population (Supplement).[3,7,21,22] Because NH residents may experience lower rates of symptom reporting, diagnostic testing and autopsy compared to the general population,[14,23] in addition to objectively-verified VTE, we also included all clinically-determined incident VTE (i.e. physician diagnosis with VTE signs/symptoms and treated by anticoagulants) [14,23] (Supplement); 96.4% of VTE events were objectively-verified. Of the four clinically-determined VTE, one was age 95 years, two had recent total knee replacement, and one, age 99 years, had recent hip fracture. Data were recorded on method of and criteria for identifying VTE and VTE type (DVT, PE, or both; chronic thromboembolic pulmonary hypertension [CTEPH]). Dates and locations (i.e., in-hospital, in NH, elsewhere) of VTE symptom-onset and death for those who died were collected.

Statistical analysis.

Incidence of VTE among NH residents: NHVTE incidence was calculated as the ratio of first lifetime (incident) VTE with symptom-onset as a NH resident, divided by the total days as a NH resident. Persons identified as experiencing VTE before earliest NH admission during the study period were excluded from analyses. CMS-MDS data first became available for research on 10/1/1998; length-of-stay was unavailable for stays with admission before that date; thus analyses were limited to NH stays with admission on or after 10/1/1998. Analyses were also limited to admissions with age $\geq$ 35 years and Olmsted County residency as of NH admission date.

NH residents were followed for each NH admission during the study period, with multiple stays possible for each resident. NH person-years-at-risk (NH-PY) was calculated only while a NH resident and was categorized by sex, age, and calendar year. To determine the timing of greatest VTE risk during a NH stay, we also categorized NH-PY as time since each admission (days 1–7, 8–14, and 15–30; months 1–3, 3–6, and 6–12; and years 1–2, 2–5, and >5). For example, categories 1–7, 8–14, and 15–30 days would each be considered

separately in a 30-day length-of-stay. Incidence was also estimated separately for DVT alone and for PE with or without DVT (**PE±DVT**).

The relationship between NHVTE incidence and each of age, sex, calendar year, and number of days from each admission, was analysed two ways: (1) Generalized linear regression with a Poisson error and a log link examined relationships between the above and VTE incidence (Supplement). All *P* values for Poisson models were based on the likelihood ratio test; (2) A Cox proportional hazards model examined time to incident NHVTE, with a robust sandwich covariance structure[24] to assess the correlation structure induced by multiple NH stays per individual. All *P* values for Cox models were based on the Wald test. NH days from each admission could not be assessed as a variable in this second way of modelling. Age also differed between the two methods (Supplement).

Survival: NH residents were continuously followed for death both in and out of the NH from earliest NH admission 10/1/1998–12/31/2005 until earliest of emigration, VTE event while not a NH resident, or 12/31/2005. Survival was analysed using the counting process formulation of Cox proportional hazards modelling.[25] NH stay was treated as a time-dependent variable toggling between being in and out of NH. The indicator variable for incident NHVTE, here also a time-dependent variable, was set to 1 on VTE date and remained at 1 until censoring for emigration, or 12/31/2005. Demographic variables were limited to sex, age (in years) at earliest NH admission 10/1/1998–12/31/2005, and calendar year of earliest NH admission. All deaths 10/1/1998–12/31/2005 were considered, regardless of whether death occurred while the individual was or was not a NH resident (Supplement).

RESULTS

Using CMS-MDS and REP resources, we identified 7,936 residents in a local NH 10/1/1998–12/31/2005. We excluded 4,471 individuals: 838 were in a NH as of 10/1/1998, but had no new admissions within that period; 565 declined use of medical records for research; 17 were not identified in REP; 17 were age <35 years at each admission; 2,646 were a non-Olmsted County resident at every admission, and 388 met criteria for VTE before earliest NH admission 10/1/1998–12/31/2005 (Figure S1).

Characteristics for all remaining 3,465 NH residents with 1 eligible NH admission 10/1/1998–12/31/2005 are provided in Table 1. The 3,465 NH residents experienced 4,762 qualifying NH stays for a cumulative total of 1,146,167 NH person-days. Table 1 provides numbers and percent distributions of all NH stays by length-of-stay for all 4,762 NH stays. Among the 3,465 NH residents, 111 met criteria for incident VTE while a NH resident during the study period; 29 (26.1%) had PE±DVT (22 PE alone, 6 PE with DVT, 1 CTEPH); 82 (73.9%) had DVT alone. Table 2 provides characteristics for the 111 individuals and the 111 stays during which incident NHVTE occurred. The 32 NH stays subsequent to NHVTE were excluded from consideration of NHVTE incidence, leaving 4,730 eligible stays.

NHVTE incidence.

The overall NHVTE incidence rate/100,000 NH-PY was 3,653 (Table 3). NHVTE incidence rates were highest in the 66–70 year-old group and lowest in the oldest age group. Women

exhibited higher rates in most age-groups, but between-sex differences were not significant overall ($P=.25$). The overall incidence/100,000 NH-PY was 2,699 for DVT alone and 954 for PE±DVT (Table 4). DVT incidence/100,000 NH-PY was highest among persons age 35–65 years. NHVTE incidence/100,000 NH-PY did not differ significantly between men and women for either DVT alone or for PE±DVT (results available on request). Table 5 and Figure reveal that NHVTE rates were highest within the first 7 days after each admission (17 incident NHVTE events during 90.6 NH-PY for a rate of 18,764/100,000 NH-PY). Rates fell to 2,138/100,000 NH-PY for days 91–180 after each NH admission, after which they remained fairly constant. It is important to note that, despite the high rate of NHVTE/100,000 NH-PY in the first week after admission, due to the large number of NH stays, only 0.4% of all stays included an incident VTE within the first 7 days after admission, and during any eligible NH stay, only 2.3% included incident VTE (Table 5).

Univariate and multivariable Poisson modelling revealed that days since each NH admission were negatively associated with incident NHVTE (multivariable coefficient=−0.3879; $P<.001$). Adjusting for sex, age at each NH admission, and calendar year of each NH admission, the standardized morbidity ratio (relative risk) of NHVTE postadmission compared to reference of >2 years was 13 within 7 days, 6–9 within 8–30 days, and 1–2 at 91+ days (Table 6). Neither sex nor age was significantly associated with NHVTE incidence after adjusting for days since each NH admission ($P=.13$ and $P=.16$, respectively). In Cox modelling, coefficients of each covariate (male sex; age; and calendar year at each NH admission) were nearly identical to those from the Poisson model (results available on request) suggesting that, of these four characteristics, days since each NH admission was the primary characteristic associated with NHVTE incidence.

Survival.

Of all 3,465 Olmsted County residents who were at risk of death after earliest admission to a local NH 10/1/1998–12/31/2005, 234 emigrated from Olmsted County and were censored at emigration date. An additional 59 people experienced incident VTE after 10/1/1998 while an Olmsted County resident but not while a NH resident and were censored at VTE date. Three additional people experienced fatal VTE while not a NH resident and were counted as a ‘death’ but not as incident NHVTE. Median length of follow-up was 1.5 years (IQR: 0.5–3.2 years). The cumulative incidence of death at weeks 1 and 4, months 3 and 6, and years 1 and 5 after earliest NH admission (total 1,650 deaths) was 1.9%, 6.8%, 13.0%, 18.3%, 24.8%, and 64.6% respectively. The remaining 1,522 individuals were alive at study end (12/31/2005).

Experiencing incident VTE while a NH resident was associated with a 2.2-fold increased univariate hazard of death (HR=2.20, 95% CI: 1.63–2.96, $P<.001$). Male sex, increasing age at earliest NH admission, and NH residency status also increased the hazard of death (1.5-fold higher than women, $P<0.001$; 4% per 10-years of age, $P<.001$; 3.0-fold higher while a NH resident compared to while not a NH resident, $P<.001$).

After adjusting for NH residency status, the hazard of death was 1.8-fold higher for individuals with versus individuals without incident NHVTE ($P<.001$). Adjusting for sex, age at earliest NH admission, NH residency status, and the interaction between sex and NH

residency status ($P=.02$), the hazard of death remained similar at 1.9-fold higher for individuals with versus individuals without incident NHVTE (HR=1.90, 95%CI: 1.38–2.62, $P<.001$).

DISCUSSION

NHVTE incidence of 3,653/100,000 NH-PY was nearly 30-fold higher than the 123/100,000 P-Y for all ages in the general Olmsted County population, 1981–2010.[3] NHVTE incidence/100,000 NH-PY (3,080 and 3,923, for males and females respectively) were 5- to 6-fold higher than VTE incidence/100,000 P-Y observed for all Olmsted County residents age 80–89 years (615 and 619 for males and females respectively, 2006–2010).[3] NHVTE incidence was as high as VTE in the first week post-partum,[26] and was 2–3 times higher than the risk of myocardial infarction for similar-aged males and females.[27]

Time since NH admission was a strong predictor of VTE incidence ($P<.001$), with extremely high rates occurring early within a stay: 15% of NHVTE events (17/111) occurred within 1-week; over 37% (42/111) occurred within 30-days. It is noted that the denominator NH-PY reflects days-at-risk for all NH stays of all individuals. Consequently, the proportion of all NH stays that included any individual who experienced incident NHVTE within 1-week after admission is small (0.4%) (Table 5). Therefore, the extraordinarily high incidence rates shortly after admission, expressed per person-years, do not correspond to high rates per person because the person-year denominator that reflects the first 7 days was very small.

The 3,465 NH residents experienced 1,650 deaths from earliest NH admission forward, regardless of whether the individual was a NH resident at time of death and regardless of death location. The cumulative incidence of death 1-year after NH admission for all NH residents was 24.8%. After adjusting for risk factors, including a time-dependent variable denoting NH residency, the hazard of death for individuals with incident NHVTE was 1.9-fold higher than for individuals without incident NHVTE.

Comparison with other studies.

Comparison with other findings is hampered by multiple between-study differences (e.g., exclusion rules, person-years-at-risk, and calendar years of study). Of very few investigations of NHVTE incidence and associated mortality,[28–31] most were limited by reliance on diagnosis/procedure codes obtained from NH administrative data and/or Medicare claims. As part of a previous study,[32] we compared characteristics of first VTE events among NH residents identified using International Classification of Diseases (**ICD-9-CM**) diagnosis codes[33] from NH administrative data[34] with those for REP-identified VTE events using detailed medical-record review among Olmsted County residents of the same nursing homes during the same time period. Only 66 cases were identified using ICD-9-CM diagnosis codes while 161 cases were identified using REP resources. Other differences noted with this comparison (i.e., the proportion with DVT alone [79% vs. 38%] and 1-year-survival [76% vs. 45%])[32] suggest that NH administrative data are biased against NHVTE cases who died before the next scheduled NH assessment. Findings confirmed conclusions by us and others[35–37] that use of administrative data for VTE ascertainment has serious limitations. In general, use of administrative diagnosis codes for

estimating VTE incidence among NH residents is limited by difficulties determining if VTE occurred, where it occurred, and whether it was first, prior, or recurrent VTE. Use of NH administrative data to assess VTE-associated mortality is also problematic (e.g., deaths occurring outside the NH are excluded).

Two previous studies[28,30] ascertained NHVTE using retrospective review of detailed medical records approximating the approach used here. Both studies classified events as definite or probable using criteria resembling our criteria for objectively-verified and clinically-determined. One study was limited to a single NH.[30] The other study identified residents of care homes in two major cities; care-home participation rates were low, refusal rates among eligible NH residents were high, and individuals with life-expectancy <6 months were excluded, as were individuals lacking capacity to consent and no available proxy.[28] The numbers of definite plus probable VTE events were 26[30] and seven[28], respectively. In both studies, a majority of individuals were long-time NH residents at study start. Thus, our finding of an inverse association between incident VTE and time since admission may contribute to lower estimates of NHVTE/100,000 NH-PY (1,390–1,580[30] and 830[28], respectively) compared to our estimate of 3,653.

Strengths.

Our cohort design had distinct advantages over prevalence estimates of the proportion of NH residents with diagnosed VTE at any point in time, as well as NHVTE incidence based on VTE diagnosis/procedure codes from administrative data. REP data contain clinical detail from all encounters (including laboratory/vascular laboratory/imaging/echocardiography/surgical reports, death certificates, and autopsy reports), affording determination of VTE symptom-onset, VTE event type, and level of diagnostic certainty. The Olmsted County REP VTE cohort for all Olmsted County residents extends from 1966–2010, containing information on VTE events, vital status, and days of Olmsted County residency from well before and throughout our study period, affording distinction between pre-existing, incident, and recurrent VTE.[3,8,22,38] NH residency on each follow-up day was available with CMS-MDS. Refusal rates for use of medical records in REP research studies are typically <5%[17] REP medical records were available for all Olmsted County residents admitted to local nursing homes; and CMS-MDS data included all certified nursing homes within or on the border of Olmsted County. Thus exclusion of individuals otherwise at high risk of VTE (e.g., with terminal illness) was greatly minimized, and potential for participation/referral bias was greatly reduced. These combined resources afforded unique estimates of first-lifetime VTE events while a NH resident, as well as consideration of time-to-event for each NH stay and VTE-associated hazard of death.

Limitations.

Estimates were for a single population (86% white in 2010). Compared with MN and all other upper-mid-west states, Olmsted County residents exhibit similar demographics and chronic disease prevalence rates, but higher income and education.[39] Low racial diversity and higher income/education levels could compromise the generalizability of findings, a limitation of any population-based study.

Few medical and NH providers potentially compromise the generalizability of findings to different health-care environments. However, published data reveal 4.1% of Olmsted County residents aged 65+ were in a nursing facility/skilled-nursing facility in 2010,[40] similar to 3.7% of MN residents age 65+ in 2011[41] and 3.9% of US white Medicare beneficiaries in 2011.[42]

We were unable to directly assess reason for NH admission, a potential NHVTE risk factor. We used two possible surrogate pieces of information regarding whether individuals were admitted for post-acute rehabilitation: 1) the proportion of NH residents for whom earliest NH admission was from hospital, and 2) the proportion of all stays ≥ 30 days, based on a published estimate of ≥ 30 days for average length-of-stay for post-acute rehabilitation in a skilled-nursing facility.[43] The proportion admitted from hospital was 80% for all NH residents versus 87% for residents with NHVTE. Among all NH stays, the proportion lasting ≥ 30 days from admission to discharge was 45% (Table 1). Table 2 reveals that 38% of incident NHVTE occurred ≥ 30 days from admission; but this is not length-of-stay; only 16% of the 111 stays lasted ≥ 30 days from NH admission to discharge. It is difficult to determine anticipated length-of-stay; the smaller proportion of stays ≥ 30 days for persons with NHVTE could reflect the necessity of staying longer due to the NHVTE.

Our approach to identifying VTE among NH residents is subject to under-ascertainment common to most VTE investigations among elderly individuals generally.[23,44,45] Autopsy rates are lower for NH residents; cognitive impairment, communication difficulties, competing co-morbidity, and/or immobility, each of which can impede symptom recognition, are higher.[5,12,46] Higher fall risk, medication use, and co-morbidity contribute to adverse consequences from anticoagulation[10,11] and may impact motivation for confirmatory testing.[47]

This study is silent regarding several putative VTE risk factors, outcomes other than death, and anticoagulation use. We previously investigated NHVTE risk factors and/or anticoagulant use using manual abstraction of REP medical records.[48,49] Our previous studies ascertained NHVTE among Olmsted County residents, using the same VTE case criteria employed in this study, and using CMS-MDS to obtain information on NH admissions for NHVTE cases and age-, sex-, calendar-year-matched NH non-VTE controls. Pharmacologic prophylaxis rates appeared higher for NH residents than for all elderly Olmsted County residents; among NH residents, the proportions receiving pharmacologic prophylaxis 3 months before index were 32% for non-VTE controls and 45% for VTE cases; [48] in our current longitudinal cohort study of NHVTE incidence, a slightly higher 54% of cases received pharmacologic prophylaxis within the 3 months before the incident NHVTE event, perhaps reflecting use of low molecular weight heparin (LMWH) in this later time period (17% of the 111 were treated with LMWH).

Additional NHVTE risk factors were identified in our two previous REP publications, the first employed REP medical record data alone,[48] the second combined REP medical record data with CMS-MDS data.[49] In the first study, NHVTE risk was significantly associated with active malignancy, recent hospitalization, and recent surgery. However, the prevalence of all evaluated VTE risk factors appeared much higher in NH controls than in

general population controls, thus the magnitude of risk appeared much lower than for general population estimates (e.g., odds ratio for major surgery = 2.5 [95% CI=1.4–4.3] for NH residents vs 11 [95% CI=7.0–17] for the general population).[48] When REP data were combined with CMS data in our second case-control investigation, only three characteristics were independently associated with NHVTE: respiratory infection vs no infection, extensive or total assistance with walking in room, and general surgery. In analyses limited to non-hospitalized cases and control subjects, only non-respiratory infection vs no infection was independently associated with VTE.[49] Both previous studies employed case-control designs. Both focused on a single index date, with index defined as NHVTE date for cases and REP encounter date for non-NHVTE NH controls; risk factors were obtained following manual review of detailed medical records over the time frame typically used in REP risk factor studies conducted for the general population (for most characteristics, this is 3 months before index, but for some conditions, the time frame can extend from date first seen by a REP provider until study end). Obtaining similar information in the present longitudinal cohort study was not feasible, as it would require obtaining risk factor information on all 3,465 NH residents, for each of 4,730 NH stays..

While our estimates of NHVTE incidence and associated mortality are unique among all studies currently in the literature, they do not extend beyond 12/31/2005. However, based on our recent REP study showing no reduction in either in-hospital or post-hospital VTE rates after achieving a near-universal in-hospital prophylaxis regimen among hospitalized Olmsted County residents,[21] we believe NHVTE estimates reported here are unlikely to have changed significantly.

Conclusion.

NH residency is a major, independent risk factor for VTE.[5,6] Many NH residents exhibit advanced age, high morbidity, and frailty, characteristics associated with increased VTE risk and adverse VTE outcomes (e.g., death, morbidity [pain, swelling, post-thrombotic syndrome], disability, recurrent VTE, and reduced quality of life).[2,3,38,50] These characteristics are also associated with risk of adverse outcomes from VTE prophylaxis.[10] Answers to important questions regarding trade-offs between these competing risks necessitate knowledge of the actual burden of VTE among NH residents.[9,13] Published estimates of NHVTE incidence and associated mortality are few, highly variable, and limited by available resources.

This study confirmed that the burden of VTE among NH residents is substantial and emphasized the need to reduce that burden. Our findings of NHVTE incidence characterized by days from each admission may inform efforts toward reducing that burden. In our study, almost half of all first NH stays for all 3,465 residents were ≤ 30 days, similar to published data showing an average length-of-stay for post-acute rehabilitation in skilled-nursing facilities of 26.4 days.[43] It is anticipated that many NH admissions for post-acute rehabilitation will result in discharge to the community. Our finding that 15% of NHVTE events occurred within 7 days after each admission and $>50\%$ occurred within the first 90 days strongly suggest that likelihood of discharge to the community would be enhanced if

NH residents were closely monitored for symptoms suggestive of VTE, especially early in their stay.

The rates of NHVTE/100,000 NH-PY found here of 3,653 overall and 18,764 the first week after NH admission compare with an average annual rate reported in a previous REP study of incident VTE among hospitalized (medical or surgical) Olmsted County residents (all ages) of 9,605 incident VTE per 100,000 hospital bed-years at risk. While such comparisons may help provide a sense of whether it might be useful to consider future research into prophylaxis against NHVTE, e.g., our finding of highest risk shortly after NH admission may support introduction of short (2–4 weeks) cluster-clinical trials, whether NH residents admitted with symptoms suggestive of VTE might benefit from prophylaxis extending up to 30–90 days post-admission requires additional information. Existing data (including ours) are not yet sufficient to recommend prophylaxis against NHVTE. While caution should be exercised regarding clinical interpretation, the estimates presented here can help inform the design of clinical trials and construction of appropriate guidelines that are currently lacking and critically needed within the NH population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Summary table.

What is known on this topic:

- The independent risk of venous thromboembolism (**VTE**) among nursing home (**NH**) residents is increased ~5-fold.
- NH residence accounts for about 13% of all incident VTE occurring in the community.

What this paper adds:

- The incidence of VTE among NH residents is ~37 per 1000 NH person-years.
- NH VTE incidence is highest within the first 7 days after NH admission.
- The hazard of death is ~2-fold higher for NH residents with incident NH VTE compared to NH residents without NH VTE.
- Data presented here can help inform clinical trials regarding short-term prophylaxis and ultimately contribute to appropriate guidelines currently lacking and critically needed within the NH population.

Figure 1.

Incidence of venous thromboembolism within the nursing home (NH) population, consisting of all 3465 Olmsted County residents admitted to a local NH 10/1/1998–12/31/2005, by time since each NH admission within that calendar period. Dashed lines represent the 95% confidence interval for the incidence rates.

Table 1.

Characteristics of all 3465 Olmsted County, MN, residents admitted to a local NH 10/1/1998–12/31/2005

Characteristic	Distribution
Unique individuals, N [*]	3465
Male, N (%)	1197 (35%)
Age at earliest NH admission, years	
Mean (SD)	80.8 (10.1)
Median (IQR)	82 (76–88)
Range	35–106
Follow-up years per individual [†]	
Mean (SD)	2.0 (1.8)
Median (IQR)	1.5 (0.5–3.2)
Range	0.0–7.2
Earliest NH admission from hospital, N (%)	2787 (80%)
Sum of NH stays per individual [‡]	
Mean (SD)	1.4 (0.8)
Median (IQR)	1 (1–2)
Range	1–15
Sum of NH days per individual [‡]	
Mean (SD)	330.8 (503.0)
Median (IQR)	73 (22–447)
Range	1–2642
All NH stays, N [§]	4762
Time from each admission to respective discharge, N (%)	
1–7 days	484 (10%)
8–14 days	621 (13%)
15–30 days	1052 (22%)
31–90 days	1020 (21%)
91–180 days	375 (7.9%)
181–365 days	254 (5.3%)
1.1–2 years	378 (7.9%)
2.1–5 years	494 (10%)
>5 years	84 (1.8%)

IQR indicates interquartile range; NH, nursing home; NHVTE, incident venous thromboembolism experienced while a nursing home resident; SD, standard deviation; VTE, venous thromboembolism.

^{*} Including individuals with (n = 111) and without (n = 3354) evidence of incident NHVTE on or after their earliest admission 10/1/1998–12/31/2005.

[†] The sum of all days during follow-up, from earliest NH admission during the study period until earliest of death, emigration, VTE while not a NH resident or 12/31/2005 (study end).

[‡]Estimates are accumulated from earliest NH admission 10/1/1998–12/31/2005 to end of follow-up. The sum of all NH days=1 146 167 across all 4762 stays. These numbers include 32 NH stays (4762 – 32 = 4730 stays) and 36 334 NH days after NHVTE (1 146 167 – 36 334 = 1 109 833 days).

[§]Includes NH stays with (n = 111) and without (n = 4651) evidence of incident NHVTE during the stay.

^{//}Time from NH admission to respective NH discharge or 12/31/2005 (study end).

Table 2.

Characteristics of the subset of 111 Olmsted County, MN, residents admitted to a local NH 10/1/1998–12/31/2005 with evidence of incident NHVTE on or after earliest admission during that time frame

Characteristic	VTE Type		
	All VTE (n = 111)	DVT alone (n = 82)	PE ± DVT (n = 29)
Unique individuals			
Male, N (%)	30 (27%)	22 (27%)	8 (28%)
Clinically determined VTE, N (%)	4 (4%)	4 (5%)	0 (0%)
Age at earliest NH admission, years			
Mean (SD)	80.6 (10.1)	80.1 (11.0)	82.2 (7.1)
Median (IQR)	82 (77–87)	82 (76–87)	83 (78–88)
Range	45–99	45–99	68–93
Age at incident NHVTE, years			
Mean (SD)	81.5 (10.3)	80.9 (11.0)	83.2 (7.7)
Median (IQR)	83 (78–89)	83 (77–88)	85 (78–89)
Range	45–99	45–99	69–95
Prophylaxis in 3 months prior to VTE, N (%)	67 (60%)	46 (56%)	21 (72%)
Earliest NH admission from hospital, N (%)	97 (87%)	70 (85%)	27 (93%)
Days to incident NHVTE per individual [*]			
Mean (SD)	203.7 (306.7)	204.8 (297.4)	200.5 (339.2)
Median (IQR)	45.5 (16–320)	49 (17–320)	37 (15–330)
Range	1–1249	2–1205	1–1249
Sum of NH stays per individual [†]			
Mean (SD)	1.2 (0.5)	1.2 (0.5)	1.2 (0.5)
Median (IQR)	1 (1–1)	1 (1–1)	1 (1–1)
Range	1–3	1–3	1–3
Sum of NH days per individual [†]			
Mean (SD)	232.8 (330.9)	225.9 (316.6)	252.4 (373.8)
Median (IQR)	55 (19–324)	59 (19–319)	47 (20–352)
Range	1–1329	2–1329	1–1249
NH stay in which incident NHVTE occurred			
Time from admission to NHVTE, N (%) [‡]			
1–7 days	17 (15%)	13 (16%)	4 (14%)
8–14 days	7 (6.3%)	5 (6.1%)	2 (6.9%)
15–30 days	18 (16%)	12 (15%)	6 (21%)
31–90 days	23 (21%)	16 (20%)	7 (24%)
91–180 days	7 (6.3%)	6 (7.3%)	1 (3.4%)
181–365 days	16 (14%)	14 (17%)	2 (6.9%)
1.1–2 years	11 (9.9%)	8 (9.8%)	3 (10%)
2.1–5 years	12 (11%)	8 (9.8%)	4 (14%)
>5 years	0 (0.0%)	0 (0.0%)	0 (0.0%)

DVT indicates deep vein thrombosis; IQR, interquartile range; NH, nursing home; NHVTE, incident venous thromboembolism experienced while a nursing home resident; PE, pulmonary embolism; SD, standard deviation; VTE, venous thromboembolism.

^{*}The sum of all days from earliest NH admission during the study period to date of incident NHVTE.

[†]Estimates are accumulated from earliest NH admission 10/1/1998–12/31/2005 to date incident NHVTE occurred. The sum of all NH days=25 843 across all 137 stays.

[‡]Time from NH admission to date of incident NHVTE.

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Table 3.

Incident NHVTE (per 100 000 NH-PY) by sex and age group among all 3465 Olmsted County, MN, residents admitted to a local NH 10/1/1998–12/31/2005

	Sex	Age group, years								Total
		35–65	66–70	71–75	76–80	81–85	86–90	91+		
NH stays, N*	Male	143	140	193	320	370	343	190	1593	
NH-PY [†]		86.0	66.4	79.4	161.2	218.6	217.1	145.4	974.1	
NHVTE events, N [‡]		3	2	3	5	8	3	6	30	
Number of NHVTE events / number of		2.1%	1.4%	1.6%	1.6%	2.2%	0.9%	3.2%	1.9%	
NH stays (%) Incidence rate		3490	3014	3779	3101	3659	1382	4126	3080	
95% CI		721–10 179	365–10 850	781–11 021	1008–7226	1580–7204	286–4031	1513–8973	2078–4397	
NH stays, N*	Female	161	160	312	548	812	763	624	3137	
NH-PY [†]		79.2	50.1	146.9	274.3	472.9	523.9	517.2	2064.5	
NHVTE events, N [‡]		5	4	5	14	20	22	11	81	
Number of NHVTE events / number of		3.1%	2.5%	1.6%	2.6%	2.5%	2.9%	1.8%	2.6%	
NH stays (%) Incidence rate		6315	7979	3404	5104	4229	4200	2127	3923	
95% CI		2052–14 714	2174–20 445	1106–7931	2789–8567	2582–6532	2631–6358	1063–3809	3116–4877	
NH stays, N*	Total	304	300	505	868	1182	1106	814	4730	
NH-PY [†]		165.1	116.5	226.3	435.5	691.6	740.9	662.6	3038.6	
NHVTE events, N [‡]		8	6	8	19	28	25	17	111	
Number of NHVTE events / number of		2.6%	2.0%	1.6%	2.2%	2.4%	2.3%	2.1%	2.3%	
NH stays (%) Incidence rate		4844	5150	3535	4363	4049	3374	2566	3653	
95% CI		2092–9538	1889–11 202	1527–6960	2625–6813	2690–5852	2183–4981	1494–4108	3005–4399	

CI indicates confidence interval; NH, nursing home; NHVTE, incident venous thromboembolism experienced while a nursing home resident; NH-PY, nursing home person-years.

* Number of NH stays that contributed nursing home person-years to each age and sex category.

[†] Individuals were followed for each NH admission during the study period, with multiple stays possible for each resident. NH person-years (NH-PY) were calculated only while a NH resident, from each admission to respective discharge date or study end (12/31/2005).

[‡] Number of incident NHVTE events that occurred within each age and sex category.

Table 4.

Incident NHVTE (per 100 000 NH-PY) by type of VTE and age group among all 3465 Olmsted County, MN, residents admitted to a local NH 10/1/1998–12/31/2005

VTE Type	Age group, years							
	35–65	66–70	71–75	76–80	81–85	86–90	91 +	Total
NH stays, N*	304	300	505	868	1182	1106	814	4730
PE ± DVT								
NH-PY [†]	165.1	116.5	226.3	435.5	691.6	740.9	662.6	3038.6
NHVTE events, N [‡]	0	2	3	7	4	8	5	29
Number of NHVTE events / number of	0.0%	0.7%	0.6%	0.8%	0.3%	0.7%	0.6%	0.6%
NH stays (%) Incidence rate	0	1717	1326	1607	578	1080	755	954
95% CI	--	208–6180	274–3867	646–3306	158–1482	466–2126	245–1758	639–1371
NH stays, N*	304	300	505	868	1182	1106	814	4730
DVT alone								
NH-PY [†]	165.1	116.5	226.3	435.5	691.6	740.9	662.6	3038.6
NHVTE events, N [‡]	8	4	5	12	24	17	12	82
Number of NHVTE events / number of	2.6%	1.3%	1.0%	1.4%	2.0%	1.5%	1.5%	1.7%
NH stays (%) Incidence rate	4844	3434	2210	2755	3470	2294	1811	2699
95% CI	2092–9538	936–8799	718–5148	1424–4810	2223–5164	1336–3674	936–3162	2146–3350

CI indicates confidence interval; DVT, deep vein thrombosis; NH, nursing home; NHVTE, incident venous thromboembolism experienced while a nursing home resident; NH-PY, nursing home person-years; PE, pulmonary embolism; VTE, venous thromboembolism.

* Number of NH stays that contributed nursing home person-years to each category.

[†] Individuals were followed for each NH admission during the study period, with multiple stays possible for each resident. NH person-years (NH-PY) were calculated only while a NH resident, from each admission to respective discharge date or 12/31/2005 (study end).

[‡] Number of incident NHVTE events that occurred within each age category.

Table 5.

Incident NHVTE (per 100 000 NH-PY) by category of time from admission for each NH stay among 4730 NH stays by all 3465 Olmsted County, MN, residents admitted to a local NH 10/1/1998–12/31/2005

	Time from each NH admission								
	1–7 days	8–14 days	15–30 days	31–90 days	91–180 days	181–365 days	1.1–2 years	2.1–5 years	>5 years
NH stays, N*	4730	4242	3621	2564	1548	1181	930	559	79
NH-PY †	90.6	79.0	129.6	316.4	327.5	527.1	728.4	777.4	62.5
NHVTE events, N‡	17	7	18	23	7	16	11	12	0
Number of NHVTE events / number of NH stays (%)	0.4%	0.2%	0.5%	0.9%	0.5%	1.4%	1.2%	2.1%	0.0%
Incidence rate	18 764	8863	13 887	7270	2138	3035	1510	1544	0.0
95% CI	10 925–30 045	3564–18 232	8226–21 949	4607–10 909	860–4397	1734–4929	755–2705	797–2695	--

Time categories were selected by reviewing the distribution of time from each NH admission and selecting round intervals. CI indicates confidence interval; NH, nursing home; NHVTE, incident venous thromboembolism experienced while a nursing home resident; NH-PY, nursing home person-years.

* Number of NH stays that contributed nursing home person-years to each category.

† Individuals were followed for each NH admission during the study period, with multiple stays possible for each resident. NH person-years (NH-PY) were calculated only while a NH resident, from each admission to respective discharge date or study end (12/31/2005). For example, the NH-PY for a 30 day stay would be broken up with the first 7 days in the first time category, the next 7 days in the second time category and the remaining 16 days in the third time category. Each subsequent NH admission would restart the clock at day zero.

‡ Number of incident NHVTE events that occurred within each time category.

Table 6.

Poisson models for incident NHVTE among all 3465 Olmsted County, MN, residents admitted to local a local NH 10/1/1998–12/31/2005

Predictor	Standardized Morbidity Ratio *	95% CI	P
Univariate models			
Female sex	1.28	0.84–1.94	.25
Age (per 10-years)	0.83	0.70–0.98	.04
Calendar year			.59
1998–1999	2.06	0.98–4.33	
2000	1.54	0.76–3.12	
2001	1.21	0.59–2.48	
2002	1.30	0.66–2.58	
2003	1.14	0.57–2.29	
2004	1.11	0.55–2.22	
2005		(reference)	
Time from each NH admission			<.001
1–7 days	13.09	6.25–27.41	
8–14 days	6.18	2.43–15.70	
15–30 days	9.70	4.67–20.13	
31–90 days	5.09	2.53–10.22	
91–180 days	1.50	0.59–3.80	
181–365 days	2.12	1.00–4.49	
1.1–2 years	1.06	0.47–2.40	
>2 years		(reference)	
Multivariable model [†]			
Male sex	1.38	0.90–2.11	.13
Age, per 10-years	0.88	0.74–1.05	.16
Calendar year			.99
1998–1999	1.06	0.50–2.26	
2000	1.20	0.59–2.45	
2001	1.13	0.55–2.32	
2002	1.25	0.63–2.49	

Predictor	Standardized Morbidity Ratio [*]	95% CI	P
2003	1.16	0.58–2.32	
2004	1.10	0.55–2.19	
2005		(reference)	
Time from each NH admission			<.001
1–7 days	12.64	5.94–26.89	
8–14 days	5.97	2.32–15.34	
15–30 days	9.39	4.45–19.81	
31–90 days	4.94	2.41–10.12	
91–180 days	1.46	0.57–3.77	
181–365 days	2.07	0.96–4.45	
1.1–2 years	1.04	0.45–2.37	
>2 years		(reference)	

CI indicates confidence interval; NH, nursing home; NHVTE, incident venous thromboembolism experienced while a nursing home resident.

^{*} Standardized morbidity ratios were calculated from generalized linear regression models with a Poisson error and log link.

[†] All two-way interactions were assessed; including the interaction terms did not significantly improve the fit over the multivariable model presented ($P = .40$).