






ORIGINAL RESEARCH

Inpatient Versus Outpatient Acute Venous Thromboembolism Management: Trends and Postacute Healthcare Utilization From 2011 to 2018

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BACKGROUND: Acute outpatient management of venous thromboembolism (VTE), which includes pulmonary embolism (PE) and deep vein thrombosis (DVT), is perceived to be as safe as inpatient management in some settings. How widely this strategy is used is not well documented.

METHODS AND RESULTS: Using MarketScan administrative claims databases for years 2011 through 2018, we identified patients with *International Classification of Diseases (ICD)* codes indicating incident VTE and trends in the use of acute outpatient management. We also evaluated healthcare utilization and hospitalized bleeding events in the 6 months following the incident VTE event. A total of 200 346 patients with VTE were included, of whom 50% had evidence of PE. Acute outpatient management was used for 18% of those with PE and 57% of those with DVT only, and for both DVT and PE its use increased from 2011 to 2018. Outpatient management was less prevalent among patients with cancer, higher Charlson comorbidity index scores, and whose primary treatment was warfarin as compared with a direct oral anticoagulant. Healthcare utilization in the 6 months following the incident VTE event was generally lower among patients managed acutely as outpatients, regardless of initial presentation. Acute outpatient management was associated with lower hazard ratios of incident bleeding risk for both patients who initially presented with PE (0.71 [95% CI, 0.61, 0.82]) and DVT only (0.59 [95% CI, 0.54, 0.64]).

CONCLUSIONS: Outpatient management of VTE is increasing. In the present analysis, it was associated with lower subsequent healthcare utilization and fewer bleeding events. However, this may be because healthier patients were managed on an outpatient basis.

Key Words: acute management ■ outpatient management ■ temporal trends ■ venous thromboembolism

Venous thromboembolism (VTE), which consists of both deep vein thrombosis (DVT) and pulmonary embolism (PE), affects ≈1.1 million Americans annually.¹ The landscape of VTE diagnosis and management has changed dramatically in the past 2 decades. In regard to acute out-of-hospital management, the 2016 American College of Chest Physicians Guideline and Expert Panel Report states that “In patients with low-risk PE and whose home circumstances are

adequate, we suggest at home or early discharge over standard discharge (eg, after the first 5 days of treatment).”² This is a Grade 2B recommendation, signifying that it is a “weak” (Grade 2) recommendation based on “moderate” (Grade B) quality evidence. Given that patients with DVT events but no documented PE are at lower risk of adverse outcomes, outpatient management in this context has been widespread for some time.^{2,3}

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Supplementary Material for this article is available at <https://www.ahajournals.org/doi/suppl/10.1161/JAHA.120.020428>

For Sources of Funding and Disclosures, see page 8.

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CLINICAL PERSPECTIVE

What Is New?

- Acute outpatient management for venous thromboembolism was used for 18% of patients with pulmonary embolism and 57% of patients with deep vein thrombosis only. Its use increased from 2011 to 2018.
- Patients managed acutely as outpatients had fewer comorbidities and in the following 6 months had lower healthcare utilization and were less frequently hospitalized for bleeding events.

What Are the Clinical Implications?

- These data provide contemporary information on the patterns of acute outpatient venous thromboembolism management.
- Our findings suggest that outpatient management is not associated with substantial harm in appropriately selected patients.

Nonstandard Abbreviations and Acronyms

DOAC	direct oral anticoagulants
OAC	oral anticoagulant

Outpatient VTE treatment has the potential to reduce medical costs,⁴ be less burdensome to patients, and in low-risk situations, yield similar outcomes.² However, there are important barriers to outpatient management; most prominently, fear of experiencing early complications and whether a local healthcare system can provide adequate initial care in the outpatient setting.³ Little is known about how widely outpatient management is presently being utilized or its real-world effectiveness.^{3,5}

Outpatient treatment rates may have increased in recent years because of both (1) primary treatment with direct oral anticoagulants (DOACs) offering an all-oral VTE treatment option, and (2) improved identification of patients with low-risk PE. The availability of several DOACs (ie, dabigatran, rivaroxaban, apixaban, and edoxaban),^{6–10} in addition to warfarin and low-molecular-weight heparin, have expanded the potential for outpatient VTE management.¹¹ The DOACs have a more stable anticoagulant effect and require less monitoring. Additionally, some (ie, rivaroxaban and apixaban) do not require initial parenteral anticoagulant therapy.

The current prevalence of outpatient VTE management is unknown, since studies that have evaluated this question ended follow-up before the era

of widespread DOAC use (ie, in the mid-2010s or before).^{11–17} Additionally, uncertainty remains about the association of outpatient versus inpatient management with subsequent healthcare utilization and bleeding risk in routine clinical settings. Herein we provide estimates of acute VTE management (outpatient versus inpatient) in an insured population for the period from 2011 to 2018, overall and by several characteristics of the patient (ie, age, sex, comorbidity burden, whether it was provoked by cancer), clinical presentation (ie, PE or DVT-only), and initial oral anticoagulant (OAC) therapy (ie, DOAC versus warfarin). Furthermore, we assess the association of acute outpatient versus inpatient management with subsequent healthcare utilization and bleeding events in the primary treatment period (ie, the first 6 months following the VTE event).

METHODS

IBM MarketScan Commercial Claims and Encounters and Medicare Supplemental and Coordination of Benefits databases for calendar years 2011 through 2018 were used in the present analysis. These administrative databases contain individual-level, de-identified, Health Insurance Portability and Accountability Act of 1996–compliant, healthcare claims information from US employers, health plans, hospitals, and Medicare programs.¹⁸ Individual-level identifiers are used to link data across enrollment records and inpatient, outpatient, ancillary, and drug claims. Given the time-frame under study, both *International Classification of Diseases Ninth Revision* and *Tenth Revision (ICD-9 and ICD-10)* codes were used. Since the MarketScan databases are commercial insurance databases, individuals with no insurance are not included and individuals working at small companies are underrepresented. The University of Minnesota Institutional Review Board deemed this research exempt from review, and waived the need to obtain informed consent. Because of licensing restrictions, we cannot make available the data and study materials to other investigators to reproduce results, but researchers may contact IBM Watson Health to obtain and license the data.

Identification of VTE Cases

We included in the present analysis individuals aged 18 to 99 years with incident VTE, at least 1 prescription for an OAC within the 31 days before or after their first VTE claim, and ≥ 3 months of continuous enrollment before their first OAC prescription.¹⁹ As is common in analyses of administrative data, a “run-in” period (in this instance 3 months) was utilized to allow for identification of incident events and to capture information on comorbidities before the incident event.²⁰

We defined VTE as having at least 1 inpatient claim for VTE or 2 outpatient claims for VTE, which were 7 to 185 days apart, in any position, based on *ICD* codes (listed in Table S1). We identified OAC prescriptions, using outpatient pharmaceutical claims data, by National Drug Codes indicating fills for apixaban, rivaroxaban, dabigatran, edoxaban, or warfarin. This VTE definition is similar to that used in a recent validation study by Sanfilippo et al, which reported a positive predictive value of 91%.²¹ The Sanfilippo definition was also based on 1 inpatient or 2 outpatient VTE claims, and required evidence of treatment. We further classified VTE cases according to whether there were *ICD* codes for PE, or if the *ICD* codes only indicated DVT (regardless of DVT site). This classification was chosen since there are less data supporting outpatient PE treatment than outpatient DVT treatment, and so the likelihood of acute outpatient management is likely to differ by whether there was evidence of PE.

The initial sample included 553 387 patients with *ICD* codes indicating VTE aged 18 to 99 years. The analytic sample was 432 950 once restricted to individuals ever prescribed an OAC between January 1, 2011 and December 31, 2018; 273 938 after requiring the first OAC prescription be within 31 days of the VTE *ICD* code date; 203 289 after requiring ≥ 90 days of continuous enrollment before the first OAC prescription; and finally, 200 346 after excluding individuals who used low-molecular-weight heparin as their sole anticoagulant prescription.

Designation as Inpatient or Outpatient Acute Management

For each year MarketScan compiles all hospitalization claims into an inpatient encounters data set, and all outpatient encounters in an outpatient claims data set. Acute management was designated as inpatient or outpatient according to dates of VTE medical encounters in the data sets. We classified patients with VTE with both inpatient and outpatient claims according to which date came first: the date of the first qualifying inpatient claim or the date of the second qualifying outpatient claim.

Postacute Management Healthcare Utilization and Hospitalized Bleeding

Healthcare utilization and hospitalized bleeding within 6 months (ie, 185 days) of the incident VTE event were evaluated. The timeframe was selected as the VTE primary treatment period is 3–6 months,² and one would expect that most repercussions following a VTE would occur within the 6 months following the incident event.

Inpatient, outpatient, and emergency department utilization during the VTE primary treatment period

were identified using the MarketScan inpatient and outpatient databases. The VTE primary treatment period was defined as beginning on the date of the first OAC prescription fill and continuing until disenrollment or 185 days post the index date (whichever came first). Inpatient claims were used to determine number of hospitalizations and days hospitalized. Emergency department and outpatient office visits were enumerated from the outpatient claims and distinguished using information on place of service.

We also evaluated number of bleeding-related hospitalizations and days hospitalized within 185 days of the incident event. Incident hospitalized bleeding was defined according to the Cunningham algorithm,²² as we have done previously.^{19,23}

Assessment of Prespecified Covariates

Information before the OAC initiation date (minimum 90-day run-in time) from all data sources in MarketScan (ie, demographic data, inpatient, outpatient, and pharmacy claims) was used to derive prespecified covariates. The Charlson comorbidity index was calculated using relevant *ICD-9* and *ICD-10* codes.²⁴ It was categorized as 0 (none noted), 1–2 (mild), 3–4 (moderate), and ≥ 5 (severe).

Statistical Analysis

Analyses were stratified by PE (regardless of DVT status) or DVT only. Logistic regression models were fit with outpatient versus inpatient management as the dependent variable and the following independent variables: calendar year, sex, age category (<65 years, ≥ 65 years), prevalent cancer, Charlson comorbidity index score category, and initial OAC prescribed (DOAC, warfarin). Results were used to estimate adjusted prevalences of outpatient management using marginal standardization.^{25,26} Adjustment was made for age, sex, and (when appropriate) calendar year, as specified in the Table and Figure footnotes.

In analyses of incident bleeding, Cox proportional hazards regression was used to calculate hazard ratios and 95% CIs. Follow-up began at the date of the first OAC prescription filled. Person-time accrued until incident hospitalized bleeding, health plan disenrollment, the end of study follow-up, or 185 days, whichever came first. In model 1, we adjusted for age, sex, and initial OAC prescribed (DOAC or warfarin). In model 2, we further adjusted for Charlson comorbidity index categories.

When healthcare utilization was the outcome of interest, all outcomes were count data and, as such, negative binomial regression was used (ie, SAS GENMOD procedure with a negative binomial distribution and a log link). An offset of log follow-up time was applied to account for variable follow-up time between

individuals. Incidence rate ratios and 95% CIs were estimated. Covariates were the same as for the incident bleeding analyses.

Sensitivity analyses were conducted requiring 6 months of enrollment in the MarketScan database before incident VTE. Stata SE version 15 and SAS version 9.4 were used for the analyses.

RESULTS

Overall, 37.6% of patients with acute VTE in our sample were initially treated as outpatients. When stratified by VTE type, 17.9% of those with PE, and 57.1% of those with DVT-only were treated as outpatients. Table 1 provides VTE patient characteristics stratified by VTE type and acute management strategy. Prevalence of outpatient management increased over time for both VTE types from 2011 to 2018, from 16% to 23% for PE, and from 54% to 65% for DVT only (Figure). Furthermore, across both the PE and DVT-only groups, outpatient management was less prevalent among patients with cancer, those with higher Charlson comorbidity index scores, and those whose primary treatment was warfarin as compared with a DOAC (Table 2). The proportion managed acutely as an outpatient did not differ significantly by age or sex.

We also evaluated whether acute management strategy was associated with differential risk of incident bleeding and healthcare utilization that occurred in the primary treatment phase (ie, the first 6 months

following the VTE event). Acute outpatient management was associated with lower incident bleeding risk for both patients who initially presented with PE (hazard ratio, 0.71; 95% CI, 0.61, 0.82) and DVT-only (hazard ratio, 0.59; 95% CI, 0.54, 0.64) in the fully adjusted model (Table 3). Also, among patients with PE, the number of hospitalizations and days hospitalized was similar regardless of acute management strategy (Table 3). However, those who were acutely managed as an outpatient incurred fewer office visits (incidence rate ratio [95% CI], 0.88 [0.87, 0.89]) and emergency department visits (0.93 [0.90, 0.96]), in the fully adjusted model. Among DVT-only patients, acute outpatient management was associated with a lower number of hospitalizations, days hospitalized, office visits, and emergency department visits. For instance, in the fully adjusted model for the DVT-only group, the mean number of hospitalizations was 48% lower (incidence rate ratio, 0.52; 95% CI, 0.50, 0.54) among patients initially managed as outpatients compared with those initially managed as inpatients.

For all analyses, sensitivity analyses were conducted requiring 6 months of enrollment in the MarketScan database before incident VTE. Findings were similar to those of the primary analyses.

DISCUSSION

In this US population of >200 000 insured patients with VTE, outpatient acute VTE management was common,

Table 1. VTE Patient Characteristics by Acute Management and Whether the Event was PE* or DVT Only: MarketScan 2011 to 2018†

Acute Management	Pulmonary Embolism*		DVT (only)	
	Inpatient	Outpatient	Inpatient	Outpatient
N (%)	17 936 (17.9%)	81 989 (82.1%)	57 372 (57.1%)	43 049 (42.9%)
Participant characteristics				
Female, %	50.9	51.4	51.7	49.4
Age, y, mean±SD	57.4±15.4	58.8±16.2	58.6±16.5	57.0±15.6
Prevalent cancer, %	22.5	25.4	26.2	17.5
Charlson comorbidity index				
Mean±SD	2.30±2.51	2.39±2.69	2.78±2.76	1.75±2.39
Score, %				
0 (none noted)	29.9	33.4	25.4	45.1
1–2 (mild)	35.1	30.1	31.4	28.8
3–4 (moderate)	15.7	14.3	17.7	11.5
≥5 (severe)	19.3	22.2	25.5	14.6
Primary treatment OAC				
DOAC	89.2	87.9	83.3	90.3
Warfarin	10.8	12.1	16.7	9.7

DOAC indicates direct oral anticoagulants; DVT, deep vein thrombosis; OAC, oral anticoagulant; PE, pulmonary embolism; and VTE, venous thromboembolism.

*PE, regardless of whether a DVT was present.

†Adjusted for age, sex, and year.

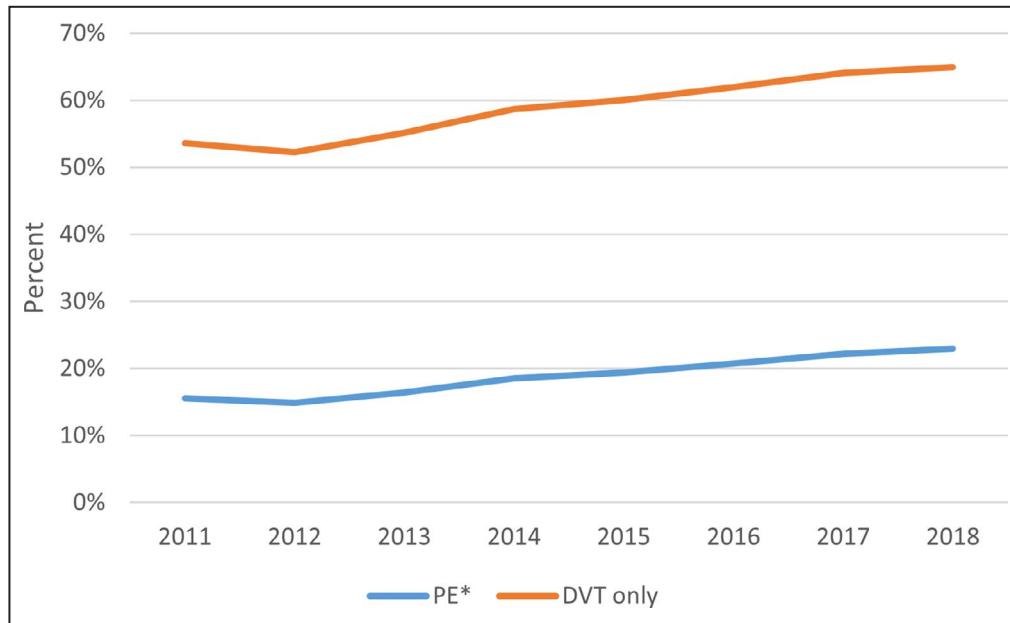


Figure. Trends in outpatient acute venous thromboembolism management by whether the event was pulmonary embolism (PE)* or DVT only: MarketScan 2011 to 2018**.

*PE, regardless of whether a DVT (deep vein thrombosis) was present. **Adjusted for age and sex.

being the selected strategy for 18% of PE cases and 57% of DVT-only cases. For both VTE types, the use of acute outpatient management increased from 2011 to 2018, the timeframe under study. As expected, outpatient management was less common among patients with VTE with cancer or higher comorbidity scores. Overall, after acute treatment, healthcare utilization and incident hospitalized bleeding in the primary treatment period were lower for patients with VTE whose acute management was as outpatients, as compared with those initially managed as inpatients. This is not surprising, because the clinical decision to treat as an outpatient would only be indicated in lower-risk individuals. These findings support current recommendations and suggest that outpatient management is not associated with substantial harm in appropriate patients.

Prevalence of, and Trends in, Outpatient Acute VTE Management

During the period from 2011 to 2018 in the MarketScan data, 18% of PE cases and 57% of DVT-only cases were initially managed on an outpatient basis. Table 4 summarizes findings from published observational studies reporting the prevalence of outpatient management in publications that included >1000 patients with VTE. As has been reviewed recently by Roy,³ numerous smaller studies of outpatient PE management have been published; however, these often were restricted to a small geographic setting and/or were

conducted as part of an intervention (randomized or practice-based). Of the large PE studies, those from Canada reported high prevalences of acute outpatient management (Quebec 2000–2009, 49%¹⁵; Ottawa 2001–2012,¹⁷ 48%), though the Quebec study reported uncertainty about the validity of PE events.¹⁵ For US-based studies, the prevalence of outpatient PE acute management was much lower (6% for 2001–2012;¹⁶ 5% for 2004–2010¹¹). For DVT, the prevalence we reported (57%) for the period 2011 to 2018 is similar to that reported by Fang (55%) for the timeframe from 2004 to 2010¹¹ but higher than that reported between 2007 and 2012 by Stein (34%).¹² Both of these DVT studies were conducted in US populations.

In comparing prevalence of outpatient management in the present analyses of MarketScan databases for years 2011 to 2018 to those of prior studies, it is crucial to be mindful of the minimal overlap in time periods. Most of the prior studies took place before the widespread use of DOACs. It has been speculated that outpatient management would become even more prevalent with the adoption of DOACs,¹¹ given their lower bleeding risk, reduced need for monitoring, and all-oral treatment approaches. Like others, we also documented that outpatient management is more likely in healthier individuals. For instance, in the Nationwide Emergency Department Sample, 63% of those relatively young (18–50 years) and with no comorbidities were treated at home.¹²

The rising use of acute outpatient management is consistent with that observed in other studies. For DVT,

Table 2. Adjusted Prevalence of VTE Patient Characteristics by Acute Management and Whether the Event was PE* or DVT Only: MarketScan 2011 to 2018†

Initial Management	% (95% CI) Outpatient VTE Management	
	PE*	DVT (only)
Sex		
Male	18.2 (18.0, 18.5)	57.9 (57.5, 58.3)
Female	17.5 (17.2, 17.8)	56.7 (56.3, 57.1)
Age category		
<45 y	18.5 (18.1, 18.9)	58.3 (57.7, 58.8)
45–54 y	19.0 (18.6, 19.4)	59.1 (58.6, 59.7)
55–64 y	16.5 (16.2, 16.8)	55.0 (54.5, 55.5)
65–74 y	18.4 (18.0, 18.8)	58.2 (57.5, 58.8)
≥75 y	17.7 (17.3, 18.1)	57.0 (56.4, 57.6)
Cancer		
Yes	15.0 (14.7, 15.4)	52.2 (51.6, 52.8)
No	18.7 (18.4, 19.0)	58.6 (58.3, 59.0)
Charlson comorbidity index score		
0 (none noted)	25.4 (25.0, 25.8)	67.6 (67.2, 68.0)
1–2 (mild)	16.4 (16.1, 16.7)	54.6 (54.1, 55.1)
3–4 (moderate)	13.2 (12.9, 13.6)	48.4 (47.7, 49.1)
≥5 (severe)	13.1 (12.8, 13.4)	48.0 (47.4, 48.6)
Primary treatment OAC		
DOAC	18.4 (18.2, 18.7)	58.5 (58.1, 58.8)
Warfarin	13.4 (13.0, 13.8)	49.1 (48.4, 49.9)

DOAC indicates direct oral anticoagulants; DVT, deep vein thrombosis; OAC, oral anticoagulant; PE, pulmonary embolism; and VTE, venous thromboembolism.

*Pulmonary embolism, regardless of whether or not a DVT was present.

†Adjusted for age, sex, and year.

the prevalence increased from 31.6% in 2007 to 37.4% in 2012, in an analysis of the Nationwide Emergency Sample.¹² Outpatient management of PE was also shown to increase from 2000 to 2009 in data from Quebec.¹⁵ As clinical experience with DOAC grows, it will be informative to evaluate how acute VTE management changes over time.¹¹

Acute Outpatient VTE Management and Subsequent Healthcare Utilization and Major Bleeding Events

Current guidelines² recommended outpatient PE management in some settings based on (1) 2 trials that randomized patients with acute PE to shorter²⁷ or no treatment in the hospital²⁸ compared with being treated in the hospital for a longer period, (2) observational studies of outpatient acute PE management,³ and (3) extrapolating from clinical experience and trials of outpatient acute DVT treatment. Furthermore, a 2017 comprehensive review of outpatient management in the context of PE, which

summarized both trials and observational studies, concluded that “outpatient management appears to be feasible and safe for many patients with PE.”³ However, the existing evidence is incomplete; the current guidelines² have a Grade 2B recommendation and state: “The quality of evidence for treatment of acute PE at home remains moderate because of marked imprecision.”

In the present evaluation of healthcare utilization and incident major bleeding postacute management (ie, in the VTE primary treatment period), we observed that in the contexts of both PE and DVT-only, patients whose initial management was outpatient had fewer bleeding events. Healthcare utilization was also lower in the DVT-only group managed acutely as outpatients, compared with the group managed acutely as inpatients. For patients with PE, hospitalization rates did not differ by acute management strategy, but office and emergency department visits were lower among patients with VTE managed initially as outpatients. We acknowledge that these results are confounded by indication; patients managed acutely as outpatients were undoubtedly healthier, as evidenced by the lower Charlson comorbidity index burden in this group. However, the findings are useful for describing the general clinical experience of patients with VTE managed acutely in outpatient and inpatient settings, respectively.

Strengths and Limitations

The primary strengths of this analysis are the large number of VTE cases in a real-world, contemporary setting. The key limitations include the likelihood of confounding because of indication and lack of detailed information to verify VTE case status, severity of VTE, and burden of comorbidities and other factors that may have influenced a clinician’s decision to manage a VTE case as inpatient or outpatient. However, throughout we used validated algorithms to define medical conditions.^{21,22,24} Our VTE definition allowed both inpatient and outpatient management, and required use of OACs around the time of the VTE event. In a validation study of this definition in an independent population, the positive predictive value was high, at 91%.²¹ We acknowledge that indication bias is almost certainly present in the determination of who is acutely managed on an outpatient basis, and in our data it is impossible to fully control for factors that influenced acute management decisions. The findings provide novel information about secular trends in acute management of VTE, though generalizability to individuals with no insurance and those working for small companies may be limited. However, these data do not reveal who should be managed as an outpatient

Table 3. Incident Hospitalized Bleeding and Healthcare Utilization According to VTE Presentation and Acute VTE Management: MarketScan 2011 to 2018

	PE*		DVT Only	
	Inpatient	Outpatient	Inpatient	Outpatient
N (%)	81 989 (82.1%)	17 936 (17.9%)	43 049 (42.9%)	57 372 (57.1%)
Hospitalized bleeding				
N hospitalized bleed	1295	210	920	506
N total	81 989	17 936	43 049	57 372
HR (95% CI)				
Model 1 [†]	1 (Ref)	0.71 (0.61, 0.82)	1 (Ref)	0.53 (0.49, 0.58)
Model 2 [‡]	1 (Ref)	0.71 (0.61, 0.82)	1 (Ref)	0.59 (0.54, 0.64)
Healthcare utilization				
Hospitalizations, N				
Crude mean±SD	0.23±0.65	0.21±0.60	0.30±0.77	0.13±0.45
IRR (95% CI)				
Model 1 [†]	1 (Ref)	0.92 (0.88, 0.97)	1 (Ref)	0.43 (0.41, 0.44)
Model 2 [‡]	1 (Ref)	0.95 (0.90, 1.00)	1 (Ref)	0.52 (0.50, 0.54)
Days hospitalized, N				
Crude mean±SD	1.69±6.17	0.21±0.60	0.30±0.77	0.13±0.45
IRR (95% CI)				
Model 1 [†]	1 (Ref)	0.90 (0.83, 0.97)	1 (Ref)	0.35 (0.33, 0.38)
Model 2 [‡]	1 (Ref)	0.96 (0.89, 1.04)	1 (Ref)	0.43 (0.40, 0.46)
Office visits, N				
Crude mean±SD	8.33±6.52	7.33±6.29	8.06±6.62	6.51±5.89
IRR (95% CI)				
Model 1 [†]	1 (Ref)	0.88 (0.87, 0.89)	1 (Ref)	0.80 (0.79, 0.81)
Model 2 [‡]	1 (Ref)	0.88 (0.87, 0.89)	1 (Ref)	0.86 (0.85, 0.87)
Emergency Department visits, N				
Crude mean±SD	0.53±1.30	0.48±1.17	0.47±1.24	0.30±0.97
IRR (95% CI)				
Model 1 [†]	1 (Ref)	0.92 (0.89, 0.96)	1 (Ref)	0.64 (0.62, 0.66)
Model 2 [‡]	1 (Ref)	0.93 (0.90, 0.96)	1 (Ref)	0.73 (0.71, 0.75)

DOAC indicates direct oral anticoagulant; DVT, deep vein thrombosis; HR, hazard ratio; IRR, incidence rate ratio; OAC, oral anticoagulant; PE, pulmonary embolism; and VTE, venous thromboembolism.

*Pulmonary embolism, regardless of whether or not a DVT was present.

[†]Model 1: Adjusted for age, sex, and initial OAC (OAC, DOAC, or warfarin).

[‡]Model 2: Adjusted for model 1+Charlson comorbidity index categories.

versus inpatient for the acute treatment of VTE. An additional limitation of the present analysis is that we did not evaluate mortality as an outcome since MarketScan lacks information on out-of-hospital death.

CONCLUSIONS

In this analysis of 200 346 patients with VTE, we demonstrated increases in the prevalence of outpatient acute management from 2011 to 2018, for both PE and DVT-only cases. In 2018, we estimate that 23% of PE cases and 65% of DVT-only cases were

managed on an outpatient basis. Cases managed as outpatients were more likely to not have cancer, have fewer comorbidities, and be prescribed a DOAC for their primary treatment. Furthermore, we show that healthcare utilization and major bleeding incidence was lower among VTE cases initially managed on an outpatient basis. These data provide a contemporary context regarding the patterns of acute outpatient VTE management, as well as outcomes, in a large, insured US population.

Further clinical studies are warranted to determine which clinical populations could most benefit from outpatient versus inpatient treatment of VTE.

Table 4. Summary of Findings From Studies Evaluating the Prevalence of Outpatient VTE Management that Included More than 1000 Patients With VTE

Publication	Study Population	Data Collection Years	N Managed Outpatient/N Patients	Percent Outpatient Management
Pulmonary embolism				
Stein ¹⁶	Nationwide Emergency Department Sample, US	2007–2012	54 464/915 702	6.0%
Kil-Drori ¹⁵	Residents of Quebec, Canada	2000–2009	7583/15 217	48.8%*
Roy ¹⁷	Ottawa Hospital, Canada	2001–2012	505/1127	48.3%
Fang ¹¹	Cardiovascular Research Network Venous Thromboembolism (CVRN VTE) consortium, US [†]	2004–2010	154/3056	5.0%
Present study	MarketScan, US	2011–2018	17 936/99 925	17.9%
Deep vein thrombosis				
Stein ¹²	Nationwide Emergency Department Sample, US	2007–2012	905 152/2 671 452	33.9%
Fang ¹¹	Cardiovascular Research Network Venous Thromboembolism (CVRN VTE) consortium, US [†]	2004–2010	1050/1928	54.5% [‡]
Present study	MarketScan, US	2011–2018	57 372/100 421	57.1%

PE indicates pulmonary embolism; and VTE, venous thromboembolism.

*Only 10.8% confirmed as PE upon evaluation of imaging and anticoagulant status.

[†]Kaiser Permanente Northern California; Kaiser Permanente Colorado, Geisinger Health System (central and northwest Pennsylvania), Marshfield Clinic (central and northwest Wisconsin).

[‡]Lower extremity thrombosis.

ARTICLE INFORMATION

Received December 11, 2020; accepted May 20, 2021.

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Sources of Funding

This work was supported by NIH National Heart Lung and Blood Institute grant R01-HL131579. Dr Alonso is also supported by NIH National Heart Lung and Blood Institute grant K24-HL148521.

Disclosures

None.

Supplementary Material

Table S1

REFERENCES

- Virani SS, Alonso A, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Chang AR, Cheng S, Delling FN, et al. Heart disease and stroke statistics-2020 update: a report from the American Heart Association. *Circulation*. 2020;141:e139–e596. DOI: 10.1161/CIR.0000000000000757.
- Kearon C, Akl EA, Ornelas J, Blaivas A, Jimenez D, Bounameaux H, Huisman M, King CS, Morris TA, Sood N, et al. Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report. *Chest*. 2016;149:315–352. DOI: 10.1016/j.chest.2015.11.026.
- Roy PM, Moumneh T, Penaloza A, Sanchez O. Outpatient management of pulmonary embolism. *Thromb Res*. 2017;155:92–100. DOI: 10.1016/j.thromres.2017.05.001.
- Tillman DJ, Charland SL, Witt DM. Effectiveness and economic impact associated with a program for outpatient management of acute deep vein thrombosis in a group model health maintenance organization. *Arch Intern Med*. 2000;160:2926–2932. DOI: 10.1001/archinte.160.19.2926.
- Fang MC, Fan D, Sung SH, Witt DM, Yale SH, Steinhilb SR, Go AS. Outcomes in adults with acute pulmonary embolism who are discharged from emergency departments: the cardiovascular research network venous thromboembolism study. *JAMA Intern Med*. 2015;175:1060–1062. DOI: 10.1001/jamainternmed.2015.0936.
- Schulman S, Kearon C, Kakkar AK, Mismetti P, Schellong S, Eriksson H, Baanstra D, Schnee J, Goldhaber SZ; RE-COVER Study Group. Dabigatran versus warfarin in the treatment of acute venous thromboembolism. *N Engl J Med*. 2009;361:2342–2352. DOI: 10.1056/NEJMoa0906598.
- EINSTEIN Investigators, Bauersachs R, Berkowitz SD, Brenner B, Buller HR, Decousus H, Gallus AS, Lensing AW, Misselwitz F, Prins MH, et al. Oral rivaroxaban for symptomatic venous thromboembolism. *N Engl J Med*. 2010;363:2499–2510. DOI: 10.1056/NEJMoa1007903.
- Hokusai-VTE Investigators, Büller HR, Décousus H, Grosso MA, Mercuri M, Middeldorp S, Prins MH, Raskob GE, Schellong SM, Schwocho L, et al. Edoxaban versus warfarin for the treatment of symptomatic venous thromboembolism. *N Engl J Med*. 2013;369:1406–1415. DOI: 10.1056/NEJMoa1306638.
- Agnelli G, Buller HR, Cohen A, Curto M, Gallus AS, Johnson M, Masiukiewicz U, Pak R, Thompson J, Raskob GE, et al. Oral apixaban for the treatment of acute venous thromboembolism. *N Engl J Med*. 2013;369:799–808. DOI: 10.1056/NEJMoa1302507.
- Schulman S, Kakkar AK, Goldhaber SZ, Schellong S, Eriksson H, Mismetti P, Christiansen AV, Friedman J, Le Maulf F, Peter N, et al. Treatment of acute venous thromboembolism with dabigatran or warfarin and pooled analysis. *Circulation*. 2014;129:764–772. DOI: 10.1161/CIRCULATIONAHA.113.004450.
- Fang MC, Fan D, Sung SH, Witt DM, Schmelzer JR, Williams MS, Yale SH, Baumgartner C, Go AS. Treatment and outcomes of acute pulmonary embolism and deep venous thrombosis: the CVRN VTE study. *Am J Med*. 2019;132:1450–1457.e1. DOI: 10.1016/j.amjmed.2019.05.040.
- Stein PD, Matta F, Hughes MJ. Home treatment of deep venous thrombosis according to comorbid conditions. *Am J Med*. 2016;129:392–397. DOI: 10.1016/j.amjmed.2015.10.022.
- Stein PD, Matta F, Hughes PG, Hourmouzis ZN, Hourmouzis NP, White RM, Ghiardi MM, Schwartz MA, Moore HL, Bach JA, et al. Home treatment of pulmonary embolism in the era of novel oral anticoagulants. *Am J Med*. 2016;129:974–977. DOI: 10.1016/j.amjmed.2016.03.035.
- Douce D, McClure LA, Lutsey P, Cushman M, Zakai NA. Outpatient treatment of deep vein thrombosis in the United States: the reasons

- for geographic and racial differences in stroke study. *J Hosp Med*. 2017;12:826–830. DOI: 10.12788/jhm.2831.
15. Kil-Drori AJ, Coulombe J, Suissa S, Hirsch A, Tagalakis V. Temporal trends in outpatient management of incident pulmonary embolism and associated mortality. *Thromb Res*. 2018;161:111–116. DOI: 10.1016/j.thromres.2017.10.026.
 16. Stein PD, Matta F, Hughes MJ. National trends in home treatment of acute pulmonary embolism. *Clin Appl Thromb Hemost*. 2018;24:115–121. DOI: 10.1177/1076029616674827.
 17. Roy PM, Corsi DJ, Carrier M, Theogene A, de Wit C, Dennie C, Le Gal G, Delluc A, Moumneh T, Rodger M, et al. Net clinical benefit of hospitalization versus outpatient management of patients with acute pulmonary embolism. *J Thromb Haemost*. 2017;15:685–694. DOI: 10.1111/jth.13629.
 18. IBM Watson Health (TM). IBM MarketScan Research Databases for Health Services Researchers (White Paper). 2018.
 19. Lutsey PL, Zakai NA, MacLehose RF, Norby FL, Walker RF, Roetker NS, Adam TJ, Alonso A. Risk of hospitalised bleeding in comparisons of oral anticoagulant options for the primary treatment of venous thromboembolism. *Br J Haematol*. 2019;185:903–911. DOI: 10.1111/bjh.15857.
 20. Schneeweiss S, Rassen JA, Brown JS, Rothman KJ, Happe L, Arlett P, Dal Pan G, Goettsch W, Murk W, Wang SV. Graphical depiction of longitudinal study designs in health care databases. *Ann Intern Med*. 2019;170:398–406. DOI: 10.7326/M18-3079.
 21. Sanfilippo KM, Wang T-F, Gage BF, Liu W, Carson KR. Improving accuracy of international classification of diseases codes for venous thromboembolism in administrative data. *Thromb Res*. 2015;135:616–620. DOI: 10.1016/j.thromres.2015.01.012.
 22. Cunningham A, Stein CM, Chung CP, Daugherty JR, Smalley WE, Ray WA. An automated database case definition for serious bleeding related to oral anticoagulant use. *Pharmacoepidemiol Drug Saf*. 2011;20:560–566. DOI: 10.1002/pds.2109.
 23. Zakai NA, Walker RF, MacLehose RF, Adam TJ, Alonso A, Lutsey PL. Impact of anticoagulant choice on hospitalized bleeding risk when treating cancer-associated venous thromboembolism. *J Thromb Haemost*. 2018;16:2403–2412. DOI: 10.1111/jth.14303.
 24. Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi JC, Saunders LD, Beck CA, Feasby TE, Ghali WA. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care*. 2005;43:1130–1139. DOI: 10.1097/01.mlr.0000182534.19832.83.
 25. Muller CJ, MacLehose RF. Estimating predicted probabilities from logistic regression: different methods correspond to different target populations. *Int J Epidemiol*. 2014;43:962–970. DOI: 10.1093/ije/dyu029.
 26. Localio AR, Margolis DJ, Berlin JA. Relative risks and confidence intervals were easily computed indirectly from multivariable logistic regression. *J Clin Epidemiol*. 2007;60:874–882. DOI: 10.1016/j.jclin.2006.12.001.
 27. Otero R, Uresandi F, Jiménez D, Cabezudo MÁ, Oribe M, Nauffal D, Conget F, Rodríguez C, Cayuela A. Home treatment in pulmonary embolism. *Thromb Res*. 2010;126:e1–e5. DOI: 10.1016/j.thromres.2009.09.026.
 28. Aujesky D, Roy PM, Verschuren F, Righini M, Osterwalder J, Egloff M, Renaud B, Verhamme P, Stone RA, Legall C, et al. Outpatient versus inpatient treatment for patients with acute pulmonary embolism: an international, open-label, randomised, non-inferiority trial. *Lancet*. 2011;378:41–48. DOI: 10.1016/S0140-6736(11)60824-6.

SUPPLEMENTAL MATERIAL

Table S1. ICD-9-CM and ICD-10-CM codes used to define incident VTE.

Revision	VTE codes
ICD-9-CM	415.1x, 451.1x, 453.2, 453.4x, 453.82, 453.83, 453.84, 453.85, 453.86, 453.87, 453.89, 453.9
ICD-10-CM	I26.0x, I26.9x, I80.1x, I80.20x, I82.210, I80.22x, I80.23x, I80.29x, I82.40x, I82.41x, I82.42x, I82.43x, I82.44x, I82.49x, I82.4Yx, I82.4Zx, I82.60x, I82.62x, I82.890, I82.A1x, I82.B1x, I82.C1x