

Pulmonary and Cardiovascular Guidelines and Consensus Statements

≋CHES1

Executive Summary Antithrombotic Therapy for VTE Disease: Second Update of the CHEST Guideline and Expert Panel Report

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16	Endorsed by the American Association for Clinical Chemistry, the American College of Clinical Pharmacy, the International Society on	71
17	Thrombosis and Haemostasis, and the American Society of Health- System Pharmacists.	72
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21	BACKGROUND: This is the 2nd update to the 9th edition of these guidelines. We provide	76
22	recommendations on 17 PICO (Population, Intervention, Comparator, Outcome) questions,	77
23 24	four of which have not been addressed previously.	70 70
24	METHODS: We generate strong and weak recommendations based on high-, moderate-, and	79 80
25 26	low-certainty evidence, using GRADE (Grading of Recommendations, Assessment, Devel-	81
20	opment, and Evaluation) methodology.	82
28	RESULTS: The panel generated 29 guidance statements, 13 of which are graded as strong	83
29	recommendations, covering aspects of antithrombotic management of VTE from initial	84
30	management through secondary prevention and risk reduction of postthrombotic syndrome	85
31	Four new guidance statements have been added that did not appear in the 9th edition (2012)	86
32	or 1st undate (2016). Fight statements have been substantially modified from the 1st undate	87
33	of 1st update (2010). Eight statements have been substantiany mounted from the 1st update.	88
34	CONCLUSION: New evidence has emerged since 2016 that further informs the standard of care	89
35	for patients with VTE. Substantial uncertainty remains regarding important management	90
36	questions, particularly in limited disease and special patient populations.	91
37	CHEST 2021; ∎(■):■-■	92
38	KEY WORDS, antithrombotic therapy: guidelines: thrombosis	93
39	KET WORDS. antumonibolic incrapy, guidelines, infolibosis	94
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49	APPREVIATIONS: AC - anticomplation, ADS - antichecological - benefits NICE - National Institute for Hackhard Core Providence	104
50	ADDREVIATIONS: $AC =$ anticoagunation; $APS =$ antiphospholipid syndrome; $ASH =$ American Society of Hematology; $AT9 =$ Antith- PE = pulmonary embolism; PICO = Population, Intervention,	105
51	rombotic Therapy and Prevention of Thrombosis, 9th ed: American Comparator, Outcome; PTS = postthrombotic syndrome; SVT =	106
52	College of Chest Physicians Evidence-Based Clinical Practice Guide- lines; CAT = cancer-associated thrombosis; CDT = catheter-directed	107

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thrombolysis; CVT = cerebral vein thrombosis; DOAC = direct-acting oral anticoagulant; ESC = European Society of Cardiology; EtD = ev-

idence-to-decision; ISSPE = isolated subsegmental pulmonary embo-

lism; IVC = inferior vena cava; LMWH = low-molecular-weight

111 Editor's Note: The online supplement to this guideline 112 [https://journal.chestnet.org/article/S0012-3692(21)01506-3/ 113 *fulltext]* contains an expanded introduction and methods 114 section with a full delineation of terminology, organization of 115 the PICO questions in the guideline, panel selection, and 116 description of conflict of interest management. For each 117 PICO, the online supplement contains the evidence profile 118 with complete summary of findings, additional comments, 119 background information, evidence-to-decision description, 120 121 and comparison with prior versions of the guideline. 122 CHEST has been developing and publishing guidelines for 123 the treatment of VTE for almost 40 years. The last full 124 edition of the guideline, Antithrombotic Therapy and 125 Prevention of Thrombosis, 9th ed: American College of Chest 126 127 Physicians Evidence-Based Clinical Practice Guidelines 128 ("AT9") was published in 2012.¹ Questions that form the 129 basis for recommendations are defined using the 130 Population, Intervention, Comparator, Outcome (PICO) 131 framework. AT9 addressed 50 PICO questions organized 132 into 11 domains and contained 91 guidance statements. 133 The 2016 update to the guideline, entitled Antithrombotic 134 135 Therapy for VTE Disease: CHEST Guideline and Expert 136 Panel Report, was published in 2016.² The 2016 update 137 ("1st update") addressed 12 PICO questions from AT9, 138 added three previously unaddressed PICOs, and contained 139 140

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166 29 guidance statements. This 2021 publication is the "2nd 167 update" to AT9. It addresses 14 PICOs contained in 168 previous editions (two of these have been merged into a 169 single PICO) and adds four previously unaddressed PICOs. 170 Thirty-two guidance statements are presented. The Q7 171 guidance statements are intended primarily for physicians 172 who treat patients with VTE, but may inform researchers in 173 selecting questions for future studies. Patients and policy 174 makers may also be informed by the guideline content. This 175 176 guideline is the first addressing this topic that will be 177 regularly updated as new evidence emerges according to 178 the Living Guidelines process of the American College of 179 Chest Physicians.³ 180

The order of presentation of the PICOs and guidance statements in the guideline is intended to follow the chronology of VTE management, and they are arranged as follows:

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186 • Whether to treat 187 Interventional and adjunctive treatments 188 Initiation phase 189 • Treatment phase 190 • Extended phase 191 • Complications of VTE 192 193 Guidance statements for antithrombotic therapy for 194 VTE are arranged according to the descriptions of the 195 phase of management: 196 • Initiation phase (\sim 5-21 days): The initial provision of 197 anticoagulants following VTE diagnosis 198 199 Treatment phase (3 months): The period after initiation that completes treatment for the acute VTE event 200 201 • Extended phase (3 months-no planned stop date): 202 The period of anticoagulant use at full or reduced 203

Precipitating factors for VTE have been characterized⁴ and are described as:

dose for the goal of secondary prevention

- VTE provoked by a major transient risk factor (present within the 3 months before VTE diagnosis)
- VTE provoked by a minor transient risk factor (present within the 2 months before VTE diagnosis)
- VTE provoked by a persistent risk factor
- Unprovoked VTE

Oral anticoagulants include vitamin K antagonists215(VKAs), direct thrombin inhibitors, and factor Xa216inhibitors (collectively referred to as *direct-acting oral*217anticoagulants [DOACs]). DOACs (apixaban,218dabigatran, edoxaban, and rivaroxaban) will be219presented in alphabetical order. The order should not be220

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interpreted as the guideline panel's order of preference for the use of these agents.

The following estimated incidences from the evidence profile for each PICO were used to classify the magnitude of desirable or undesirable effects of an intervention:

- Trivial: Fewer than 5 events per 1,000 subjects
- Small: Between 5 and 20 events per 1,000 subjects
- Moderate: Between 21 and 50 events per 1,000 subjects
- Large: More than 50 events per 1,000 subjects

To facilitate understanding of the magnitude of any outcome, the symbols \leftrightarrow , \uparrow , and \downarrow accompany each selected summary of findings to indicate whether the outcome addressed by the PICO does not cross unity (\leftrightarrow), is increased (\uparrow), or is decreased (\downarrow). Each summary reports a point estimate per 1,000 cases for the outcome and the CIs.

Certainty of evidence was based on the GRADE
(Grading of Recommendations, Assessment,
Development, and Evaluation) approach and
categorized as high, moderate, low, or very low.

PICO Topics and Guidance Statements

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 249 Whether and How to Prescribe Anticoagulants to
 250 Patients With Isolated Distal DVT

PICO Question: Should anticoagulant therapy vs no
anticoagulant therapy be given to patients with
isolated distal DVT?:

254 Guidance statements:

255 1. In patients with acute isolated distal DVT of the leg 256 and (i) without severe symptoms or risk factors for 257 extension (see text), we suggest serial imaging of the deep 258 veins for 2 weeks over anticoagulation (weak 259 recommendation, moderate-certainty evidence); or (ii) 260 with severe symptoms or risk factors for extension (see 261 text), we suggest anticoagulation over serial imaging of 262 the deep veins (weak recommendation, low-certainty 263 evidence). 264

265 2. In patients with acute isolated distal DVT of the leg 266 08 who are managed with serial imaging, we (i) 267 recommend no anticoagulation if the thrombus does 268 not extend (strong recommendation, moderate-269 certainty evidence), (ii) suggest anticoagulation if the 270 thrombus extends but remains confined to the distal 271 272 veins (weak recommendation, very low-certainty 273 evidence), and (iii) recommend anticoagulation if the 274 thrombus extends into the proximal veins (strong 275 recommendation, moderate-certainty evidence).

276 *Remarks:* Serial imaging refers to repeating ultrasound 277 once weekly, or with worsening symptoms, for 2 weeks 278 and anticoagulating only if distal thrombi propagate. 279 Patients at high risk for bleeding are more likely 280 to benefit from serial imaging. Evidence 281 suggests uncertainty that anticoagulation is superior 282 to no anticoagulation. Patients who place a high 283 value on avoiding the inconvenience of repeat 284 imaging and a low value on the inconvenience of 285 treatment and on the potential for bleeding are 286 likely to favor initial anticoagulation over serial imaging. 287

In patients with acute isolated distal DVT of the leg who are managed with anticoagulation, the same anticoagulation regimen as for patients with acute proximal should be used.

Selected summary of findings:

- ↓ Recurrent VTE at 3 months: 60 fewer events per 1,000 cases (from 77 fewer to 21 fewer)
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- ↔ Major bleeding at 3 months: 2 fewer events per 1,000 297 cases (from 7 fewer to 29 more) 298
- ↔ Overall mortality at 3 months: 0 fewer events per 1,000 cases (from 0 fewer to 0 more)
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301 **Comments:** Isolated distal DVT is defined as thrombus 302 affecting deep veins of the lower extremity with most 303 proximal extent distal to the popliteal vein. The key 304 management decision when isolated distal DVT is diagnosed 305 is whether to offer anticoagulation or perform serial 306 ultrasound (weekly for 2 weeks or with worsening symptoms) 307 and offer anticoagulation only if proximal propagation is 308 observed. Several factors that encapsulate patient preference 309 and risk influence this decision, further detailed in the online 310 supplement to this guideline [https://journal.chestnet.org/ 311 312 article/S0012-3692(21)01506-3/fulltext]. 313

Other guidelines:

2018 American Society of Hematology (ASH) guideline: 315 No specific guidance.⁵ 316

2020 National Institute for Health and Care Excellence (NICE) guideline: Recommendations for only proximal DVT.⁶ 320

Whether to Treat Isolated Subsegmental Pulmonary Embolism

PICO Question: Should anticoagulant therapy vs no
anticoagulant therapy be given to patients with
isolated subsegmental pulmonary embolism?:324
325Guidance statement:3263. In patients with subsegmental PE (no involvement
of more proximal pulmonary arteries) and no329

proximal DVT in the legs who have a (i) low risk for ³³⁰

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331	recurrent VTE (see text), we suggest clinical
332	surveillance over anticoagulation (weak
333	recommendation, low-certainty evidence) or (ii) high
334	risk for recurrent VTE (see text), we suggest
335	anticoagulation over clinical surveillance (weak
336	recommendation low containty avidence)
337	recommendation, low-certainty evidence).

338 **Comments:** Because isolated subsegmental PE (ISSPE) 339 is associated with DVT, the panel endorsed excluding 340 proximal DVT with bilateral leg ultrasound, or at 341 another location if clinically suspected (eg, upper 342 extremity if DVT is suspected), before choosing to 343 withhold anticoagulation for ISSPE. Clinical surveillance 344 involves patient education to ensure an understanding of 345 clinical signs and symptoms worrisome for progressive 346 thrombosis that would require return for reassessment. 347 Considering whether ISSPE is a true positive finding, 348 and the likelihood of progressive thrombosis, informs 349 350 decision-making regarding anticoagulation, further 351 detailed in the online supplement to this guideline 352 [https://journal.chestnet.org/article/S0012-3692(21)015 353 06-3/fulltext]. 354

355 Other guidelines:

2019 European Society of Cardiology (ESC)
guideline: Suggests further imaging to confirm PE
when isolated subsegmental filling defects are seen on
CT pulmonary angiography.⁷

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Whether to Treat an Incidentally Diagnosed Asymptomatic Acute PE

PICO Question: Should anticoagulant therapy vs no anticoagulant therapy be given to patients with incidentally diagnosed asymptomatic acute pulmonary embolism?:

368 Guidance statement:

4. In patients who are incidentally found to have
asymptomatic PE, we suggest the same initial and
long-term anticoagulation as for comparable patients
with symptomatic PE (weak recommendation,
moderate-certainty evidence).

Comments: Asymptomatic PE is diagnosed in about 375 376 1% of outpatients and about 4% of inpatients who have 377 contrast-enhanced chest CT scans (notably performed 378 during a diagnostic workup in patients with cancer) and 379 may represent false-positive imaging findings; therefore 380 it is important to ensure a false-positive result is not 381 likely. Observational data suggest that asymptomatic PE 382 carries a similar prognosis to symptomatic PE (data 383 predominantly from patients with cancer), implying a 384 similar approach to treatment is needed.⁸ 385

Other guidelines:

2019 ESC: Suggests anticoagulation for asymptomatic/
incidental PE in patients with cancer but notes387
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treatment of asymptomatic/incidental PE in otherpatient groups represents an important evidence gap.390
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Whether to Treat Cerebral Vein Thrombosis PICO Question: Should anticoagulant therapy vs no anticoagulant therapy be given to patients with cerebral vein or cerebral venous sinus thrombosis?:

Guidance statement:

5. In patients with cerebral vein/venous sinus thrombosis, we recommend anticoagulation therapy for at least the treatment phase (first 3 months) over no anticoagulant therapy (strong recommendation, low-certainty evidence).

Remark: While the formal evidence-to-decision (EtD) assessment warrants a weak recommendation in favor of anticoagulation ("suggest"), the panelists upgraded the guidance to a strong recommendation, placing a very high value on an uncertain but potentially life-preserving benefit.⁹

Selected summary of findings:

\leftrightarrow	Overall mortality at 90 days: 108 fewer events per
	1,000 cases (from 162 fewer to 47 more)

↔ New intracranial hemorrhage or PE at 90 days: 69
 fewer events per 1,000 cases (from – fewer to 83 more) 011
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Comments: Anticoagulation therapy (with most evidence regarding the use of low-molecular-weight heparin [LMWH]) appears safe and effective for the treatment of cerebral vein thrombosis (CVT). The guidance statement applies both to patients who have and have not experienced intracranial hemorrhage as a complication of CVT. No randomized controlled trial evidence currently evaluates the use of DOACs among patients with CVT.

Other guidelines:

2016 Anticoagulation (AC) Forum guidance statement: Includes six guidance statements related to CVT. Two statements relate to initial and treatment-phase anticoagulant therapy and are similar to this guidance statement.¹⁰

2014 American Heart Association/American Stroke Association guideline: Contains similar guidance and includes an additional statement on duration of anticoagulation and subsequent use of antiplatelet therapy.¹¹

4 Guidelines and Consensus Statements

4 4 1	Thrembolytic and Machanical Interventions in	11 10 01 / / 011 1 00/ 1	406
441	Acute DVT	bleeding risk, we suggest systemically administered	490
442	NGC Oregins Should through the mathemical or	thrombolytic therapy over no such therapy (weak	498
444	PICO Question: Should thrombolytic, mechanical, or	recommendation, low-certainty evidence).	499
445	the second	Remark: Studies of systemically administered	500
446	therapy alone be given to patients with acute deep vein	thrombolytic therapy have utilized different agents at	5 01
447	thrombosis:	varving doses. Due to lack of comparative data between	502
448	Guidance statement:	these approaches, the panel does not endorse one agent	503
449	6. In patients with acute DVT of the leg we suggest	or dosing strategy over another	504
450	anticoagulant therapy alone over interventional	of dooling strategy over another.	505
451	(thrombolytic, mechanical, or pharmacomechanical)	8. In most patients with acute PE not associated with	506
452	therapy (weak recommendation, moderate-certainty	hypotension, we recommend against systemically	507
453	evidence).	administered thrombolytic therapy (strong	508
454	Selected summary of findings	recommendation, low-certainty evidence).	509
455	Destthement at is seen draws (Concentrates to Forecase of		510
456	Postthrombotic syndrome (6 months to 5 years of	Remark: While the formal EtD assessment warrants a	511
457	follow-up): 116 fewer events per 1,000 cases (from	weak recommendation in favor of anticoagulation	512
458	180 fewer to 37 fewer)	("suggest"), the panelists upgraded the guidance to a	513
459	\downarrow Postthrombotic syndrome at > 5 years: 308 fewer	strong recommendation, placing a very high value on	514
460	events per 1,000 cases (from 400 fewer to 189 fewer)	avoiding the potential increase in harm when the	515
461	↑ Bleeding (excluding intracranial and minor	magnitude of benefit is variable. ⁹	516
462	bleeding): 33 more events per 1,000 cases (from 13		517
463	more to 64 more)	9. In selected patients with acute PE who deteriorate (see	518
464	\leftrightarrow Early stroke or intracerebral bleeding: 0 fewer per	remarks) after starting anticoagulant therapy but have	519
465	1,000 cases (from 0 fewer to 0 fewer)	yet to develop hypotension and who have an acceptable	520
400	↔ All-cause mortality (1-30 days of follow-up): 3 fewer	bleeding risk, we suggest systemically administered	521
407	events per 1,000 cases (from 9 fewer to 11 more)	thrombolytic therapy over no such therapy (weak	522
408	Comments: In patients with very severe limb	recommendation, low-certainty evidence).	523 524
409	threatening DVT (such as these with phlagmasis or		525
470	threatening DV1 (such as those with philegmasia of	Remark: Such patients should be treated with full	526
472	threatened venous gangrene) the benefits of more rapid	anticoagulation and monitored for evidence of clinical	527
472	thrombus resolution may outweigh the risk of harm. In	deterioration (decrease in systolic BP, increase in heart	528
474	contrast, a systematic review and meta-analysis	rate, worsening gas exchange, signs of inadequate	529
475	suggested no benefit of thrombolysis for either	perfusion, worsening RV function, or increasing cardiac	014 530
476	iliofemoral or femoropopliteal DVT. ^{12,13} All catheter-	biomarkers). Such deterioration should prompt	531
477	directed methods (thrombolytic, mechanical, or	consideration of thrombolytic therapy in the absence of	532
478	pharmacomechanical) were pooled for comparison.	frank shock if the bleeding risk is deemed acceptable.	533
479	Other guidelines:		534
480	2016 AC Forum: Suggests individual risk-to-benefit	Selected summary of findings:	535
481	analysis for catheter-directed therapy (CDT) and suggests	\downarrow Recurrent PE (7 days to 12 months of follow-up): 19	536
482	against systemic thrombolysis for DVT ¹⁴	fewer events per 1,000 cases (from 27 fewer to 4	537
483	against systemic unombolysis for D v 1.	fewer)	538
484	2020 NICE: Suggests considering CDT in patients	↑ Major bleeding (7 days to 12 months of follow-up): 65	539
485	with iliofemoral DVT who have symptoms lasting less	more events per 1,000 cases (from 33 more to 107	540
486	than 14 days, good functional status, a life expectancy of	more)	541
487	1 year or more, and low risk for bleeding. ⁶	\downarrow All-cause mortality (7 days to 12 months of follow-up):	542
488	Thrombolytic Therapy in Patients With Acute PF	20 fewer events per 1,000 cases (from 30 fewer to 6 fewer)	543
489	NICO Question Should systemic thromholytic	Commenter Agreement existed among the penalists to	544
490	thereby we anticeequilant thereby clone he given to	administer thrombolicies to most nation to (in the choose	545
491	netionte with costs pulmoners embolicer?	of a contraindication) with acute DE and prolonged	540 547
492 102	Cuidenes statements	by a contraindication) with acute PE and protonged	54/ 578
493	Guidance statements:	DE with out hymotoneion ¹⁵ has been successful at	540
495	/. In patients with acute PE associated with hypotension	PE without nypotension has been associated with a	550
	(eg, systolic BP < 90 mm Hg) who do not have a high	reduction in risk for cardiovascular collapse but	500

increased major (including intracranial) bleeding, with
the benefits and harms finely balanced and with no
convincing net benefit from thrombolytic therapy.

555 Other guidelines:

2016 AC Forum: Suggests an individual risk-to-benefit
analysis for use of thrombolysis in patients with acute PE,
and suggests that the benefit-to-risk ratio is more

559 favorable for PE with hypotension.¹⁴

560 2019 ESC: Recommends thrombolysis for high-risk PE 561 and indicates CDT should be considered in high-risk 562 563 patients with PE in whom systemic thrombolysis is 564 contraindicated or has failed. They recommend systemic 565 thrombolysis in patients with intermediate- or low-risk 566 PE who have hemodynamic deterioration, but are 567 against the routine use of such therapy.⁷ 568

2020 NICE: Recommends that thrombolysis be considered
in patients with hemodynamic instability, but against its
use in patients who are hemodynamically stable, regardless
of the presence of right ventricular dysfunction.⁶

574 Catheter-Assisted Thrombus Removal in Patients575 With Acute PE

576 PICO Question: Should mechanical or

pharmacomechanical interventions vs anticoagulant
therapy alone be given to patients with acute
pulmonary embolism?:

581 Guidance statements:

10. In patients with acute PE who are treated with a
thrombolytic agent, we suggest systemic thrombolytic
therapy using a peripheral vein over catheter-directed
thrombolysis (CDT) (weak recommendation, lowcertainty evidence).

587 11. In patients with acute PE associated with 588 hypotension who also have (i) a high bleeding risk, 589 (ii) failed systemic thrombolysis, or (iii) shock that is 590 likely to cause death before systemic thrombolysis 591 592 can take effect (eg, within hours), if appropriate 593 expertise and resources are available, we suggest 594 catheter-assisted thrombus removal over no such 595 intervention (weak recommendation, low-certainty 596 evidence). 597

598 Comments: No randomized trials or observational
599 studies have compared contemporary CDT with
500 systemic thrombolytic therapy. Evidence for the use of
501 mechanical or pharmacomechanical interventions
502 compared with anticoagulation alone is of low certainty,
503 and our recommendations are weak.

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Other guidelines:

2016 AC Forum: Suggests both systemic and catheterdirected or pharmacomechanical therapy are effective options for massive PE in appropriately selected patients.¹⁴

2019 ESC: Recommends percutaneous catheter-directed treatment should be considered for patients with high-risk PE, in whom thrombolysis is contraindicated or has failed.⁷

2020 NICE: Addresses	only systemic thrombolytic
therapy for PE. ⁶	

Inferior Vena Cava Filter in Addition to Anticoagulation in Patients With Acute PE

PICO Question: Should an inferior vena cava filter (permanent or retrievable) be used in addition to anticoagulant therapy vs anticoagulant therapy alone in patients with acute pulmonary embolism?: Guidance statements:

12. In patients with acute DVT of the leg, we recommend against the use of an inferior vena cava (IVC) filter in addition to anticoagulants (strong recommendation, moderate-certainty evidence).

Selected summary of findings²:

- ↔ All-cause mortality at 90 days: 15 more events per 1,000 cases (from 24 fewer to 96 more)
- ↔ Recurrent PE at 90 days: 15 more events per 1,000 cases (from 7 fewer to 104 more)
- ↔ Major bleeding at 90 days: 10 fewer events per 1,000 cases (from 34 fewer to 49 more)

13. In patients with acute proximal DVT of the leg and a contraindication to anticoagulation, we recommend the use of an IVC filter (strong recommendation, moderate-certainty evidence).

Comments: IVC filters are overused and, given the known risks of harm and significant uncertainty of benefit of IVC filters,¹⁶ the panel endorses a conservative approach to their placement by suggesting use only in patients with acute VTE (eg, diagnosed in the preceding 1 month) with an absolute contraindication to anticoagulation (eg, active major bleeding, severe thrombocytopenia, high bleeding risk, CNS lesion).

Other guidelines:

2016 AC Forum: Suggests IVC filter placement in patients with acute PE or proximal DVT and a contraindication to anticoagulation.¹⁴

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661 662 663 664 665 666	2019 ESC: Recommends considering an IVC filter in patients with acute PE and an absolute contraindication to anticoagulation and in patients with progressive PE despite anticoagulation. It recommends against routine use of IVC filter. ⁷	Other guidelines: 2016 AC Forum: Suggests many patients with PE can be treated as outpatients, and suggests evaluation with laboratory, imaging, and risk prediction models to select suitable patients. ¹⁹	716 717 718 719 720 721
667 668 669 670 671	2020 NICE: Suggests considering an IVC filter in patients with proximal DVT or PE when anticoagulation is contraindicated, and when new or progressive PE occurs during anticoagulation. Filter use is also	 2019 ESC: Suggests that patients with low-risk PE can be treated with early discharge or at home.⁷ 2020 NICE: Suggests considering outpatient treatment in patients with low-risk PE, using a validated risk- 	722 723 724 725 726
672 673 674 675	suggested in the setting of a clinical trial. ⁶ Setting of Initial Anticoagulation PICO Question: Should treatment in hospital	stratification tool. ⁶ Choice of Treatment-Phase Anticoagulant PICO Question: Should standard anticoagulation	727 728 729 730
676 677 678 679	vs outpatient treatment be provided to patients with acute pulmonary embolism?: Guidance statement:	(LMWH transitioned to an oral VKA) vs DOAC be provided for treatment-phase therapy in patients with acute venous thromboembolism?:	731 732 733 734
680 681 682 683	14. In patients with low-risk PE we recommend outpatient treatment over hospitalization provided access to medications, ability to access outpatient care, and home circumstances are adequate (strong	15. In patients with VTE (DVT of the leg or PE) we recommend apixaban, dabigatran, edoxaban, or rivaroxaban over VKA as treatment-phase (first	735 736 737 738
684 685 686 687	<i>Remark:</i> While the formal EtD assessment warrants a weak recommendation in favor of outpatient treatment	3 months) anticoagulant therapy (strong recommendation, moderate-certainty evidence). <i>Remark:</i> While the certainty of the evidence is moderate, the papelists choice a strong recommendation, placing a	739 740 741 742
688 689 690 691	to a strong recommendation, placing a very high value on avoiding the potential increase in risk of harm (including much greater cost) related to hospitalization	very high value on avoiding the potential increase in harm in the setting of a similar magnitude of benefit. ⁹ Selected summary of findings: Comparison: Dabigatran	743 744 745 746
692 693 694 695	even though the magnitude of benefit is similar. ⁹ Selected summary of findings: ↔ Long-term all-cause mortality (at 90 days): 0 fewer	 etexilate vs standard anticoagulation ↔ Recurrent VTE at 6 months: 2 fewer events per 1,000 cases (from 15 fewer to 20 more) 	747 748 749 750
696 697 698 699	 events per 1,000 cases (from 4 fewer to 64 more) ↔ Major bleeding at 90 days: 0 fewer events per 1,000 cases (from 0 fewer to 0 more) ↔ Recurrent PE at 90 days: 0 fewer events per 1,000 	 ? All-cause mortality: Not estimable ↔ Major bleeding: 5 fewer events per 1,000 cases (from 9 fewer to 7 more) 	751 752 753 754
700 701 702 703	cases (from 0 fewer to 0 more) Comments: Home treatment is more convenient and less expensive than hospital treatment and is preferred	 Comparison: Oral Xa infibitor vs standard anticoagulation ↔ Recurrent VTE at 6 months: 5 fewer events per 1,000 cases (from 12 fewer to 4 more) 	755 756 757 758
704 705 706 707	by most patients." Patients who satisfy all the following criteria are suitable for treatment of acute PE out of the hospital: (1) clinically stable with good cardiopulmonary reserve; (2) no contraindications such as recent bleeding,	 ↔ All-cause mortality: 3 more events per 1,000 cases (from 4 fewer to 14 more) ↔ Major bleeding: 1 fewer event per 1,000 cases (from 6 four to 7 more) 	759 760 761 762
708 709 710 711	severe renal or liver disease, or severe thrombocytopenia (ie, $< 50,000/\text{mm}^3$); (3) expected to be compliant with treatment; and (4) the patient feels well enough to be treated at home. In addition, a system to ensure	Comments: The choice of anticoagulant for the treatment phase of VTE necessitates consideration of patient-specific factors (eg, renal function, direct patient	763 764 765 766
712 713 714 715	outpatient follow-up and access to prompt care in the event of patients' questions or worsening of symptoms should be in place. ¹⁸	expense, payor considerations, bleeding risk, anticipated compliance), drug availability, and the patient's preferences. Guidance is driven by the comparable	767 768 769 770

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 \leftrightarrow Major GI bleeding (6-12 months of follow-up): 2

therapy. DOACs also offer greater convenience. Certain more events per 1,000 cases (from 7 fewer to 22 more) 773 clinical situations favor VKA (eg, extremes of weight, Comments: In patients with VTE and cancer (cancer-774 severe renal impairment, or presence of associated thrombosis [CAT]) there is a higher risk for 775 antiphospholipid syndrome). Cost may also drive the recurrence as well as a higher risk for major bleeding 776 clinical decision. than in patients with VTE without cancer.²⁰ Because DOACs have not been compared head-to-head among 778 Other guidelines: 779 patients with cancer, the panelists remarked that 2016 AC Forum: Suggests DOACs as an alternative to 780 standard anticoagulation in appropriately selected apixaban or LMWH may be the preferred option in 781 patients.19 patients with luminal GI malignancies who place higher 782 value on avoiding GI major bleeding, whereas others 2018 ASH: Suggests VKA or LMWH rather than DOAC 783 may elect the convenience of once-daily DOAC therapy 784 in patients requiring administration of inhibitors or (edoxaban or rivaroxaban). However, LMWH has the 785 inducers of P-glycoprotein or strong inhibitors or potential advantages of bypassing the GI system in 786 inducers of cytochrome P450 enzymes.⁵ patients with nausea or mucositis and may be more 787 2019 ESC: Recommends DOAC in preference to VKA in easily dose-adjusted in patients with thrombocytopenia 788 eligible patients ready to start an oral anticoagulant.⁷ 789 due to cancer therapy.^{20,21} 790 2020 NICE: Recommends apixaban or rivaroxaban as Other guidelines: 791 initial choices, and suggests other regimens for patients 792 2016 AC Forum: Suggests LMWH for a minimum of not suitable for one of these two drugs.⁶ 793 6 months in patients with CAT.²² 794 DOACs in Cancer-Associated Thrombosis 2018 National Comprehensive Cancer Network 795 PICO Question: Should LMWH vs oral Xa inhibitor guideline: Indicates that LMWH is the preferred agent 796 be provided for treatment-phase therapy in patients for the first six months in patients with CAT.²¹ 797 798 with acute venous thromboembolism in the setting of 2019 European Society of Cardiology guideline: 799 cancer ("cancer-associated thrombosis")?: Recommends LMWH, edoxaban, or rivaroxaban for 800 Guidance statement: management of CAT. 801 16. In patients with acute VTE in the setting of cancer 802 (cancer-associated thrombosis) we recommend an oral 2019 International clinical practice guidelines (for the 803 Xa inhibitor (apixaban, edoxaban, rivaroxaban) over treatment and prophylaxis of VTE in patients with 804 LMWH for the initiation and treatment phases of cancer): Recommend LMWH for the initial treatment of 805 therapy (strong recommendation, moderate-certainty established VTE in CAT, or rivaroxaban or edoxaban in 806 evidence). patients who do not have a high risk of GI or 807 808 genitourinary bleeding.²³ Remark: Edoxaban and rivaroxaban appear to be 8<mark>0</mark>9 associated with a higher risk of gastrointestinal major 2020 NICE: Suggests considering a DOAC for patients 810 bleeding than LMWH in patients with CAT and a with CAT, and LMWH alone or LMWH transitioned to 811 luminal gastrointestinal malignancy, while apixaban warfarin in patients unsuitable for DOAC.⁶ 812 does not. Apixaban or LMWH may be the preferred 813 option in patients with luminal GI malignancies. 814 DOACs in Patients With Antiphospholipid Syndrome 815 Selected summary of findings: **PICO Question: Should standard anticoagulation** 816 ↓ Recurrent VTE at 6 months: 31 fewer events per (heparinoid transitioned to an oral VKA inhibitor) 817 1,000 cases (from 47 fewer to 7 fewer) vs DOAC be provided for treatment- and extended-818 \leftrightarrow Major bleeding at 6 months: 10 more events per phase therapy in patients with acute venous 819 1,000 cases (from 6 fewer to 36 more) thromboembolism in the setting of antiphospholipid 820 syndrome?: 821 Comparison: Edoxaban/rivaroxaban vs LMWH 822 **Guidance statement:**

↑ Major GI bleeding (6-12 months of follow-up): 25 823 more events per 1,000 cases (from 5 more to 65 more) 824

825 Comparison: Apixaban vs LMWH

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efficacy and improved safety of DOACs over traditional

17. In patients with confirmed antiphospholipid

syndrome being managed with anticoagulant therapy, Q18

we suggest adjusted-dose VKA (target INR 2.5) over Q19

8 Guidelines and Consensus Statements

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881	DOAC therapy during the treatment phase (weak	19 In natients with SVT who are treated with	936
882	recommendation. low-certainty evidence).	anticoagulation, we suggest fondaparinux 2.5 mg	937
883		daily over other anticoagulant treatment regimens	938
884	Remark: Initiating VKA therapy should include an	such as (prophylactic or therapeutic) dose of	939
885	overlapping period of parenteral anticoagulation.	IMWH (weak recommendation low-certainty	940
886	Selected summary of findings	evidence)	941
887	\leftrightarrow Any thrombosis at 6 months: 0 fewer events per	evidence).	942
888	1 000 cases (from 0 fewer to 0 more)	20. In patients with SVT who refuse or are unable to	943
889	\leftrightarrow Any thrombosis at 36 months: 63 more events per	use parenteral anticoagulation, we suggest	944
890	Any thromosis at 50 months. 05 more events per	rivaroxaban 10 mg daily as a reasonable alternative	945
891	1,000 cases (from 14 fewer to 200 filore)	for fondaparinux 2.5 mg daily (weak	946
892 802	↔ Major bleeding at 6 months: 1 more event per 1,000	recommendation, low-certainty evidence).	947
804	Cases (110111 9 lewer to 65 11101e)	Salastad summary of findings, Comparison,	940
895	\leftrightarrow Major bleeding at 36 months: To lewer events per	Deschalastic LMMUL as all sales	949
896	1,000 cases (from 52 fewer to 108 more)	Prophylactic LMWH vs placebo	951
897	\leftrightarrow All-cause mortality at 6 months: 2 more events per	↔ VTE at 3 months: 10 more events per 1,000 cases	952
898	1,000 cases (from 21 fewer to 86 more)	(from 28 fewer to 129 more)	953
899	\leftrightarrow All-cause mortality at 36 months: 21 more events	↓ Extension or recurrence of SVT: 185 fewer events	954
900	per 1,000 cases (from 19 fewer to 183 more)	per 1,000 cases (from 244 fewer to 86 fewer)	955
901	Comments: Panelists agreed that DOACs should be	? Major bleeding at 97 days: Not estimable	956
902	avoided in patients with antiphospholipid syndrome	Comparison. Therepoutic I MWH vs placebo	957
903	(APS), especially if positive for lupus anticoagulant, anti-	Comparison. Therapeutic Livi will vs placebo	958
904	cardiolipin, and anti- β_2 -glycoprotein-I antibodies (ie,	\leftrightarrow VTE at 3 months: 7 fewer events per 1,000 cases	959
905	"triple-positive"), and in those with arterial thrombosis.	(from 34 fewer to 92 more)	960
906	For these patients VKA should be elected as first-line	↓ Extension or recurrence of SVT: 178 fewer events	961
907	therapy.	per 1,000 cases (from 241 fewer to 76 fewer)	962
908	Other guidelines	? Major bleeding at 97 days: Not estimable	903
910	2018 ASH. No specific guidence statement on treatment	Comparison: Fondaparinux ys rivaroxaban	965
911	2018 ASH: No specific guidance statement on treatment		966
912	of patients with APS.	\leftrightarrow VTE at 90 days: 9 fewer events per 1,000 cases (from	967
913	2020 International Society on Thrombosis and	12 fewer to 28 more)	968
914	Haemostasis Scientific Subcommittee guidance	? Major bleeding at 45 days: Not estimable	969
915 <mark>Q20</mark>	statement: Recommends VKA over DOAC for most	\leftrightarrow All-cause mortality at 90 days: 3 fewer events per	970
916	patients with APS. ²⁴	1,000 cases (from 4 fewer to 30 more)	971
917		Comments: SVT has been less well studied than DVT,	972
918	2020 16th International Congress on Antiphospholipid	likely occurs more often, ²⁶ and usually affects the lower	973
919	Antibodies Task Force report on antipnospholipid	limbs. Although historically considered a benign disease,	974
920	syndrome: Guidance is similar to our statement.	more recent appreciation of the seriousness of SVT has	975
921	Dela of Antionan Jatim in Country Countries	informed treatment studies. The anticoagulants	970
922	Kole of Anticoagulation in Spontaneous Superficial	fondaparinux and rivaroxaban 10 mg orally once daily	977
924		for 45 days prevent progression of SVT, DVT, PE, or	979
925	PICO Question: Should anticoaguiant therapy vs no	death among select patients with SVT. ²⁷ Factors that	980
926	anticoaguiant therapy be provided to patients with	favor the use of anticoagulation for the treatment of SVT	981
927	acute superficial venous thrombosis of the lower	include extensive SVT; involvement above the knee,	982
928	extremities::	particularly if close to the saphenofemoral junction;	983
929	Guidance statements:	severe symptoms; involvement of the greater saphenous	984
930	10. In patients with superficial venous thrombosis	vein; history of VTE or SVT; active cancer; and recent	985
931	$(5 \vee 1)$ of the lower limb at increased risk of clot	surgery.	986
932	progression to DVI or PE (see text), we suggest the	Other guidelines	987
933	use of anticoagulation for 45 days over no	No recent avidence based muidelines for management of	988
934 025	anticoagulation (weak recommendation, moderate-	No recent evidence-based guidennes for management of	989 000
200	certainty evidence).	Sv 1 were identified.	390

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991 A review commissioned by the American Society of 992 Hematology's Education Program included a 993 management algorithm that suggested either 994 fondaparinux or rivaroxaban in selected patients with 995 more extensive SVT, risk factors for VTE, and no 996 contraindications to anticoagulant therapy.²⁶ 997 998 Duration of Anticoagulation in Patients With Acute 999 VTE 1000 PICO Question: Should extended-phase anticoagulant 1001 therapy vs no extended-phase anticoagulant therapy 1002 be provided to patients with venous 1003 thromboembolism who have completed the treatment 1004 1005 phase of therapy?: 1006 **Guidance statements:** 1007 **Duration of Treatment Phase of Anticoagulation** 1008 21. In patients with acute VTE who do not have a 1009 contraindication we recommend a 3-month treatment 1010 phase of anticoagulation (strong recommendation, 1011 1012 moderate-certainty evidence). 1013 Remark: On completion of the 3-month treatment phase 1014 of therapy, all patients should be assessed for extended-1015 phase therapy. 1016 1017 **Extended-Phase Therapy** 1018 1019 22. In patients with VTE diagnosed in the setting of a 1020 major transient risk factor (see text), we recommend 1021 against offering extended-phase anticoagulation 1022 (strong recommendation, moderate-certainty 1023 evidence). 1024 1025 23. In patients with VTE diagnosed in the setting of a 1026 minor transient risk factor (see text), we suggest 1027 against offering extended-phase anticoagulation 1028 (weak recommendation, moderate-certainty 1029 evidence). 1030 1031 24. In patients with VTE diagnosed in the absence of 1032 transient provocation (unprovoked VTE or provoked 1033 by persistent risk factor), we recommend offering 1034 extended-phase anticoagulation with a DOAC (strong 1035 recommendation, moderate-certainty evidence). 1036 1037 25. In patients with VTE diagnosed in the absence of 1038 transient risk factor (unprovoked VTE or provoked by 1039 a persistent risk factor) who cannot receive a DOAC, 1040 we suggest offering extended-phase anticoagulation 1041 with a VKA (weak recommendation, moderate-1042 certainty evidence). 1043 1044 Remarks: The recommendation to offer extended-phase 1045 anticoagulation would not automatically imply that all

patients with unprovoked VTE receive extended1046therapy. Patient preference and predicted risk of1047recurrent VTE or bleeding should also influence the1048decision to proceed with, or continue, extended-phase1049anticoagulation therapy.1051

Patients who receive extended-phase anticoagulation should have this decision reevaluated at least on an annual basis, and at times of significant change in health status.

Extended-phase anticoagulation does not have a 1056 predefined stop date. However, studies of extended-1057 phase anticoagulation followed patients for durations of Q22 1058 1059 about 2 to 4 years. While most patients in these studies 1060 did not stop anticoagulation therapy at the end of 1061 follow-up, the risk:benefit balance of continuing 1062 extended anticoagulation therapy beyond this time is 1063 uncertain. It is advised that this decision involve shared 1064 decision-making with the patient, taking into 1065 consideration her/his values and preferences. 1066

Selected summary of findings:

- ↓ Recurrent VTE at 7 to 48 months of follow-up: 64 fewer events per 1,000 cases (from 80 fewer to 37 fewer)
 ↑ Major bleeding (7-48 months of follow-up): 6 more events per 1,000 cases (from 1 more to 14 more)
- ↔ All-cause mortality (7-48 months of follow-up): 4 fewer events per 1,000 cases (from 10 fewer to 5 more)

Comments: Duration of anticoagulation refers to the length of the initiation and treatment phases of anticoagulant therapy as well as the decision on whether to offer extended-phase therapy. While extended-phase therapy is defined as having no planned stop date, the longest duration of follow up to assess outcomes was about four years. Although participants in these trials generally did not discontinue anticoagulants at the conclusion of follow-up, the risk-to-benefit balance of continuing anticoagulants beyond this period is less certain. Patients receiving extended-phase anticoagulation should be periodically reassessed for bleeding risk, burdens of therapy, and any change in values and preferences. Categorization of risk factors is further detailed in the online supplement to this guideline [https://journal.chestnet.org/article/S0012-36 92(21)01506-3/fulltext].

Other guidelines:

2016 AC Forum: Suggests 3 months of anticoagulation for patients with surgical risk factor-associated VTE, for at least 3 months in patients with medical illness or travelassociated VTE, and extended anticoagulation for

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1101 1102 1103 1104	patients with unprovoked VTE. They note uncertainty regarding extended anticoagulation of longer than 2 years. ¹⁹	 ↔ Major or clinically relevant nonmajor bleeding at 12 months: 10 fewer events per 1,000 cases (from 18 fewer to 2 more) ? Mortality: Not estimable 	1156 1157 1158 1159
1105	after 3 months in patients with DE secondary to a major	Comments : When electing extended -phase	1160
1100	transient/asserble rick forten recommende in definite	antithromhotic therapy the choice of a particular drug	1161
1107	transient/reversible risk factor, recommends indefinite	and dose is informed by multiple veriables. We suggest	1162
1100	anticoagulation for patients with recurrent unprovoked	choice of low does ve full does (treatment phase)	1164
1110	PE and in patients with PE and APS, and suggests	entire or low-dose vs full-dose (treatment phase)	1165
1110	considering indefinite anticoagulation in patients with	anticoaguiants when available, while considering	1166
1112	initial unprovoked PE, PE provoked by a persistent risk	patient-specific variables including BMI, renal function,	1167
1113	factor other than APS, and in patients with PE	adherence to dosing regimen, and cost." Should	1168
1114	associated with a minor transient or reversible risk	cessation of anticoagulation be elected, then we suggest	1169
1115	factor. ⁷	aspirin over no such therapy (see Aspirin for Extended	1170
1116	2020 NICE, Suggests considering stopping	Treatment of VTE for discussion).	1171
1117	anticoorgulants after 3 months (or 3.6 months in patients	Other guidelines:	1172
1118	with active concern following VTE in the acting of a	2016 AC Forum: Notes that reduced-dose DOAC "may	1173
1119	with active cancer) following vie in the setting of a	be attractive" for some nationts undergoing extended	1174
1120	provoking factor that is no longer present; and suggests	thereasy. ¹⁹	1175
1121	continuing anticoagulation beyond 3 months (3-	tilerapy.	1176
1122	6 months in patients with active cancer) following an	2019 ESC: Recommends reducing the dose of	1177
1123	unprovoked VTE.	apixaban or rivaroxaban after 6 months of full-dose	1178
1124	2020 ASH: Describes transient risk factors as	therapy in patients receiving extended	1179
1125	surgical/trauma or nonsurgical, that risk for	anticoagulation. ⁷	1180
1126	recurrent VTE is lower following surgery/trauma	0	1181
1127	compared with a nonsurgical risk factor, but that the	Aspirin for Extended Treatment of VTE	1182
1128	risk is low for both groups and that patients with	PICO Question: Should aspirin vs anticoagulant	1183
1129	VTE provoked by a transient risk factor typically do	therapy he provided to patients with venous	1184
1130	not require entithrembetic thereasy after completion	thromboombolism who have been selected to	1185
1131	not require antitinombotic therapy after completion	thromboembonsm who have been selected to	1186
1132	of primary treatment (3-6 months of $\frac{1}{28}$	receive extended-pnase therapy::	1187
1133	anticoagulation).	Guidance statements:	1188
1134	Reduced-Dose vs Full-Dose Anticoagulation for	27. In patients offered extended-phase	1109
1135	Extended Treatment of VTE	anticoagulation, we recommend reduced-dose	1190
1130	PICO Question: Should reduced-dose Xa inhibitor	DOAC over aspirin or no therapy (strong	1191
1128	(anivaban or rivarovaban) vs full dose Va inhibitor	recommendation, low-certainty evidence) and	1192
1130	(apixaban or rivarovaban) be provided to patients	suggest reduced-dose rivaroxaban over aspirin	1195
1140	(apixabali of fivaroxabali) be provided to patients	(weak recommendation, moderate-certainty	1195
1141	with vehous thromodelindonsin who have been	evidence).	1196
1142	selected to receive extended-phase anticoaguiant	Remarks: While the formal EtD accommont warrants a	1197
1143	therapy::	<i>Remarks.</i> while the formal EtD assessment warrants a	1198
1144	Guidance statement:	("suggest") the penalists upgraded the suidenes to a	1199
1145	26. In patients offered extended-phase	(suggest), the panelists upgraded the guidance to a	1200
1146	anticoagulation, we suggest the use of reduced-dose	strong recommendation, placing a very high value on	1201
1147	apixaban or rivaroxaban over full-dose apixaban or	an uncertain but potentially life-preserving benefit."	1202
1148	rivaroxaban (weak recommendation, very low-	Reduced dose refers to apixaban 2.5 mg twice daily and	1203
1149	certainty evidence).	rivaroxaban 10 mg once daily.	1204
1150	Remark: Reduced dose refers to anixaban 2.5 mg twice		1205
1151	daily and rivarovaban 10 mg once daily	Rivaroxaban is the only DOAC to be directly compared to	1206
1152	and inversionabili to hig once dally.	aspirin for secondary prevention of VTE. Several other	1207
1153	Selected summary of findings:	DOACs, as well as warfarin, are also acceptable for	1208
1154	\leftrightarrow Recurrent symptomatic VTE at 12 months: 2 more	secondary prevention (extended-phase therapy) after	1209
1155	events per 1,000 cases (from 5 fewer to 12 more)	VTE.	1210

1211 28. In patients with an unprovoked proximal DVT
1212 or PE who are stopping anticoagulant therapy and
1213 do not have a contraindication to aspirin, we
1214 suggest aspirin over no aspirin to prevent recurrent
1215 VTE (weak recommendation, low-certainty
1216 evidence).

1218 Remark: Because aspirin has been shown to be much 1219 less effective at preventing recurrent VTE than 1220 anticoagulants, and because some anticoagulants 1221 confer a similar risk of bleeding to aspirin, we do not 1222 consider aspirin a reasonable alternative to 1223 anticoagulant therapy in patients who want extended 1224 therapy. However, if a patient has decided to stop 1225 anticoagulants, prevention of recurrent VTE is one of 1226 the benefits of aspirin that needs to be balanced 1227 against aspirin's risk of bleeding and inconvenience. 1228 Use of aspirin should also be reevaluated when 1229 1230 patients stop anticoagulant therapy because aspirin 1231 may have been stopped when anticoagulants were 1232 started. 1233

1234 Selected summary of findings: Comparison: Reduced-1235 dose DOAC vs aspirin or placebo

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1237 ↓ Recurrent symptomatic VTE at 12 months: 46 fewer
1238 events per 1,000 cases (from 54 fewer to 34 fewer)

- August An August Andrew August August
- 1242 ? Mortality: Not estimable
- ¹²⁴³ 1244 Comparison: Rivaroxaban vs aspirin
- 1245 ↓ Recurrent VTE (2-4 years of follow-up): 39 fewer
 1246 events per 1,000 cases (from 47 fewer to 25 fewer)
- Hajor bleeding (2-4 years of follow-up): 4 more
 events per 1,000 cases (from 1 fewer to 52 more)

1250 Comparison: Aspirin vs no aspirin (placebo)

- Recurrent VTE (2-4 years of follow-up): 53 fewer
 events per 1,000 cases (from 84 fewer to 13 fewer)
- Major bleeding (2-4 years of follow-up): 3 more
 events per 1,000 cases (from 6 fewer to 28 more)
- All-cause mortality (2-4 years of follow-up): 2 fewer
 events per 1,000 cases (from 18 fewer to 26 more)

Comments: Aspirin is not a recommended alterative
to anticoagulation, based on direct and indirect
comparisons demonstrating that the net benefit of
extended anticoagulant therapy in patients with
unprovoked VTE is substantially greater than the
benefits of extended aspirin therapy. However, if a

patient has decided to stop anticoagulants, prevention1266of recurrent VTE is one of the benefits of aspirin and1267these benefits must be balanced against aspirin's risk1268of bleeding and inconvenience.1270

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Other guidelines:

2016 AC Forum: Suggests aspirin should be considered an option for patients at risk for recurrent VTE who are not considered candidates for an anticoagulant, or who choose to stop anticoagulant therapy.¹⁹

2019 ESC: Suggests that aspirin or sulodexide (not available in the United States) may be considered for extended VTE prophylaxis.⁷

2020 NICE: Suggests considering aspirin 75 mg or 150 mg daily in people who decline extended anticoagulation treatment.⁶

Compression Stockings in Preventing Postthrombotic Syndrome

PICO Question: Should graduated compression stockings vs no graduated compression stockings be provided to patients with acute DVT to reduce the risk of PTS?:

Guidance statement:

29. In patients with acute DVT of the leg, we suggest against using compression stockings routinely to prevent PTS (weak recommendation, low-certainty evidence).

Selected summary of findings:

- ↔ Any PTS of the leg (6-37 months of follow-up): 139 fewer events per 1,000 cases (from 268 fewer to 76 more).
- ↔ Severe PTS of the leg (6-37 months of follow-up): 23 fewer events per 1,000 cases (from 58 fewer to 57 more).

Comments: Graduated compression stockings may
reduce acute symptoms of DVT or chronic symptoms in
those who have developed PTS; but there is no evidence
demonstrating reduction in the risk for developing PTS.
There is also no evidence that the use of graduated
compression stockings DVT reduces risk for recurrent
DVT.1305
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DVT.1312

Other guidelines:

2016 AC Forum: Suggests that graduated compression13142016 AC Forum: Suggests that graduated compression1315stockings do not increase the risk of recurrent VTE but1316do not have any beneficial effect on leg discomfort in1317patients with acute DVT. No statements are made1318regarding prevention of PTS.¹⁹1319

1321 2020 NICE: Recommends against offering graduated 1322 compression stockings for the prevention of PTS, but 1323 notes that they can be offered to manage leg symptoms 1324 after DVT.⁶ 1325

Acknowledgments

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1331²²⁶ Role of sponsors: The sponsor had no role in the design of the study, the collection and analysis of the data, or the preparation of the 1332 manuscript. 1333

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