

# Error in Funding Information in: Management of Cardiac Sarcoidosis in the United States: A Delphi Study

In "Management of Cardiac Sarcoidosis in the United States: A Delphi Study," published in the January 2012 issue of *CHEST* (2012;141[1]:154-162), grant # UL1 RR025780 was incorrectly attributed to the Colorado Clinical and Translational Science Institute rather than the National Institutes of Health.

The funding information should have read: Supported by NIH/NCATS Colorado CTSI Grant Number UL1 TR000154. Contents are the authors' sole responsibility and do not necessarily represent official NIH views.

The article has been corrected, and the authors regret the error.

## Missing Attribution in: Pulmonary Rehabilitation: A Classic Tune With a New Beat, But Is Anyone Listening?

The article entitled, "Pulmonary Rehabilitation: A Classic Tune With a New Beat, But Is Anyone Listening?" published in the July 2011 issue of *CHEST* (2011;139[6]:1498-1502) repurposed a portion of text that had been previously published without attribution. The online article has been amended with an Editor's note as follows:

Editor's Note: Some of the content in this article previously appeared in Coding for Chest Medicine 2010.<sup>22</sup>

In addition, the following reference has been appended to the reference list as reference #22:

22. Birnbaum S, Carlin BW. Pulmonary rehabilitation programs and respiratory therapy service. In: Manaker S, ed. *Coding for Chest Medicine 2010*. 14th ed. Northbrook, IL: American College of Chest Physicians; 2009:225-232.

### Correction to Online Text: Executive Summary: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

The article "Executive Summary: Antithrombotic Therapy and Prevention of Thrombosis,  $9^{th}$  ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines" published in the February 2012 supplement of *CHEST* (2012; 141[2][Suppl]:7S-47S) contained an error in the online text. The error was on page 31S on recommendation 2.0.2.

The corrected text reads:

2.0.2. In patients with rheumatic mitral valve disease and normal sinus rhythm with a left atrial diameter > 55 mm, we suggest VKA therapy (target INR, 2.5; range, 2.0-3.0) over no VKA therapy or antiplatelet (Grade 2C).

This error occurred only in the online version of the text; the PDF and print version are correct. The text has been corrected online.

## Error in Tables in Antithrombotic Therapy for VTE Disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

The article: "Antithrombotic Therapy for VTE Disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines," published in the February 2012 supplement of *CHEST* (2012;141[2][Suppl]:e419S-e494S) contained errors in Table 18 and Table 19.

There were also errors in Table S27, included in the online supplement for this chapter.

The online article has been corrected with the updated tables.

Table 18—[Section 3.1.1-3.1.4] Summary of Findings: Extended Anticoagulation vs No Extended Anticoagulation for Different Groups of Patients with VTE and Without Cancer<sup>a,b,48,161,182,207</sup>

|                  |   |  |                                      | Anticipated   | d Absolute Effects   |
|------------------|---|--|--------------------------------------|---|--|
| Outcomes         | No. of Participants<br>(Studies), Follow-up | Quality of<br>the Evidence<br>(GRADE)            | Relative Effect<br>(95% CI)          | Risk With No<br>Extended Duration<br>Oral Anticoagulation | Risk Difference With<br>Extended Duration Ora<br>Anticoagulation (95% CI |
| Mortality        | 1,184 (4 studies),<br>10-36 mo              | Moderate <sup>c-e</sup><br>due to<br>imprecision | RR 0.57 (0.31-1.03)                  | 63 per 1,000  | 27 fewer per 1,000 (from<br>44 fewer to 2 more)                          |
| Recurrent VTE at | 1,184 (4 studies),                          | High   | RR 0.12 (0.05-0.25)                  | First VTE pr  | rovoked by surgery <sup>f-j</sup>  |
| 1 y              | 10-36 mo                                    |  |                                      | 10 per 1,000  | 9 fewer per 1,000 (from<br>7 fewer to 9 fewer)                           |
|                  |   |  |                                      | first unprov  | or PE provoked nonsurgical/<br>voked distal DVT <sup>[-j</sup>           |
|                  |   |  |                                      | 50 per 1,000  | 44 fewer per 1,000 (from<br>38 fewer to 47 fewer)                        |
|                  |   |  |                                      |   | provoked VTE <sup>f-j</sup>  |
|                  |   |  |                                      | 100 per 1,000   | 88 fewer per 1,000 (from<br>75 fewer to 95 fewer)                        |
|                  |   |  |                                      |   | nprovoked VTE <sup>f-j</sup>   |
|                  |   |  |                                      | 150 per 1,000   | 132 fewer per 1,000<br>(from 113 fewer to<br>142 fewer)                  |
| Major bleeding   | 1,184 (4 studies),                          | Moderate   | RR 2.63 (1.02-6.76)                  | Low <sup>k,l</sup>  | (see Table 3)  |
| at 1 y           | 10-36 mo                                    | due to imprecision                               |                                      | 3 per 1,000   | 5 more per 1,000 (from<br>0 more to 17 more)                             |
|                  |   | •  |                                      | Moderate  | e <sup>k,l</sup> (see Table 3)   |
|                  |   |  |                                      | 6 per 1,000   | 10 more per 1,000 (from<br>0 more to 35 more)                            |
|                  |   |  |                                      | High <sup>k,l</sup>                                       | (see Table 3)  |
|                  |   |  |                                      | 24 per 1,000  | 39 more per 1,000 (from<br>0 more to 138 more)                           |
| Recurrent VTE    | 1,184 (4 studies),                          | High   | ${\rm RR}\ 0.12\ (0.05\text{-}0.25)$ | First VTE pr  | rovoked by surgery <sup>f-j</sup>  |
| at 5 y           | 10-36 mo                                    |  |                                      | 30 per 1,000  | 26 fewer per 1,000 (from<br>22 fewer to 29 fewer)                        |
|                  |   |  |                                      | first unprov  | or PE provoked nonsurgical/<br>voked distal DVT <sup>f-j</sup>           |
|                  |   |  |                                      | 150 per 1,000   | 132 fewer per 1,000<br>(from 113 fewer to<br>142 fewer)                  |
|                  |   |  |                                      | Firet un  | provoked VTE <sup>f-j</sup>  |
|                  |   |  |                                      | 300 per 1,000   | 264 fewer per 1,000<br>(from 225 fewer to                                |
|                  |   |  |                                      | l   | 285 fewer)   |
|                  |   |  |                                      | 450 per 1,000   | nprovoked VTE <sup>f-j</sup>   |
|                  |   |  |                                      | 450 per 1,000   | 396 fewer per 1,000<br>(from 337 fewer to<br>427 fewer)                  |
| Major bleeding   | 1,184 (4 studies),                          | Moderate   | RR 2.63 (1.02-6.76)                  | Low <sup>k,l</sup>  | (see Table 3)  |
| at 5 y           | 10-36 mo                                    | due to<br>imprecision                            | 111 2.05 (1.02 0.10)                 | 15 per 1,000  | 24 more per 1,000 (from<br>0 more to 87 more)                            |
|                  |   | 1  |                                      | Moderate  | e <sup>k,l</sup> (see Table 3)   |
|                  |   |  |                                      | 30 per 1,000  | 49 more per 1,000 (from<br>1 more to 173 more)                           |
|                  |   |  |                                      | High <sup>k,l</sup>                                       | (see Table 3)  |
|                  |   |  |                                      | 120 per 1,000   | 196 more per 1,000<br>(from 2 more to                                    |
|                  |   |  |                                      |   | 692 more)  |
|                  |   |  |                                      |   | (Continued   |

### Table 18—Continued

|  |   |                                       |                             | Anticipated  | Absolute Effects   |
|--|---|---------------------------------------|-----------------------------|--|--|
| Outcomes                                     | No. of Participants<br>(Studies), Follow-up | Quality of<br>the Evidence<br>(GRADE) | Relative Effect<br>(95% CI) | Risk With No<br>Extended Duration<br>Oral Anticoagulation  | Risk Difference With<br>Extended Duration Oral<br>Anticoagulation (95% CI) |
| Burden of<br>anticoagulation<br>not reported |   |                                       |                             | Warfarin: daily medication, dietary and activity restrictions, frequent blood testing/monitoring, increased hospital/ clinic visits <sup>m</sup> |  |
| PTS not reported                             |   |                                       |                             | *  |  |

The basis for the assumed risk (eg, the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). Working group grades of evidence are as follow: High quality, further research is very unlikely to change our confidence in the estimate of effect; moderate quality, further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low quality, further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; very-low quality, we are very uncertain about the estimate. PREVENT = Prevention of Recurrent Venous Thromboembolism. See Table 1 and 3 legends for expansion of other abbreviations.

<sup>a</sup>Studies vary in follow-up duration (10 mo to 3 y) and in duration of time-limited VKA (3-6 mo).

<sup>b</sup>We excluded PREVENT trial because target INR was 1.75 (low intensity), which has been shown in an RCT<sup>44</sup> to be less effective than a target of 2.5.

 $cI^2 = 0\%$ .

<sup>d</sup>CI includes both values suggesting no effect and values suggesting either appreciable harms or appreciable benefit.

<sup>e</sup>Small number of events. Decision to rate down also takes into account that two studies were stopped early for benefit.

<sup>f</sup>Annual risk of VTE recurrence after discontinuing oral anticoagulation therapy in patients with first VTE provoked by surgery: 1% (Iorio et al<sup>171</sup>); we assumed a 0.5% yearly risk thereafter (3% over 5 y).

gAnnual risk in patients with first VTE provoked by nonsurgical factor:  $\sim$ 5% the first year (Iorio et all<sup>171</sup>); we assumed a 2.5% yearly thereafter (15% over 5 y).

hAnnual risk in patients with first episode of unprovoked VTE: 9.3% over 1 y in Rodger et all 185; 11.0% over 1 y, 19.6% over 3 y, and 29.1% over 5 y in Prandoni et al. 208 We assumed a risk of 10% the first year after discontinuation and 5% yearly thereafter (30% over 5 y).

Annual risk in patients with second episode of unprovoked VTE: we assumed an RR of 1.5 compared with a first episode of unprovoked VTE: 15% the first year after discontinuation, 7.5% yearly thereafter (45% over 5 y).

Case fatality rate of recurrent VTE after discontinuing oral anticoagulation therapy: 3.6% (Carrier et al<sup>12</sup>).

 $^k$ Annual risk of major bleeding is based on three risk levels: low, intermediate, and high. The corresponding 0.3%, 0.6%, and 1.2% risks are estimates based on control arms of included studies (see Table 2).

'Case fatality rate of major bleeding during initial oral anticoagulation therapy: 11.3% (Carrier et al<sup>12</sup>) (no data available for after discontinuing oral anticoagulation therapy).

"Burden of anticoagulation: endured by all patients who continue extended-duration anticoagulation (100%) and applies to patients who stop anticoagulation (no extended duration anticoagulation) who subsequently experienced a recurrent VTE (5%/10%/15% at 1 y; 15%/30%/45% at 5 y).

<sup>n</sup>PTS: baseline risk over 2 y of 58.8% for PTS and 13.8% for severe PTS (Kahn et al<sup>102</sup>). There was a threefold (Prandoni et al<sup>202</sup>) to 10-fold (van Dongen et al<sup>209</sup>) increase in PTS with recurrent VTE in the ipsilateral leg.

Table 19—[Section 3.1.1-3.1.4] Estimated Absolute Difference in Recurrent VTE and Major Bleeding Events (Including Fatal Events) With 5 Years of vs No Extended Anticoagulation

|   | Outcomes After            |  | Risk of Bleeding                           |  |
|---|---------------------------|--|--|--|
|   | 5 y of Treatment          | Low  | Intermediate                               | Higha                                      |
| First VTE provoked by                             | Recurrent VTE reduction % | 12.6 (2.2-2.9) (0.1 fatal)b                | 12.6 (2.2-2.9) (0.1 fatal)b                | 12.6 (2.2-2.9) (0.1 fatal) <sup>b</sup>    |
| surgery   | Major bleeding increase % | 12.4 (0-8.7) (0.3 fatal) <sup>b</sup>      | 14.9 (0.1-17.3) (0.5 fatal)b               | 19.6 (0.2-69.2) (2.2 fatal)b               |
| First VTE provoked by a                           | Recurrent VTE reduction % | ↓13.2 (11.3-14.2) (0.5 fatal) <sup>c</sup> | ↓13.2 (11.3-14.2) (0.5 fatal) <sup>c</sup> | 13.2 (11.3-14.2) (0.5 fatal) <sup>b</sup>  |
| nonsurgical factor/first<br>unprovoked distal DVT | Major bleeding increase % | 12.4 (0-8.7) (0.3 fatal) <sup>c</sup>      | 14.9 (0.1-17.3) (0.5 fatal) <sup>c</sup>   | 19.6 (0.2-69.2) (2.2 fatal) <sup>b</sup>   |
| First unprovoked proximal                         | Recurrent VTE reduction % | 126.4 (22.5-28.5) (1 fatal)d               | 126.4 (22.5-28.5) (1 fatal)d               | 126.4 (22.5-28.5) (1 fatal)b               |
| DVT or PE   | Major bleeding increase % | 12.4 (0-8.7) (0.3 fatal) <sup>d</sup>      | 14.9 (0.1-17.3) (0.5 fatal)d               | 19.6 (0.2-69.2) (2.2 fatal)b               |
| second unprovoked VTE                             | Recurrent VTE reduction % | ↓39.6 (33.7-42.7) (1.4 fatal) <sup>e</sup> | ↓39.6 (33.7-42.7) (1.4 fatal) <sup>d</sup> | 139.6 (33.7-42.7) (1.4 fatal) <sup>c</sup> |
| -   | Major bleeding increase % | 12.4 (0-8.7) (0.3 fatal)e                  | 14.9 (0.1-17.3) (0.5 fatal) <sup>d</sup>   | 19.6 (0.2-69.2) (2.2 fatal) <sup>c</sup>   |

### Recommendations:

Risk of dying in patients with a recurrent VTE or a major bleed:

- Case fatality rate of recurrent VTE after discontinuing oral anticoagulation therapy: 3.6% (Carrier et al<sup>12</sup>).
- Case fatality rate of major bleeding during initial oral anticoagulation therapy: 11.3% (Carrier et al<sup>12</sup>) (no data available for after discontinuing oral anticoagulation therapy).

Annual risks of recurrent VTE after discontinuation of anticoagulation:

- First VTE provoked by surgery: 1% (Iorio et al<sup>171</sup>); we assumed a 0.5% yearly risk thereafter (3% over 5 y).
- First episode of VTE provoked by nonsurgical factor: ~5% the first year (Iorio et all<sup>171</sup>); we assumed a 2.5% yearly thereafter (15% over 5 y)
- First episode of unprovoked VTE: 9.3% over 1 y (Rodger et al<sup>185</sup>); 11.0% over 1 y, 19.6% over 3 y, 29.1% over 5 y (Prandoni et al<sup>208</sup>). We assumed a risk of 10% the first year after discontinuation and 5% yearly thereafter (30% over 5 y).
- Second episode of unprovoked VTE: we assumed that this inflicts 1.5 the risk of recurrent VTE relative to first episode of unprovoked VTE: 15% the first year after discontinuation, 7.5% yearly thereafter (45% over 5 y).

Relative risk reduction with extended anticoagulant therapy:

• 82% based on Table 18

Annual risks of major bleeding in patients not on anticoagulant therapy:

• Low risk, 0.3%/y; intermediate risk 0.6%/y; high risk, 2.4%/y (Table 2).

Relative risk of major bleeding with extended anticoagulant therapy:

2.6 based on Table 18.

Criteria used to decide on direction and strengths of recommendations:

- Criterion for a strong recommendation against whenever the estimated number of fatal bleeding events exceeded the estimated number of fatal recurrent VTE prevented.
- Criterion to go from a strong recommendation against to weak recommendation against: difference between the lower boundary of increased major bleeding and upper boundary of reduction in recurrent VTE < 2% (risk over 5 y averaged per year).
- Criterion to go from a weak recommendation against to a weak recommendation in favor of: difference between point estimate of reduction of recurrent VTE and point estimate for increase in major bleeding is >2% (risk over 5 y averaged per year) (2% to account for the burden and cost of VKA).
- Criterion to go from a weak recommendation for to strong recommendation for: difference between the lower boundary of reduction in VTE and upper boundary of increased major bleeding >4% (risk over 5 y averaged per year).

Another way of interpreting the direction and strength of recommendation based on the number of deaths (related to either bleeding or recurrent VTE) is as follows:

- A strong recommendation against: extended anticoagulation is estimated to be associated with an increase in deaths.
- A weak recommendation against: extended anticoagulation is estimated to be associated with from no effect on deaths to only a very small reduction in deaths (0-4/1,000 prevented over 5 y or < 0.5%/patient-y).
- A weak recommendation for: extended anticoagulation is estimated to be associated with a small reduction in deaths (5 to 9/1,000 prevented over 5 y or 0.5%-0.9%/patient-y).
- A strong recommendation for: extended anticoagulation is estimated to be associated with a large reduction in deaths (> 10/1,000 prevented over 5 y or > 1%/patient-y).

<sup>a</sup>With an eightfold risk of bleeding in the high-risk group compared with the low-risk group, a strong recommendation against extended anticoagulation for a second unprovoked VTE is justified. The high-risk group, however, includes patients who have a risk of bleeding that is less than this estimate (eg, patients aged >75 y without additional risk factors for bleeding [Table 2]) and, therefore, may benefit from extended anticoagulant therapy. For this reason, we provide a weak rather than a strong recommendation against extended anticoagulation for patients with a second unprovoked VTE in the high-bleeding-risk group.

bStrong against

<sup>c</sup>Weak against

dWeak in favor

<sup>e</sup>Strong in favor

Table \$27—[Sections 3.1.1-3.1.4] Extended Anticoagulation vs No Extended Anticoagulation for Different Groups of Patients With VTE and Without Cancerab

|  |   |                            |                 |                     |  |  |                                  | 0                           | Simon   |   |
|--|---|----------------------------|-----------------|---------------------|--|--|----------------------------------|-----------------------------|---|---|
|  |   |                            |                 |                     |  | Study Eve                              | Study Event Rates (%)            |                             | Anticipat                                     | Anticipated Absolute Effects  |
| Participants<br>(Studies),<br>Follow-up Risk of Bias | ias Inconsistency                               | Indirectness               | Imprecision     | Publication<br>Bias | Overall Quality<br>of Evidence                   | With No<br>Extended<br>Anticoagulation | With Extended<br>Anticoagulation | Relative Effect<br>(95% CI) | Risk With No<br>t Extended<br>Anticoagulation | Risk Difference<br>With Extended<br>Anticoagulation (95% CI)            |
|  |   |                            |                 | Mort                | Mortality (important outcome)                    | outcome)                               |                                  |                             |   |   |
| 1,184 (4 No serious studies), risk of bias 10-36 mo  | s No serious<br>bias inconsistency <sup>c</sup> | No serious<br>indirectness | $Serious^{d,e}$ | Undetected          | Moderate <sup>c-e</sup><br>due to<br>imprecision | 38/599 (6.3%)                          | 16/585 (2.7%)                    | RR 0.57<br>(0.31-1.03)      | 63 per 1,000                                  | 27 fewer per 1,000 (from<br>44 fewer to 2 more)                         |
|  |   |                            |                 | Recurren            | Recurrent VTE at 1 y (critical outcome)          | tical outcome)                         |                                  |                             |   |   |
| Z  | Z   | No serious                 | No serious      | Undetected High     | High   | 102/599 (17%)                          | 21/585 (3.6%)                    | RR 0.12                     | First VTE                                     | First VTE provoked by surgery <sup>f-j</sup>                            |
| studies), risk of bias<br>10-36 mo                   | otas inconsistency                              | indirectness               | ımprecision     | _                   |  |  |                                  | (0.05-0.25)                 | 10 per 1,000                                  | 9 fewer per 1,000 (from 7 fewer to 9 fewer)                             |
|  |   |                            |                 |                     |  |  |                                  |                             | First VTE pr<br>unpre                         | First VTE provoked nonsurgical/first unprovoked distal DVT <sup>E</sup> |
|  |   |                            |                 |                     |  |  |                                  |                             | 50 per 1,000                                  | 44 fewer per 1,000 (from 38 fewer to 47 fewer)                          |
|  |   |                            |                 |                     |  |  |                                  |                             | First u                                       | First unprovoked VTE <sup>f.j</sup>                                     |
|  |   |                            |                 |                     |  |  |                                  |                             | 100 per 1,000                                 | 88 fewer per 1,000 (from 75 fewer to 95 fewer)                          |
|  |   |                            |                 |                     |  |  |                                  |                             | Second  | Second unprovoked VTE <sup>f.j</sup>                                    |
|  |   |                            |                 |                     |  |  |                                  |                             | $150 \; \mathrm{per} \; 1,000$                | 132 fewer per 1,000<br>(from 113 fewer to                               |
|  |   |                            |                 |                     |  |  |                                  |                             |   | 142 fewer)  |
|  |   |                            |                 | Major ble           | Major bleeding at 1 y (critical outcome)         | tical outcome)                         |                                  |                             |   |   |
| Z  | Z   | No serious                 | Serious         | Undetected          | Moderate   | 7/599 (1.2%)                           | $21/585 \ (3.6\%)$               | RR 2.63                     | Low   | Low risk of bleeding <sup>k,l</sup>                                     |
| studies), risk of bias<br>10-36 mo                   | bias inconsistency                              | indirectness               |                 |                     | due to<br>imprecision                            |  |                                  | (1.02-6.76)                 | 3 per 1,000                                   | 5 more per 1,000 (from 0 more to 17 more)                               |
|  |   |                            |                 |                     |  |  |                                  |                             | Modera  | Moderate risk of bleeding <sup>k,1</sup>                                |
|  |   |                            |                 |                     |  |  |                                  |                             | $6  \mathrm{per}  1,000$                      | 10 more per 1,000 (from 0 more to 35 more)                              |
|  |   |                            |                 |                     |  |  |                                  |                             | High  | High risk of bleeding <sup>k.1</sup>                                    |
|  |   |                            |                 |                     |  |  |                                  |                             | 24 per 1,000                                  | 39 more per 1,000 (from 0 more to 138 more)                             |
|  |   |                            |                 |                     |  |  |                                  |                             |   | : 0   |

Table S27—Continued

|                     | ffects                       | ference<br>tended<br>on (95% CI)   |   | urgery <sup>f.j</sup>                        | 1,000 (from 29 fewer)                          | gical/first<br>VT <sup>F</sup> j  | r 1,000             | fewer to           | E6                                 | 1,000               | ewer to            |            | re <sup>6</sup>                     | r 1,000             | ewer to            |            |  | rk,l                                | 1,000 (from             | 87 more)           | $ing^{k,l}$                              | 1,000 (from             | 173 more)           | بابر ح                               | 1,000 (from)               | 392 more)           | (Continued)                            |
|---------------------|------------------------------|--|---|--|--|---|---------------------|--------------------|------------------------------------|---------------------|--------------------|------------|-------------------------------------|---------------------|--------------------|------------|--|-------------------------------------|-------------------------|--------------------|--|-------------------------|---------------------|--------------------------------------|----------------------------|---------------------|--|
|                     | Anticipated Absolute Effects | Risk Difference<br>With Extended<br>Anticoagulation (95%                                     |   | First VTE provoked by surgery <sup>f.j</sup> | 26 fewer per 1,000 (from 22 fewer to 29 fewer) | First VTE provoked nonsurgical/first unprovoked distal DVT <sup>F</sup> | 132 fewer per 1,000 | (from 113 fewer to | First unprovoked VTE <sup>F3</sup> | 264 fewer per 1,000 | (from 225 fewer to | 285 fewer) | Second unprovoked VTE <sup>Fj</sup> | 396 fewer per 1,000 | (from 337 fewer to | 427 fewer) |  | Low risk of bleeding <sup>k,1</sup> | 24 more per 1,000 (from | 0 more to 87 more) | Moderate risk of bleeding <sup>k,1</sup> | 49 more per 1,000 (from | 1 more to 173 more) | High risk of bleeding <sup>k,l</sup> | 196 more per $1,000$ (from | 2 more to 692 more) |  |
| indings             | Anticipat                    | Risk With No Risk Difference Extended With Extended Anticoagulation Anticoagulation (95% CI) |   | First VTE 1                                  | 30 per 1,000                                   | First VTE pro   | 150 per 1,000       |                    | First un                           | 300 per 1,000       |                    |            | Second                              | 450 per 1,000       |                    |            |  | Low r                               | 15 per 1,000            |                    | Moderat                                  | 30  per  1,000          | ,                   | High 1                               | $120  \mathrm{per}  1,000$ |                     |  |
| Summary of Findings |                              | Relative Effect (95% CI)   |   | RR 0.12                                      | (0.05-0.25)                                    |   |                     |                    |                                    |                     |                    |            |                                     |                     |                    |            |  | RR 2.63                             | (1.02-6.77)             |                    |  |                         |                     |                                      |                            |                     |  |
|                     | Study Event Rates (%)        | With No<br>Extended With Extended<br>Anticoagulation Anticoagulation                         |   | 21/585 (3.6%)                                |  |   |                     |                    |                                    |                     |                    |            |                                     |                     |                    |            |  | 21/585 (3.6%)                       |                         |                    |  |                         |                     |                                      |                            |                     |  |
|                     | Study Ever                   | With No<br>Extended<br>Anticoagulation   | tical outcome)                          | 102/599 (17%)                                |  |   |                     |                    |                                    |                     |                    |            |                                     |                     |                    |            | tical outcome)                           | 7/599 (1.2%)                        |                         |                    |  |                         |                     |                                      |                            |                     | not reported                           |
|                     |                              | Overall Quality<br>of Evidence   | Recurrent VTE at 5 y (critical outcome) | High   |  |   |                     |                    |                                    |                     |                    |            |                                     |                     |                    |            | Major bleeding at 5 y (critical outcome) | M                                   | to<br>imprecision       | 4                  |  |                         |                     |                                      |                            |                     | Burden of anticoagulation not reported |
|                     |                              | Publication<br>Bias  | Recurre                                 | Undetected                                   | п  |   |                     |                    |                                    |                     |                    |            |                                     |                     |                    |            | Major bl                                 | Undetected                          |                         |                    |  |                         |                     |                                      |                            |                     | Burden                                 |
| nt                  |                              | Imprecision  |   | ~  | imprecision                                    |   |                     |                    |                                    |                     |                    |            |                                     |                     |                    |            |  | Serious                             |                         |                    |  |                         |                     |                                      |                            |                     |  |
| Quality Assessment  |                              | Indirectness   |   | No serious                                   | indirectness                                   |   |                     |                    |                                    |                     |                    |            |                                     |                     |                    |            |  | No serious                          | indirectness            |                    |  |                         |                     |                                      |                            |                     |  |
| δ                   |                              | Inconsistency  |   | No serious                                   | inconsistency                                  |   |                     |                    |                                    |                     |                    |            |                                     |                     |                    |            |  | No serious                          | inconsistency           |                    |  |                         |                     |                                      |                            |                     |  |
|                     |                              | Risk of Bias   |   | No serious                                   | risk of bias                                   |   |                     |                    |                                    |                     |                    |            |                                     |                     |                    |            |  | No serious                          | risk of bias            |                    |  |                         |                     |                                      |                            |                     |  |
|                     | _                            | Participants<br>(Studies),<br>Follow-up  |   | 1,184 (4                                     | studies),<br>10-36 mo                          |   |                     |                    |                                    |                     |                    |            |                                     |                     |                    |            |  | 1,184 (4                            | studies),<br>10-36 mo   |                    |  |                         |                     |                                      |                            |                     |  |

# Table S27—Continued

|   |                   | )  | Quality Assessment | nt               |              |   |  |  | Summary of Findings         | indings   |  |
|---|-------------------|--|--------------------|------------------|--------------|---|--|--|-----------------------------|---|--|
|   |                   |  |                    |                  |              |   | Study Even                                 | Study Event Rates (%)  |                             | Anticipat   | Anticipated Absolute Effects   |
| Participants<br>(Studies),<br>Follow-up | s<br>Risk of Bias | Participants Studies), Follow-up Risk of Bias Inconsistency Indirectness Imprecision   | Indirectness       | Imprecision      |              | Publication Overall Quality Bias of Evidence An | <br>With No<br>Extended<br>Anticoagulation | With No Extended With Extended Relative Effect Extended riticoagulation Anticoagulation (95% CI) Anticoagulation | Relative Effect<br>(95% CI) | Risk With No<br>Extended<br>Anticoagulation       | With No Risk Difference Overall Quality Extended With Extended Relative Effect Extended With Extended of Evidence Anticoagulation Anticoagulation (95% CI) |
| :                                       | :                 | :  | :                  | :                | :            | :   | :  | :  | :                           | See comment <sup>m</sup> See comment <sup>m</sup> | See comment <sup>m</sup>   |
|   |                   |  |                    |                  |              | PTS not reported                                | pa   |  |                             |   |  |
| :                                       | :                 | :  | :                  | :                | :            | :   | :  | :  | :                           | See comment <sup>n</sup> See comment <sup>n</sup> | See comment <sup>n</sup>   |
| Bibliograph                             | v: Schulman et    | Bibliography. Schulman et al (DHBAC 2) 97 Kearon et al (LAFIT) 36 Farrai 38 Palareti (PBOLONG) 35 See Table S1 S2 S7 and S10 legends for expansion of alphreviations | Kearon et al (LA   | FIT 96 Farrai 98 | Palareti (PR | J.ONG) 95 See T                                 | able S1 S2 S7 a                            | nd S10 levends fo  | r expansion of a            | hreviations                                       |  |

"Studies vary in follow-up duration (10 mo to 3 y) and in duration of time-limited VKA (3 to 6 mo).

We excluded Ridker et al (PREVENT) we because target INR was 1.75 (low intensity), which has been shown in an RCT to be less effective than a target of 2.5.

\*CI includes both values suggesting no effect and values suggesting either appreciable harms or appreciable benefit.

Small number of events. Decision to rate down also takes into account that two studies were stopped early for benefit.

Annual risk of VTE recurrence after discontinuing oral anticoagulation therapy in patients with first VTE provoked by surgery: 1% (Iorio A, Kearon C, Filippucci E, et al. Risk of recurrence after a first episode of symptomatic venous thromboembolism provoked by a transient risk factor: a systematic review. Arch Intern Med. 2010;170(19):1710-1716); we assumed a 0.5% yearly risk thereafter (3% over 5 y).

"Annual risk in patients with first episode of unprovoked VTE: 9.3% over 1 y in Rodger MA, Kahn SR, Wells PS, et al. Identifying unprovoked thromboembolism patients at low risk for recurrence who can discontinue anticoagulant therapy. CMAJ. 2008;179(5):417-426; 11.0% over 1 y, 19.6% over 3 y, and 29.1% over 5 y in Prandoni et al (2007). We assumed a risk of 10% the first year after discontinuation \*Annual risk in patients with first VTE provoked by non surgical factor: about 5% the first year (Iorio et al); we assumed 2.5% yearly thereafter (15% over 5 y).

and 5% yearly thereafter (30% over 5 y).

Amual risk in patients with second episode of unprovoked VTE: we assumed an RR of 1.5 compared with a first episode of unprovoked VTE: 15% the first year after discontinuation, 7.5% yearly thereafter (45% over 5 v).

Annual risk of major bleeding is based on three risk levels: low, intermediate, and high. The corresponding 0.3%, 0.6%, and 1.2% risks are estimates based on control arms of included studies (see Table 3). Case fatality rate of recurrent VTE after discontinuing oral anticoagulation therapy: 3.6% (Carrier 2010).

and applies to patients who stended-duration anticoagulation (100%) and applies to patients who stop anticoagulation (no extended-duration anticoagulation) who Case fatality rate of major bleeding during initial oral anticoagulation therapy: 11.3% (Carrier et al) (no data available for after discontinuing oral anticoagulation therapy) subsequently experience a recurrent VTE (5%, 10%, 15% at 1 y; 15%, 30%, 45% at 5 y).

Baseline risk over 2 y of 58.8% for PTS and 13.8% for severe PTS (VETO [Venous Thrombosis Outcomes study]; Ann Intern Med. 2008) and threefold (Prandoni. Ann Intern Med. 2004) to 10-fold (Van Dongen. J Thromb Haemost. 2005) increase in PTS.