National Institute for Health and Care Excellence

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Draft for consultation

Venous thromboembolic diseases: diagnosis, management and thrombophilia testing

[H] Evidence review for the use of inferior vena caval filters in people with venous thromboembolism

NICE guideline

Evidence review

November 2019

Draft for Consultation

This evidence review was developed by the NICE Guideline Updates Team

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Inferior vena caval filters for people with venous thromboembolism (VTE)

Review question

What is the effectiveness of inferior vena caval filters to prevent PE in people with confirmed VTE?

Introduction

The inferior vena cava (IVC) drains the blood from the lower parts of the body and legs into the right atrium of the heart. If a DVT in the lower body or legs becomes dislodged, it will pass through the inferior vena cava and right heart into the pulmonary arteries, causing a pulmonary embolus which damages the lungs and may cause death. IVC filters are devices placed within the IVC to trap larger travelling thromboemboli and stop them reaching the pulmonary circulation.

An IVC filter is placed through a needle puncture operation in a groin or neck vein by an interventional radiologist. It is reserved for more serious cases of VTE. In recent years, IVC filters have seen increasing usage in certain groups of people with VTE, such as those people with VTE and a contraindication to anticoagulation or those people thought to be at particularly high risk of a PE (such as those people who have already had a PE, and people with iliac vein (proximal) DVTs). The 2012 NICE guideline recommended temporary inferior vena caval filters for people with proximal DVT or PE who cannot have anticoagulation treatment, with the filter being removed when the person becomes eligible for anticoagulation treatment. However, these recommendations were informed by relatively few studies and only one RCT assessing the use of filters, and concerns have been raised that in light of new evidence, these recommendations may no longer be appropriate.

This review aims to examine the current evidence for the use of IVC filters to prevent PE in people with VTE. It identified studies that fulfilled the conditions listed in Table 1. For full details of the review protocol, see appendix A.

Table 1 PICO for IVC filters for people with VTE

Population	Adults (18+ years) with: • VTE (DVT and/or PE) who cannot have anticoagulants **or** • VTE who have had a filter inserted because they could not take anticoagulants, but retain the filter once they start taking anticoagulants **or** • VTE who have a PE whilst taking anticoagulants **or** • VTE who have the filters inserted for prophylaxis before a potential provoking event (e.g. surgery) **or** • VTE who can receive anticoagulants but are at high risk of poor outcomes if they had further PEs or • VTE who can receive anticoagulants but are at high risk of PE.
Intervention	• IVC filter
Comparator	• No filter
Outcomes	• Recurrent VTE (PE and DVT)

- All-cause mortality
- VTE-related mortality
- Post-thrombotic syndrome
- Pulmonary hypertension (PH)
- Quality of life
  - Generic and disease-specific measures will be reported
  - Overall score will be reported (data on subscales will not be reported)
- Adverse events
  - Total serious adverse events
  - Major bleeding
  - Clinically relevant non-major bleeding
  - Surgical complications at the time of placement and removal
  - Sepsis (or serious infections) for filters that are in place for longer periods
- Resource use and costs

Methods and process

This evidence review was developed using the methods and process described in developing NICE guidelines: the manual (2014). Methods specific to this review question are described in the review protocol in appendix A and the methods section in Appendix B.

Additional methodological issues were as follows:

1. During protocol development. the committee identified six distinct clinical scenarios where filters may be used in people with VTE:

- who cannot have anticoagulants, or
- who have had a filter inserted because they could not take anticoagulants, but retain the filter once they start taking anticoagulants, or
- who have a PE whilst taking anticoagulants, or
- who have the filters inserted for prophylaxis before a potential provoking event (e.g. surgery), or
- who can receive anticoagulants but are at high risk of poor outcomes if they had further PEs, or
- who can receive anticoagulants but are at high risk of PE occurrence (for people with an initial event that was DVT) or recurrence (for people with an initial event that was PE). (See note 9 below.)

These groups were analysed in separate meta-analyses. In cases where there was a mixed population studies were excluded unless data could be extracted for the populations separately or if the majority of participants fell into a single population based on committee judgement. Downgrading for indirectness was considered in the latter case with the final decision being based on committee judgement.

2. In addition, the committee identified people with VTE and cancer as a subgroup of interest for all of the above scenarios. Several studies were identified that included people with VTE and cancer, but it was unclear whether these participants fell under the group of people who can receive anticoagulants but are at high risk of PE or whether having cancer put the participants at high risk of poor outcomes if they had

further PEs. As a result, with committee agreement, these studies were analysed separately. No data for people with VTE and cancer was identified for the other scenarios.

3. Outcomes of relevance to this review were reported at different time points:
   - during the procedure (this outcome is only relevant to those people undergoing surgery)
   - in-hospital
   - in the short term (up to 30 days)
   - at 3 months
   - in the long term (after 3 months).

When a study reported data on two time points within the same grouping (for example, 1 year and 8 years) the later time point was extracted.

4. RCTs, prospective cohort studies and retrospective cohort studies were not pooled in the meta-analyses (see protocol deviation). However, they were shown on the same forest plots to facilitate visual comparison of the results.
5. Risk of bias was assessed using the modified version of the first Cochrane risk of bias tool (Higgins, 2011) for RCTs and ROBINS-I for cohort studies. Risk of bias was assessed at the study (as opposed to the being conducted for each outcome). However, in instances where an additional risk of bias applied specifically to one outcome or group of outcomes (for example subjective versus objective outcomes), this was noted in the evidence table and reflected in the relevant GRADE table.
6. The ROBINS-I risk of bias checklist has 5 possible overall ratings for risk of bias: low, moderate, serious, critical and no information. In the forest plots, cohort studies at moderate, serious and critical risk of bias were included in the same plots. However, sensitivity analyses were carried out as follows:
   - In cases where studies were at low to critical risk of bias, studies at serious and critical risk of bias were removed
   - In cases where studies were at low to critical risk of bias, studies at critical risk of bias were removed
   - In cases where studies were at serious to critical risk of bias, studies at critical risk of bias were removed.
7. In the GRADE tables, cohort studies at low risk of bias from ROBINS-I were deemed to have no serious risk of bias, those at moderate risk of bias were deemed to be at serious risk of bias, while those at serious and critical risk were grouped as very serious risk of bias. There were no studies in the no information category. Pooled results were presented for each study type (RCT, prospective and retrospective cohort) separately and then for the sensitivity analyses.
8. Data was available for subgroup analyses for people aged at least 80 years of age who were classed as being at high risk of poor outcomes in the event of a PE recurrence. Due to a lack of data no other subgroup analyses were performed.
9. PE-recurrence in this chapter refers to a PE developing in a person who already has confirmed VTE (DVT and/or PE). Unless otherwise stated, it does not mean that the person specifically had a PE and then went on to have another PE, but also includes people with DVT who then go onto have a PE. Subgroup analyses by index event were carried out where data was available.
10. PE-recurrence in some studies was separated into symptomatic and asymptomatic PE-recurrence, whereas most studies simply reported the number of PE events without indicating whether they were symptomatic or asymptomatic. As these studies are retrospective they are unlikely to have captured asymptomatic events. Therefore,

unless otherwise stated, PE-recurrence will be assumed to relate to symptomatic PE for the purposes of this review.

Declarations of interest were recorded according to NICE's 2018 conflicts of interest policy.

Protocol deviation

Priority screening was not used for this review. All references returned by the search were screened at title and abstract level.

The committee decided that due to the serious/critical risk of bias associated with the included retrospective cohort studies, these should not be pooled with RCTs. Therefore, these study types were analysed separately and no sensitivity analysis by study type was necessary.

Clinical evidence

Included studies

This review was conducted as part of a larger update of the 2012 NICE VTE management guideline (CG144). A systematic literature search for randomised controlled trials (RCTs), cohort studies (retrospective or prospective) and systematic reviews (SRs) was conducted for this review and this returned 2,416 references (see appendix C for literature search strategy). Based on title and abstract, 2,373 references were excluded because they did not meet the review protocol, and 43 references were ordered for full text screening.

Of the 43 references screened as full texts, 21 references, reporting data on 20 unique studies met the inclusion criteria specified in the review protocol for this question (appendix A). The clinical evidence study selection is presented as a diagram in appendix D. Systematic reviews were used as a source of primary studies and were then excluded.

This review was carried out at the end of the update of the VTE management guideline and as a result, no rerun searches were carried out for this question.

Please see appendix E for the full evidence tables. The references of individual included studies are listed in appendix K.

Excluded studies

See Appendix J for a list of references for excluded studies, with reasons for exclusion.

Summary of clinical studies included in the evidence review

The 20 included studies were assigned to the categories as follows (see note below):

- 2 retrospective cohort studies for people with VTE who cannot have anticoagulants (Table 2)
- 2 cohort studies (1 retrospective, 1 retrospective analysis of a prospective cohort) for people with VTE who had a PE whilst taking anticoagulants (Table 3)
- 4 studies (3 retrospective cohort studies, 1 RCT) for people with VTE who have filters inserted for prophylaxis before a potential provoking event (Table 4)

- 7 retrospective cohort studies for people with VTE who are at high risk of poor outcomes in the event of PE-recurrence (Table 5)
- 2 RCTs (3 papers) for people with VTE who are at high risk of PE recurrence (Table 6)
- 5 studies (4 retrospective cohort studies, 1 RCT) for people with VTE and cancer (Table 7)

Note: Decousus 1998 and PREPIC 2005 reported data on the same study. Stein 2018a and White 2016 each reported data for two distinct relevant populations and so are included in the tables below twice (and twice in the lists above).

Table 2 Studies including people with VTE who cannot have anticoagulants

Author (year)	Design	Sample size	Population	Comparison	Follow up
Turner 2018	Retrospective cohort study	126,030	VTE with contraindication to anticoagulants, identified by presence of any of the following criteria: • intracranial bleeding • other major bleeding • thrombocytopenia • active gastrointestinal bleeding • aortic dissection • pericardial disease • bacterial endocarditis • threatened abortion • preeclampsia and eclampsia • malignant hypertension • brain surgery • spinal surgery • spinal puncture • eye surgery • haemophilia, von Willebrand disease or cerebral aneurysm coded at the index hospitalization or within the prior year	• Filter • No filter	30 days
White 2016	Retrospective cohort study	3,017	PE or lower extremity DVT with contraindication to anticoagulants, identified by presence of active bleeding (on admission or during hospital stay)	• Filter • No filter	• 30 days • 90 days • 1 year

1 **Table 3 Studies including people with VTE who had a PE whilst taking anticoagulants**

Author (year)	Design	Sample size	Population	Comparison	Follow-up
Mellado 2016	Retrospective analysis of prospective cohort	139	Acute VTE with recurrent PE within 3 months of index event, whilst taking anticoagulation.	• Filter • No filter	30 days
Stein 2019a	Retrospective cohort study	814	Had a recurrent PE within 3 months of an index VTE. Anticoagulation status of participants is uncertain – study makes assumption that they were on anticoagulants.	• Filter • No filter	• In-hospital • 3 months

2 **Table 4 Studies including people with VTE who have the filters inserted for**
3 **prophylaxis before a potential provoking event**

Author (year)	Design	Sample size	Population	Comparison	Follow-up
Pan 2016	Retrospective cohort study	1,471	Pelvic or lower extremity fracture complicated with lower extremity DVT, who underwent orthopedic surgery	• Filter • No filter	In-hospital
Sharifi 2012	RCT	141	DVT involving the popliteal vein or more proximal venous segments, scheduled to undergo percutaneous endovenous intervention.	• Filter • No filter	• During procedure • 24 hours post-procedure • Up to 24 months
Stein 2018a	Retrospective cohort study	369	Stable PE and underwent surgical pulmonary embolectomy	• Filter • No filter	In-hospital
White 2016	Retrospective cohort study	1,445	PE and underwent major surgical procedure during hospital stay	• Filter • No filter	• 30 days • 90 days • 1 year

4 **Table 5 Studies including people with VTE who are at high risk of poor outcomes in**
5 **the event of PE recurrence.**

Author (year)	Design	Sample size	Population	Comparison	Follow-up
Jha 2010	Retrospective cohort study	67	PE with right heart strain	• Filter • No filter	• In-hospital
Liang 2017	Retrospective cohort study	11,218	Hemodynamically unstable PE	• Filter • No filter	• In-hospital

Author (year)	Design	Sample size	Population	Comparison	Follow-up
Stein 2018a	Retrospective cohort study	369	Population 1: Stable PE and underwent surgical pulmonary embolectomy	• Filter • No filter	• In-hospital
		4,279	Population 2: Unstable (in shock or on ventilator support) PE		
Stein 2018b	Retrospective cohort study	479	Unstable (in shock or on a ventilator) PE	• Filter • No filter	In-hospital
Stein 2019b	Retrospective cohort study	16,486	PE and heart failure	• Filter No filter	In-hospital
Tanabe 2014	Retrospective cohort study	375	Massive or sub-massive PE, or PE with collapse.	• Filter • No filter	• Up to 30 days
Wadhwa 2018	Retrospective cohort study	425,877	PE and chronic heart failure	• Filter • No filter	• In-hospital

1 **Table 6 Studies including people with VTE who are at high risk of PE recurrence**

Author (year)	Design	Sample size	Population	Comparison	Follow up
PREPIC 2005 and Decousus 1998	RCT	400	Proximal DVT (with/without PE), considered to be at high risk for PE by physician.	• Filter • No filter	• 12 days • 3 months • 8 years
Mismetti 2015 (PREPIC II)	RCT	399	PE with at least one of the following indicators of severity: • older than 75 years • active cancer • chronic cardiac or respiratory insufficiency ischemic stroke with leg paralysis within the last 6 months (but more than 3 days before randomization) • deep vein thrombosis that involved the iliocaval segment or was bilateral • at least 1 sign of right ventricular dysfunction or myocardial injury	• Filter • No filter	• 3 months • 6 months

Table 7 Studies including people with VTE and cancer

Author (year)	Design	Sample size	Population	Comparison	Follow-up
Bargine ar 2009	Retrospective cohort study	104	VTE and active cancer	• Filter plus anticoagulation (treated with VKA) • Anticoagulation only (40% had LMWH alone, 60% had VKA)	• Unclear length of follow-up but was likely into the long term.
Bargine ar 2012	RCT	64	DVT (with or without PE) and active cancer	• Fondaparinux + filter • Fondaparinux only	• 90 days
Brunson 2017	Retrospective cohort study	14,000	VTE and active cancer	• Filter • No filter	• 30 days • 6 months • 1 year
Coombs 2017	Retrospective cohort study	1,270	PE and active cancer	• Filter • No filter	• 1 year
Stein 2018c	Retrospective cohort study	35,024	PE with solid malignant tumor	• Filter • No filter	• In-hospital • 3 months

See appendix E for full evidence tables.

Quality assessment of clinical studies included in the evidence review

See appendix E for the risk of bias assessments for individual studies, appendix F for forest plots and appendix G for full GRADE tables. Please refer to the evidence statement section for an overall summary of the evidence.

Economic evidence

Included studies

A systematic search was conducted to identify economic evaluations published since the 2012 update of the guideline. The search returned 233 records. In addition, 1 paper from the economic evidence review for the 2012 guideline was identified. Of the 234 records, 231 were excluded on the basis of title and abstract. The 3 remaining papers were screened in full and only the 1 study (from the 2012 guideline) met the criteria for inclusion in the evidence review.

Excluded studies

Details of excluded studies with reasons for their exclusion are provided in appendix J. For full references of excluded studies, please see appendix K.

Summary of economic studies included in the evidence review

Sarasin (1993) conducted a cost-utility analysis comparing the use of an IVC filter to observation (no treatment) in people with cancer and confirmed VTE. The analysis also

considered a third strategy, immediate long-term anticoagulation but this strategy does not fall within the scope of the protocol for this review question. Separate analyses were conducted for the DVT and PE subpopulations. A decision tree was used to simulate the short-term impact of the interventions and a Markov model was used to capture the lifelong differences in recurrence, bleeding, mortality and filter-related complications. The Markov model was run over a lifetime horizon using monthly cycles. The analysis was carried out from the health provider perspective in the US.

The probabilities of VTE, bleeding, mortality and relative treatment effects were sourced from published observational studies or single arm trials. Because there was no study reporting the risk of VTE in people with cancer not receiving anticoagulation, the authors assumed that the probability of developing PE after a DVT was the same as in a population without cancer. It was also assumed that all embolic events would occur in the first month following index DVT or PE. Death was associated to specific events such as acute bleeding, long term consequences of bleeding, IVC filter insertion and PE recurrence, or to excess cancer mortality. The model accounted for the costs of the interventions, complications (VTE, IVC filter insertion) and death, which were expressed in US dollars (1989/91). Utility values were obtained from consensus of clinicians' opinions. Both costs and outcomes were discounted annually at 5%.

In the base case, the IVC filter option dominated the no treatment strategy as the IVC filter was both cheaper and generated more QALYs. IVC filter and anticoagulation remained more cost effective than no treatment when parameters were varied deterministically. The cost of filter insertion was estimated to be $1500 but the model assumed much higher costs ($3100 to $4600) in the event of a thromboembolic recurrence such that overall, costs for the IVC filter strategy were lower than no treatment. The analysis was strongly influenced by the short life expectancy of people with cancer, which reduced the likelihood of complications from the device.

The study was classified as being partially applicable because it was conducted from a non-UK NHS perspective. Full incremental cost-effectiveness results were reported only for people with lung cancer and costs were discounted at 5% annually. The study was categorised as having very serious limitations because utilities were estimated from expert opinion, the source of funding was not reported, it was unclear how studies for some clinical parameters were identified and probabilistic sensitivity analysis was not conducted.

Evidence statements

Clinical evidence statements

People with VTE who cannot take anticoagulation

Very low quality evidence from up to 2 retrospective cohort studies reporting data on up to 129,047 people with VTE who cannot take anticoagulation **could not differentiate** any-cause mortality (in the 30 days following admission) or PE-recurrence (in the year following admission) between in people with a filter compared to people without a filter.

Very low-quality evidence from 1 retrospective cohort study reporting data on 3,017 people with VTE who cannot take anticoagulation **found a reduction** in any-cause mortality (in the 3 months following admission) in people with a filter compared to people without a filter.

Very low-quality evidence from 1 retrospective cohort study reporting data on 3,017 people with VTE who cannot take anticoagulation **found an increase** in DVT-recurrence (in the 3 months following admission) in people with a filter compared to people without a filter.

People with VTE who have a PE whilst taking anticoagulants

Very-low quality evidence from 1 prospective cohort study reporting data on 139 people who experienced a PE within 3 months of an initial VTE **found a reduction** in all-cause mortality and PE related mortality at 30 days in people with a filter compared to people without a filter.

Very-low quality evidence from 1 retrospective cohort study reporting data on 814 people who experienced a PE within 3 months of an initial VTE **found a reduction** in all-cause mortality during hospital stay and at 3 months in people with a filter compared to people without a filter.

Very-low quality evidence from 1 prospective cohort study reporting data on 139 people who experienced a PE within 3 months of an initial VTE **could not differentiate** VTE-recurrence and major bleeding at 30 days between people with a filter and people without a filter.

People with VTE who have the filters inserted for prophylaxis before a potential provoking event

Low to moderate quality evidence from 1 RCT reporting data on 141 people with VTE undergoing surgery **found a reduction** in PE-recurrence (during the surgical procedure, during hospital stay and up to 2 years of follow-up) in people with a filter compared to people without a filter.

Very low quality evidence from 1 RCT reporting data 141 people with VTE undergoing surgery **could not differentiate** DVT-recurrence up to 2 years between people with a filter compared to people without a filter.

Moderate quality evidence from 1 RCT reporting data on 141 people **could not estimate** an effect for all-cause mortality (during the surgical procedure or in-hospital) and DVT-recurrence (during the surgical procedure or in-hospital) as both arms reported 0 events.

Very low quality evidence from up to 2 retrospective cohort studies reporting data on up to 1,787 people with VTE undergoing surgery **found a reduction** in in-hospital all-cause mortality, all-cause mortality at 3 months, PE-related mortality (in-hospital and at 3-months), in-hospital PE-recurrence (overall population and specifically in those people who received anticoagulation following the procedure) in people with a filter compared to people without a filter.

Very low quality evidence from up to 2 retrospective cohort studies reporting data on up to 1,787 people with VTE undergoing surgery **could not differentiate** the following outcomes between people with a filter compared to people without a filter:

- in-hospital all-cause mortality (specifically in those people at least 80 years old)
- in-hospital PE-recurrence (specifically in those with a contraindication to anticoagulation during their hospital stay)
- all-cause mortality at 30 days, 3 months and 2 years.
- PE-recurrence at 1 year
- DVT-recurrence at 1 year

People with VTE who are at high risk of poor outcomes in the event of a PE

Very low quality evidence from up to 6 retrospective cohort studies reporting data on 446,762 people with VTE at high risk of poor outcomes in the event of a PE **found a reduction** in in-hospital all-cause mortality (overall, specifically in those at least 80 years of age and specifically in those with massive PE) and all-cause mortality at 3 months in people with a filter compared to people without a filter.

Very low quality evidence from 1 retrospective cohort study reporting data on 11, 218 people with VTE at high risk of poor outcomes in the event of a PE **found an increase** in in-hospital all-cause mortality in people with a filter compared to people without a filter.

Very low quality evidence from 1 prospective cohort study reporting data on 375 people with VTE at high risk of poor outcomes in the event of a PE **found a reduction** in all-cause mortality at 30 days in people with a filter compared to people without a filter.

Very low quality evidence from 2 retrospective cohort studies reporting data on 3,380 people with VTE at high risk of poor outcomes in the event of a PE **could not differentiate** PE-related mortality in-hospital or at 3 months between people with a filter and people without a filter.

Sensitivity analysis excluding studies at critical risk of bias

Very low quality evidence from 1 retrospective cohort study reporting data on 425,875 people with VTE at high risk of poor outcomes in the event of a PE found a **reduction** in all-cause mortality (in-hospital) in people with a filter compared to people without a filter.

People with VTE who are at high risk of PE-recurrence

High quality evidence from 1 RCT reporting data on 400 people with VTE at high risk of recurrence **found a reduction** in symptomatic PE-recurrence at 8 years in people with a filter compared to people without a filter.

High quality evidence from 1 RCT reporting data on 400 people with VTE at high risk of recurrence found **no meaningful difference** in rates of post-thrombotic syndrome at 8 years between people with a filter compared to people without a filter.

Very low to moderate quality evidence from up to 2 RCTs reporting data on up to 799 people with VTE at high risk of recurrence **could not differentiate** the following outcomes between people with a filter compared to people without a filter:

- all-cause mortality at 12 days, 3 months, 6 months and 8 years.
- VTE-recurrence at 3 months, 6 months and 8 years.
- PE-related mortality at 3 months, 6 months and 8 years.
- symptomatic PE-recurrence at 12 days, 3 months and 6 months.
- DVT-recurrence at 3 months, 6 months and 8 years.
- major bleeding at 12 days, 3 months, 6 months and 8 years.
- asymptomatic or symptomatic PE recurrence at 12 days.

People with VTE and cancer

Low quality evidence from 1 RCT reporting data on 64 participants **could not differentiate** all-cause mortality, PE-recurrence, major bleeding or IVC complications all at 3 months between people with a filter compared to people without a filter.

High quality evidence from 1 RCT reporting data on 64 people **could not estimate** an effect for DVT-recurrence at 3 months as both arms reported 0 events.

Very low quality evidence from 1 retrospective cohort study reporting data on up to 35,034 people with VTE and cancer **found a reduction** in in-hospital all-cause mortality (overall and specifically in those aged 80 years or older) and in all-cause mortality at 3 months, in people with a filter compared to people without a filter.

Very low quality evidence from 3 retrospective cohort studies reporting data on up to 15,374 people with VTE and cancer **found an increase** in long-term DVT-recurrence in people with a filter compared to people without a filter.

Very low quality evidence from 2 retrospective cohort studies reporting data on up to 15,270 people with VTE and cancer **found an increase** in all-cause mortality at 30 days, 3 months and 1 year and in VTE recurrence at 1 year in people with a filter compared to people without a filter.

Very low quality evidence from 3 retrospective cohort studies reporting data on up to 15,374 people with VTE and cancer **could not differentiate** the following outcomes between people with a filter compared to people without a filter:

- PE recurrence (long term)
- major bleeding (long-term)

Sensitivity analysis excluding studies at critical risk of bias

Very low quality evidence from 1 retrospective cohort study reporting data on up to 1,270 people with VTE and cancer **found an increase** in DVT recurrence at 1 year between people with a filter compared to people without a filter.

Very low quality evidence from 1 retrospective cohort study reporting data on up to 1,270 people with VTE and cancer **could not differentiate** the PE recurrence at 1 year between people with a filter compared to people without a filter.

Economic evidence statements

A partially applicable study with very serious limitations (Sarasin et al.,1993) assessed the cost effectiveness of IVC filter versus no treatment in people with cancer and confirmed VTE. The IVC filter strategy was found to be dominant (more effective and less expensive). The results were robust to one-way sensitivity analysis. No probabilistic sensitivity analysis was conducted.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

IVC filters are used to prevent thromboemboli from travelling into the pulmonary circulation in a number of clinical scenarios (see Table 1 and discussions below). VTE-recurrence (particularly PE-recurrence) is therefore one of the most important outcomes when assessing the effectiveness of IVC-filters. PE-recurrence can increase the risk of mortality, therefore

VTE and all-cause mortality are also important outcomes. It may also lead to chronic thromboembolic pulmonary hypertension.

The committee agreed that the use of IVC filters is accompanied by a risk of filter complications (such as filter migration and filter-site thrombosis) and that these were also important outcomes to consider and could be linked to increased mortality in some cases.

The committee noted the importance of having results for outcomes in the short and long term. Short term outcomes (outcomes up 3 months) are important because IVC filters are often placed in people with an acute risk of thrombosis (such as people at high risk of PE and people undergoing surgery or other provoking events) and short term follow up will capture the effects of the filter in these situations. Additionally, complications may arise as a result of placing the filter or in the period immediately following insertion. Long-term evidence (outcomes occurring after 3 months) is important in people receiving filters that are expected to be left in for a longer duration (such as those people who had a recurrent event whilst taking anticoagulation). Filters have a risk of delayed complications such as filter migration, infection, fracture and perforation which may occur at a differential rate in the long-term. It is therefore important that both time points are captured.

The quality of the evidence

The committee agreed that the best evidence available was from RCTs but that most of the available evidence came from retrospective cohort studies which compared groups of people with VTE who received a filter to those who did not. The committee agreed that the decision to place a filter is usually based on a variety of important clinical characteristics (including severity of the PE, general health etc.) and therefore a group of people who received a filter and a group who did not are likely to be very different populations. Some studies attempted to account for this disparity by identifying important clinical characteristics (such as indicators of PE severity) which contribute to making a filter more likely to be placed and adjusting for these factors.

Studies typically account for these confounders either by using propensity matching (matching the participants in the filter group to a pair in the no-filter group based on important clinical characteristics and excluding non-matched participants) or adjusting their analysis by propensity score (attributing a score to each participant for the likelihood of receiving a filter based on important clinical characteristics and applying this score as a coefficient in the analysis). However, the committee were concerned that differences between groups are likely to remain even after adjustment, and many studies either did not adjust their analysis or adjusted for only a few confounders.

All the cohort studies suffered from immortal time bias as follow-up began at the point of admission to hospital, but filters were placed at a later point in time. Therefore, the filter group cannot die in the period between admission and when the filter is placed (deaths in this period would have been placed in the no-filter group), however all deaths in the no-filter group were counted. This can lead to an overestimation of the benefit of filters in reducing mortality. Some studies attempted to account for immortal time bias by excluding all events occurring within 24 hours of admission, however as filters are often placed after 24 hours, this inadequately accounts for the bias. A more appropriate method (as used in White 2016) was to match participants across groups based on the propensity for receiving a filter, with people in the no-filter group having to be alive on the day their matched pair had their filter placed.

The committee agreed with the risk of bias assessments of the cohort studies and with marking down for risk of bias those studies that adjusted for a limited number of confounding factors or failed to adjust/adjusted poorly for immortal time bias. The committee were particularly concerned about studies judged to be at critical risk of bias because these studies typically did not adjust for confounders and /or immortal time bias. The committee agreed that it was important to include these studies in the review due to the scarcity of other studies, but that it was useful to conduct sensitivity analyses in which these studies were excluded from meta-analysis (along with additional sensitivity analyses excluding those studies at serious risk of bias).

There was high heterogeneity between the included cohort studies in the confounders the studies adjusted for, in the inclusion criteria and in the results obtained in some scenarios when meta-analysis was possible.

There were only two retrospective cohort studies looking at people with VTE who cannot take anticoagulation, both of which suffered from methodological issues. Data on actual use of (and contraindication to) anticoagulation was not captured by the sources these studies used to obtain their data. Instead, these studies used other available clinical characteristics to indicate a contraindication (such as active bleeding). The committee advised that the criteria used in these studies would very likely indicate a contraindication to anticoagulation but agreed that studies using active bleeding alone (White, 2016) are unlikely to capture all relevant participants.

Both of these studies adjusted for the likelihood of receiving a filter using various important clinical characteristics. The committee agreed that this improved their confidence in the evidence but advised that the inclusion of people with distal DVT (in Turner, 2018) is a risk of bias as these people are typically not candidates for a filter and will likely be over-represented in the no-filter group. Additionally, the evidence was inconsistent as the larger study (Turner, 2018) showed increased all-cause mortality at 30 days and White (2016) showed a reduction at 30 days and 3 months.

The committee were concerned with the very low quality of the limited evidence available for people with VTE who have had a PE whilst taking anticoagulants, noting that Stein (2019a) could not determine whether participants were on anticoagulation when the recurrent event occurred and did not adjust for confounders or immortal time bias. The committee agreed that there were fewer methodological concerns surrounding Mellado (2016) as this study used a prospective collected database and used propensity matching, however the sample size was small.

The evidence for people having filters inserted for prophylaxis before a potential provoking event came from people with VTE who were having a filter placed before surgery. The committee were concerned with the differences in study populations contained within this group as the type of surgery differed between studies. Additionally, three of the studies only included people undergoing a specific intervention (such as percutaneous endovenous intervention) whereas one study (White 2016) included all people with VTE undergoing major surgery. The committee advised that the nature of these interventions is very diverse. Consequently, it is difficult to generalise the available evidence to all people with VTE undergoing surgery. The committee agreed that there is a need for better evidence for specific types of surgery for which IVC filters may be more appropriate as a prophylactic measure (such as cancer surgery).

The committee advised that there were considerable population differences in the studies looking at people at high risk of poor outcomes in the event of a PE (as the conditions that

predisposed them to poor outcomes varied between studies) and studies looking at people with VTE who were having a filter fitted prior to surgery (as the type of surgery differed between studies). The evidence for this population subgroup was of very-low quality and came from retrospective cohort studies, the majority of which were at critical risk of bias. As such, it was hard to draw conclusions from the meta-analyses for these groups.

The committee noted that there were two RCTs looking at the use of filters in people at high risk of PE recurrence; that these studies were at low risk of bias and reported outcomes into the long-term (PREPIC 2005 reported outcomes up to 8 years). However, these studies were unable to differentiate between filter and no-filter for the majority of outcomes. Additionally, the criteria for high risk of PE differed between studies: PREPIC (2005) defined risk according to physician's judgement whereas Mismetti (2015) required that the person meet pre-specified criteria for risk. The committee noted that based on these criteria, Mismetti (2015) included a mixture of people at high risk of PE, at high risk of poor outcomes, and people with VTE who do not meet the inclusion criteria for this review. The committee agreed that this evidence should be downgraded for indirectness because of this, but that it should remain in this section of the review. In addition, they noted that despite the differences in the characteristics of the participants, the studies showed similar results for most outcomes.

There were 4 retrospective cohort studies at moderate to critical risk of bias and 1 RCT with low risk of bias reporting data on people with VTE and cancer. The committee were concerned that the evidence for people with VTE and cancer was inconsistent. Stein (2018c) noted a reduction in all-cause mortality associated with filter use, Coombs (2017) and Brunson (2017) found an increase (along with an increase in DVT-recurrence and VTE-recurrence) and the only RCT in this group (Barginear 2012) could not differentiate between filter and no filter for all of the outcomes reported.

Benefits and harms

The committee noted that IVC filters are used in a variety of circumstances in people with VTE, but there is a lack of consensus about their efficacy in most of these contexts. However, most of the evidence for the use of IVC filters in people with VTE that was identified in this review was of very low quality and the committee agreed that this limited their ability to make recommendations.

The committee discussed the potential harms associated with placing an IVC filter in a person with VTE. They agreed that there is an inherent harm associated with placing a filter due to the invasive nature of the procedure. In addition, the use of filters is also associated with a risk of filter complications, such as migration and infection, and these potential harms must be considered when a decision is made to place a filter. The committee were aware of a review by Jia (2015) that reported high rates of IVC filter complications (>15%), with major complications (typically requiring that the filter be retrieved) occurring in around 5% of people. However, the committee noted that many of the complications in this study are likely to be minor and there is uncertainty as to how important certain complications (such as IVC wall transgression by components of the filter) as clinically. The committee agreed that the evidence available does not adequately consider filter complications. The committee also noted that in some circumstances, filters may be placed prophylactically to reduce the perceived risk of PE recurrence rather than based on clinical need. They agreed that there are financial costs to the health system and risks to the individual if filters are placed unnecessarily.

The committee were very concerned with the limited amount of long-term evidence available, leaving uncertainty surrounding treatment beyond 30 days, which is particularly important for

certain groups of people (such as those people who had a recurrent event whilst taking anticoagulation) who typically receive long-term filters.

The committee discussed the benefits of using filters in the different scenarios. Firstly, the committee noted that the evidence for people at high risk of poor outcomes if they develop a PE was of very-low quality and that only two of the studies (Liang 2017 and Wadhwa 2018) attempted to adjust for confounders (and these were the only two that were not at critical risk of bias) produced conflicting results. Secondly, the committee agreed that as the evidence for people at high risk of a recurrent PE could not differentiate most outcomes at any point in time, they were unable to determine a benefit or harm associated with filter use in these people. Thirdly, they noted that the results from studies in people with VTE and cancer were contradictory with Stein (2018c) showing a reduction in all-cause mortality, while other studies (Coombs, 2017 and Brunson, 2017) showed an increase and the only RCT available for this group of people (Barginear, 2012) could not differentiate outcomes between people given a filter and those without a filter. Finally, in people with VTE who are undergoing surgery, there was very-low quality evidence from a retrospective cohort study suggesting reduced all-mortality associated with the use of filters and low quality evidence from an RCT suggesting a reduction in PE-recurrence (due to a reduction in PEs occurring during surgery) in people given a filter, but this was in disagreement with another retrospective cohort study that could not differentiate between the filer and no filter groups for both outcomes. In addition, the committee were concerned with the heterogeneity of the studies contained within the grouping as each study involved a different type of surgery.

The committee agreed they were unable to recommend the use of filters for these groups due to the poor quality and contradictory or inconclusive nature of the evidence identified. However, they recognised there was a need for higher quality research to try to fill in the gaps in the evidence base and address the remaining uncertainty in these areas. They therefore made a recommendation to not offer filters people with DVT or PE unless it is part of a clinical trial or was covered by their other recommendations for people in whom anticoagulation is contraindicated or who have a PE while taking anticoagulation treatment (see below for details of these recommendations). In addition, they made an accompanying research recommendation to try to determine the short and long term clinical and cost effectiveness of filters in people with VTE. The recommendation was for a large prospective study to follow-up people with VTE and capture information regarding IVC filter use. They envisaged that this cohort study would enrol everyone with VTE, with the intention of recording information regarding filter use and no filter use for each of the key population subgroups groups identified (see appendix Q for more details). They also included the option of an RCT to investigate all the population subgroups (with the exception of people who are at high risk of PE as this group was already covered by 2 RCTs). However, they noted that an RCT study design was likely to be less feasible than a prospective cohort study because it might be difficult to recruit sufficient people in the different subgroups to be able to detect a difference in outcomes between people who or do not have a filter.

The committee noted that people with VTE and a contraindication to anticoagulation are at a particularly high risk of VTE-recurrence. Therefore, IVC filters are typically seen as a viable and important alternative treatment (or secondary prophylactic measure) in these people. However, the committee agreed that in light of new evidence, which did not show a clear benefit to IVC filters in this group of people, and some evidence suggesting harm, the 2012 guideline recommendation - that IVC filters be offered to people with VTE with a contraindication to anticoagulants - was too strong. The committee noted that these recommendations were made by consensus and that the only evidence available at the time was from the PREPIC 2005 study (which contained a population of people receiving

anticoagulation). Based on the limited evidence base and inconsistencies in the results between studies, the committee agreed that the recommendation should be downgraded to consider. They agreed that when filters are placed, they should be removed as soon as they are no longer needed (i.e. as soon as the individual is able to take anticoagulants and is on stable treatment with them).

The committee discussed the use of IVC filters in people who have a PE whilst taking therapeutic anticoagulation treatment. The committee noted a reduction in short term all-cause mortality (30 days) associated with the use of filters in the Mellado (2016) study. The committee agreed that the very serious risk of bias associated with Stein (2019a) limited their confidence in the findings of this study but noted that the trend was consistent with that of Mellado (2016). The committee recommended that IVC filters be considered in people with VTE who have a PE whilst taking therapeutic treatment, but only after various clinical checks are performed. They agreed that adherence to anticoagulation treatment should be checked, as a recurrent event associated with poor adherence may be more suitably treated by increasing the awareness of the person with VTE of the importance of taking the anticoagulants at the correct time and in the correct manner. If adherence to treatment is not an issue, then an increased dose of anticoagulant or alternative treatment regimen should be investigated as other anticoagulants may prove more effective for that individual. Finally, hypercoagulability should be assessed. The committee made a weaker 'consider' recommendation due to the limited and low quality of the evidence base.

The committee agreed that it is important that there is a strategy in place for removing the IVC filter as soon as this is clinically advisable and that this plan is clearly documented. The committee agreed that they could not specify how frequently the strategy should be reviewed but agreed that a review should take place if the individual's clinical situation changes. The committee made a recommendation to reflect these points to ensure that the filter is removed as soon as it is no longer needed.

Cost effectiveness and resource use

The committee discussed evidence from one published cost-utility study (Sarasin 1993) that compared the use of IVC filters to no treatment in people with cancer and confirmed VTE. The authors of the study concluded that using an IVC filter was more effective and less costly than no treatment. The study was classified as partially applicable with very serious limitations. The committee decided to include the study in the evidence review for transparency but felt it had limited value in informing the recommendations for several reasons. Firstly, the analysis was not conducted from a UK perspective. Secondly, the analysis was published in 1993 and therefore the evidence informing the effectiveness of the IVC filter strategy in the model did not reflect any of the more recent studies identified in the clinical evidence review and was unlikely to reflect the efficacy of IVC filters in current use. Finally, there were a number of methodological weaknesses in the modelling approach, including a lack clarity about the source of some model parameters, utility values that were elicited from healthcare professionals and an absence of probabilistic sensitivity analysis.

No published economic evidence on the cost effectiveness of IVC filters was identified for any of the other subgroups of interest and de novo modelling was not conducted for this review question. The committee reflected on the costs of placement and removal of IVC filters (£3,500 and £930 respectively based on 2017/2018 NHS Reference Costs YR22A – YR22C). By making more specific recommendations about the clinical situations in which to consider the use of IVC filters, the committee felt that this could lead to a reduction in the use

of IVC filters in patients for whom there is no clear evidence of benefit and could potentially result in cost savings.

1 Appendices

1 Appendix A – Review protocol

Field (based on PRISMA-P	Content
Review question	What is the effectiveness of inferior vena caval filters to prevent PE in people with confirmed VTE?
Type of review question	Intervention
Objective of the review	To determine the effectiveness of filters in people with VTE who cannot take anticoagulants or those people with VTE who might need filters in addition to anticoagulants.
Eligibility criteria – population/disease	Adults (18+ years) with: • VTE (DVT and/or PE) who cannot have anticoagulants **or** • VTE who have had a filter inserted because they could not take anticoagulants, but retain the filter once they start taking anticoagulants **or** • VTE who have a PE whilst taking anticoagulants **or** • VTE who have the filters inserted for prophylaxis before a potential provoking event (e.g. surgery) **or** • VTE who can receive anticoagulants but are at high risk of PE* **or** are at high risk of poor outcomes if they had further PEs** *High risk was defined by the committee as people with free floating DVTs. **This includes massive /sub-massive PE patients and those with severe pre-existing cardio-pulmonary disease.
Eligibility criteria – intervention(s)	Vena cava filters with or without: • anticoagulation treatment and/or • mechanical interventions

Eligibility criteria – comparator(s)	No filter with: • mechanical intervention and/or • anticoagulant treatment and/or • placebo or no treatment. We will include studies that allow participants to have mechanical interventions, anticoagulation treatment or both, but these must be included in both arms of the trial so that the only difference in treatment between arms is the inclusion or exclusion of IVC filters.

Outcomes and prioritisation	• Recurrent VTE (PE and DVT)
	• All-cause mortality
	• VTE-related mortality
	• Post-thrombotic syndrome
	• Pulmonary hypertension (PH)
	• Quality of life
	  • Generic and disease-specific measures will be reported
	  • Overall score will be reported (data on subscales will not be reported)
	• Adverse events
	  • Total serious adverse events (as defined by the European medicines agency) will be reported if data is available.
	  • Major bleeding (as *defined by* International Society on Thrombosis and Haemostasis)
	  • Clinically relevant non-major bleeding *(*as defined by International Society on Thrombosis and Haemostasis)
	  • Surgical complications at the time of placement and removal
	  • Sepsis (or serious infections) for filters that are in place for longer periods
	• Resource use and costs

Eligibility criteria – study design	• RCTs • Cohort studies (prospective or retrospective)
Other inclusion/ exclusion criteria	Inclusion: • English language papers only

	Exclusion: • Filters in studies from before 1990 that are no longer used in clinical practice
Proposed sensitivity/sub-group analysis	Populations: • People with cancer • Very elderly people (defined as people over the age of 80) • Intravenous drug users • People with chronic liver disease • People with obesity (a BMI of over 30 kg/m^2 or more). Other factors: • Index event (DVT-only or PE with or without DVT) • Study type (RCT, prospective and retrospective cohort) • Filter type (retrievable or permanent) • Intervention type
Selection process – duplicate screening/selection/analysis	10% of the abstracts were reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. If meaningful disagreements were found between the different reviewers, a further 10% of the abstracts were reviewed by two reviewers, with this process continued until agreement is achieved between the two reviewers. From this point, the remaining abstracts will be screened by a single reviewer. This review made use of the priority screening functionality with the EPPI-reviewer systematic reviewing software. See Appendix B for more details.
Data management (software)	See Appendix B
Information sources –	• Sources to be searched

databases and dates	○ Clinical searches - Medline, Medline in Process, PubMed, Embase, Cochrane CDSR, CENTRAL, DARE (legacy records) and HTA. ○ Economic searches - Medline, Medline in Process, PubMed, Embase, NHS EED (legacy records) and HTA, with economic evaluations and quality of life filters applied. • Supplementary search techniques ○ None identified • Limits ○ Studies reported in English ○ Study design RCT, SR and Observational filter will be applied (as agreed) ○ Animal studies will be excluded from the search results ○ Conference abstracts will be excluded from the search results ○ Date limit from August 2011 for search for RCTs, but no date limits for cohort studies search.
Identify if an update	This question is an update of a question in CG144. Original search date up to 01.08.2011 but only included RCTs. <u>Recommendations that may change as a result of this review:</u> 1.2.10 Offer temporary inferior vena caval filters to patients with proximal DVT or PE who cannot have anticoagulation treatment, and remove the inferior vena caval filter when the patient becomes eligible for anticoagulation treatment. **[2012]** 1.2.11 Consider inferior vena caval filters for patients with recurrent proximal DVT or PE despite adequate anticoagulation treatment only after considering alternative treatments such as: • increasing target INR to 3–4 for long-term high-intensity oral anticoagulant therapy **or** • switching treatment to LMWH. **[2012]** 1.2.12 Ensure that a strategy for removing the inferior vena caval filter at the earliest possible opportunity is planned

	and documented when the filter is placed, and that the strategy is reviewed regularly. **[2012]**
Author contacts	https://www.nice.org.uk/guidance/indevelopment/gid-ng10087
Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual
Search strategy – for one database	For details please see appendix C of the evidence review
Data collection process – forms	A standardised evidence table format will be used, and published as appendix E (clinical evidence tables) or I (economic evidence tables) of the evidence review.
Data items – define all variables to be collected	For details please see evidence tables in appendix E (clinical evidence tables) or I (economic evidence tables) of the evidence review.
Methods for assessing bias at outcome/study level	See appendix B
Criteria for quantitative synthesis	See appendix B
Methods for quantitative analysis – combining studies and exploring (in)consistency	See appendix B
Meta-bias assessment – publication bias, selective reporting bias	See appendix B
Confidence in cumulative evidence	See appendix B
Rationale/context – what is known	In CG144, temporary inferior vena caval filters were recommended for people with proximal DVT or PE who cannot have anticoagulation treatment, with the filter being removed when the person becomes eligible for

	anticoagulation treatment (2012 recommendations). The guideline committee raised concerns that this recommendation was no longer appropriate given the results from new clinical trials and that additional guidance is needed concerning how long a person should be unable to take anticoagulant treatment before an inferior vena caval filter (IVC) is fitted. For more detail please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the guideline. The committee was convened by the NICE Guidelines Updates Team and chaired by Susan Bewley in line with section 3 of Developing NICE guidelines: the manual. Staff from the NICE Guidelines Updates Team undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the guideline in collaboration with the committee. For details please see the methods section of the evidence review in appendix B.
Sources of funding/support	The NICE Guideline Updates Team is an internal team within NICE
Name of sponsor	The NICE Guideline Updates Team is an internal team within NICE
Roles of sponsor	The NICE Guideline Updates Team is an internal team within NICE
PROSPERO registration number	[If registered, add PROSPERO registration number]

1
2

Appendix B – Methods

Priority screening

The reviews undertaken for this guideline all made use of the priority screening functionality with the EPPI-reviewer systematic reviewing software. This uses a machine learning algorithm (specifically, an SGD classifier) to take information on features (1, 2 and 3 word blocks) in the titles and abstract of papers marked as being 'includes' or 'excludes' during the title and abstract screening process, and re-orders the remaining records from most likely to least likely to be an include, based on that algorithm. This re-ordering of the remaining records occurs every time 25 additional records have been screened.

Research is currently ongoing as to what are the appropriate thresholds where reviewing of abstract can be stopped, assuming a defined threshold for the proportion of relevant papers it is acceptable to miss on primary screening. As a conservative approach until that research has been completed, the following rules were adopted during the production of this guideline:

- In every review, at least 50% of the identified abstract (or 1,000 records, if that is a greater number) were always screened.
- After this point, screening was only terminated if a pre-specified threshold was met for a number of abstracts being screened without a single new include being identified. This threshold was set according to the expected proportion of includes in the review (with reviews with a lower proportion of includes needing a higher number of papers without an identified study to justify termination), and was always a minimum of 250.
- A random 10% sample of the studies remaining in the database when the threshold were additionally screened, to check if a substantial number of relevant studies were not being correctly classified by the algorithm, with the full database being screened if concerns were identified.

As an additional check to ensure this approach did not miss relevant studies, the included studies lists of included systematic reviews were searched to identify any papers not identified through the primary search.

Incorporating published systematic reviews

For all review questions where a literature search was undertaken looking for a particular study design, systematic reviews containing studies of that design were also included. All included studies from those systematic reviews were screened to identify any additional relevant primary studies not found as part of the initial search.

Quality assessment

Individual systematic reviews were quality assessed using the ROBIS tool, with each classified into one of the following three groups:

- High quality – It is unlikely that additional relevant and important data would be identified from primary studies compared to that reported in the review, and unlikely that any relevant and important studies have been missed by the review.
- Moderate quality – It is possible that additional relevant and important data would be identified from primary studies compared to that reported in the review, but unlikely that any relevant and important studies have been missed by the review.

- Low quality – It is possible that relevant and important studies have been missed by the review.

Each individual systematic review was also classified into one of three groups for its applicability as a source of data, based on how closely the review matches the specified review protocol in the guideline. Studies were rated as follows:

- Fully applicable – The identified review fully covers the review protocol in the guideline.
- Partially applicable – The identified review fully covers a discrete subsection of the review protocol in the guideline (for example, some of the factors in the protocol only).
- Not applicable – The identified review, despite including studies relevant to the review question, does not fully cover any discrete subsection of the review protocol in the guideline.

Using systematic reviews as a source of data

If systematic reviews were identified as being sufficiently applicable and high quality, and were identified sufficiently early in the review process (for example, from the surveillance review or early in the database search), they were used as the primary source of data, rather than extracting information from primary studies. The extent to which this was done depended on the quality and applicability of the review, as defined in Table 8. When systematic reviews were used as a source of primary data, and unpublished or additional data included in the review which is not in the primary studies was also included. Data from these systematic reviews was then quality assessed and presented in GRADE tables as described below, in the same way as if data had been extracted from primary studies. In questions where data was extracted from both systematic reviews and primary studies, these were cross-referenced to ensure none of the data had been double counted through this process.

Table 8: Criteria for using systematic reviews as a source of data

Quality	Applicability	Use of systematic review
High	Fully applicable	Data from the published systematic review were used instead of undertaking a new literature search or data analysis. Searches were only done to cover the period of time since the search date of the review.
High	Partially applicable	Data from the published systematic review were used instead of undertaking a new literature search and data analysis for the relevant subsection of the protocol. For this section, searches were only done to cover the period of time since the search date of the review. For other sections not covered by the systematic review, searches were undertaken as normal.
Moderate	Fully applicable	Details of included studies were used instead of undertaking a new literature search. Full-text papers of included studies were still retrieved for the purposes of data analysis. Searches were only done to cover the period of time since the search date of the review.
Moderate	Partially applicable	Details of included studies were used instead of undertaking a new literature search for the relevant subsection of the protocol. For this section, searches were only done to cover the period of time since the search date of the review. For other sections not covered by the systematic review, searches were undertaken as normal.

Evidence synthesis and meta-analyses

Where possible, meta-analyses were conducted to combine the results of quantitative studies for each outcome. For continuous outcomes analysed as mean differences, where change from baseline data were reported in the trials and were accompanied by a measure of spread (for example standard deviation), these were extracted and used in the meta-analysis. Where measures of spread for change from baseline values were not reported, the corresponding values at study end were used and were combined with change from baseline values to produce summary estimates of effect. These studies were assessed to ensure that baseline values were balanced across the treatment groups; if there were significant differences at baseline these studies were not included in any meta-analysis and were reported separately. For continuous outcomes analysed as standardised mean differences, where only baseline and final time point values were available, change from baseline standard deviations were estimated, assuming a correlation coefficient of 0.5.

Evidence of effectiveness of interventions

Quality assessment

Individual RCTs and quasi-randomised controlled trials were quality assessed using the Cochrane Risk of Bias Tool. Other studies were quality assessed using the ROBINS-I tool. Each individual RCT was classified into one of the following three groups:

- Low risk of bias – The true effect size for the study is likely to be close to the estimated effect size.
- Moderate risk of bias – There is a possibility the true effect size for the study is substantially different to the estimated effect size.
- High risk of bias – It is likely the true effect size for the study is substantially different to the estimated effect size.

Each individual cohort study was classified into one of the following five groups:

- Low risk of bias – The true effect size for the study is likely to be close to the estimated effect size.
- Moderate risk of bias – There is a possibility the true effect size for the study is substantially different to the estimated effect size.
- Serious risk of bias – It is likely the true effect size for the study is substantially different to the estimated effect size.
- Critical risk of bias – It is likely the true effect size for the study is substantially different to the estimated effect size.
- No information – There is no clear indication that the study is at serious or critical risk of bias *and* there is a lack of information in one or more key domains of bias.

Each individual study (RCT and cohort study) was also classified into one of three groups for directness, based on if there were concerns about the population, intervention, comparator and/or outcomes in the study and how directly these variables could address the specified review question. Studies were rated as follows:

- Direct – No important deviations from the protocol in population, intervention, comparator and/or outcomes.
- Partially indirect – Important deviations from the protocol in one of the population, intervention, comparator and/or outcomes.

- Indirect – Important deviations from the protocol in at least two of the following areas: population, intervention, comparator and/or outcomes.

Methods for combining intervention evidence

Meta-analyses of interventional data were conducted with reference to the Cochrane Handbook for Systematic Reviews of Interventions (Higgins et al. 2011).

Where different studies presented continuous data measuring the same outcome but using different numerical scales (e.g. a 0-10 and a 0-100 visual analogue scale), these outcomes were all converted to the same scale before meta-analysis was conducted on the mean differences. Where outcomes measured the same underlying construct but used different instruments/metrics, data were analysed using standardised mean differences (Hedges' g).

A pooled relative risk was calculated for dichotomous outcomes (using the Mantel–Haenszel method) reporting numbers of people having an event, and a pooled incidence rate ratio was calculated for dichotomous outcomes reporting total numbers of events. Both relative and absolute risks were presented, with absolute risks calculated by applying the relative risk to the pooled risk in the comparator arm of the meta-analysis (all pooled trials).

Fixed- and random-effects models (der Simonian and Laird) were fitted for all syntheses, with the presented analysis dependent on the degree of heterogeneity in the assembled evidence. Fixed-effects models were the preferred choice to report, but in situations where the assumption of a shared mean for fixed-effects model were clearly not met, even after appropriate pre-specified subgroup analyses were conducted, random-effects results are presented. Fixed-effects models were deemed to be inappropriate if one or both of the following conditions was met:

- Significant between study heterogeneity in methodology, population, intervention or comparator was identified by the reviewer in advance of data analysis. This decision was made and recorded before any data analysis was undertaken.
- The presence of significant statistical heterogeneity in the meta-analysis, defined as $I^2 \geq 50\%$.

In any meta-analyses where some (but not all) of the data came from studies at high risk of bias, a sensitivity analysis was conducted, excluding those studies from the analysis. Results from both the full and restricted meta-analyses are reported. Similarly, in any meta-analyses where some (but not all) of the data came from indirect studies, a sensitivity analysis was conducted, excluding those studies from the analysis.

Meta-analyses were performed in Cochrane Review Manager V5.3, with the exception of incidence rate ratio analyses which were carried out in R version 3.3.4.

Minimal clinically important differences (MIDs)

The Core Outcome Measures in Effectiveness Trials (COMET) database was searched to identify published minimal clinically important difference thresholds relevant to this guideline. MIDs were assessed to ensure they had been developed and validated in a methodologically rigorous way, and were applicable to the populations, interventions and outcomes specified in this guideline. No MIDs were identified through this process. In addition, the Guideline Committee were asked to prospectively specify any outcomes where they felt a consensus MID could be defined from their experience. The committee agreed that any difference in mortality would be clinically meaningful, and therefore the line of no effect was used as an MID. The committee chose not to specify any other MIDs by consensus.

For continuous outcomes expressed as a mean difference where no other MID was available, an MID of 0.5 of the median standard deviations of the comparison group arms was used (Norman et al. 2003). For continuous outcomes expressed as a standardised mean difference where no other MID was available, an MID of 0.5 was used. For relative risks where no other MID was available, a default MID interval for dichotomous outcomes of 0.8 to 1.25 was used.

The 'Evidence to Recommendations' section of each review makes explicit the committee's view of the expected clinical importance and relevance of the findings. In particular, this includes consideration of whether the whole effect of a treatment (which may be felt across multiple independent outcome domains) would be likely to be clinically meaningful, rather than simply whether each individual sub outcome might be meaningful in isolation.

GRADE for pairwise meta-analyses of interventional evidence

GRADE was used to assess the quality of evidence for the selected outcomes as specified in 'Developing NICE guidelines: the manual (2014)'. Data from RCTs were initially rated as high quality, data from observational studies were originally rated as low quality. The quality of the evidence for each outcome was downgraded or not from this initial point, based on the criteria given in Table 9.

Table 9: Rationale for downgrading quality of evidence for intervention studies

GRADE criteria	Reasons for downgrading quality
Risk of bias	Not serious: If less than 33.3% of the weight in a meta-analysis came from studies at moderate or high risk of bias, the overall outcome was not downgraded. Serious: If greater than 33.3% of the weight in a meta-analysis came from studies at moderate or high risk of bias, the outcome was downgraded one level. Very serious: If greater than 33.3% of the weight in a meta-analysis came from studies at high risk of bias, the outcome was downgraded two levels. Outcomes meeting the criteria for downgrading above were not downgraded if there was evidence the effect size was not meaningfully different between studies at high and low risk of bias.
Indirectness	Not serious: If less than 33.3% of the weight in a meta-analysis came from partially indirect or indirect studies, the overall outcome was not downgraded. Serious: If greater than 33.3% of the weight in a meta-analysis came from partially indirect or indirect studies, the outcome was downgraded one level. Very serious: If greater than 33.3% of the weight in a meta-analysis came from indirect studies, the outcome was downgraded two levels. Outcomes meeting the criteria for downgrading above were not downgraded if there was evidence the effect size was not meaningfully different between direct and indirect studies.
Inconsistency	Concerns about inconsistency of effects across studies, occurring when there is unexplained variability in the treatment effect demonstrated across studies (heterogeneity), after appropriate pre-specified subgroup analyses have been conducted. This was assessed using the I^2 statistic. N/A: Inconsistency was marked as not applicable if data on the outcome was only available from one study. Not serious: If the I^2 was less than 33.3%, the outcome was not downgraded. Serious: If the I^2 was between 33.3% and 66.7%, the outcome was downgraded one level.

GRADE criteria	Reasons for downgrading quality
	Very serious: If the I^2 was greater than 66.7%, the outcome was downgraded two levels. Outcomes meeting the criteria for downgrading above were not downgraded if there was evidence the effect size was not meaningfully different between studies with the smallest and largest effect sizes.
Imprecision	If an MID other than the line of no effect was defined for the outcome, the outcome was downgraded once if the 95% confidence interval for the effect size crossed one line of the MID, and twice if it crosses both lines of the MID. If the line of no effect was defined as an MID for the outcome, it was downgraded once if the 95% confidence interval for the effect size crossed the line of no effect (i.e. the outcome was not statistically significant), and twice if the sample size of the study was sufficiently small that it is not plausible any realistic effect size could have been detected. Outcomes meeting the criteria for downgrading above were not downgraded if the confidence interval was sufficiently narrow that the upper and lower bounds would correspond to clinically equivalent scenarios.

Publication bias

Where 10 or more studies were included as part of a single meta-analysis, a funnel plot was produced to graphically assess the potential for publication bias.

Evidence statements

Evidence statements for pairwise intervention data are classified in to one of four categories:

- Situations where the data are only consistent, at a 95% confidence level, with an effect in one direction (i.e. one that is 'statistically significant'), and the magnitude of that effect is most likely to meet or exceed the MID (i.e. the point estimate is not in the zone of equivalence). In such cases, we state that the evidence showed that there is an effect.
- Situations where the data are only consistent, at a 95% confidence level, with an effect in one direction (i.e. one that is 'statistically significant'), but the magnitude of that effect is most likely to be less than the MID (i.e. the point estimate is in the zone of equivalence). In such cases, we state that the evidence showed there is an effect, but it is less than the defined MID.
- Situations where the confidence limits are smaller than the MIDs in both directions. In such cases, we state that the evidence demonstrates that there is no meaningful difference.
- In all other cases, we state that the evidence could not differentiate between the comparators.

For outcomes without a defined MID or where the MID is set as the line of no effect (for example, in the case of mortality), evidence statements are divided into 2 groups as follows:

- We state that the evidence showed that there is an effect if the 95% CI does not cross the line of no effect.
- The evidence could not differentiate between comparators if the 95% CI crosses the line of no effect.

Appendix C – Literature search strategies

A systematic search was conducted on 4th July 2019. The following databases were searched; Medline, Medline in Process, Medline epub ahead of Print, Embase (all via the Ovid platform), Cochrane Database of Systematic Reviews and the Cochrane Register of Controlled Trials (via the Wiley platform) and the Database of Abstracts of Reviews (via the Centre for Reviews and Dissemination platform). Date limits were applied to the date of the previous guideline for RCT and systematic review evidence. No date limits were applied for observational studies evidence. McMaster balanced RCT health-evidence.ca Systematic Review and NICE in house observational studies filters were used.

The Medline strategy is presented below. This was translated for other databases.

1 Venous Thrombosis/
2 (phlegmasia adj2 dolens).tw.
3 (thrombo* adj2 (vein* or venous)).tw.
4 (venous adj stasis).tw.
5 (dvt or vte).tw.
6 Venous Thromboembolism/ or Embolism, paradoxical/
7 exp pulmonary embolism/
8 ((pulmonary or lung) adj4 (embol* or thromboembo* or microembol*)).tw.
9 (pulmonary adj infarction).tw.
10 or/1-9
11 Vena Cava Filters/
12 vena cava, inferior/su or venae cavae/su
13 ((((ivc or vena) adj (cava or caval)) or umbrella) adj2 (filter or filters)).tw.
14 (ALN or Amplatz or Antheor or "Bird's Nest" or Celect or Crux or Denali or G2 or Greenfield or "Gunther Tulip" or LGM or "Mobin-Uddin" or Ninitol or OptEase or Prolyser or Tempofilter or TrapEase or "Vena Tech" or Venatech).tw.
15 or/11-14
16 10 and 15
17 randomized controlled trial.pt.
18 randomi?ed.mp.
19 placebo.mp.
20 or/17-19
21 (MEDLINE or pubmed).tw.
22 systematic review.tw.
23 systematic review.pt.
24 meta-analysis.pt.
25 intervention$.ti.
26 or/21-25
27 20 or 26
28 16 and 27
29 limit 28 to ed=20110801-20190704
30 Observational Studies as Topic/
31 Observational Study/
32 Epidemiologic Studies/
33 exp Case-Control Studies/

1	34	exp Cohort Studies/
2	35	Cross-Sectional Studies/
3	36	Controlled Before-After Studies/
4	37	Historically Controlled Study/
5	38	Interrupted Time Series Analysis/
6	39	Comparative Study.pt.
7	40	case control$.tw.
8	41	case series.tw.
9	42	(cohort adj (study or studies)).tw.
10	43	cohort analy$.tw.
11	44	(follow up adj (study or studies)).tw.
12	45	(observational adj (study or studies)).tw.
13	46	longitudinal.tw.
14	47	prospective.tw.
15	48	retrospective.tw.
16	49	cross sectional.tw.
17	50	or/30-49
18	51	16 and 50
19	52	29 or 51
20	53	limit 52 to english language
21	54	animals/ not humans/
22	55	53 not 54

23

24 Searches to identify economic evidence were run on 9th July 2019 in Medline, Medline in
25 Process, Econlit and Embase (all va the Ovid platform), NHS EED and the Health
26 Technology Database (via the Centre for Reviews and Dissemination platform). NICE
27 inhouse economic evaluation and Quality of Life filters were attached to lines 1 to 29 of the
28 core strategy in the Medline and Embase databases. The Medline version of the filters is
29 displayed below.

30 Economic evaluations

31	1	Economics/
32	2	exp "Costs and Cost Analysis"/
33	3	Economics, Dental/
34	4	exp Economics, Hospital/
35	5	exp Economics, Medical/
36	6	Economics, Nursing/
37	7	Economics, Pharmaceutical/
38	8	Budgets/
39	9	exp Models, Economic/
40	10	Markov Chains/
41	11	Monte Carlo Method/
42	12	Decision Trees/
43	13	econom$.tw.
44	14	cba.tw.
45	15	cea.tw.
46	16	cua.tw.
47	17	markov$.tw.
48	18	(monte adj carlo).tw.

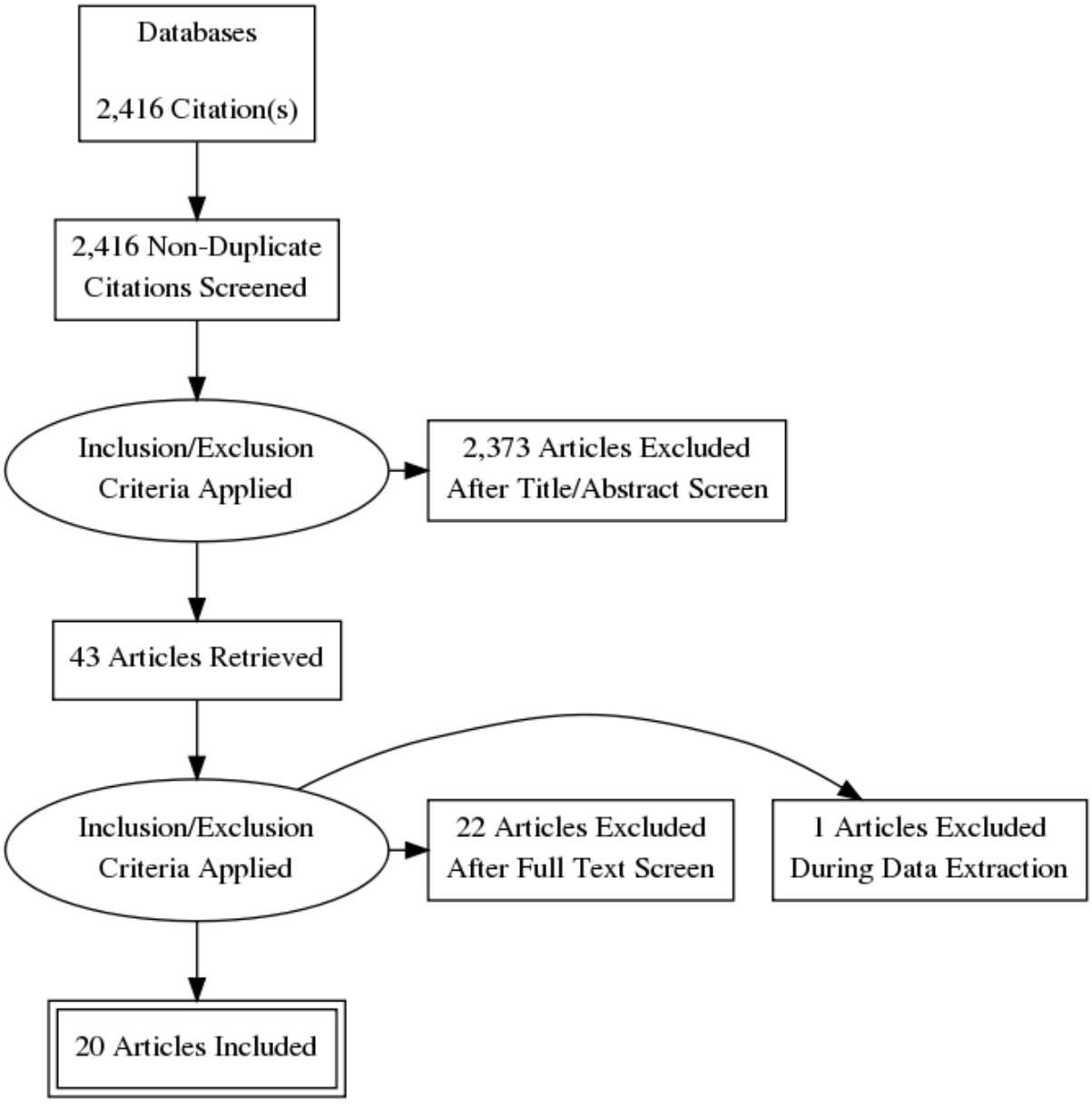
19	(decision adj3 (tree$ or analys$)).tw.
20	(cost or costs or costing$ or costly or costed).tw.
21	(price$ or pricing$).tw.
22	budget$.tw.
23	expenditure$.tw.
24	(value adj3 (money or monetary)).tw.
25	(pharmacoeconomic$ or (pharmaco adj economic$)).tw.
26	or/1-25

Quality of Life

1	"Quality of Life"/
2	quality of life.tw.
3	"Value of Life"/
4	Quality-Adjusted Life Years/
5	quality adjusted life.tw.
6	(qaly$ or qald$ or qale$ or qtime$).tw.
7	disability adjusted life.tw.
8	daly$.tw.
9	Health Status Indicators/ (22343)
10	(sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw.
11	(sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw.
12	(sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw.
13	(sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw.
14	(sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw.
15	(euroqol or euro qol or eq5d or eq 5d).tw.
16	(qol or hql or hqol or hrqol).tw.
17	(hye or hyes).tw.
18	health$ year$ equivalent$.tw.
19	utilit$.tw.
20	(hui or hui1 or hui2 or hui3).tw.
21	disutili$.tw.
22	rosser.tw.
23	quality of wellbeing.tw.
24	quality of well-being.tw.
25	qwb.tw.
26	willingness to pay.tw.
27	standard gamble$.tw.
28	time trade off.tw.
29	time tradeoff.tw.
30	tto.tw.

1 or/1-30

Appendix D – Clinical evidence study selection



Appendix E – Clinical evidence tables

Barginear, 2009

Bibliographic Reference	Barginear, M. F.; Lesser, M.; Akerman, M. L.; Strakhan, M.; Shapira, I.; Bradley, T.; Budman, D. R.; Need for inferior vena cava filters in cancer patients: a surrogate marker for poor outcome; Clinical & Applied Thrombosis/Hemostasis; 2009; vol. 15 (no. 3); 263-9

Study arms

Filter + anticoagulation (N = 36)	Anticoagulation only (N = 68)
% female: 61.1%	% female: 66.2%
% PE only: 16.7%	% PE only: 29.4%
% PE + DVT: 36.1%	% PE + DVT: 22.1%
Treated with VKA: 100%	Treated with VKA: 60% treated with LMWH alone: 40%

Study details

Study type	Retrospective cohort study
Study location	USA
Study setting	Patients at a single hospital in New York, USA
Study dates	January 2002 - December 2004
Duration of follow-up	Unclear
Sources of funding	None reported
Inclusion criteria	VTE Active cancer
Sample size	201; 104 relevant to this review
Loss to follow-up	Unclear

Interventions	Filter + anticoagulant versus no filter + anticoagulant *All participants received anticoagulation. All participants in the filter + AC group received LMWH + VKA however 40% in the AC group received LMWH alone*
Outcome measures	All-cause mortality *Not extractable for this review.* Major bleeding VTE-recurrence

1

1. Bias due to confounding
Risk of bias judgement for confounding Critical *(The reason for the filter being placed was likely based on confounding variables. Attempts were made to adjust for confounders however these were insufficient and important confounders were not controlled for. Additionally, different courses of anticoagulation were used between the treatment groups (none of the filter group received LMWH alone, whereas 40% of the AC-only group did). These treatments are known to have different effectiveness)*
2. Bias in selection of participants into the study
Risk of bias judgement for selection of participants into the study Serious *(Immortal time bias was not adjusted for)*
3. Bias in classification of interventions
Risk of bias judgement for classification of interventions Low
4. Bias due to deviations from intended interventions
Risk of bias judgement for deviations from intended interventions Moderate *(There was no information regarding deviations from the intended intervention.)*
5. Bias due to missing data

Risk of bias judgement for missing data

Critical

(Hazard ratio and event data for mortality are not provided)

6. Bias in measurement of outcomes

Risk of bias judgement for measurement of outcomes

Low

7. Bias in selection of the reported result

Risk of bias judgement for selection of the reported result

Moderate

(Unclear length of hospital stay. It is possible that the filter group had a longer follow-up time and this has the potential for bias)

Overall bias

Risk of bias judgement

Critical

Directness

Directly applicable

1

Barginear, 2012

2

Bibliographic Reference	Barginear, M. F.; Gralla, R. J.; Bradley, T. P.; Ali, S. S.; Shapira, I.; Greben, C.; Nier-Shoulson, N.; Akerman, M.; Lesser, M.; Budman, D. R.; Investigating the benefit of adding a vena cava filter to anticoagulation with fondaparinux sodium in patients with cancer and venous thromboembolism in a prospective randomized clinical trial; Supportive Care in Cancer; 2012; vol. 20 (no. 11); 2865-72

3 **Study arms**

Filter + fondaparinux sodium (N = 31)	Fondaparinux sodium (N = 33)
Mean age (SD): 63 (12) years	Mean age (SD): 67 (14) years
% female: 52%	% female: 73%

% Chemotherapy: 90%	% Chemotherapy: 94%
% TNM stage II: 3%	% TNM stage II: 9%
% TNM stage III: 19%	% TNM stage III: 15%
% TNM stage IV: 77%	% TNM stage IV: 75%
% brain metastases: 9%	% brain metastases: 15%

1

2 **Study details**

Study type	Randomised controlled trial (RCT)
Study location	USA
Study setting	Single centre
Study dates	May 2007 - May 2010
Duration of follow-up	Pp to 3 years
Sources of funding	This study is supported in part by a grant from GlaxoSmithKline.
Inclusion criteria	VTE *Acute DVT, confirmed by duplex/Doppler ultrasound, with or without a concomitant PE, confirmed by a ventilation/perfusion scan (V/Q) or computed tomography pulmonary angiogram (CTPA).* Active cancer *Definitive diagnosis of cancer hospitalized or ambulatory.* At least 18 years of age
Exclusion criteria	Previous filter placement Indication for thrombolysis Other conditions *"Allergy to iodine, hereditary thrombophilia, pregnancy, platelet count of <50,000/µL, bleeding requiring blood transfusion, intracranial bleeding, and/or brain metastasis secondary to melanoma, choriocarcinoma, renal cell carcinoma, or medullary thyroid carcinoma."* CrCl <30mL/min Active AC lasting more than 72h

Sample size	64
Interventions	Filter versus no filter *"Permanent VCFs (Vena Tech Vena LP, B. Braun Medical) were used. These percutaneous filters were inserted within 3 days of randomization, to patients assigned to a VCF, under fluoroscopic guidance".* *"Patients were anticoagulated with an age and weight-adjusted dose of subcutaneous fondaparinux sodium (5 mg for patients <50 kg or age >65 years, 7.5 mg for patients 50– 100 kg and 10 mg for patients >100 kg) for 90 days. The study period of 90 days was established as a conservative approach to evaluate the specified endpoints while taking into account the lack of safety data with fondaparinux sodium in cancer patients (IND# 76,762). After 90 days, patients were given further anticoagulant therapy at the discretion of their physician."*
Outcome measures	Adverse events *VCF complications. Major VCF complications were defined as thrombosis at the filter site, erosion into the wall of the vena cava, infection, prolonged Cancer Acute DVT + PE Fondaparinux Sodium Fondaparinux Sodium + Vena Cava Filter Day 1 Day 3 Day 14 Repeat Imaging Day 30 Repeat Imaging Day 56 Repeat Imaging Fig. 1 Schema of the trial. Eligible patients were randomized within 72 h of enrolment to an age and weight-adjusted dose of subcutaneous fondaparinux sodium with or without a vena cava filter. Upon study entry, patients enrolled secondary to an acute DVT were evaluated for a PE and patients enrolled secondary to an acute PE were evaluated for a DVT. Repeat imaging to evaluate the clot burden as specified below Support Care Cancer (2012) 20:2865–2872 2867 hospitalization, and/or migration of the filter.* Major bleeding VTE-recurrence *In patients with a confirmed PE at baseline, a CTPA was systematically performed on day 56 to evaluate the clot burden. If a clinically suspected PE occurred before day 56 or at any time during the first 90 days after randomization, a V/Q scan was obtained. A CTPA was performed if the V/Q scan could not be obtained. patients with a confirmed DVT at baseline, a bilateral duplex/doppler ultrasound of the lower extremities was systematically performed on days 14, 30, and 56 to evaluate the Vote. Initially, bilateral duplex/doppler ultrasound of the lower extremities was performed on day 56 in all patients in whom a baseline DVT was confirmed to evaluate the clot burden. Diagnoses of recurrent or residual PEs or DVTs were based on a comparison between baseline findings and those obtained at previously specified follow up intervals. Recurrence of a DVT was defined as a lack of compressibility at a new site or an extension to a new venous segment of the thrombus on duplex/Doppler ultrasound [24]. The angiographic diagnosis of a recurrent PE required the visualization of a new intraluminal filling defect or a sudden new arterial cut-off. When Tawas unavailable, the diagnosis based on the V/Q scan required the visualization of at least two new segmental mismatched perfusion defects, with no current improvement in other areas in cases of initial extensive perfusion defects.*

1

Selection bias

Random sequence generation

Low risk of bias

("Subjects were randomly assigned in a 1:1 ratio, using a permuted block design")

Allocation concealment

Unclear risk of bias

(No information regarding allocation concealment)

Performance bias

Blinding of participants and personnel

High risk of bias

(unblinded)

Detection bias

Blinding of outcome assessment

High risk of bias

(No information given. "All events were evaluated and validated by an independent Data Safety Monitoring Board." however it is unclear whether these this committee was blinded.)

Attrition bias

Incomplete outcome data

Low risk of bias

Reporting bias

Selective reporting

Low risk of bias

Other sources of bias

Any other sources of bias

Low risk of bias

Overall risk of bias and directness
Risk of bias Low – *Although this study was at serious risk of bias due to a lack of blinding, the overall risk of bias for this study remains low as the outcomes of relevance to this review are objectively assessed and therefore unlikely to be significantly influenced by a lack of blinding.* *Directness* Directly applicable

Brunson, 2017

1

Bibliographic Reference	Brunson, A.; Ho, G.; White, R.; Wun, T.; Inferior vena cava filters in patients with cancer and venous thromboembolism (VTE) does not improve clinical outcomes: A population-based study; Thrombosis Research; 2017; vol. 153; 57-64

2 **Study arms**

With filter (N = 2747)	Without filter (N = 11253)
% >80 years old: 21.2%	% >80 years old: 19.8%
% female: 47.7%	% female: 51.4%
% metastatic cancer: 48.9%	% metastatic cancer: 42.3%
% bleeding present on admission: 9.6%	% bleeding present on admission: 2.8%
% bleeding acquired in hospital: 3.9%	% bleeding acquired in hospital:1.0%
% GI bleed: 7.7%	% GI bleed: 1.9%
% intracranial bleed: 1.0%	% intracranial bleed: 0.1%
% major surgery in hospital: 7.7%	% major surgery in hospital: 1.3%
% PE (with/without DVT): 50.2%	% PE (with/without DVT): 58.8%

3 **Study details**

Study type	Retrospective cohort study
Study location	USA
Study setting	Data from the California Patient Discharge Database (PDD)
Study dates	January 1, 2005 - December 31, 2009
Duration of follow-up	up to 1 year

Inclusion criteria	VTE *Acute DVT (without PE) in the lower extremity or acute with PE (with or without DVT). Identified using diagnosis codes* Active cancer *At time of admission or within 6 months prior*
Sample size	14,000
Interventions	Filter versus no filter
Outcome measures	All-cause mortality *Within 30 days* Major bleeding *At 180 and 365 days* VTE-recurrence *Within 180 days*

1

1. Bias due to confounding
Risk of bias judgement for confounding Moderate *(The decision to place a filter was likely due to confounding variables. Baseline characteristics are poorly matched between groups. The study attempted to adjust for many relevant clinical factors that likely influenced decision to place filter)*
2. Bias in selection of participants into the study
Risk of bias judgement for selection of participants into the study Moderate *(Potential for immortal time bias. Attempts were made to correct for this however it is unclear whether these were adequate.)*
3. Bias in classification of interventions
Risk of bias judgement for classification of interventions Low

4. Bias due to deviations from intended interventions

Risk of bias judgement for deviations from intended interventions

Serious

(There was no information regarding deviations from the intended intervention and in particular, no information about whether participants could later receive a filter or have a filter removed. Information on post-intervention anticoagulant usage was not available however the analysis did control for baseline characteristics indicative of contraindication to anticoagulation (such as active bleeding and undergoing major surgery. This will in part correct for this bias. However, bleeds could have occurred at any point in the hospital stay, therefore participants could still have received some post-intervention anticoagulation and have been wrongly classified as being contraindicated.)

5. Bias due to missing data

Risk of bias judgement for missing data

Low

6. Bias in measurement of outcomes

Risk of bias judgement for measurement of outcomes

Low

7. Bias in selection of the reported result

Risk of bias judgement for selection of the reported result

Moderate

(There is no indication of selective reporting but there is no evidence of a pre-registered protocol so it is possible that the analysis was matched to the available data rather than being pre-specified.)

Overall bias

Risk of bias judgement

Moderate

Directness

Directly applicable

1

Coombs, 2017

2

Bibliographic Reference	Coombs, C.; Kuk, D.; Devlin, S.; Siegelbaum, R. H.; Durack, J. C.; Parameswaran, R.; Mantha, S.; Deng, K.; Soff, G.; Outcomes after inferior vena cava filter placement in cancer patients diagnosed with pulmonary embolism: risk for recurrent venous thromboembolism; Journal of Thrombosis & Thrombolysis; 2017; vol. 44 (no. 4); 489-493

1 **Study arms**

With filter (N = 317)	**Without filter (N = 953)**
Mean (range): 64.1 (20.8-93.4) years	Mean (range): 63.8 (18.3 - 92.4) years
% female: 49%	% female: 55%
% therapeutic anticoagulation on admission: 86%	% therapeutic anticoagulation on admission: 99%
% metastatic tumor: 79%	% metastatic tumor: 82%
% primary CNS tumor: 7%	% primary CNS tumor: 2%
% liquid tumor: 5%	% liquid tumor: 7%
% localized solid tumor: 8%	% localized solid tumor: 9%

2 **Study details**

Study type	Retrospective cohort study
Study location	USA
Study setting	Single institution (cancer centre)
Study dates	2008 - 2009
Duration of follow-up	Up to 12 months
Sources of funding	This research was funded in part through the NIH/NCI, Cancer Center Support Grant P30 CA008748.
Inclusion criteria	PE *Radiographically-confirmed PE. "All PE cases were initially identified by billing code, followed by manual review of the electronic medical record by two study physicians."* Active Cancer *Treated at cancer centre.*

Sample size	1270
Interventions	Filter versus no filter
Outcome measures	All-cause mortality *Up to 12 months*

1

1. Bias due to confounding
Risk of bias judgement for confounding Serious *(The decision to fit a filter was likely due to the presence of confounding variables. Attempts were made to adjust for confounders however only a limited number of factors were included.)*
2. Bias in selection of participants into the study
Risk of bias judgement for selection of participants into the study Serious *(Follow-up began at admission however it is likely that the filter was filter at a later point in time. The paper outlines that participants could be included if they had a filter placed within 30 days following admission. There is potential for immortal time bias. This was not adjusted for.)*
3. Bias in classification of interventions
Risk of bias judgement for classification of interventions Low
4. Bias due to deviations from intended interventions
Risk of bias judgement for deviations from intended interventions Moderate *(It is unclear whether participants classified as having no filter could later have one placed during follow-up, or whether those with a filter could have it retrieved. Additionally, AC use on admission was recorded however post-intervention AC use in not known.)*
5. Bias due to missing data
Risk of bias judgement for missing data Moderate

(Adjusted outcome data was not available for recurrent PE or DVT (only present overall, for recurrent VTE))

6. Bias in measurement of outcomes

Risk of bias judgement for measurement of outcomes

Low

7. Bias in selection of the reported result

Risk of bias judgement for selection of the reported result

Moderate

(There is no indication of selective reporting but there is no evidence of a pre-registered protocol so it is possible that the analysis was matched to the available data rather than being pre-specified.)

Overall bias

Risk of bias judgement

Serious

Directness

Directly applicable

Decousus, 1998

Bibliographic Reference	Decousus, H.; Leizorovicz, A.; Parent, F.; Page, Y.; Tardy, B.; Girard, P.; Laporte, S.; Faivre, R.; Charbonnier, B.; Barral, F. G.; Huet, Y.; Simonneau, G.; A clinical trial of vena caval filters in the prevention of pulmonary embolism in patients with proximal deep-vein thrombosis. Prevention du Risque d'Embolie Pulmonaire par Interruption Cave Study Group; New England Journal of Medicine; 1998; vol. 338 (no. 7); 409-15

Study details

Study type	Associate study *This study is part of the longer duration, PREPIC study (2005). Shorter term outcomes are reported here however the inclusion/exclusion criteria, sample and outcomes (reported in the present paper at the following time points: up to 3 months, 3months - 1year and 1-2 years) are the same.*

PREPIC Group, 2005

Bibliographic Reference	Group, Prepic Study; Eight-year follow-up of patients with permanent vena cava filters in the prevention of pulmonary embolism: the PREPIC (Prevention du Risque d'Embolie Pulmonaire par Interruption Cave) randomized study; Circulation; 2005; vol. 112 (no. 3); 416-22

Study arms

Filter plus anticoagulation (N = 200)	**Anticoagulation alone (N = 200)**
Mean age (SD): 73 (11) years	Mean age (SD): 72 (11) years
% female: 54%	% female: 51%
% history of VTE: 35%	% history of VTE: 36%
% cancer at point of inclusion: 16%	% cancer at point of inclusion: 12%
% post-thrombotic syndrome: 23%	% post-thrombotic syndrome: 24%

Study details

Study type	Randomized controlled trial
Study location	France
Study setting	44 centres
Study dates	Patients were randomly assigned between September 1991 and February 1995. Patients were followed for up to 8 years from inclusion.
Duration of follow-up	Visits schedules at 3 months, 1 year, 2 years and then yearly via telelphone call from the coordinating centre for up to 8 years.
Sources of funding	"This study was supported by grants from Ministère Français de la Santé (PHRC), Paris, France, and from Fondation de l'Avenir"
Inclusion criteria	DVT *Confirmed by bilateral venography, with or without concomitant symptomatic pulmonary embolism, and considered to be at high risk for pulmonary embolism (by their physician)* At least 18 years of age

Exclusion criteria	Previous filter placement Pregnancy Contraindication to or failure of anticoagulant therapy *Or curative anticoagulant therapy lasting more than 48 hours* Indication for thrombolysis Short life expectancy Allergy to iodine Hereditary thrombophilia Severe renal or hepatic failure Likelihood of noncompliance
Sample size	400 (outcomes available in 396)
Mean age (SD)	Data were unavailable for 4 participants.
Interventions	Filter plus AC versus AC alone *"Four types of permanent vena cava filter were used: Vena Tech LGM (B. Braun), titanium Greenfield (Boston Scientific), Cardial (Bard), and Bird's Nest (Cook Group).5 All filters were inserted percutaneously under fluoroscopic control through a femoral or jugular vein. For patients in the filter group, cavography was performed immediately to ensure that the upper extremity of the filter was located in the inferior vena cava, immediately below the renal veins."* *"Nineteen percent of patients in both groups wore elastic stockings for only 3 months after the index thromboembolic event; they were worn during the entire study period by 45% and 47% of patients in the filter and no-filter group. At 8 years, 61% and 63%, respectively, of living patients were still using elastic stockings."* *All participants received anticoagulation (LMWH or UFH) 94% were assigned heparin treatment for at least 8 days. At discharge, 91% were on oral anticoagulants and 8% were on subcutaneous UFH (1% received no anticoagulants).*
Outcome measures	All-cause mortality *Up to 8 years* Major bleeding *Up to 8 years* VTE-recurrence *symptomatic PE up to 8 years. considered to have occurred if it was documented objectively (positive angiography, high-probability lung scan, spiral computed tomography (CT), or chest radiograph) or, in the event of death, at autopsy or if there was strong evidence that pulmonary embolism was the cause of death. The*

	angiographic diagnosis of pulmonary embolism required the visualization of a new intraluminal defect or a sudden new arterial cutoff in comparison with the most recent angiographic examination. On ventilation/perfusion lung scanning, diagnosis was based on the visualization of at least 2 new segmental mismatched perfusion defects with no improvement in other areas in cases of initial extensive perfusion defects on the more recent lung scan. On spiral CT, pulmonary embolism was diagnosed if a central filling defect outlined by contrast material or complete occlusion was seen in a segmental or more proximal pulmonary artery. Diagnosis of recurrent pulmonary embolism could be based on abnormal chest radiograph suggestive of pulmonary embolism if there was strong clinical evidence of pulmonary embolism and associated acute proximal deep-vein thrombosis. Recurrence of deepvein thrombosis, including deep-vein thrombosis of the lower limbs and filter thrombosis, was diagnosed if there was a new intraluminal filling defect on venography, a lack of compressibility at a new site or an extension to a new venous segment of the thrombus on ultrasonography, or a partial or complete occlusion of an abdominal vein (iliac or caval) on contrast-enhanced CT scan. Post-thrombotic syndrome *Up to 8 years* Mechanic filter complications *Up to 8 years*

1

Selection bias
Random sequence generation Low risk of bias *(randomization (stratified according to center) was performed by means of a central 24-hour computer telephone system.)* *Allocation concealment* Low risk of bias *(use of a computer telephone system likely concealed allocation)*
Performance bias
Blinding of participants and personnel High risk of bias
Detection bias
Blinding of outcome assessment Low risk of bias

(unblinded however as the outcomes were objectively measured this is not likely to represent a risk of bias)

Attrition bias

Incomplete outcome data

Low risk of bias

(8 participants assigned to no filter went on to recieve a filter in the first 8 days due to PE occurence or major bleeding. Outcome data were available for all patients at 2 years and only unavailable for 3 patients at 8 years)

Reporting bias

Selective reporting

Low risk of bias

Other sources of bias

Any other sources of bias

Low risk of bias

Overall risk of bias and directness

Risk of bias

Low – *Although this study was at serious risk of bias due to a lack of blinding, the overall risk of bias for this study remains low as the outcomes of relevance to this review are objectively assessed and therefore unlikely to be significantly influenced by a lack of blinding.*

Directness

Directly applicable

1

Jha, 2010

Bibliographic Reference	Jha, V. M.; Lee-Llacer, J.; Williams, J.; Ubaissi, H.; Gutierrez, G.; Adjunctive inferior vena cava filter placement for acute pulmonary embolism; Cardiovascular & Interventional Radiology; 2010; vol. 33 (no. 4); 739-43

2 **Study arms**

Filter + anticoagulation (N = 18)	**Anticoagultion alone (N = 49)**
Demographic characteristics were available for the entire study group only:	Demographic characteristics were available for the entire study group only:

Mean age: 54 years, % female: 57.7%, % cardiac disease: 16.1%, % elevated Troponin I: 17.7%, % Troponin I within normal limits: 49.2%, % oxygen required >4L by nasal canula: 9.3%, % admitted to intensive care unit due to PE: 27.8%.	Mean age: 54 years, % female: 57.7%, % cardiac disease: 16.1%, % elevated Troponin I: 17.7%, % Troponin I within normal limits: 49.2%, % oxygen required >4L by nasal canula: 9.3%, % admitted to intensive care unit due to PE: 27.8%.

1

2 **Study details**

Study type	Retrospective cohort study *Retrospective chart review performed at a 371- bed academic medical center*
Study location	USA
Study setting	Single centre
Study dates	January 1, 2006 to September 22, 2008
Duration of follow-up	During hospital stay
Sources of funding	No external funding
Inclusion criteria	PE *Newly diagnosed PE by means of either a chest CT with PE protocol or a high-probability ventilation–perfusion (V/Q) scan, defined by two or more large mismatched segmental perfusion defects* Taking anticoagulation *Treatment with therapeutic-dose intravenous heparin or low-molecular-weight heparin, or with a factor Xa inhibitor such as fondaparinux* Right heart strain *"Any of the following: right atrial or ventricular enlargement, pulmonary hypertension, or the loss of inspiratory collapse of the IVC by echocardiogram; mean pulmonary artery pressure of[25 mm Hg, demonstrated by right heart catheterization [2]; or enlarged pulmonary artery or shift of the interventricular septum by chest CT scan."*
Exclusion criteria	Contraindications *Contraindication to full-dose anticoagulation* Previous filter placement Recent treatment for PE

	"Preexisting treatment with anticoagulation for PE any time within 6 weeks of the current hospital visit, which would indicate that the current PE was not acute;" Other conditions *Acute PE associated with refractory hypotension or refractory hypoxemia;* Concomitant use of thrombolytic agents
Sample size	248; 67 of relevance to this review (those with right heart strain).
Interventions	Filter + anticoagulation versus anticoagulation alone
Outcome measures	All-cause mortality *In-hospital mortality*

1

1. Bias due to confounding
Risk of bias judgement for confounding Critical *(No baseline characteristics given for subgroups of relevance to this review. No adjustments were made to analysis for confounders.)*
2. Bias in selection of participants into the study
Risk of bias judgement for selection of participants into the study Serious *(no adjustments for immortal time bias)*
3. Bias in classification of interventions
Risk of bias judgement for classification of interventions Low
4. Bias due to deviations from intended interventions
Risk of bias judgement for deviations from intended interventions Moderate *(There was no information regarding deviations from the intended intervention. However, as outcomes are restricted to those occurring in the hospital, this is not a great concern. There is limited*

information regarding anticoagulation use after the intervention, or whether this was comparable between groups.)

5. Bias due to missing data

Risk of bias judgement for missing data

Low

6. Bias in measurement of outcomes

Risk of bias judgement for measurement of outcomes

Moderate

(unclear length of hospital stay. It is possible that the filter group had a longer follow-up time and this has the potential for bias)

7. Bias in selection of the reported result

Risk of bias judgement for selection of the reported result

Moderate

(There is no indication of selective reporting but there is no evidence of a pre-registered protocol so it is possible that the analysis was matched to the available data rather than being pre-specified.)

Overall bias

Risk of bias judgement

Critical

Directness

Directly applicable

1

Liang, 2017

2

Bibliographic Reference	Liang, N. L.; Genovese, E. A.; Avgerinos, E. D.; Singh, M. J.; Makaroun, M. S.; Chaer, R. A.; Impact of Inferior Vena Cava Filter Placement on Short-Term Outcomes in Patients with Acute Pulmonary Embolism; Annals of Vascular Surgery; 2017; vol. 42; 71-77

3

1 **Study arms**

With a filter (N = 2507)	**Without a filter (N = 8711)**
Mean age (SD): 66.3 (15.9) years	Mean age (SD): 62.3 (17.3) years
% female: 50.6%	% female: 52.9%
% hemodynamic instability: 6.8%	% hemodynamic instability: 3.8%
% respiratory failure: 12.1%	% respiratory failure: 11.2%
% DVT: 32.8%	% DVT: 13.9%
% any cancer: 22.7%	% any cancer: 15.6%
% congestive heart failure: 16.6%	% congestive heart failure: 14.7%
% hypertension: 56.7%	% hypertension: 54.6%
% peripheral arterial disease: 6.8%	% peripheral arterial disease: 5.5%
% Chronic renal failure: 11.2%	% Chronic renal failure: 10.9%
% given thrombolytic therapy: 5.9%	% given thrombolytic therapy: 1.6%
% given thrombectomy 0.7%.	% given thrombectomy 0.1%.

2

3 **Study details**

Study type	Retrospective cohort study *Using data obtained from the National Inpatient Sample (NIS) from 2009–2012.*
Study location	USA
Study setting	The NIS contains data from inpatient admissions nationwide.
Study dates	Used data from 2009 - 2012.
Duration of follow-up	During hospital stay
Sources of funding	This study was funded in part by grant 2T32HL098036-06 from the National Institutes of Health.
Inclusion criteria	PE Primary or secondary diagnosis of acute pulmonary embolism At least 18 years of age
Exclusion criteria	Pregnancy

	Diagnosis of chronic PE
Sample size	265,955; 11,218 of interest to this review (those with hemodynamic instability).
Interventions	Filter versus no filter
Outcome measures	All-cause mortality In-hospital mortality

1

1. Bias due to confounding

Risk of bias judgement for confounding

Moderate

(The study controlled for propensity score based on many clinically important factors that likely influenced receiving of filter. Filter was inserted as a time-dependent covariate in the time-varying analysis. It is likely that the complexity of the clinical situtation that led to the filter being placed is not accurately accounted for in the controlled for factors.)

2. Bias in selection of participants into the study

Risk of bias judgement for selection of participants into the study

Moderate

(The study has potential for immortal time bias. This was adjusted for however it is unclear whether the method of correction was adequate.)

3. Bias in classification of interventions

Risk of bias judgement for classification of interventions

Low

4. Bias due to deviations from intended interventions

Risk of bias judgement for deviations from intended interventions

Moderate

(There was no information regarding deviations from the intended intervention. However, as outcomes are restricted to those occurring in the hospital, this is not a great concern. There is limited information regarding anticoagulation use after the intervention, or whether this was comparable between groups.)

5. Bias due to missing data

Risk of bias judgement for missing data

Low

6. Bias in measurement of outcomes

Risk of bias judgement for measurement of outcomes

Low

7. Bias in selection of the reported result

Risk of bias judgement for selection of the reported result

Moderate

(There is no indication of selective reporting but there is no evidence of a pre-registered protocol so it is possible that the analysis was matched to the available data rather than being pre-specified.)

Overall bias

Risk of bias judgement

Moderate

Directness

Directly applicable

Mellado, 2016

Bibliographic Reference	Mellado, M.; Pijoan, J. I.; Jimenez, D.; Muriel, A.; Aujesky, D.; Bertoletti, L.; Decousus, H.; Barrios, D.; Clara, A.; Yusen, R. D.; Monreal, M.; Investigators, Riete; Outcomes Associated With Inferior Vena Cava Filters Among Patients With Thromboembolic Recurrence During Anticoagulant Therapy; Jacc: Cardiovascular Interventions; 2016; vol. 9 (no. 23); 2440-2448

Study arms

With filter (N = 17)	Without filter (N = 49)
Mean age: 61.6 (14.2) years	Mean age: 60.1 (12.5) years
% co-morbid cancer: 41.2%	% co-morbid cancer: 44.9%

% immobilized: 11.8% % active or recent bleeding: 5.9% Duration of anticoagulation (SD): 17.0 (17.0) days	% immobilized: 26.5% % active or recent bleeding: 4.1% Duration of anticoagulation (SD): 19.6 (17.7)

1 **Study details**

Study type	Retrospective analysis of prospective cohort study *Propensity-matched retrospective cohort study used prospectively collected data from patients enrolled in the multicenter international RIETE (Registro Informatizado de la Enfermedad Tromboembólica) registry*
Study location	Spain (approximately 18-19% of participants in the RIETE registry came from regions outside of Spain).
Study setting	Participating sites in the RIETE registry, a database supplied by 25 Spanish Physicians.
Study dates	Enrolled in RIETE from January 1, 2001, through September 31, 2015
Duration of follow-up	30 days
Sources of funding	Sanofi Spain for supporting this registry with an unrestricted educational grant; Bayer Pharma AG for supporting this registry. Bayer Pharma AG's support was limited to the part of RIETE outside Spain, which accounts for 22.88% of the total patients included in the RIETE registry.
Inclusion criteria	Recurrent VTE *Acute symptomatic or asymptomatic VTE confirmed by objective testing, who also had a recurrent VTE within 3 months of index event* Taking anticoagulation *Receiving anticoagulation for the first VTE event.*
Exclusion criteria	Previous filter placement *Pre-existing IVC filters or received filter therapy for the index VTE event* Died with 24 of VTE recurrence
Sample size	139
Interventions	Filter versus no filter
Outcome measures	All-cause mortality *All-cause mortality through 30 days after VTE recurrence* VTE-related mortality

	PE-related mortality through 30 days after VTE recurrence Major bleeding *Up to 30 days* VTE-recurrence *30 day recurrence after recurrent event at point of recruitment*

1

1. Bias due to confounding
Risk of bias judgement for confounding Serious *(As the study was not randomized, the decision to treat with filters was likely based on clinical characteristics which may reflect confounding differences between groups. The study used propensity matching, after which baseline characteristics were roughly comparable between groups Analysis was adjusted (generalized estimating equation modelling) for variables not achieving 10% standardized difference after matching. Most domains are routinely measured during hospital stay and are likely to be captured validly and reliably in the database.)*
2. Bias in selection of participants into the study
Risk of bias judgement for selection of participants into the study Moderate *(There is immortal time bias because follow-up begins at enrollment however filters are likely placed at a later point in time. The study corrected for this by excluding events occurring within 24 hours from enrollment, assuming most people would have their filter placed within this time. However, this is unlikely to be the case for all participants.)*
3. Bias in classification of interventions
Risk of bias judgement for classification of interventions Low
4. Bias due to deviations from intended interventions
Risk of bias judgement for deviations from intended interventions Moderate *(There was no information regarding deviations from the intended intervention and in particular, no information about whether participants could later receive a filter or have a filter removed. There is some difference in anticoagulant usage after admission to study.)*

5. Bias due to missing data
Risk of bias judgement for missing data
Low
6. Bias in measurement of outcomes
Risk of bias judgement for measurement of outcomes
Low
7. Bias in selection of the reported result
Risk of bias judgement for selection of the reported result
Moderate
(There is no indication of selective reporting but there is no evidence of a pre-registered protocol.)
Overall bias
Risk of bias judgement
Moderate
Directness
Directly applicable

1

Mismetti, 2015

2

Bibliographic Reference	Mismetti, P.; Laporte, S.; Pellerin, O.; Ennezat, P. V.; Couturaud, F.; Elias, A.; Falvo, N.; Meneveau, N.; Quere, I.; Roy, P. M.; Sanchez, O.; Schmidt, J.; Seinturier, C.; Sevestre, M. A.; Beregi, J. P.; Tardy, B.; Lacroix, P.; Presles, E.; Leizorovicz, A.; Decousus, H.; Barral, F. G.; Meyer, G.; Group, Prepic Study; Effect of a retrievable inferior vena cava filter plus anticoagulation vs anticoagulation alone on risk of recurrent pulmonary embolism: a randomized clinical trial; JAMA; 2015; vol. 313 (no. 16); 1627-35

3 **Study arms**

Filter plus anticoagulation (N = 200)	Anticoagulation alone (N = 199)
Mean age (SD): 74.2 (10.8) years	Mean age (SD): 72.7 (12.4) years
% female: 51%	% female: 52.8%

% unprovoked PE: 74% % aged >75 years: 55% % active cancer: 16.6% %Chronic heart failure: 9.0% %Chronic respiratory failure: 17.5% % at least 1 sign of right ventricular dysfunction or myocardial injury: 66.7% %DVT involving iliocaval segment: 9.0% % Bilateral DVT: 13.0%	% unprovoked PE: 79.4% % aged >75 years: 49.7% % active cancer: 14.6% %Chronic heart failure: 8.5% %Chronic respiratory failure: 9.5% % at least 1 sign of right ventricular dysfunction or myocardial injury: 65.2% %DVT involving iliocaval segment: 8.5% % Bilateral DVT: 13.6%

1 **Study details**

Study type	Prospective cohort study
Study location	France
Study setting	Members of the Prévention du Risque d'Embolie Pulmonaire par Interruption Cave 2 (PREPIC2) Study Group (all in France).
Study dates	August 2006 to January 2013
Duration of follow-up	Up to 6 months
Sources of funding	"The study was supported by grants from the Programme Hospitalier de Recherche Clinique (French Department of Health), Fondation de l'Avenir and Fondation de France. Filters were packaged and provided free of charge by ALN Implants Chirurgicaux. The study sponsor was the University Hospital of Saint-Etienne. An academic steering committee assumed overall responsibility for all these steps. An independent data and safety monitoring committee periodically reviewed the main safety outcomes."
Inclusion criteria	PE with high risk of recurrent PE "hospitalized for acute, symptomatic pulmonary embolism associated with acute lower-limb deep vein or superficial vein thrombosis, confirmed by means of standard objective tests, were eligible for randomization. Objective tests included spiral computed tomography, ventilation-perfusion lung scan, or pulmonary angiography to confirm pulmonary embolism, and bilateral compression ultrasonography and/or venography to confirm lower-limb vein thrombosis. Patients had to present at least 1 additional criterion for severity: older than 75 years, active cancer, chronic cardiac or respiratory insufficiency, ischemic stroke with leg paralysis within the last 6 months (but more than 3 days before randomization), deep vein thrombosis that involved the iliocaval segment or was bilateral, or at least 1 sign of right ventricular dysfunction or myocardial injury. Signs of right ventricular dysfunction or myocardial injury included

	evidence of right ventricular dilatation or pulmonary hypertension on echocardiography, or abnormal levels of at least 1 of the following biomarkers: brain natriuretic peptide, N-terminal pro-brain natriuretic peptide, or cardiac troponin T or I."
Exclusion criteria	Contraindications *Allergy to iodinated contrast media* Previous filter placement Pregnancy Contraindication to or failure of anticoagulant therapy Short life expectancy *<6 months* Unable to place filter *Due to thrombosis in the vena cava* Recent anticoagulation treatment *"If full-dose anticoagulant treatment had been administered during more than 72 hours before randomization"* Surgery *If they had undergone noncancer surgerywithin the past 3months or cancer surgerywithin the past 10 days* Serum creatinine greater than 2.04 mg/dL per liter
Sample size	399
Loss to follow-up	37 did not attend 6 months follow-up, 28 did not attend 3-month follow-up. However, all were included in ITT analysis.
Interventions	Filter plus anticoagulation versus anticoagulation alone *filter group received retrievable vena cava filter (ALN filter, ALN Implants Chirurgicaux)19-22 inserted within 72 hours from randomization.* *“In patients who had received thrombolytic therapy for the index event, insertion of the filter was to be postponed to more than 36 hours after thrombolysis. Filters were to be retrieved at 3 months. In all participating centers, filters were placed and retrieved by experienced vascular and interventional radiologists according to a standardized procedure, based on the technical documentation provided by themanufacturer. All patients underwent cavography before and after filter placement and conventional abdominal x-ray 24 hours to 48 hours after implan-tation. Before filter retrieval, ultrasonography or venography wasperformedtodetect filter thrombosis. Cavography was performed after retrieval in all patients."* *"Patients in both study groups received full-dose anticoagulant therapy according to guidelines for at least 6 months (eMethods in Supplement 2). Continuation of anticoagulation thereafter was at the investigator's discretion. Although the choice of anticoagulant therapy was left to the investigators' discretion (ie, any injectable*

	anticoagulant agent followed by vitaminKantagonist as soon as possible), investigators were strongly encouraged to use unfractionated heparin as the injectable agent in patients with a creatinine clearance of less than 30 mL/min, and, whenever possible, a lowmolecular- weight heparin for 6months rather than a vitaminK antagonist in patients with cancer."
Outcome measures	VTE-related mortality *PE-related mortality at 3 months and 6 months* VTE-recurrence *DVT/PE recurrence at 3 and 6 months* All-cause mortality *At 3 and 6 months*

1

Selection bias
Random sequence generation Low risk of bias *(Patients were randomized to the filter group or control group by a central, 24-hour, interactive voice response system, which ensured concealed allocation. Randomization was performed in randomly permuted blocks of 4 or 6with stratification according to center and patient creatinine clearance (estimated using the Cockcroft and Gault formulas; 30 mL/L or less vs more than 30 mL/L).")* *Allocation concealment* Low risk of bias *(interactive voice response system, which ensured concealed allocation)*
Performance bias
Blinding of participants and personnel High risk of bias *(unblinded)*
Detection bias
Blinding of outcome assessment Low risk of bias

(All efficacy and safety outcomes were reviewed by the central adjudication committee, the members of which were blinded to treatment assignments.)

Attrition bias

Incomplete outcome data

Low risk of bias

(all participants were included in ITT analysis, those that did not attend follow-up was typically due to death)

Reporting bias

Selective reporting

Low risk of bias

Other sources of bias

Any other sources of bias

Low risk of bias

Overall risk of bias and directness

Risk of bias

Low -Although this study was at serious risk of bias due to a lack of blinding, the overall risk of bias for this study remains low as the outcomes of relevance to this review are objectively assessed and therefore unlikely to be significantly influenced by a lack of blinding.

Directness

Partially applicable

Due to a mixed population of people with VTE being included in the study. The inclusion criteria for being at “high risk of PE-recurrence” covered a wide range of characteristics including those that the committee thought were more indicative of being at high risk of poor outcomes.

1

Pan, 2016

2

Bibliographic Reference	Pan, Y.; Zhao, J.; Mei, J.; Shao, M.; Zhang, J.; Wu, H.; Evaluation of nonpermanent inferior vena cava filter placement in patients with deep venous thrombosis after lower extremity fracture: A single-center retrospective study; Phlebology; 2016; vol. 31 (no. 8); 564-72

3 **Study arms**

With filter (N = 823)	Without filter 2008-2014 (N = 648)	Without filter 2003-2007 (excluded from present analysis) (N = 1052)
Mean age (SD): 51.8 (20.5) years % female: 44% % Anticoagulation: 84.0% % iliofemoral thrombosis: 52% % Popliteal thrombosis: 40% %Calf thrombosis: 8%	Mean age (SD): 48.2 (17.9) years % female: 36.4% % anticoagulation: 96.0% % iliofemoral thrombosis: 0.5% % Popliteal thrombosis: 34.7% %Calf thrombosis: 64.8%	

1 **Study details**

Study type	Retrospective cohort study
Study location	China
Study setting	Single centre
Study dates	January 2003 - October 2014
Sources of funding	No funding
Inclusion criteria	DVT *People with pelvic or lower extremity fracture complicated with lower extremity DVT, who underwent orthopedic surgery. The hospital inserted IVC filters for acute trauma patients with lower limb DVT in three circumstances: 1) pelvic and/or lower limb fracture requiring surgery complicated with DVT and with proxmial end located above knee. 2) free floating DVT, 3) peripheral DVT scheduled for bone fracture surgery of the knee or areas below the knee.*
Sample size	2763
Interventions	Filter versus no filter *Two control groups, both not receiving filters, were compared to the filter group. Control group 1 were matched to the filter group 1 includes all participants between 2008 - 2014 who did not get a filter (the same time period as the filter group). Control group 2 included all participants between 2003 - 2007, during which time filters were not permitted in the hospital.* Anticoagulation was permitted but not compulsory. "*For those people without contraindication to anticoagulation, LMWH was given for 3-4 days followed by*

	warfarin or rivaroxaban, for 3-6 months. If the filter was not removed oral anticoagulants should continue for 6-12 months, followed by aspirin for life. (see details on the study arms for more information on anticoagulation use).”
Outcome measures	All-cause mortality *During hospital stay* VTE-recurrence *Incidence of in-hospital PE*

1

1. Bias due to confounding
Risk of bias judgement for confounding Critical *(Controls are poorly matched to filter cohort and there is a high potential for confounding variables)*
2. Bias in selection of participants into the study
Risk of bias judgement for selection of participants into the study Low
3. Bias in classification of interventions
Risk of bias judgement for classification of interventions Low
4. Bias due to deviations from intended interventions
Risk of bias judgement for deviations from intended interventions Serious *(There was no information regarding deviations from the intended intervention. However, as the outcomes recorded all took place during hospital stay, this is not expected to be a big cause for concern. There are some differences in anticoagulant usage after admission to study.)*
5. Bias due to missing data
Risk of bias judgement for missing data Low
6. Bias in measurement of outcomes

Risk of bias judgement for measurement of outcomes

Low

7. Bias in selection of the reported result

Risk of bias judgement for selection of the reported result

Moderate

(There is no indication of selective reporting but there is no evidence of a pre-registered protocol so it is possible that the analysis was matched to the available data rather than being pre-specified.)

Overall bias

Risk of bias judgement

Critical

Directness

Directly applicable

1

Sharifi, 2012

2

Bibliographic Reference	Sharifi, M.; Bay, C.; Skrocki, L.; Lawson, D.; Mazdeh, S.; Role of IVC filters in endovenous therapy for deep venous thrombosis: the FILTER-PEVI (filter implantation to lower thromboembolic risk in percutaneous endovenous intervention) trial; Cardiovascular & Interventional Radiology; 2012; vol. 35 (no. 6); 1408-13

3 **Study arms**

Filter plus anticoagulation (N = 70)	**Anticoagulation alone (N = 71)**
% female: 45.7%	% female: 45.1%
Mean age (SD): 56 (9) years	Mean age (SD): 54 (10) years
% hypertension: 47%	% hypertension: 44%
% active cancer: 10%	% active cancer: 13%
% previous VTE: 19%	% previous VTE: 17%

4 **Study details**

Study type	Randomised controlled trial (RCT)
Study location	USA
Study dates	June 2009 - June 2010
Duration of follow-up	Up to 24 months
Inclusion criteria	DVT *DVT involving the popliteal vein or more proximal venous segments were eligible* Underwent procedure *People scheduled to undergo PEVI procedure - "The objective of PEVI was to restore streamline flow from the popliteal vein into the unobstructed portion of IVC and to lyse or extract as much thrombus as possible. Initial venography would dictate the approach to PEVI. For acute DVT with otherwise preserved venous architecture (Fig. 1), thrombectomy was performed with the Trellis device (Covidien, Mansfield, MA) or the AngioJet DVX catheter (Medrad/Possis, Warrendale, PA), which were followed with manual aspiration of the residual clot with a guide catheter. For severely distorted venous anatomy with residual diameter stenosis of C80% and calcification, which we called venosclerotic disease, a venous conduit was reconstructed by using balloon venoplasty and stents."*
Exclusion criteria	Thrombocytopenia *Severe thrombocytopenia (platelet count\30,000/mm3)* Contraindications *Contraindication to unfractionated or low-molecular-weight heparin* Previous filter placement Major bleeding *In previous 2 weeks*
Sample size	141
Interventions	Filter plus anticoagulation versus anticoagulation alone *"All interventions were performed through the popliteal vein. The filters implanted consisted of 8 Celect, 14 Tulip (Cook Medical, Bloomington, IN), 42 Optease (Cordis, Miami, FL), and 6 Eclipse (Bard, Tempe, AZ) filters. Of these, 41 filters were placed through the common femoral and 11 through the right internal jugular veins with the patient initially in the supine position. After filter placement, the patients were placed in the prone position, and access to the popliteal vein was obtained by a micropuncture needle with ultrasound guidance. Subsequently, a 6–8F sheath was placed through which venography and intervention were performed. In 18 patients, the filter was placed using the same popliteal access site, thereby eliminating the*

	need for repositioning the patient. Only one company (Cordis) has developed a long delivery system allowing for this approach." *"The anticoagulation regimen was similar in both groups. For most patients, it consisted of enoxaparin at 1 mg/kg twice daily administered subcutaneously. For those with renal insufficiency (creatinine clearance\30 ml/min) or concomitant massive PE, unfractionated heparin was provided at 80 IU/kg intravenously as loading dose, followed by 18 IU/kg/h. Adjustments were subsequently made to keep the activated partial thromboplastin time between 1.5 and 2 times baseline. Warfarin and aspirin were initiated at admission for all patients."*
Outcome measures	VTE-recurrence *"primary end point of this study was development of iatrogenic PE by objective testing in patients who developed suggestive signs and symptoms during the first 24 h after PEVI. The secondary end points were recurrent venous thromboembolism and filter integrity at the last follow-up. PE was defined as the development of new defects on a high-probability V/Q scan or multislice CT pulmonary angiogram. Only symptomatic patients were objectively evaluated. The suggestive signs and symptoms triggering testing for iatrogenic PE consisted of the following: cough, chest pain, bradycardia, tachycardia, hypotension, unresponsiveness, and oxygen desaturation."*

1

Selection bias
Random sequence generation Unclear risk of bias *(refers to participant randomization however it is unclear how this was conducted)* *Allocation concealment* Unclear risk of bias *(no mention of randomization procedures therefore unclear whether allocation was effectively concealed)*
Performance bias
Blinding of participants and personnel High risk of bias *(not reported however blinding is infeasible for this intervention)*
Detection bias
Blinding of outcome assessment Unclear risk of bias

(no information provided)

Attrition bias

Incomplete outcome data

Low risk of bias

Reporting bias

Selective reporting

Low risk of bias

Other sources of bias

Any other sources of bias

Unclear risk of bias

("By study design, this study evaluated only symptomatic patients for iatrogenic PE. It is well known that most PEs are asymptomatic, and hence the efficacy of IVC filters in their reduction is not clarified in this study." Additionally, the short follow-up time was noted by the author as being a limitation that will likely limit the number of events seen)

Overall risk of bias and directness

Risk of bias

Moderate

(No information on randomization or blinding. Lack of blinding is not thought to be a major risk of bias as blinding of participants and personnel is difficult/ infeasible in this context and is not likely to have a major impact on results as outcomes are objectively assessed)

Directness

Directly applicable

1

Stein, 2018a

2

Bibliographic Reference	Stein, P. D.; Matta, F.; Lawrence, F. R.; Hughes, M. J.; Usefulness of Inferior Vena Cava Filters in Unstable Patients With Acute Pulmonary Embolism and Patients Who Underwent Pulmonary Embolectomy; American Journal of Cardiology; 2018; vol. 121 (no. 4); 495-500

3 **Study arms**

Unstable with filter (N = 1272) Age (SD): 65 (15) years % female: 48.6% % aged >80: 16.2% % underwent thrombolytic therapy: 15.7% *34 patients in this group underwent pulmonary embolectomy (for which subgroup data is available)	**Unstable without filter (N = 3002)** Age (SD): 65 (15) years % female: 53.6% % aged >80: 17.2% % underwent thrombolytic therapy: 13.4% *9 patients in this group underwent pulmonary embolectomy (for which subgroup data is available)	**Stable with pulmonary embolectomy with filter (N = 245)** Age (SD): 58 (15) years % female: 43.3% % aged >80: 4.5%	**Stable with pulmonary embolectomy without filter (N = 124)** Age (SD): 55 (18) years % female: 50.0% % aged >80: 8.9%

1 **Study details**

Study type	Retrospective cohort study *an analysis of administrative data from the Premier Healthcare Database (Charlotte, North Carolina)*
Study location	USA
Study setting	The Premier Healthcar eDatabase contains data from 700 to 3,600 hospitals in the United States, depending on the year. The data include 20% to 40% of all discharges in the United States. Since 2011, the database has included 6 million discharges per year.
Study dates	2010 - 2014
Sources of funding	"This investigation was supported by a grant 2412.ll from the Blue Cross Blue Shield of Michigan Foundation (Detroit, Michigan)."
Inclusion criteria	VTE *hospitalized with PE* Underwent procedure *in shock or on ventilator support OR stable and underwent surgical pulmonary embolectomy* Unstable

	in shock or on ventilator support OR stable and underwent surgical pulmonary embolectomy
Sample size	4,274 participants were unstable. (604 received thrombolytic therapy and 43 underwent pulmonary embolectomy). 369 participants were stable and underwent pulmonary embolectomy.
Interventions	Filter versus no filter
Outcome measures	All-cause mortality *in-hospital mortality and at 3 months*

1

1. Bias due to confounding
Risk of bias judgement for confounding Critical *(The reason for filter being placed is likely due to confounding variables and no attempts were made to try to control for these.)*
2. Bias in selection of participants into the study
Risk of bias judgement for selection of participants into the study Moderate *(Potential for immortal time bias and this was not accounted for.)*
3. Bias in classification of interventions
Risk of bias judgement for classification of interventions Low
4. Bias due to deviations from intended interventions
Risk of bias judgement for deviations from intended interventions Moderate *(There was no information regarding deviations from the intended intervention. However, as outcomes are restricted to those occurring in the hospital, this is not a great concern. There is limited information regarding anticoagulation use after the intervention, or whether this was comparable between groups.)*

5. Bias due to missing data

Risk of bias judgement for missing data

Moderate

(There was no information regarding deviations from the intended intervention. However, as outcomes are restricted to those occurring in the hospital, this is not a great concern. There is limited information regarding anticoagulation use after the intervention, or whether this was comparable between groups.)

6. Bias in measurement of outcomes

Risk of bias judgement for measurement of outcomes

Moderate

(unclear length of hospital stay. It is possible that the filter group had a longer follow-up time and this has the potential for bias)

7. Bias in selection of the reported result

Risk of bias judgement for selection of the reported result

Moderate

(There is no indication of selective reporting but there is no evidence of a pre-registered protocol so it is possible that the analysis was matched to the available data rather than being pre-specified.)

Overall bias

Risk of bias judgement

Critical

Directness

Directly applicable

Stein, 2018b

Bibliographic Reference	Stein, P. D.; Matta, F.; Lawrence, F. R.; Hughes, M. J.; Importance of Early Insertion of Inferior Vena Cava Filters in Unstable Patients with Acute Pulmonary Embolism; American Journal of Medicine; 2018; vol. 131 (no. 9); 1104-1109

Study arms

With filter (N = 180) with thrombolysis: 35.6%	**Without filter (N = 299)** With thrombolysis: 31.1% *no other demographic information was reported

1 **Study details**

Study type	Retrospective cohort study
Study location	USA
Study setting	Using admin data from Premier Healthcare Database (Charlotte, North Carolina)
Study dates	2010 - 2015
Duration of follow-up	Hospital stay
Sources of funding	None
Inclusion criteria	PE Unstable *In shock or on ventilator*
Sample size	479
Interventions	Filter versus no filter
Outcome measures	All-cause mortality *In-hospital*

2

1. Bias due to confounding
Risk of bias judgement for confounding Critical *(Baseline characteristics were not provided and confounding variables were not controlled for. It is likely that the decision to place a filter was due to confounding variables.)*
2. Bias in selection of participants into the study

Risk of bias judgement for selection of participants into the study

Serious

(Potential for immortal time bias however no attempts were made to adjust for this.)

3. Bias in classification of interventions

Risk of bias judgement for classification of interventions

Low

4. Bias due to deviations from intended interventions

Risk of bias judgement for deviations from intended interventions

Moderate

(There was no information regarding deviations from the intended intervention. However, as outcomes are restricted to those occurring in the hospital, this is not a great concern. There is limited information regarding anticoagulation use after the intervention, or whether this was comparable between groups.)

5. Bias due to missing data

Risk of bias judgement for missing data

Low

6. Bias in measurement of outcomes

Risk of bias judgement for measurement of outcomes

Moderate

(unclear length of hospital stay. It is possible that the filter group had a longer follow-up time and this has the potential for bias)

7. Bias in selection of the reported result

Risk of bias judgement for selection of the reported result

Moderate

(There is no indication of selective reporting but there is no evidence of a pre-registered protocol so it is possible that the analysis was matched to the available data rather than being pre-specified.)

Overall bias

Risk of bias judgement

Critical
Directness
Directly applicable

1

Stein, 2018c

2

Bibliographic Reference	Stein, P. D.; Matta, F.; Lawrence, F. R.; Hughes, M. J.; Inferior Vena Cava Filters in Patients with Acute Pulmonary Embolism and Cancer; American Journal of Medicine; 2018; vol. 131 (no. 4); 442.e9-442.e12

3 **Study arms**

With filter (N = 6589) % over 80 years old: 14.4% % female: 50.2% Mean age (SD): 67.0 (12) years	**Without filter (N = 28435)** % over 80 years old: 14.0% % female: 51.9% Mean age (SD): 66.7 (12) years

4 **Study details**

Study type	Retrospective cohort study
Study location	USA
Study setting	Using admin data from Premier Healthcare Database (Charlotte, North Carolina)
Study dates	2010 - 2014
Duration of follow-up	Up to 3 months
Sources of funding	None
Inclusion criteria	PE Active cancer *Solid malignant tumor* At least 18 years of age

Exclusion criteria	Surgery *Underwent pulmonary embolectomy* Other conditions *Unstable (in shock or on ventilator).* Concomitant use of thrombolytic agents
Sample size	35,024
Interventions	Filter versus no filter
Outcome measures	All-cause mortality *In-hospital and at 3 months*

1

1. Bias due to confounding
Risk of bias judgement for confounding Critical *(The decision to place a filter was likely based on clinical characteristics and no attempts were made to adjust the analysis for important clinical characteristics which make a filter being placed more likely.)*
2. Bias in selection of participants into the study
Risk of bias judgement for selection of participants into the study Serious *(Potential for immortal time bias as the follow-up began before the filter was likely to have been placed and no attempts were made to adjust for this.)*
3. Bias in classification of interventions
Risk of bias judgement for classification of interventions Low
4. Bias due to deviations from intended interventions
Risk of bias judgement for deviations from intended interventions Moderate

(There was no information regarding deviations from the intended intervention. For outcomes occurring in the hospital, this is not a great concern as all placed filter will be captured in the study. However, at 3 months it is unclear whether participants had subsequent filters placed or removed. There is limited information regarding anticoagulation use after the intervention, or whether this was comparable between groups.)

5. Bias due to missing data

Risk of bias judgement for missing data

Moderate

(There was no information regarding deviations from the intended intervention. However, as outcomes are restricted to those occurring in the hospital, this is not a great concern. There is limited information regarding anticoagulation use after the intervention, or whether this was comparable between groups.)

6. Bias in measurement of outcomes

Risk of bias judgement for measurement of outcomes

Moderate

(length of hospital stay is unclear and therefore it is possible that the filter group remained in the hospital for longer, allowing more time for the outcome to occur.)

7. Bias in selection of the reported result

Risk of bias judgement for selection of the reported result

Moderate

(There is no indication of selective reporting but there is no evidence of a pre-registered protocol so it is possible that the analysis was matched to the available data rather than being pre-specified.)

Overall bias

Risk of bias judgement

Critical

Directness

Directly applicable

1

Stein, 2019a

2

Bibliographic Reference	Stein, P. D.; Matta, F.; Lawrence, F. R.; Hughes, M. J.; Inferior Vena Cava Filters in Patients with Recurrent Pulmonary Embolism; American Journal of Medicine; 2019; vol. 132 (no. 1); 88-92

1 **Study arms**

With filter (N = 603) Mean age (SD): 66 (15) years % female: 50.4%	**Without filter (N = 211)** Mean age (SD): 66 (16) years % female: 54.0%

2 **Study details**

Study type	Retrospective cohort study *of administrative data from Premier Healthcare Database*
Study location	USA.
Study setting	The Premier Healthcare Database contains inpatient discharges in the USA primarily fro mnon-profit, non-governmental community and teaching hospitals in rural and urban areas. >5 million inpatient admissions per year were included since 2011, representing around 20% of annual inpatient hospitalisations. From 2009 - 2014 data came from 397 - 615 different hospitals.
Study dates	2009 - 2014
Duration of follow-up	Up to 3 months
Sources of funding	None reported
Inclusion criteria	Recurrent PE *People who suffered a recurrent PE within 3 months of an index PE.* At least 18 years of age
Exclusion criteria	Previous filter placement *Those who received filter during index PE event (prior to recurrence) were excluded*
Sample size	814
Interventions	Filter versus no filter
Outcome measures	All-cause mortality

	Reported during in-hospital stay and during 3 month follow-up. Subgroup analysis was also reported which only included stable people who did not receive thrombolytic therapy or pulmonary embolectomy.

1

1. Bias due to confounding

Risk of bias judgement for confounding

Critical

(The decision to give a filter was likely due to confounding variables and the study does not attempt to adjust for these.)

2. Bias in selection of participants into the study

Risk of bias judgement for selection of participants into the study

Moderate

(Potential for immortal time bias however attempts were made to correct for this.)

3. Bias in classification of interventions

Risk of bias judgement for classification of interventions

Low

4. Bias due to deviations from intended interventions

Risk of bias judgement for deviations from intended interventions

Moderate

(There was no information regarding deviations from the intended intervention. However, as outcomes are restricted to those occurring in the hospital, this is not a great concern. There is limited information regarding anticoagulation use after the intervention, or whether this was comparable between groups.)

5. Bias due to missing data

Risk of bias judgement for missing data

Low

6. Bias in measurement of outcomes

Risk of bias judgement for measurement of outcomes

Moderate

(unclear length of hospital stay. It is possible that the filter group had a longer follow-up time and this has the potential for bias)

7. Bias in selection of the reported result

Risk of bias judgement for selection of the reported result

Moderate

(There is no indication of selective reporting but there is no evidence of a pre-registered protocol so it is possible that the analysis was matched to the available data rather than being pre-specified.)

Overall bias

Risk of bias judgement

Critical

Directness

Directly applicable

1

Stein, 2019b

2

Bibliographic Reference	Stein, P. D.; Matta, F.; Hughes, M. J.; Inferior Vena Cava Filters in Stable Patients With Pulmonary Embolism and Heart Failure; American Journal of Cardiology; 2019; vol. 124 (no. 2); 292-295

3 **Study arms**

With filter (N = 2423)	Without filter (N = 14063)
*demographic information not reported.	*demographic information not reported.

4 **Study details**

Study type	Retrospective cohort study
Study location	USA
Study setting	Using admin data from Premier Healthcare Database (Charlotte, North Carolina)
Study dates	2009 - 2015

Duration of follow-up	Hospital stay
Sources of funding	None
Inclusion criteria	PE Heart failure *PE with a discharge code of heart failure* At least 18 years of age
Exclusion criteria	Surgery *If the person underwent pulmonary embolectomy* Other conditions *Unstable (on ventilator or in shock) or any other co-morbid conditions*
Sample size	16,486
Interventions	Filter versus no filter
Outcome measures	All-cause mortality *In-hospital mortality*

1

1. Bias due to confounding
Risk of bias judgement for confounding Serious *(The reason for receiving a filter was likely due to confounding variables. The study attempted to control for this by matching participants based on comorbid conditions however this does not adequately account for confounders. Additionally, baseline characteristics are not provided.)*
2. Bias in selection of participants into the study
Risk of bias judgement for selection of participants into the study Serious *(Potential for immortal time bias and no attempts were made to adjust for this.)*
3. Bias in classification of interventions

Risk of bias judgement for classification of interventions

Low

4. Bias due to deviations from intended interventions

Risk of bias judgement for deviations from intended interventions

Moderate

(There was no information regarding deviations from the intended intervention. However, as outcomes are restricted to those occurring in the hospital, this is not a great concern. There is limited information regarding anticoagulation use after the intervention, or whether this was comparable between groups.)

5. Bias due to missing data

Risk of bias judgement for missing data

Low

6. Bias in measurement of outcomes

Risk of bias judgement for measurement of outcomes

Moderate

(unclear length of hospital stay. It is possible that the filter group had a longer follow-up time and this has the potential for bias)

7. Bias in selection of the reported result

Risk of bias judgement for selection of the reported result

Moderate

(moderate There is no indication of selective reporting but there is no evidence of a pre-registered protocol so it is possible that the analysis was matched to the available data rather than being pre-specified.)

Overall bias

Risk of bias judgement

Critical

Directness

Directly applicable

1

Tanabe, 2014

Bibliographic Reference	Tanabe, Y.; Obayashi, T.; Yamamoto, T.; Nakata, J.; Yagi, H.; Takayama, M.; Nagao, K.; Current status of the use of inferior vena cava filters in cases of pulmonary embolism in CCUs: From the Tokyo CCU Network; Journal of Cardiology; 2014; vol. 63 (no. 5); 385-9

1 **Study arms**

Sub-massive PE with filter (N = 129)	**Sub-massive PE without filter (N = 123)**	**Massive PE with filter (N = 38)**	**Massive PE without filter (N = 41)**	**PE 201 with collapse, with filter (N = 15)**	**PE with collapse, without filter (N = 29)**
*demographic information was not reported.	*demographic information was not reported.	*demographic information was not reported.	*demographic information was not reported.	*demographic information was not reported.	*demographic information was not reported.

2 **Study details**

Study type	Retrospective cohort study *Retrospective review of records of routinely collected data in CCUs*
Study location	Japan
Study setting	62 hospitals. The study anaylsed data from the Tokyo CCU Net-work. The Tokyo CCU Network is operated through 62 hospitalswith the help of ambulance units through the control room of theTokyo Fire Department. Institutions belonging to the Tokyo CCUNetwork routinely record and submit details of all patients treatedin their CCUs on survey forms
Study dates	January 2005 - December 2010
Duration of follow-up	Up to 30 days
Sources of funding	None reported
Inclusion criteria	VTE *Participants had PE*
Sample size	375 extracted for this review (only those participants with sub-massive or massive PE, or collapse).
Interventions	Filter versus no filter
Outcome measures	All-cause mortality *30 day mortality*

1

1. Bias due to confounding

Risk of bias judgement for confounding

Critical

(Baseline characteristics were not provided. No adjustments for confounders were made in the analysis.)

2. Bias in selection of participants into the study

Risk of bias judgement for selection of participants into the study

Serious

(Potential for immortal time bias and the study did not attempt to correct for this.)

3. Bias in classification of interventions

Risk of bias judgement for classification of interventions

Low

4. Bias due to deviations from intended interventions

Risk of bias judgement for deviations from intended interventions

Moderate

(There is no information given regarding co-interventions given after filter. There was no information regarding deviations from the intended intervention and in particular, no information about whether participants could later receive a filter or have a filter removed.)

5. Bias due to missing data

Risk of bias judgement for missing data

Moderate

(Outcome data is available for most included participants however the response rate regarding the use of IVC filters is not known.)

6. Bias in measurement of outcomes

Risk of bias judgement for measurement of outcomes

Low

7. Bias in selection of the reported result
Risk of bias judgement for selection of the reported result
Moderate
(There is no indication of selective reporting but there is no evidence of a pre-registered protocol so it is possible that the analysis was matched to the available data rather than being pre-specified.)
Overall bias
Risk of bias judgement
Critical
Directness
Directly applicable

1

Turner, 2018

2

Bibliographic Reference	Turner, T. E.; Saeed, M. J.; Novak, E.; Brown, D. L.; Association of Inferior Vena Cava Filter Placement for Venous Thromboembolic Disease and a Contraindication to Anticoagulation With 30-Day Mortality; JAMA Network Open; 2018; vol. 1 (no. 3); e180452

3 **Study arms**

With filter (N = 45771)	**Without filter (N = 80259)**
% female: 49.4%	% female: 48.2%
Mean age (SD): 69.1 (15.6) years	Mean age (SD): 65.7 (17.1) years
% PE only: 21.7%	% PE only: 33.6%
%DVT only: 56.4%	%DVT only: 51.1%
% PE and DVT: 21.9%	% PE and DVT: 15.3%
Reason for not being able to take AC: • 13.4% Intracranial bleeding • 61.7% other major bleeding • 26.0% thrombocytopenia	Reason for not being able to take AC: • 4.5% Intracranial bleeding • 53.8% other major bleeding • 32.1% thrombocytopenia

4 **Study details**

Study type	Retrospective cohort study

	Retrospective review of State Inpatient Database
Study location	USA
Study setting	Hospitals in California, Florida and New York
Study dates	January 1, 2005 to December 31, 2013 (data from California and New York ended in 2011 and 2012, respectively).
Duration of follow-up	Until end of data collection.
Sources of funding	"This work was supported by grant UL1 TR000448 to theWashington University Institute of Clinical and Translational Sciences from the National Center for Advancing Translational Sciences, grant R24 HS19455 from the Agency for Healthcare Research and Quality, and grant KM1CA156708 from the National Cancer Institute at the National Institutes of Health."
Inclusion criteria	VTE *Hospitalization of a patient with PE or DVT was defined as the index hospitalization and was required to have the preceding 12-month period free of inpatient records coded for PE, DVT, or IVC filter insertion.* Cannot take anticoagulation *Contraindications to anticoagulation were identified by ICD-9-CM diagnosis or procedure codes and included any of the following: intracranial bleeding, other major bleeding, thrombocytopenia, active gastrointestinal bleeding, aortic dissection, pericardial disease, bacterial endocarditis, threatened abortion, preeclampsia and eclampsia, malignant hypertension, brain surgery, spinal surgery or spinal puncture, and eye surgery coded at the index hospitalization or within the prior 15 days (Table 1). In addition, hemophilia, von Willebrand disease, and cerebral aneurysm coded at the index hospitalization or within the prior year were considered contraindications to anticoagulation.*
Exclusion criteria	Missing data *Index hospitalizations with missing sex* Residence outside hospital state Hospitalisation length of stay over 6 months
Sample size	126,030
Interventions	Filter versus no filter
Outcome measures	All-cause mortality *"Our primary method of analysis was a multivariable Cox model with IVC filter status as a timedependent variable to account for immortal time bias. The start time for this analysis was the date of index hospitalization. Patients were followed up until the time of an event or censored at 30 days."*

1

1. Bias due to confounding

Risk of bias judgement for confounding

Serious

(The study adjusted for many potential confounders and most of the confounding domains that the study adjusted for are routinely measured during hospital stay and are likely to be captured validly and reliably in the database. However, participants with Distal-DVT were included in the study. These participants are not typically candidates for an IVC filter and are therefore likely more likely (or exclusively) to be represented in the no-follow up group. This does not seem to have been controlled for.)

2. Bias in selection of participants into the study

Risk of bias judgement for selection of participants into the study

Moderate

(Follow-up starts at the point of recurrence (criteria for enrolment) however the filter will have been placed after this point. Therefore those in the filter group are immortal from the point of admission until the filter is placed. However, the study adjusted for this adding filter status as a variable within the analysis, such that events occurring before this point were excluded.)

3. Bias in classification of interventions

Risk of bias judgement for classification of interventions

Low

4. Bias due to deviations from intended interventions

Risk of bias judgement for deviations from intended interventions

Moderate

(overall There was no information regarding deviations from the intended intervention and in particular, no information about whether participants could later receive a filter or have a filter removed.)

5. Bias due to missing data

Risk of bias judgement for missing data

Low

6. Bias in measurement of outcomes

Risk of bias judgement for measurement of outcomes

Low
7. Bias in selection of the reported result
Risk of bias judgement for selection of the reported result Moderate *(There is no indication of selective reporting but there is no evidence of a pre-registered protocol so it is possible that the analysis was matched to the available data rather than being pre-specified.)*
Overall bias
Risk of bias judgement Serious *Directness* Directly applicable

1

Wadhwa, 2018

2

Bibliographic Reference	Wadhwa, V.; Gutta, N. B.; Trivedi, P. S.; Chatterjee, K.; Ahmed, O.; Ryu, R. K.; Kalva, S. P.; In-Hospital Mortality Benefit of Inferior Vena Cava Filters in Patients With Pulmonary Embolism and Congestive Heart Failure; AJR. American Journal of Roentgenology; 2018; vol. 211 (no. 3); 672-676

3

4 **Study arms**

Without filter (N = 358638)	With filter (N = 67237)
% >80 years old: 34.6%	% >80 years old: 38.8%
% Female: 56.2%	% Female: 55.0%
median length of stay: 6 days metastatic cancer: 4.7%	median length of stay: 10 days metastatic cancer: 7.8%
obesity: 18.4%	obesity: 15.3%
chronic renal failure: 22%	chronic renal failure: 21%

5

6 **Study details**

Study type	Retrospective cohort study
Study location	USA
Study setting	Data from the Nationwide Inpatient Sample, the largest all-payer inpatient database in the US, encompassing over 95% of US population.
Study dates	2005 - 2014
Duration of follow-up	In-hospital stay
Inclusion criteria	PE Chronic heart failure
Exclusion criteria	Incomplete outcome data
Sample size	425,877
Interventions	Filter versus no filter
Outcome measures	All-cause mortality *In-hospital*

1

1. Bias due to confounding
Risk of bias judgement for confounding Moderate *(The reason for the filter being placed was likely due to confounding variables that are prognostic of the outcome. However, the study adjusted for many different relevant confounders that are indicative of propensity to receive a filter. Most variables controlled for are routinely assessed in hospital and are therefore likely to have been measured reliably and validly.)*
2. Bias in selection of participants into the study
Risk of bias judgement for selection of participants into the study Serious *(Potential for immortal time bias and no attempts were made to correct for this.)*
3. Bias in classification of interventions

Risk of bias judgement for classification of interventions

Low

4. Bias due to deviations from intended interventions

Risk of bias judgement for deviations from intended interventions

Moderate

(There was no information regarding deviations from the intended intervention. However, as outcomes are restricted to those occurring in the hospital, this is not a great concern. There is limited information regarding anticoagulation use after the intervention, or whether this was comparable between groups.)

5. Bias due to missing data

Risk of bias judgement for missing data

Low

6. Bias in measurement of outcomes

Risk of bias judgement for measurement of outcomes

Moderate

(length of stay was 10 days in the filter group and only 6 days in the non-filter group therefore there was more time for the outcome to occur in the filter group.)

7. Bias in selection of the reported result

Risk of bias judgement for selection of the reported result

Moderate

(There is no indication of selective reporting but there is no evidence of a pre-registered protocol so it is possible that the analysis was matched to the available data rather than being pre-specified.)

Overall bias

Risk of bias judgement

Serious

Directness

Directly applicable

1

White, 2016

1

Bibliographic Reference	White, R. H.; Brunson, A.; Romano, P. S.; Li, Z.; Wun, T.; Outcomes After Vena Cava Filter Use in Noncancer Patients With Acute Venous Thromboembolism: A Population-Based Study; Circulation; 2016; vol. 133 (no. 21); 2018-29

2 **Study arms**

Surgery with filter (N = 489)	**Surgery without filter (N = 956)**	**Contraindication to anticoagulation, with filter (N = 1095)**	**contraindication to anticoagulation, without filter (N = 1922)**
% aged over 80 years: 24.5% % female: 49.9% % bleeding on admission: 12.3% % bleeding during hospitalization: 12.3% % thrombolytic treatment: 9.0%	% aged over 80 years: 19.2% % female: 52.5% % bleeding on admission: 6.0% % bleeding during hospitalization: 4.2% % thrombolytic treatment: 7.1%	% aged over 80 years: 36.7% % female: 56.8% % bleeding on admission: 71.6% % bleeding during hospitalization: 31.0% % thrombolytic treatment: 7.3%	% aged over 80 years: 27.8% % female: 51.0% % bleeding on admission: 79.1% % bleeding during hospitalization: 22.0% % thrombolytic treatment: 4.0%

3 **Study details**

Study location	USA
Study setting	California Patient Discharge Database (PDD). *"The PDD contains administrative hospital discharge data, as required (and audited) by the Centers for Medicare & Medicaid Services. The database includes demographic information, a principal diagnosis for the hospitalization and up to 25 additional clinical diagnoses, and a list of up to 20 major procedures performed on every patient hospitalized in all nonfederal acute care hospitals in California (the PDD includes 95%–97% of all discharges in the state). The ED records include similar data for patients evaluated at but not admitted to all hospital-affiliated EDs. Serial hospital/ ED records can be linked with the use of an encrypted form of the Social Security number called the record linkage number that is generated by California Office of Statewide Planning and Design for the 95% of patients who have a Social Security number. The PDD and ED data sets do not list the medications prescribed to the patient."*
Study dates	2005-2010

Duration of follow-up	Up to 1 year
Inclusion criteria	VTE *"PE or lower-extremity DVT. For each linked record, only the first hospitalization for acute VTE was analyzed. Patients coded as having both DVT and PE were classified as having a PE."* Cannot take anticoagulation **For subgroup analysis. "To isolate the patients who were likely not to have received anticoagulation during all or part of the hospital stay, we identified all patients with active bleeding". It is likely that these participants did not receive AC during hospital stay (and at time of IVC filter) however it is not known whether these participants went on to receive AC.* Underwent procedure **For subgroup analysis. "To isolate another subgroup of patients who were likely to have had anticoagulation withheld during all or part of the hospital stay, we identified patients who underwent a major surgical operation during the hospital stay. Major diagnostic or therapeutic operating room procedures were defined with the use of a modification of the Centers for Medicare & Medicaid Services reference codes,19 specifically excluding VCF insertion (code 38.7) as a surgical procedure. Vascular procedures for venous thrombectomy or procedures used in conjunction with thrombolysis were not included in the definition of major surgery"* At least 18 years of age
Exclusion criteria	Previous filter placement *Placed since July 1, 1991* Active cancer (except for melanoma skin cancer)
Sample size	4462
Interventions	Filter versus no filter *"VCF placement was identified by the presence of the ICD-9-CM code 38.7 (interruption of the vena cava). VCF removal is ICD-9-CM code 39.99 or Current Procedural Terminology code 037203, but these codes were encountered so infrequently (314 of 9346 patients, 3.4%) that retrieval was not incorporated into any analysis"* *The author noted that parenteral anticoagulation used was inadequately captured by the database due to no information on AC intensity, duration or adequacy.*
Outcome measures	All-cause mortality *At 30 and 90 days* VTE-recurrence *At 1-year*

1. Bias due to confounding

Risk of bias judgement for confounding

Moderate

(The reason for the filter being placed is likely due to confounding variables. The study adjusted for many relevant confounders to account for this.)

2. Bias in selection of participants into the study

Risk of bias judgement for selection of participants into the study

Moderate

(There is the potential for immortal time bias however the study attempted to account for this using a method which was likely adequate (VCF use was entered as a time-dependent covariate in the inverse probability-weighted proportional hazard models for death. In propensity-matched analyses, patients not treated with a VCF had to be alive on the hospital day when the matched VCF case had the filter inserted).)

3. Bias in classification of interventions

Risk of bias judgement for classification of interventions

Low

4. Bias due to deviations from intended interventions

Risk of bias judgement for deviations from intended interventions

Low (for surgery prophylaxis groups)

Serious (for contraindication to anticoagulation groups)

(Actual anticoagulation status during hospital stay and over the course of the study was not available. This bring into question the validity of the "contraindication to AC" intervention groups. Turner 2018 used a much wider range of criteria, including various comorbid conditions, to indicate a contraindication to anticoagulation. Additionally, a lack of information regarding anticoagulation use means that there is uncertainty as to whether participants deviated from their intended intervention.)

5. Bias due to missing data

Risk of bias judgement for missing data

Low

6. Bias in measurement of outcomes

Risk of bias judgement for measurement of outcomes

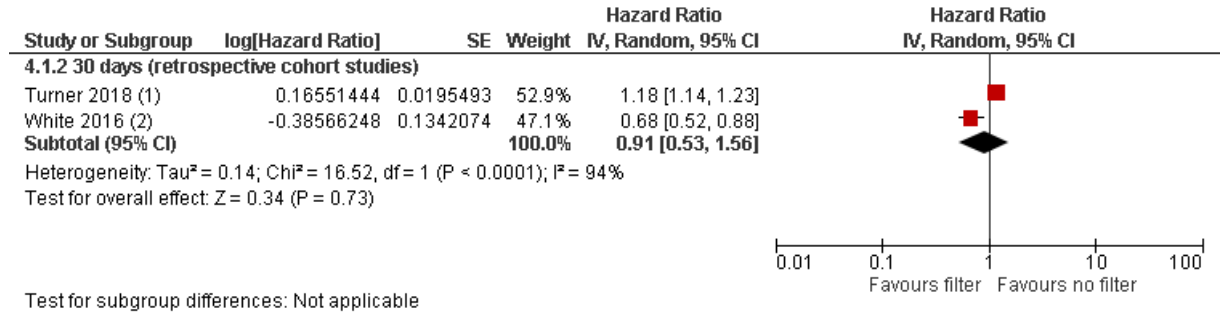
Low
7. Bias in selection of the reported result
Risk of bias judgement for selection of the reported result Moderate *(There is no indication of selective reporting but there is no evidence of a pre-registered protocol so it is possible that the analysis was matched to the available data rather than being pre-specified.)*
Overall bias
Risk of bias judgement Moderate (Surgery groups) Serious (contrainidication groups) *Directness* Directly applicable

1

Appendix F – Forest plots

Filter versus no filter in people who cannot have anticoagulants

Figure 1: All-cause mortality (30 days)



Test for subgroup differences: Not applicable

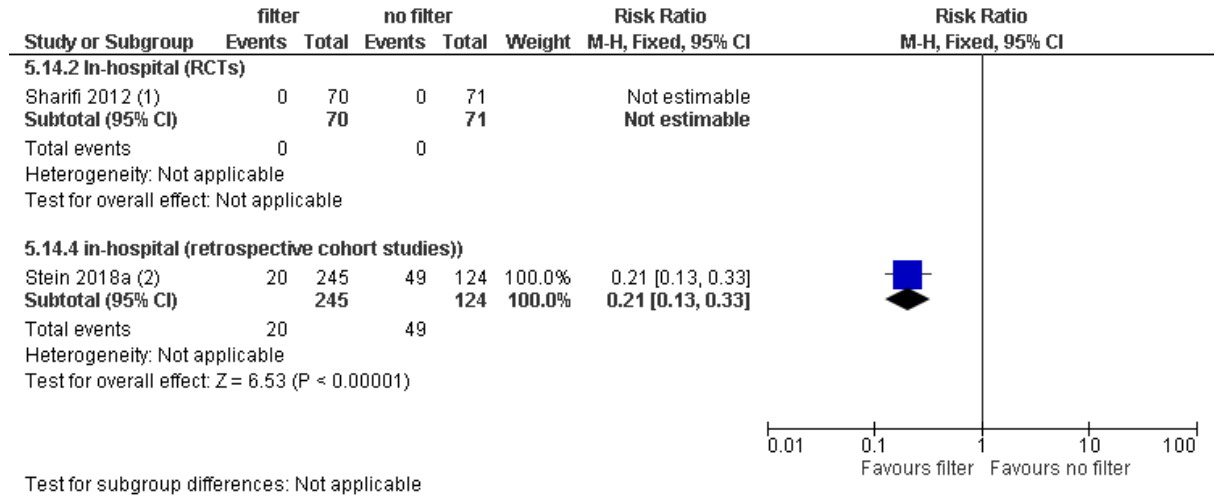
Footnotes

(1) contraindication identifed by any one of many relevant clinical factors (see evidence table); analysis adjusted for immortal time bias...

(2) contraindication identified by active bleeding; analysis adjusted for immortal time bias and used inversed probability of treatment...

Filter versus no filter in people with VTE who have the filters inserted for prophylaxis before a potential provoking event

Figure 2: All-cause mortality (in-hospital)



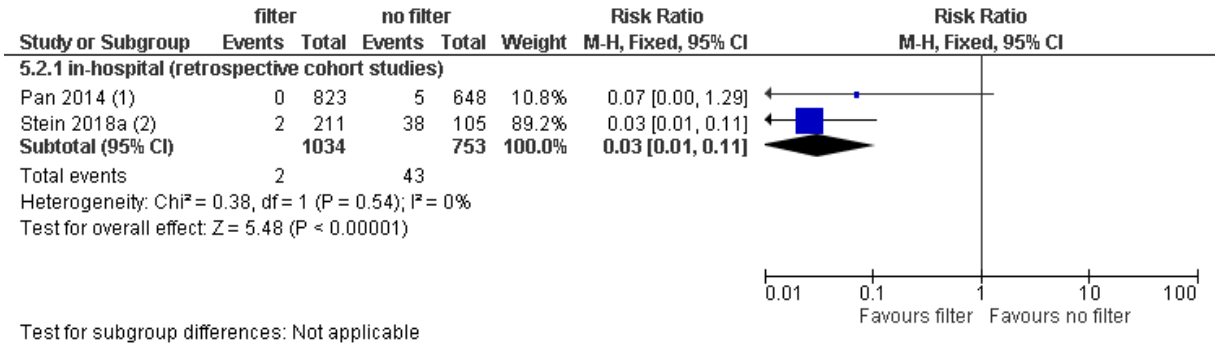
Test for subgroup differences: Not applicable

Footnotes

(1) at 24 hours

(2) PE, undergoing surgical pulmonary embolectomy

Figure 3: PE-related mortality (in-hospital)



Test for subgroup differences: Not applicable

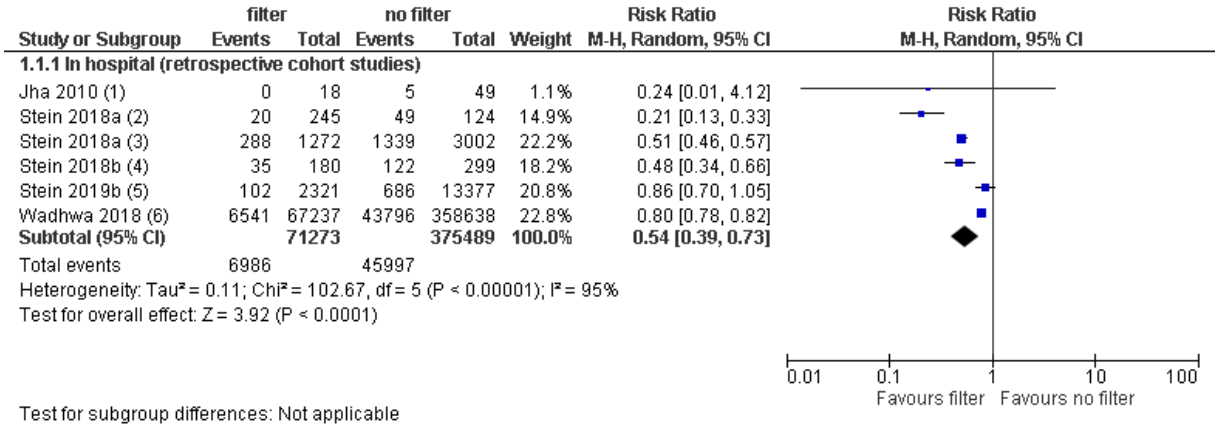
Footnotes

(1) undergoing orthopedic surgery for pelvic or lower extremity fracture, complicated with lower extremity DVT

(2) PE, undergoing surgical pulmonary embolectomy

Filter versus no filter in people with VTE who are at high risk of poor outcomes in the event of PE recurrence

Figure 4: All-cause mortality (in-hospital)



Test for subgroup differences: Not applicable

Footnotes

(1) PE with right heart strain

(2) PE undergoing surgical pulmonary embolectomy

(3) unstable (in shock or on ventilator support) PE

(4) unstable (in shock or on ventilator support) PE

(5) PE and heart failure

(6) PE and congestive heart failure

Figure 5: Subgroup analysis: all-cause mortality (in-hospital) in people aged over 80 years old

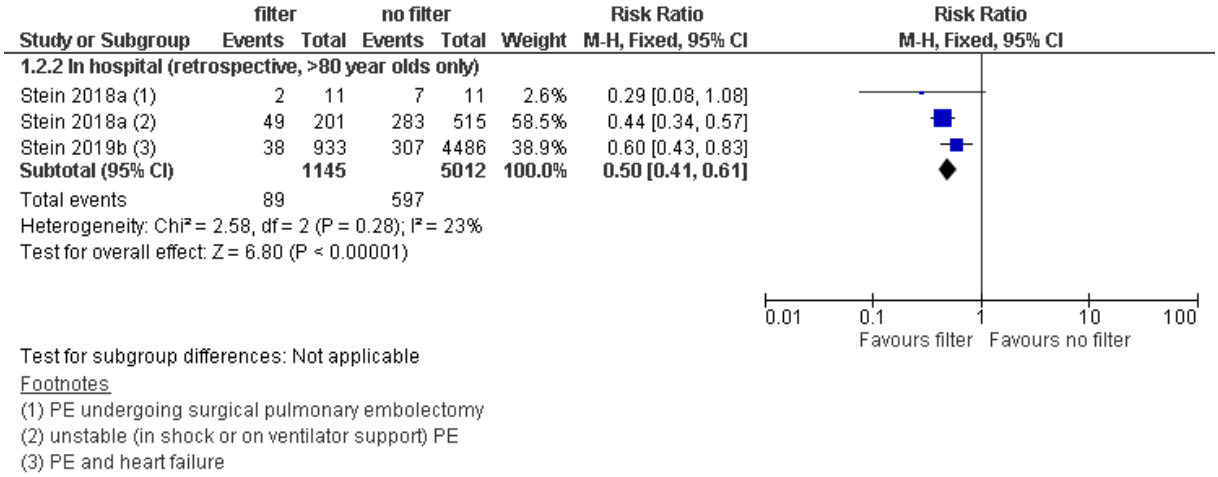


Figure 6: All-cause mortality (3 months)

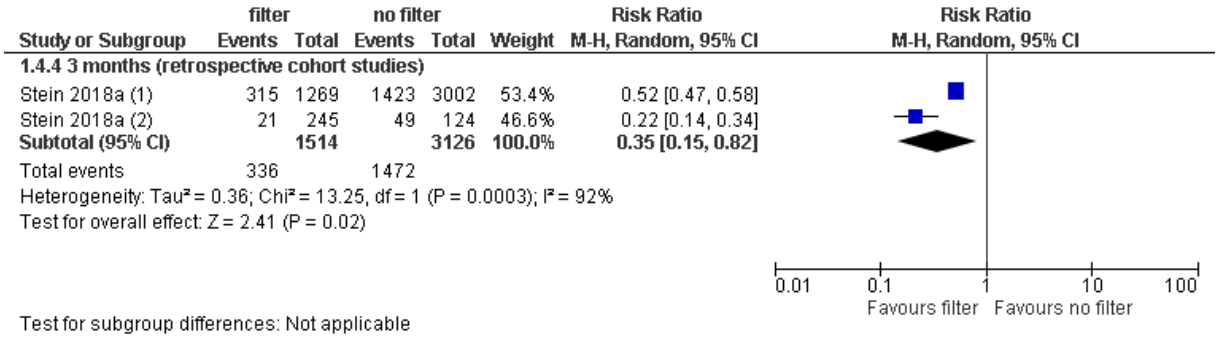


Figure 7: PE-related mortality (in-hospital)

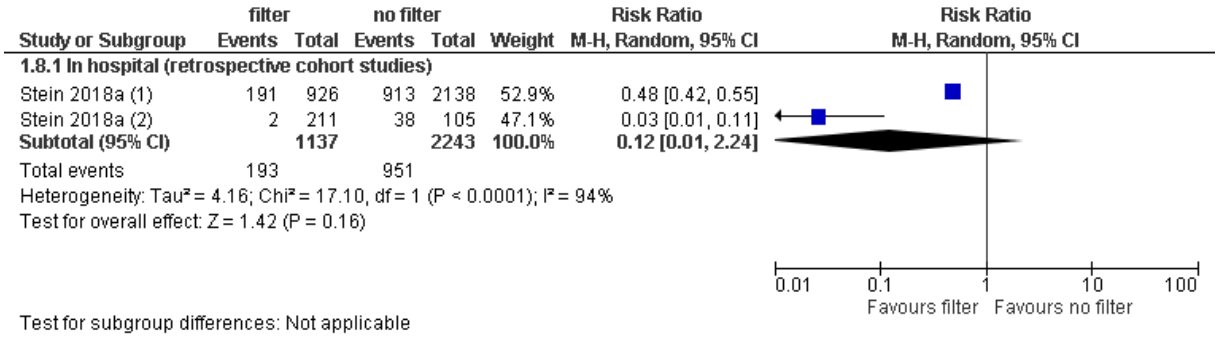
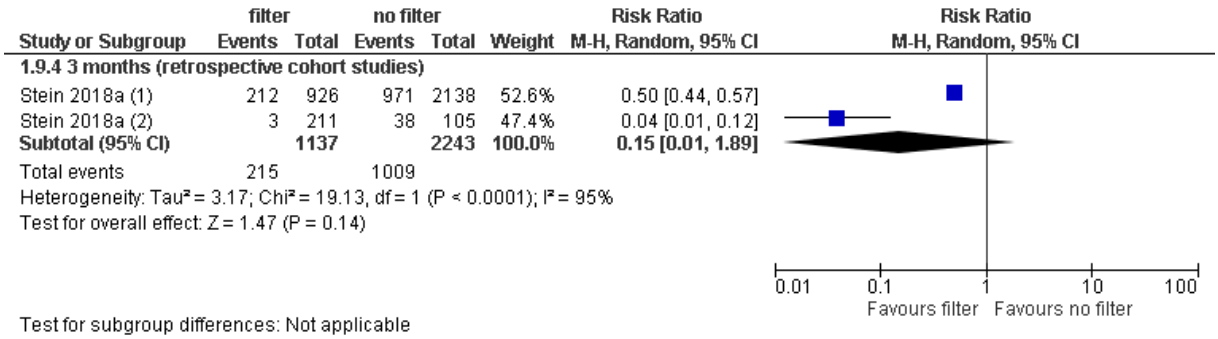


Figure 8: PE-related mortality (3 months)



Test for subgroup differences: Not applicable

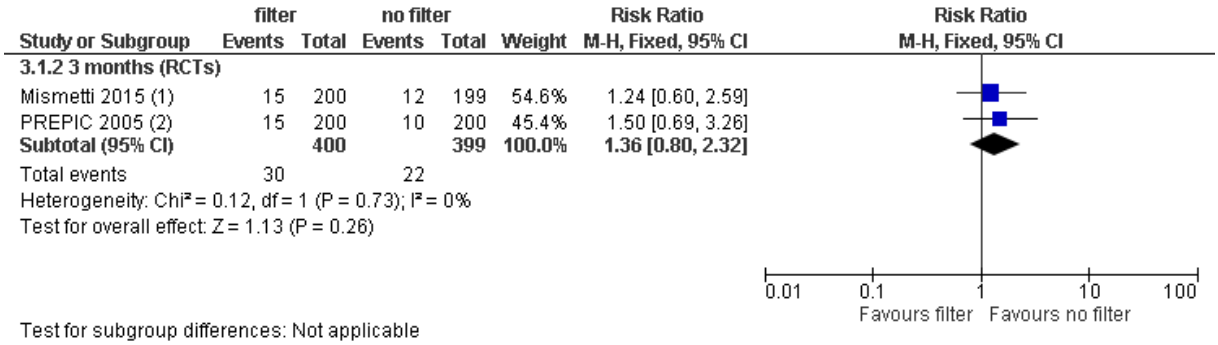
Footnotes

(1) unstable (in shock or on ventilator support) PE

(2) PE undergoing surgical pulmonary embolectomy

Filter versus no filter in people with VTE who are at high risk of PE-recurrence

Figure 9: All-cause mortality (3 months)



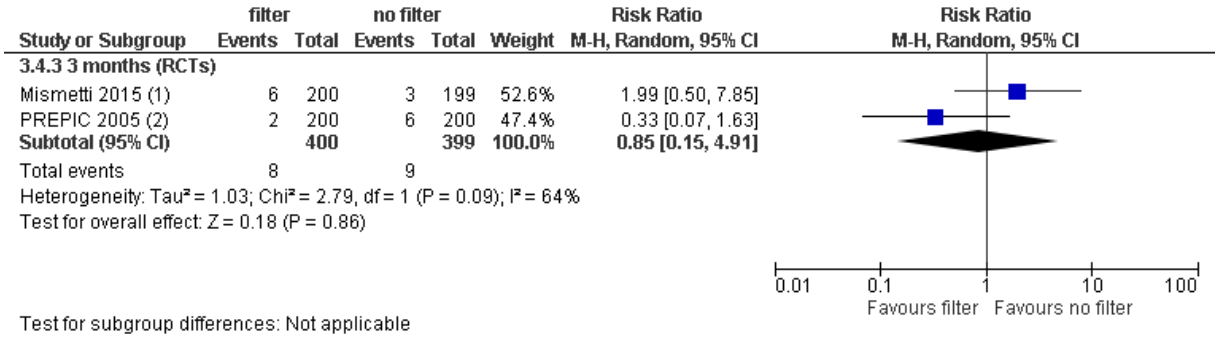
Test for subgroup differences: Not applicable

Footnotes

(1) at least 1 criterion for severity (see evidence table).

(2) see (1)

Figure 10: Symptomatic PE-recurrence (3 months)



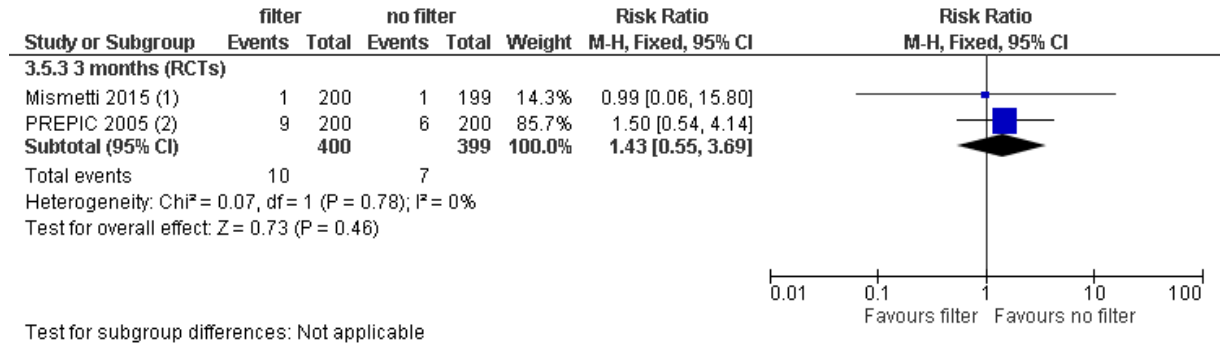
Test for subgroup differences: Not applicable

Footnotes

(1) at least 1 criterion for severity (see evidence table).

(2) see (1)

Figure 11: DVT-recurrence (3 months)



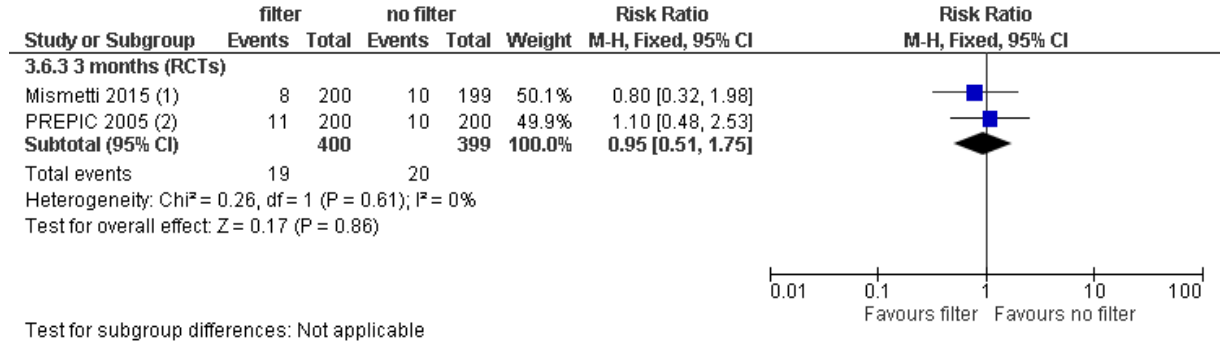
Test for subgroup differences: Not applicable

Footnotes

(1) at least 1 criterion for severity (see evidence table).

(2) see (1)

Figure 12: Major bleeding (3 months)



Test for subgroup differences: Not applicable

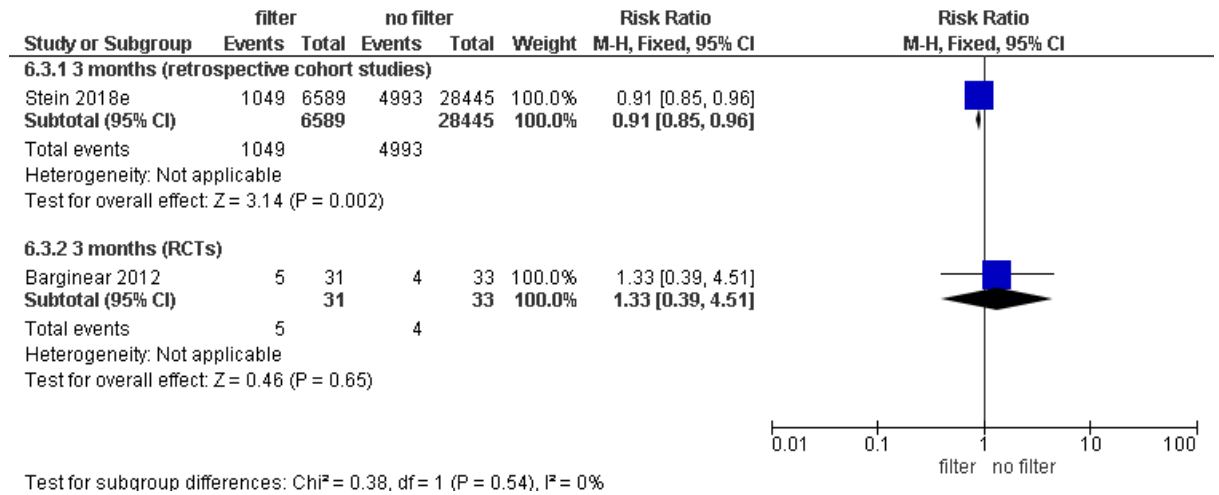
Footnotes

(1) at least 1 criterion for severity (see evidence table).

(2) see (1)

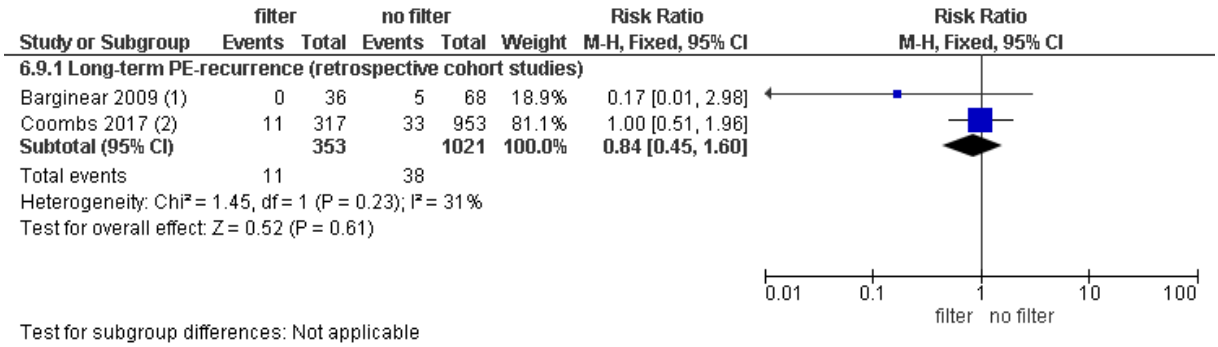
Filter versus no filter in people with VTE and cancer

Figure 13: All-cause mortality (3 months)



Test for subgroup differences: Chi² = 0.38, df = 1 (P = 0.54), I² = 0%

Figure 14: PE-recurrence (long-term)



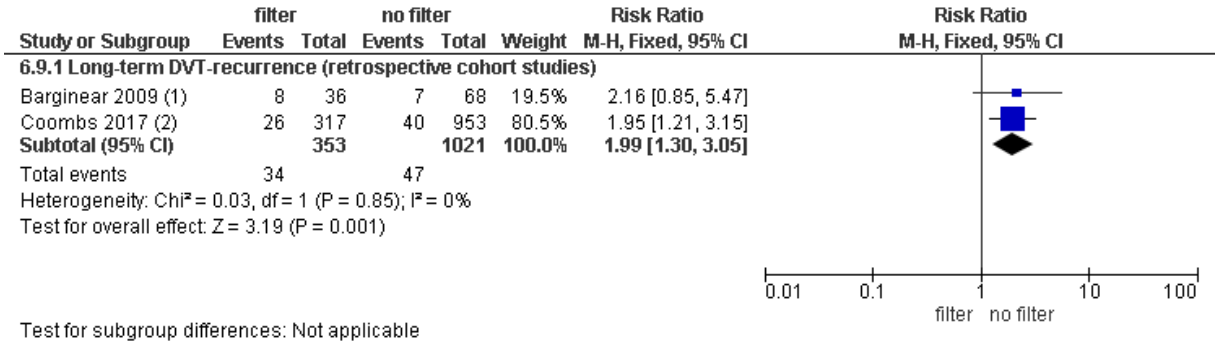
Test for subgroup differences: Not applicable

Footnotes

(1) unclear length of follow-up although participants were followed until death.

(2) up to 1 year

Figure 15: DVT-recurrence (long-term)



Test for subgroup differences: Not applicable

Footnotes

(1) unclear length of follow-up although participants were followed until death.

(2) up to 1 year

Appendix G – GRADE profiles

Filter versus no filter in people with VTE who cannot have anticoagulants

Quality assessment						No. patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	imprecision	Filter	No filter	Relative (95% CI)	Absolute risk control	Absolute risk intervention	Quality
All-cause mortality (30 days): HR <1 favours filter (Figure 1)											
2	Retrospective cohort study	Very serious[2]	Very serious	Not serious	Serious[3]	N/A	N/A	HR 0.91 (0.53, 1.56)	N/A	N/A	Very low
All-cause mortality (3 months): HR <1 favours filter											
1 White 2016	Retrospective cohort study	Very serious[1]	N/A	Not serious	Not serious	N/A	N/A	HR 0.73 (0.59, 0.90)	N/A	N/A	Very low
PE-recurrence (1 year): HR <1 favours filter											
1 White 2016	Retrospective cohort study	Very serious[1]	N/A	Not serious	Serious[3]	N/A	N/A	HR 1.04 (0.67, 1.61)	N/A	N/A	Very low
DVT-recurrence (1 year): HR <1 favours filter											
1 White 2016	Retrospective cohort study	Very serious[1]	N/A	Not serious	Not serious	N/A	N/A	HR 2.35 (1.56, 3.53)	N/A	N/A	Very low

1. Study was at serious risk of bias for this population (people with contraindication for anticoagulants).
2. >33.3% of studies were at serious risk of bias.
3. 95% CI crosses line of no effect.

1 **Filter versus no filter in people with VTE who have a PE whilst taking anticoagulants.**

Quality assessment						No. patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	imprecision	Filter	No filter	Relative (95% CI)	Absolute risk control	Absolute risk intervention	Quality
All-cause mortality (in-hospital): RR <1 favours filter											
1 Stein 2019a	Retrospective cohort study	Very serious[4]	N/A	Not serious	Not serious	18/603	83/211	RR 0.08 (0.05, 0.12)	39.34 per 100	2.99 per 100 (1.84, 4.85)	Very low
All-cause mortality (30 days): RR <1 favours filter											
1 Mellado 2016	Retrospective analysis of prospective cohort	Serious[4]	N/A	Not serious	Not serious	1/48	23/91	RR 0.08 (0.01, 0.59)	25.27 per 100	2.08 per 100 (0.29, 14.96)	Very low
All-cause mortality (3 months): RR <1 favours filter											
1 Stein 2019a	Retrospective cohort study	Very serious[4]	N/A	Not serious	Not serious	18/603	83/211	RR 0.08 (0.05, 0.12)	39.34 per 100	2.99 per 100 (1.84, 4.85)	Very low
VTE:-recurrence (30 days): RR <1 favours filter											
1 Mellado 2016	Retrospective analysis of prospective cohort	Serious[3]	N/A	Not serious	Very serious[1]	2/48	2/91	RR 1.90 (0.28, 13.04)	2.20 per 100	4.17 per 100 (0.61, 28.66)	Very low
PE-related mortality (30 days): RR <1 favours filter											
1 Mellado 2016	Retrospective analysis of prospective cohort	Very serious[3]	N/A	Not serious	Serious[5]	1/48	16/91	RR 0.12 (0.02, 0.87)	17.58 per 100	2.08 per 100 (0.28, 15.24)	Very low

Quality assessment						No. patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	imprecision	Filter	No filter	Relative (95% CI)	Absolute risk control	Absolute risk intervention	Quality
Major bleeding (30 days): RR <1 favours filter											
1 Mellado 2016	Retrospective analysis of prospective cohort	Serious[3]	N/A	Not serious	Very serious [1]	2/48	3/91	RR 1.26 (0.22, 7.31)	3.30 per 100	4.17 per 100 (0.72, 24.09)	Very low

1. 95% confidence interval crosses both ends of a defined MID interval.
2. I^2 >66.6%.
3. The study was at Moderate risk of bias.
4. The study was at critical risk of bias.
5. 95% confidence interval crosses one end of a defined MID interval.

1

1 **Filter versus no filter in people with VTE who have the filters inserted for prophylaxis before a potential provoking event**

Quality assessment						No. patients		Effect			Quality
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	imprecision	Filter	No filter	Relative (95% CI)	Absolute risk control	Absolute risk intervention	
All-cause mortality (peri-procedure): RR <1 favours filter											
1 Sharifi 2012	RCT	Serious[1]	N/A	Not serious	Not estimable[7]	0/70	0/71	Not estimable[7]	Not estimable[7]	Not estimable[7]	Moderate
All-cause mortality (in-hospital): RR <1 favours filter (Figure 2)											
1 Sharifi 2012	RCT	Serious[1]	N/A	Not serious	Not estimable[7]	0/70	0/71	Not estimable[7]	Not estimable[7]	Not estimable[7]	Moderate
All-cause mortality (in-hospital): RR <1 favours filter (Figure 2)											
1 Stein 2018a	Retrospective cohort study	Very serious[2]	N/A	Not serious	Not serious	20/245	49/124	RR 0.21 (0.13, 0.33)	39.52 per 100	8.16 per 100 (5.09, 13.10)	Very low
All-cause mortality (in-hospital, >80 year olds only): RR <1 favours filter											
1 Stein 2018a	Retrospective cohort study	Very serious[2]	N/A	Not serious	Serious[6]	2/11	7/11	RR 0.29 (0.08, 1.08)	63.64 per 100	18.18 per 100 (4.80, 68.80)	Very low
All-cause mortality (30 days): HR <1 favours filter											
1 White 2016	Retrospective cohort study	Serious[1]	N/A	Not serious	Serious[6]	N/A	N/A	HR 1.12 (0.71, 1.77)	N/A	N/A	Very low
All-cause mortality (3 months): RR <1 favours filter											
1 Stein 2018a	Retrospective cohort study	Very serious[2]	N/A	Not serious	Not serious	21/245	49/124	RR 0.22 (0.14, 0.34)	39.52 per 100	8.57 per 100 (5.39, 13.62)	Very low

Quality assessment						No. patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	imprecision	Filter	No filter	Relative (95% CI)	Absolute risk control	Absolute risk intervention	Quality
All-cause mortality (3 months): HR <1 favours filter											
1 White 2016	Retrospective cohort studies	Serious[1]	N/A	Not serious	Serious[6]	N/A	N/A	HR 1.10 (0.76, 1.60)	N/A	N/A	Very low
All-cause mortality (2 years): RR <1 favours filter											
1 Sharifi 2012	RCT	Serious[1]	N/A	Not serious	Not serious	2/70	2/71	RR 1.01 (0.15, 7.00)	2.82 per 100	2.85 per 100 (0.42, 19.72)	Moderate
PE-related mortality (in-hospital): RR <1 favours filter (Figure 3)											
2	Retrospective cohort study	Very serious[3]	Not serious	Not serious	Not serious	2/1034	43/753	RR 0.03 (0.01, 0.11)	5.71 per 100	0.18 per 100 (0.05, 0.62)	Very low
PE-related mortality (3-months): RR <1 favours filter											
1 Stein 2018a	Retrospective cohort study	Very serious[2]	N/A	Not serious	Not serious	3/211	38/105	RR 0.04 (0.01, 0.12)	36.19 per 100	1.42 per 100 (0.45, 4.50)	Very low
DVT-recurrence (peri-procedure): RR <1 favours filter											
1 Sharifi 2012	RCT	Serious[1]	N/A	Not serious	Not estimable[7]	0/70	0/71	Not estimable[7]	Not estimable[7]	Not estimable[7]	Moderate
DVT-recurrence (in-hospital): RR <1 favours filter											
1 Sharifi 2012	RCT	Serious[1]	N/A	Not serious	Not estimable[7]	0/70	0/71	Not estimable[7]	Not estimable[7]	Not estimable[7]	Moderate
DVT-recurrence (1 year): HR <1 favours filter											

Quality assessment						No. patients		Effect			Quality
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	imprecision	Filter	No filter	Relative (95% CI)	Absolute risk control	Absolute risk intervention	
1 White 2016	Retrospective cohort studies	Serious[1]	N/A	Not serious	Serious[6]	N/A	N/A	HR 1.15 (0.57, 2.32)	N/A	N/A	Very low
DVT-recurrence (2 years): RR <1 favours filter											
1 Sharifi 2012	RCT	Serious[1]	N/A	Not serious	Very serious[4]	2/70	2/71	RR 1.01 (0.15, 7.00)	2.82 per 100	2.86 per 100 (0.41, 19.72)	Very low
PE-recurrence (peri-procedure): RR <1 favours filter											
1 Sharifi 2012	RCT	Serious[1]	N/A	Not serious	Serious[5]	1/70	8/71	RR 0.13 (0.02, 0.99)	11.27 per 100	1.43 per 100 (0.18, 11.12)	Low
PE-recurrence (in-hospital): RR <1 favours filter											
1 Sharifi 2012	RCT	Serious[1]	N/A	Not serious	Serious[5]	1/70	8/71	RR 0.13 (0.02, 0.99)	11.27 per 100	1.43 per 100 (0.18, 11.12)	Low
PE-recurrence (in-hospital): RR <1 favours filter											
1 Pan 2014	Retrospective cohort study	Very serious[2]	N/A	Not serious	Not serious	1/823	11/648	RR 0.09 (0.01, 0.51)	1.70 per 100	0.15 per 100 (0.02, 0.87)	Very low
PE-recurrence (in-hospital, only those with contraindication to AC during stay): RR <1 favours filter											
1 Pan 2014	Retrospective cohort study	Very serious[2]	N/A	Not serious	Serious[5]	0/132	1/26	RR 0.07 (0.00, 1.62)	3.85 per 100	0.26 per 100 (0.01, 6.22)	Very low
PE-recurrence (in-hospital, only those with AC following surgery): RR <1 favours filter											
1 Pan 2014	Retrospective cohort study	Very serious[2]	N/A	Not serious	Not serious	1/691	10/622	RR 0.09 (0.01, 0.70)	1.61 per 100	0.14 per 100 (0.02, 1.13)	Very low
PE-recurrence (1 year): HR <1 favours filter											

Quality assessment						No. patients		Effect			Quality
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	imprecision	Filter	No filter	Relative (95% CI)	Absolute risk control	Absolute risk intervention	
1 White 2016	Retrospective cohort study	Serious[1]	N/A	Not serious	Serious[6]	N/A	N/A	HR 0.85 (0.35, 2.08)	N/A	N/A	Very low
PE-recurrence (2 years): RR <1 favours filter											
1 Sharifi 2012	RCT	Serious[1]	N/A	Not serious	Serious[5]	1/70	8/71	RR 0.13 (0.02, 0.99)	11.27 per 100	1.43 per 100 (0.18, 11.12)	Low

1. Study was at moderate risk of bias.
2. Study was at critical risk of bias.
3. Both studies were at critical risk of bias.
4 95% confidence interval crosses both ends of a defined MID interval.
5 95% confidence interval crosses one end of a defined MID interval
6 95% CI crosses line of no effect.
7 Effect estimate not calculable as both arms have 0 events.

1

1 Filter versus no filter in people with VTE who are at high risk of poor outcomes in the event of PE recurrence

2 The characteristics predisposing the populations to poor outcomes varied considerably between studies (see the corresponding forest plots and
3 evidence tables for further detail).

Quality assessment						No. patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	imprecision	Filter	No filter	Relative (95% CI)	Absolute risk control	Absolute risk intervention	Quality
All-cause mortality (in-hospital): RR <1 favours filter (Figure 4)											
6*	Retrospective cohort study	Very serious[4]	Very serious[2]	Not serious	Not serious	6986/71273	45997/375489	RR 0.54 (0.39, 0.73)	12.25 per 100	6.59 per 100 (4.83, 8.98)	Very low
All cause mortality (in-hospital): HR <1 favours filter											
1 Liang 2017	Retrospective cohort study	Serious[6]	N/A	Not serious	Not serious	N/A	N/A	HR 1.24 (1.11, 1.38)	N/A	N/A	Very low
All-cause mortality (in-hospital, sensitivity analysis excluding studies at critical risk of bias): RR <1 favours filter											
1 Wadhwa 2018	Retrospective cohort study	Very serious[5]	N/A	Not serious	Not serious	6541/67237	43796/358638	RR 0.80 (0.78, 0.82)	9.73 per 100	7.78 per 100 (7.59, 7.98)	Very low
All-cause mortality (in-hospital, only in people aged 80 years or older): RR <1 favours filter (Figure 5)											
3**	Retrospective cohort study	Very serious[4]	Not serious	Not serious	Not serious	89/1145	597/5012	RR 0.50 (0.41, 0.61)	11.91 per 100	5.96 per 100 (4.88, 7.27)	Very low

Quality assessment						No. patients		Effect			Quality
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	imprecision	Filter	No filter	Relative (95% CI)	Absolute risk control	Absolute risk intervention	
All-cause mortality (in-hospital, only in people with massive-PE): RR <1 favours filter											
1 Wadhwa 2018	Retrospective cohort study	Very serious[5]	N/A	Not serious	Not serious	3815/15411	21553/52708	RR 0.61 (0.59, 0.62)	40.89 per 100	24.76 per 100 (24.04, 25.49)	Very low
All-cause mortality (30 days): RR <1 favours filter											
1 Tanabe 2014	Retrospective cohort study	Very serious[3]	N/A	Not serious	Not serious	14/182	42/193	RR 0.35 (0.20, 0.63)	21.76 per 100	7.69 per 100 (4.35, 13.60)	Very low
All-cause mortality (3 months): RR <1 favours filter (Figure 6)											
2***	Retrospective cohort study	Very serious[4]	Very serious[2]	Not serious	Not serious	336/1514	1472/3126	RR 0.35 (0.15, 0.82)	47.09 per 100	16.36 per 100 (6.91, 38.72)	Very low
PE-related mortality (in-hospital): RR <1 favours filter (Figure 7)											
2***	Retrospective cohort study	Very serious[4]	Very serious[2]	Not serious	Serious[1]	193/1137	951/2243	RR 0.12 (0.01, 2.24)	42.40 per 100	5.18 per 100 (0.28, 95.03)	Very low
PE-related mortality (3 months): RR <1 favours filter (Figure 8)											
2***	Retrospective	Very serious[4]	Very serious[2]	Not serious	Serious[1]	215/1137	1009/2243	RR 0.15 (0.01, 1.89)	44.98 per 100	6.76 per 100	Very low

Quality assessment						No. patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	imprecision	Filter	No filter	Relative (95% CI)	Absolute risk control	Absolute risk intervention	Quality
	cohort study									(0.54, 84.89)	

1. 95% confidence interval crosses the line of no effect.
2. I^2 >66.6%
3. The study was at critical risk of bias
4.>33.3% of studies were at serious/critical risk of bias.
5. The study was at serious risk of bias.
6. The study was at moderate risk of bias.
* The data for this analysis came from 5 individual studies, one of which (Stein 2018) contained data on two distinct populations.
** The data for this analysis came from 2 individual studies, one of which (Stein 2018) contained data on two distinct populations.
***The data for this analysis is from a single study (Stein 2018) containing data on two distinct populations.

1

1 **Filter versus no filter in people with VTE who are at high risk of PE-recurrence**

Quality assessment						No. patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	imprecision	Filter	No filter	Relative (95% CI)	Absolute risk control	Absolute risk intervention	Quality
All-cause mortality (12 days): RR <1 favours filter											
1 PREPIC 2005	RCT	Not serious	N/A	Not serious	Serious[3]	5/200	5/200	RR 1.00 (0.29, 3.40)	2.50 per 100	2.50 per 100 (0.74, 8.50)	Moderate
All-cause mortality (3 months): RR <1 favours filter (Figure 9)											
2	RCT	Not serious	Not serious	Serious[5]	Serious[3]	30/400	22/399	RR 1.36 (0.80, 2.32)	5.51 per 100	7.50 per 100 (4.40, 12.77)	Low
All-cause mortality (6 months): RR <1 favours filter											
1 Mismetti 2015	RCT	Not serious	N/A	Serious[4]	Serious[3]	21/200	15/199	RR 1.39 (0.74, 2.62)	7.54 per 100	10.50 per 100 (5.58, 19.77)	Low
All-cause mortality (8 years): RR <1 favours filter											
1 PREPIC 2005	RCT	Not serious	N/A	Not serious	Serious[3]	98/200	103/200	RR 0.95 (0.78, 1.16)	51.50 per 100	49.00 per 100 (40.31, 59.56)	Moderate
VTE-recurrence (3 months): RR <1 favours filter											
1 Mismetti 2015	RCT	Not serious	N/A	Serious[4]	Very serious[1]	7/200	4/199	RR 1.74 (0.52, 5.86)	2.01 per 100	3.50 per 100 (1.04, 11.77)	Very-low
VTE-recurrence (6 months): RR <1 favours filter											
1 Mismetti 2015	RCT	Not serious	N/A	Serious[4]	Very serious[1]	8/200	6/199	RR 1.33 (0.47, 3.75)	3.02 per 100	4.00 per 100 (1.41, 11.32)	Very-low

Quality assessment						No. patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	imprecision	Filter	No filter	Relative (95% CI)	Absolute risk control	Absolute risk intervention	Quality
VTE-recurrence (8 years): RR <1 favours filter											
1 PREPIC 2005	RCT	Not serious	N/A	Not serious	Very serious[1]	58/200	55/200	RR 1.05 (0.77, 1.44)	27.50 per 100	29.00 per 100 (21.22, 39.64)	Low
PE-related mortality (3 months): RR <1 favours filter											
1 Mismetti 2015	RCT	Not serious	N/A	Serious[4]	Very serious[1]	6/200	2/199	RR 2.99 (0.61, 14.61)	1.01 per 100	3.00 per 100 (0.61, 14.69)	Very low
PE-related mortality (6 months): RR <1 favours filter											
1 Mismetti 2015	RCT	Not serious	N/A	Serious[4]	Very serious[1]	6/200	3/199	RR 1.99 (0.50, 7.85)	1.51 per 100	3.00 per 100 (0.76, 11.83)	Very low
PE-related mortality (8 years): RR <1 favours filter											
1 PREPIC 2005	RCT	Not serious	N/A	Not serious	Very serious[1]	2/200	5/200	RR 0.40 (0.08, 2.04)	2.50 per 100	1.00 per 100 (0.20, 5.09)	Low
Symptomatic PE-recurrence (12 days): RR <1 favours filter											
1 PREPIC 2005	RCT	Not serious	N/A	Not serious	Very serious[1]	2/200	5/200	RR 0.40 (0.08, 2.04)	2.50 per 100	1.00 per 100 (0.20, 5.09)	Low
Asymptomatic and symptomatic PE-recurrence (12 days): RR <1 favours filter											
1 PREPIC 2005	RCT	Not serious	N/A	Not serious	Serious[2]	2/200	9/200	RR 0.22 (0.05, 1.02)	4.50 per 100	1.00 per 100 (0.22, 4.57)	Moderate
Symptomatic PE-recurrence (3 months): RR <1 favours filter (Figure 10)											

Quality assessment						No. patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	imprecision	Filter	No filter	Relative (95% CI)	Absolute risk control	Absolute risk intervention	Quality
2	RCT	Not serious	Serious	Serious[5]	Very serious[1]	8/400	9/399	RR 0.85 (0.15, 4.91)	2.26 per 100	1.92 per 100 (0.33, 11.09)	Low
Symptomatic PE-recurrence (6 months): RR <1 favours filter											
1 Mismetti 2015	RCT	Not serious	N/A	Serious[4]	Very serious[1]	7/200	4/199	RR 1.74 (0.52, 5.86)	2.01 per 100	3.50 per 100 (1.04, 11.77)	Very low
Symptomatic PE-recurrence (8 years): RR <1 favours filter											
1 PREPIC 2005	RCT	Not serious	N/A	Not serious	Not serious	9/200	24/200	RR 0.38 (0.18, 0.79)	12.00 per 100	4.50 per 100 (2.15, 9.44)	High
DVT-recurrence (3 months): RR <1 favours filter (Figure 11)											
2	RCT	Not serious	Not serious	Serious[5]	Very serious[1]	10/400	7/399	RR 1.43 (0.55, 3.69)	1.75 per 100	2.50 per 100 (0.97, 6.48)	Very low
DVT-recurrence (6 months): RR <1 favours filter											
1 Mismetti 2015	RCT	Not serious	N/A	Serious[4]	Very serious[1]	1/200	2/199	RR 0.50 (0.05, 5.44)	1.01 per 100	0.50 per 100 (0.05, 5.47)	Very low
DVT-recurrence (8 years): RR <1 favours filter											
1 PREPIC 2005	RCT	Not serious	N/A	Not serious	Serious[2]	57/200	41/200	RR 1.39 (0.98, 1.97)	20.50 per 100	28.50 per 100 (20.08, 40.45)	Moderate
Major bleeding (12 days) (RR <1 favours filter)											
1 PREPIC 2005	RCT	Not serious	N/A	Not serious	Very serious[1]	9/200	6/200	RR 1.50 (0.54, 4.14)	3.00 per 100	4.50 per 100 (1.63, 12.41)	Low

Quality assessment						No. patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	imprecision	Filter	No filter	Relative (95% CI)	Absolute risk control	Absolute risk intervention	Quality
Major bleeding (3 months) (RR <1 favours filter) (Figure 12)											
2	RCT	Not serious	Not serious	Serious[5]	Very serious[1]	19/400	20/399	RR 0.95 (0.51, 1.75)	5.01 per 100	4.75 per 100 (2.58, 8.76)	Low
Major bleeding (6 months): RR <1 favours filter											
1 Mismetti 2015	RCT	Not serious	N/A	Serious[4]	Very serious[1]	13/200	15/199	RR 0.86 (0.42, 1.77)	7.54 per 100	6.50 per 100 (3.18, 13.30)	Very low
Major bleeding (8 years): RR <1 favours filter											
1 PREPIC 2005	RCT	Not serious	N/A	Not serious	Very serious[1]	26/200	31/200	RR 0.84 (0.52, 1.36)	15.50 per 100	13.00 per 100 (8.02, 21.07)	Low
Post-thrombotic syndrome (8 years): RR <1 favours filter											
1 PREPIC 2005	RCT	Not serious	N/A	Not serious	Not serious	109/200	107/200	RR 1.02 (0.85, 1.22)	53.50 per 100	54.50 per 100 (45.48, 65.31)	High

1. 95% confidence interval crosses both ends of a defined MID interval.
2. 95% confidence interval crosses one end of a defined MID interval.
3. 95% CI crosses line of no effect.
4. Study was partially applicable to the review question.
5. >33.3% of studies were partially applicable to the review question.

1

1 **Filter versus no filter in people with VTE and cancer**

Quality assessment						No. patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	imprecision	Filter	No filter	Relative (95% CI)	Absolute risk control	Absolute risk intervention	Quality
All-cause mortality (in-hospital): RR <1 favours filter											
1 Stein 2018c	Retrospective cohort study	Very serious[1]	N/A	Not serious	Not serious	532/6589	3175/28445	RR 0.72 (0.66, 0.79)	11.16 per 100	8.07 per 100 (7.40, 8.82)	Very low
All-cause mortality (in-hospital, >80 year olds only): RR <1 favours filter											
1 Stein 2018c	Retrospective cohort study	Very serious[1]	N/A	Not serious	Not serious	56/952	469/3969	RR 0.50 (0.38, 0.65)	11.82 per 100	5.88 per 100 (4.50, 7.69)	Very low
All-cause mortality (30 days): HR <1 favours filter											
1 Brunson 2017	Retrospective cohort study	Serious[4]	N/A	Not serious	Not serious	N/A	N/A	HR 1.22 (1.15, 1.30)	N/A	N/A	Very low
All-cause mortality (3 months): RR <1 favours filter (Figure 13)											
1 Bargingear 2012	RCT	Not serious	N/A	Not serious	Serious[6]	5/31	4/33	RR 1.33 (0.39, 4.51)	12.12 per 100	16.13 per 100 (4.76, 54.63)	Moderate
All-cause mortality (3 months): RR <1 favours filter (Figure 13)											
1 Stein 2018c	Retrospective cohort study	Very serious[1]	N/A	Not serious	Not serious	1049/6589	4993/28445	RR 0.91 (0.85, 0.96)	17.55 per 100	15.92 per 100 (14.98, 16.92)	Very low
All-cause mortality (3 months): HR <1 favours filter											

Quality assessment						No. patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	imprecision	Filter	No filter	Relative (95% CI)	Absolute risk control	Absolute risk intervention	Quality
1 Brunson 2017	Retrospective cohort study	Serious[4]	N/A	Not serious	Not serious	N/A	N/A	HR 1.26 (1.16, 1.37)	N/A	N/A	Very low
All-cause mortality (1 year): HR <1 favours filter											
1 Coombs 2017	Retrospective cohort study	Very serious[2]	N/A	Not serious	Not serious	N/A	N/A	HR 1.26 (1.08, 1.46)	N/A	N/A	Very low
PE-recurrence (3 months): RR <1 favours filter											
1 Bargingear 2012	RCT	Not serious	N/A	Not serious	Very serious[5]	1/31	1/33	RR 1.06 (0.07, 16.29)	3.03 per 100	3.23 per 100 (0.21, 49.37)	Low
PE recurrence (long term)*: RR <1 favours filter (Figure 14)											
2	Retrospective cohort study	Very serious[3]	Not serious	Not serious	Very serious[5]	11/353	38/1021	RR 0.84 (0.45, 1.60)	3.72 per 100	3.14 per 100 (1.66, 5.96)	Very low
PE recurrence (up to 1 year) sensitivity analysis excluding study at critical risk of bias: RR <1 favours filter											
1 Coombs 2017	Retrospective cohort study	Serious[4]	N/A	Not serious	Very serious[6]	11/317	33/953	RR 1.00 (0.51, 1.96)	3.72 per 100	3.14 per 100 (1.66, 5.96)	Very low
PE-recurrence (long-term): HR <1 favours filter											
1 Brunson 2017	Retrospective cohort study	Serious[4]	N/A	Not serious	Serious[6]	N/A	N/A	HR 0.81 (0.52, 1.27)	N/A	N/A	Very low
DVT-recurrence (3 months): RR <1 favours filter											

Quality assessment						No. patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	imprecision	Filter	No filter	Relative (95% CI)	Absolute risk control	Absolute risk intervention	Quality
1 Bargin ear 2012	RCT	Not serious	N/A	Not serious	Not estimable[8]	0/31	0/33	Not estimable[8]	Not estimable[8]	Not estimable[8]	High
DVT-recurrence (long-term)*: RR <1 favours filter (Figure 15)											
2	Retrospective cohort study	Very serious[1]	Not serious	Not serious	Not serious	34/353	47/1021	RR 1.99 (1.30, 3.05)	4.60 per 100	9.18 per 100 (6.00, 14.03)	Very low
DVT recurrence (up to 1 year) sensitivity analysis excluding study at critical risk of bias: RR <1 favours filter											
1 Coombs 2017	Retrospective cohort study	Serious[4]	N/A	Not serious	Serious[7]	26/317	40/953	RR 1.95 (1.21, 3.15)	3.72 per 100	3.14 per 100 (1.66, 5.96)	Very low
DVT-recurrence (long-term): HR <1 favours filter											
1 Brunson 2017	Retrospective cohort study	Serious[4]	N/A	Not serious	Not serious	N/A	N/A	HR 1.73 (1.31, 2.28)	N/A	N/A	Very low
VTE-recurrence (long term): RR <1 favours filter											
1 Coombs 2017	Retrospective cohort study	Very serious[1]	N/A	Not serious	Serious[7]	37/317	73/953	RR 1.52 (1.05, 2.22)	N/A	N/A	Very low
Major bleeding (3 months): RR <1 favours filter											
1 Bargin ear 2012	RCT	Not serious	N/A	Not serious	Very serious[5]	1/31	2/33	RR 0.53 (0.05, 5.58)	6.06 per 100	3.23 per 100 (0.31, 33.82)	Low

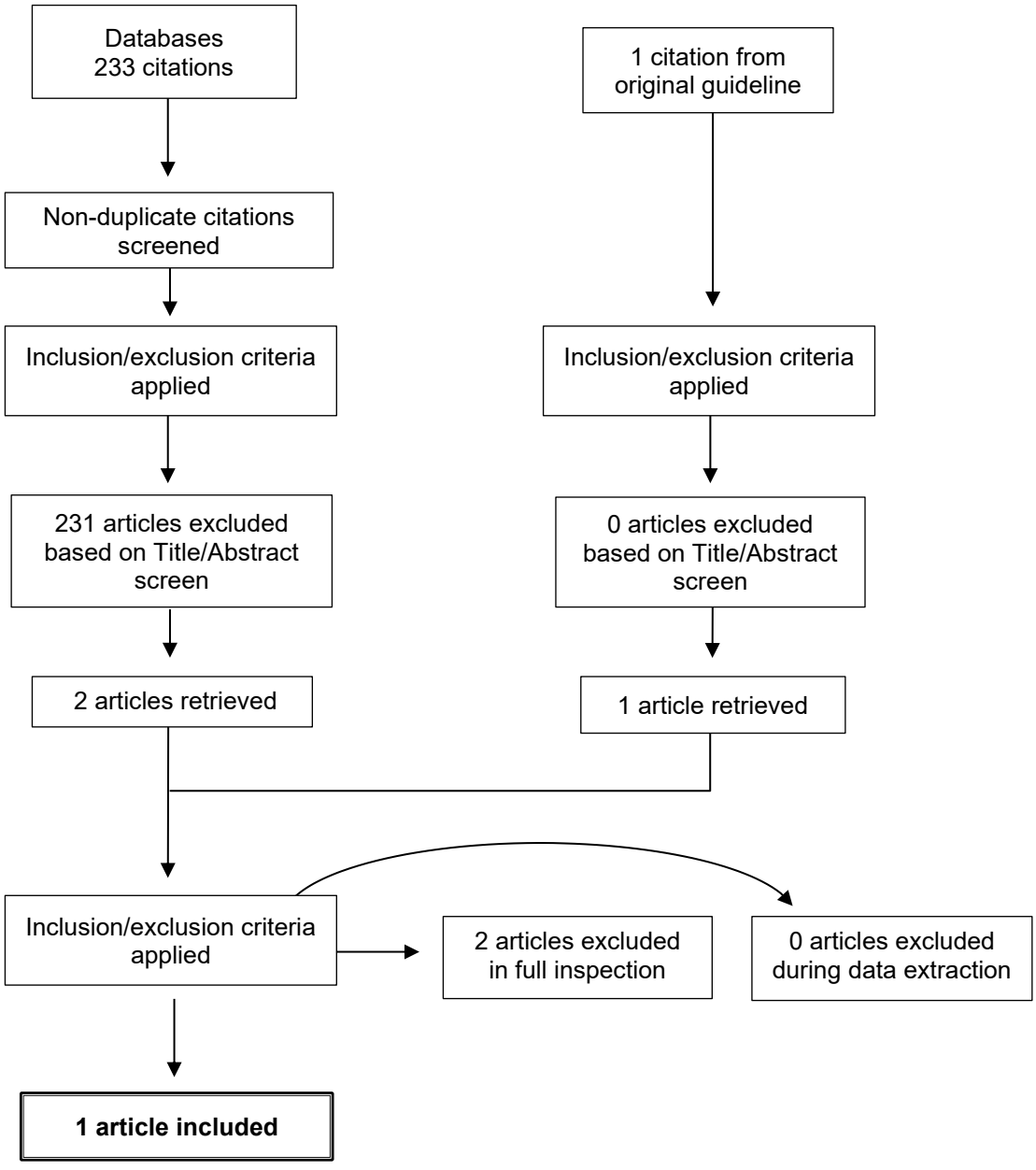
Quality assessment						No. patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	imprecision	Filter	No filter	Relative (95% CI)	Absolute risk control	Absolute risk intervention	Quality
Major bleeding (long-term, participants followed until death): RR <1 favours filter											
1 Barginear 2009	Retrospective cohort study	Very serious[1]	N/A	Not serious	Very serious[5]	0/36	9/68	RR 0.10 (0.01, 1.64)	13.24 per 100	1.30 per 100 (0.08, 21.70)	Very low
Major bleed (long-term): HR <1 favours filter											
Brunson 20-17	Retrospective cohort study	Not serious	N/A	Not serious	Serious[6]	N/A	N/A	HR 1.11 (0.94, 1.31)	N/A	N/A	Very low
IVC complications (3 months): RR <1 favours filter											
1 Barginear 2012	RCT	Not serious	N/A	Not serious	Very serious[5]	2/31	0/33	RR 5.31 (0.27, 106.46)	0.00 per 100	0.00 per 100 (0.00, 0.00)	Low

1. The study was at critical risk of bias.
2. The study was at serious risk of bias.
3. >33.3% of studies were at serious or critical risk of bias.
4. The study was at moderate risk of bias.
5. 95% confidence interval crosses both ends of a defined MID interval.
6. 95% CI crosses line of no effect.
7. 95% confidence interval crosses one end of a defined MID interval.
8. Effect estimate not calculable as both arms have 0 events.

* Coombs (2017) had a follow-up of 1 year and Barginear (2009) had an unclear follow, lasting until the participants' death.

1

Appendix H – Economic evidence study selection



Appendix I – Economic evidence profiles

Study	1. Applicability 2. Limitations	Comparison(s)	Setting	Duration Discount rate(s)	Results / conclusion	Uncertainty
Sarasin et al. (1993)	1. Partially applicable[(a)] 2. Very serious limitations[(b)]	IVC filter versus no treatment[(c)]	US	Lifetime 5% for costs and health effects	The IVC filter strategy dominates no treatment (cheaper and more effective)	The IVC filter strategy remained more cost effective than no treatment when parameters were varied deterministically. Probabilistic sensitivity analysis was not conducted

(a) The study was conducted in the US. Incremental cost-effectiveness results were reported for people with lung cancer only although other types of cancer are described in the study. Effectiveness of the IVC filter was based on a single study that pre-dated 1990 and is unlikely to reflect filters in current use.
(b) Utilities estimated from expert opinion; source of funding not reported. No data was available on the incidence of PE in patients with cancer and DVT so it was assumed this was the same as in patients with no cancer. Unclear how studies for clinical parameters were identified and which study was eventually selected for base case values. Probabilistic sensitivity analysis was not conducted.
(c) Immediate anticoagulation was included in the model as an additional comparator but is not reported here because it is not an eligible comparator for this subgroup.

1 Appendix J – Excluded studies

2 Clinical studies

Study	Reason for exclusion
Akhtar, O. S., Lakhter, V., Zack, C. J. et al. (2018) Contemporary Trends and Comparative Outcomes With Adjunctive Inferior Vena Cava Filter Placement in Patients Undergoing Catheter-Directed Thrombolysis for Deep Vein Thrombosis in the United States: Insights From the National Inpatient Sample. Jacc: Cardiovascular Interventions 11(14): 1390-1397	- Does not contain a population of people fitting into the categories of interest to this review, as outlined in the protocol [Participants had DVT and were undergoing catheter directed thrombolysis.]
Billett, H. H., Jacobs, L. G., Madsen, E. M. et al. (2007) Efficacy of inferior vena cava filters in anticoagulated patients. Journal of Thrombosis & Haemostasis 5(9): 1848-53	- Does not contain a population of people fitting into the categories of interest to this review, as outlined in the protocol [Population does not meet protocol as the study contained anyone with VTE who received filter]
Bikdeli, B., Chatterjee, S., Desai, N. R. et al. (2017) Inferior Vena Cava Filters to Prevent Pulmonary Embolism: Systematic Review and Meta-Analysis. Journal of the American College of Cardiology 70(13): 1587-1597	- Systematic review used as source of primary studies
Calligaro, K. D., Bergen, W. S., Haut, M. J. et al. (1991) Thromboembolic complications in patients with advanced cancer: anticoagulation versus Greenfield filter placement. Annals of Vascular Surgery 5(2): 186-9	- Study does not contain a relevant intervention [One arm were treated with anticoagulation and the other was not.]
Chen, M., Goodin, A., Xiao, H. et al. (2018) Hospitalization metrics associated with hospital-level variation in inferior vena cava filter utilization for patients with venous thromboembolism in the United States: Implications for quality of care. Vascular Medicine 23(4): 365-371	- Does not contain a population of people fitting into one the categories of interest to this review, as outlined in the protocol [Contained all people with VTE.]
Ghanim, A. J., Daskalakis, C., Eschelman, D. J. et al. (2007) A five-year, retrospective, comparison review of survival in neurosurgical patients diagnosed with venous thromboembolism and treated with either inferior vena cava filters or anticoagulants. Journal of Thrombosis & Thrombolysis 24(3): 247-54	- Does not contain a population of people fitting into the categories of interest to this review, as outlined in the protocol [Participants had VTE and a significant risk of bleeding. Other studies have used this as a proxy for contraindication to anticoagulation however in the present study the majority of participants were noted to be receiving anticoagulation. Therefore, the population does not meet those outlined in the protocol.]
Isogai, T., Yasunaga, H., Matsui, H. et al. (2015) Effectiveness of inferior vena cava filters on mortality as an adjuvant to antithrombotic therapy. American Journal of Medicine 128(3): 312.e23-31	- Does not contain a population of people fitting into the categories of interest to this review, as outlined in the protocol [The study included people with PE on anticoagulation (without additional characteristics indicating risk level)]

Study	Reason for exclusion
Jiang, J.; Jiao, Y.; Zhang, X. (2017) The short-term efficacy of vena cava filters for the prevention of pulmonary embolism in patients with venous thromboembolism receiving anticoagulation: Meta-analysis of randomized controlled trials. Phlebology 32(9): 620-627	- Systematic review used as source of primary studies
Leiderman, D. B. D., Zerati, A. E., Vieira Mariz, M. P. et al. (2019) The Need for a Vena Cava Filter in Oncological Patients with Acute Venous Thrombosis: A Marker of a Worse Prognosis. Annals of Vascular Surgery 23: 23	- Study does not contain a relevant intervention [Compared IVC without AC to AC alone]
Mismetti, P. (2013) Prevention of pulmonary embolism recurrences by retrievable vena cava filter: results of the randomized multicenter trial PREPIC 2. Journal of thrombosis and haemostasis : JTH 11(suppl2): 28	- Conference abstract
Mismetti, P. (2008) Randomized trial assessing the efficacy of the partial interruption of the inferior vena cava by an optional vena caval filter in the prevention of the recurrence of pulmonary embolism. PREPIC 2 trial: prevention of embolic recurrences by caval interruption (prospective, multicentric, randomised, open trial). Revue de pneumologie clinique 64(6): 328-331	- Study not reported in English
Muriel, A., Jimenez, D., Aujesky, D. et al. (2014) Survival effects of inferior vena cava filter in patients with acute symptomatic venous thromboembolism and a significant bleeding risk. Journal of the American College of Cardiology 63(16): 1675-83	- Does not contain a population of people fitting into the categories of interest to this review, as outlined in the protocol [Although significant bleeding risk has been used by other studies as being indicative of a contraindication to anticoagulation, the study identified that most participants received anticoagulation. Additionally, the level of anticoagulation usage was considerably different between intervention groups]
Olin, J. W., Young, J. R., Graor, R. A. et al. (1987) Treatment of deep vein thrombosis and pulmonary emboli in patients with primary and metastatic brain tumors. Anticoagulants or inferior vena cava filter?. Archives of Internal Medicine 147(12): 2177-9	- Study does not contain a relevant intervention [One arm received anticoagulation but the other did not.]
Rojas-Hernandez, C. M.; Zapata-Copete, J. A.; Garcia-Perdomo, H. A. (2018) Role of vena cava filters for the management of cancer-related venous thromboembolism: Systematic review and meta-analysis. Critical Reviews in Oncology-Hematology 130: 44-50	- Systematic review used as source of primary studies
Senties, A. C.; Carrera, N. F.; Gordillo, O. G. (1977) Inferior vena cava ligation versus the Mobin-Uddin filter for prevention of recurrent pulmonary embolism. International Surgery 62(8): 420-5	- Study does not contain a relevant intervention [Study compared ligation versus filters]

Study	Reason for exclusion
Stein, P. D.; Matta, F.; Hughes, M. J. (2019) Usefulness of Inferior Vena Cava Filters in Stable Patients with Acute Pulmonary Embolism. American Journal of Cardiology 123(11): 1874-1877	- Systematic review used as source of primary studies
Stein, P. D.; Matta, F.; Hughes, M. J. (2017) Inferior Vena Cava Filters in Elderly Patients with Stable Acute Pulmonary Embolism. American Journal of Medicine 130(3): 356-364	- Does not contain a population of people fitting into the categories of interest to this review, as outlined in the protocol [Study population does not match the groups outlined in the protocol]
Stein, P. D.; Matta, F.; Hughes, M. J. (2018) Inferior Vena Cava Filters in Stable Patients with Acute Pulmonary Embolism Who Receive Thrombolytic Therapy. American Journal of Medicine 131(1): 97-99	- Does not contain a population of people fitting into the categories of interest to this review, as outlined in the protocol [Contained all people with PE who underwent thrombolytic therapy.]
White, R. H., Zhou, H., Kim, J. et al. (2000) A population-based study of the effectiveness of inferior vena cava filter use among patients with venous thromboembolism. Archives of Internal Medicine 160(13): 2033-41	- Does not contain a population of people fitting into the categories of interest to this review, as outlined in the protocol [Study is a general population of people with VTE. There is a subgroup analysis of people who have had previous VTEs however it is not possible to tell whether these occurred whilst taking anticoagulation.]
Yamashita, Y., Unoki, T., Takagi, D. et al. (2016) Indications, applications, and outcomes of inferior vena cava filters for venous thromboembolism in Japanese patients. Heart & Vessels 31(7): 1084-90	- Does not contain a population of people fitting into the categories of interest to this review, as outlined in the protocol [Population did not meet protocol (included all people with VTE + IVC)]
Zektser, M., Bartal, C., Zeller, L. et al. (2016) Effectiveness of Inferior Vena Cava Filters without Anticoagulation Therapy for Prophylaxis of Recurrent Pulmonary Embolism. Rambam Maimonides Medical Journal 7(3): 28	- Does not contain a population of people fitting into the categories of interest to this review, as outlined in the protocol [Compared IVC without anticoagulation to group with anticoagulation]
Zuin, M., Rigatelli, G., Zonzin, P. et al. (2019) Inferior Vena Cava Filters in Hemodynamically Unstable Patients with Acute Pulmonary Embolism: How Often are They Used? Data from Multicenter Prospective Registries on Acute Pulmonary Embolism. Cardiovascular & Interventional Radiology 42(8): 1073-1079	- Systematic review used as source of primary studies

1 Economic studies

Author (year)	Title	Reason for exclusion
Raphael (2014)	Pulmonary embolism after total joint arthroplasty: cost and effectiveness of four treatment modalities	Not a cost-effectiveness analysis
Spangler (2010)	Cost-effectiveness of guidelines for insertion of inferior vena cava filters in high-risk trauma patients	The IVC filter strategy was not compared with an

Author (year)	Title	Reason for exclusion
		option without IVC filter

1 Appendix K – References

2 Included clinical studies

Barginear, M. F., Gralla, R. J., Bradley, T. P. et al. (2012) Investigating the benefit of adding a vena cava filter to anticoagulation with fondaparinux sodium in patients with cancer and venous thromboembolism in a prospective randomized clinical trial. Supportive Care in Cancer 20(11): 2865-72

Barginear, M. F., Lesser, M., Akerman, M. L. et al. (2009) Need for inferior vena cava filters in cancer patients: a surrogate marker for poor outcome. Clinical & Applied Thrombosis/Hemostasis 15(3): 263-9

Brunson, A., Ho, G., White, R. et al. (2017) Inferior vena cava filters in patients with cancer and venous thromboembolism (VTE) does not improve clinical outcomes: A population-based study. Thrombosis Research 153: 57-64

Coombs, C., Kuk, D., Devlin, S. et al. (2017) Outcomes after inferior vena cava filter placement in cancer patients diagnosed with pulmonary embolism: risk for recurrent venous thromboembolism. Journal of Thrombosis & Thrombolysis 44(4): 489-493

Decousus, H., Leizorovicz, A., Parent, F. et al. (1998) A clinical trial of vena caval filters in the prevention of pulmonary embolism in patients with proximal deep-vein thrombosis. Prevention du Risque d'Embolie Pulmonaire par Interruption Cave Study Group. New England Journal of Medicine 338(7): 409-15

Group, Prepic Study (2005) Eight-year follow-up of patients with permanent vena cava filters in the prevention of pulmonary embolism: the PREPIC (Prevention du Risque d'Embolie Pulmonaire par Interruption Cave) randomized study. Circulation 112(3): 416-22

Jha, V. M., Lee-Llacer, J., Williams, J. et al. (2010) Adjunctive inferior vena cava filter placement for acute pulmonary embolism. Cardiovascular & Interventional Radiology 33(4): 739-43

Liang, N. L., Genovese, E. A., Avgerinos, E. D. et al. (2017) Impact of Inferior Vena Cava Filter Placement on Short-Term Outcomes in Patients with Acute Pulmonary Embolism. Annals of Vascular Surgery 42: 71-77

Mellado, M., Pijoan, J. I., Jimenez, D. et al. (2016) Outcomes Associated With Inferior Vena Cava Filters Among Patients With Thromboembolic Recurrence During Anticoagulant Therapy. Jacc: Cardiovascular Interventions 9(23): 2440-2448

Mismetti, P., Laporte, S., Pellerin, O. et al. (2015) Effect of a retrievable inferior vena cava filter plus anticoagulation vs anticoagulation alone on risk of recurrent pulmonary embolism: a randomized clinical trial. JAMA 313(16): 1627-35

Pan, Y., Zhao, J., Mei, J. et al. (2016) Evaluation of nonpermanent inferior vena cava filter placement in patients with deep venous thrombosis after lower extremity fracture: A single-center retrospective study. Phlebology 31(8): 564-72

Sharifi, M., Bay, C., Skrocki, L. et al. (2012) Role of IVC filters in endovenous therapy for deep venous thrombosis: the FILTER-PEVI (filter implantation to lower thromboembolic risk in percutaneous endovenous intervention) trial. Cardiovascular & Interventional Radiology 35(6): 1408-13

Stein, P. D., Matta, F., Lawrence, F. R. et al. (2018a) Usefulness of Inferior Vena Cava Filters in Unstable Patients With Acute Pulmonary Embolism and Patients Who Underwent Pulmonary Embolectomy. American Journal of Cardiology 121(4): 495-50

Stein, P. D., Matta, F., Lawrence, F. R. et al. (2018b) Importance of Early Insertion of Inferior Vena Cava Filters in Unstable Patients with Acute Pulmonary Embolism. American Journal of Medicine 131(9): 1104-1109

Stein, P. D., Matta, F., Lawrence, F. R. et al. (2018c) Inferior Vena Cava Filters in Patients with Acute Pulmonary Embolism and Cancer. American Journal of Medicine 131(4): 442.e9-442.e12

Stein, P. D., Matta, F., Lawrence, F. R. et al. (2019a) Inferior Vena Cava Filters in Patients with Recurrent Pulmonary Embolism. American Journal of Medicine 132(1): 88-92

Stein, P. D.; Matta, F.; Hughes, M. J. (2019b) Inferior Vena Cava Filters in Stable Patients With Pulmonary Embolism and Heart Failure. American Journal of Cardiology 124(2): 292-295

Tanabe, Y., Obayashi, T., Yamamoto, T. et al. (2014) Current status of the use of inferior vena cava filters in cases of pulmonary embolism in CCUs: From the Tokyo CCU Network. Journal of Cardiology 63(5): 385-9

Turner, T. E., Saeed, M. J., Novak, E. et al. (2018) Association of Inferior Vena Cava Filter Placement for Venous Thromboembolic Disease and a Contraindication to Anticoagulation With 30-Day Mortality. JAMA Network Open 1(3): e180452

Wadhwa, V., Gutta, N. B., Trivedi, P. S. et al. (2018) In-Hospital Mortality Benefit of Inferior Vena Cava Filters in Patients With Pulmonary Embolism and Congestive Heart Failure. AJR. American Journal of Roentgenology 211(3): 672-676

White, R. H., Brunson, A., Romano, P. S. et al. (2016) Outcomes After Vena Cava Filter Use in Noncancer Patients With Acute Venous Thromboembolism: A Population-Based Study. Circulation 133(21): 2018-29

Other included clinical studies

Higgins, J.P., Altman, D.G., Gøtzsche, P.C., Jüni, P., Moher, D., Oxman, A.D., Savović, J., Schulz, K.F., Weeks, L. and Sterne, J.A., 2011. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJj*, *343*, p.d5928

Jia, Z., Wu, A., Tam, M., Spain, J., McKinney, J. M., & Wang, W. (2015). Caval penetration by inferior vena cava filters: a systematic literature review of clinical significance and management. *Circulation*, *132*(10), 944-952.

Excluded clinical studies

Akhtar, O. S., Lakhter, V., Zack, C. J. et al. (2018) Contemporary Trends and Comparative Outcomes With Adjunctive Inferior Vena Cava Filter Placement in Patients Undergoing Catheter-Directed Thrombolysis for Deep Vein Thrombosis in the United States: Insights From the National Inpatient Sample. Jacc: Cardiovascular Interventions 11(14): 1390-1397

Bikdeli, B., Chatterjee, S., Desai, N. R. et al. (2017) Inferior Vena Cava Filters to Prevent Pulmonary Embolism: Systematic Review and Meta-Analysis. Journal of the American College of Cardiology 70(13): 1587-1597

Billett, H. H., Jacobs, L. G., Madsen, E. M. et al. (2007) Efficacy of inferior vena cava filters in anticoagulated patients. Journal of Thrombosis & Haemostasis 5(9): 1848-53

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1 Appendix L – Research recommendation

Research question	What is the short and long term clinical and cost effectiveness of inferior vena caval filters in people with VTE?
Population	Adults (aged 18+) with confirmed VTE
Intervention(s)	IVC filter with or without: • mechanical intervention and/or • anticoagulant treatment.
Comparator	No filter with: • mechanical intervention and/or • anticoagulant treatment and/or • placebo or no treatment. Studies can allow participants to have mechanical interventions, anticoagulation treatment or both, but these must be included in both arms of the trial so that the only difference in treatment between arms is the inclusion or exclusion of IVC filters.

Outcomes	• Recurrent VTE (PE and DVT)
	• All-cause mortality
	• VTE-related mortality
	• Post-thrombotic syndrome
	• Pulmonary hypertension (PH)
	• Quality of life
	  • Generic and disease-specific measures will be reported
	  • Overall score will be reported (data on subscales will not be reported)
	  • Adverse events
	  • Total serious adverse events (as defined by the European medicines agency) will be reported if data is available.
	  • Major bleeding (as defined by International Society on Thrombosis and Haemostasis)
	  • Clinically relevant non-major bleeding (as defined by International Society on Thrombosis and Haemostasis)
	  • Surgical complications at the time of placement and removal
	  • Sepsis (or serious infections) for filters that are in place for longer periods
	  • Resource use and costs

Outcome measures	• Risk ratios • hazard ratios • Event data
Study designs	• Randomised controlled trial **or** • Prospective cohort study
Subgroups of interest	Adults (aged 18+) with confirmed VTE: • who cannot have anticoagulants **or** • who have a PE whilst taking anticoagulants **or** • who have the filters inserted for prophylaxis before a potential provoking event (e.g. surgery) **or** • who are at high risk of poor outcomes if they had further PEs **or**

Research question	What is the short and long term clinical and cost effectiveness of inferior vena caval filters in people with VTE?
	• who are at high risk of a PE (only for prospective cohort study as RCTs are available for this group) **or** • and cancer Other subgroups of the above populations: • Type of surgery • People with chronic liver disease • Intravenous drug users • People who are obese (BMI ≥ 40 kg/m^2)

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Potential criterion	Explanation
Importance to patients, service users or the population	IVC filters are currently placed in people with VTE in a range of different clinical scenarios (see population subgroups in PICO table above). However, there is continuing uncertainty about their clinical and cost-effectiveness in these different situations. More and higher quality evidence could help to establish in which clinical scenarios it would be beneficial to use filters in people with VTE. Further RCT evidence will help to add to the evidence base and would be likely to provide the best quality evidence. However, the feasibility of carrying out RCTs in the above clinical scenarios may be limited by the number of people they can recruit and lack statistical power as a result. In contrast, a large prospective cohort study could provide a sufficiently large sample to capture enough events to clearly establish the efficacy of IVC filters in people with VTE and the subgroups specified above.
Relevance to NICE guidance	High priority: the research is essential to inform future updates of key recommendations in the guidance. (The committee agreed that because of the lack of high quality evidence they could not make positive recommendations for the use of filters in several of the population subgroups they identified.)
Current evidence base	There is limited high quality evidence comparing the use of IVC filters to no filters in people with VTE. There are very few RCTs and most of the evidence came from retrospective cohort studies which have serious methodological limitations. The evidence base for each population subgroup is summarised below. In people with VTE and a contraindication to anticoagulation, filters are being used as an alternative to anticoagulation. Evidence for the use of IVC filters in this population comes from two retrospective studies that have methodological shortcomings and report conflicting results for short-term all-cause mortality. In people with VTE who are undergoing a provoking event, the evidence is very heterogeneous (the studies contain people undergoing different surgical procedures) and inconclusive. Several of the studies were at critical risk of bias. The only RCT suggests a benefit for PE-recurrence associated with filter use however the committee agreed that further evidence is needed to confirm this result.

Potential criterion	Explanation
	There are two studies looking at filters in people with VTE who had a recurrent PE whilst taking anticoagulation. One study was at critical risk of bias due to very serious methodological problems. The other study suggested a benefit of filters at 30 days for all-cause and PE-related mortality. The committee again advised that further evidence is needed to clarify this effect. Two RCTs were available for the use of filters in people with VTE who are at high risk of PE. However, for most outcomes these studies could not differentiate outcomes between the filter and no-filter group, and therefore a clear benefit or harm to filters is not established for this group of people. In people with VTE who are at high risk of poor outcomes if they were to have a PE, evidence was again conflicting, and the committee felt unable to make recommendations without further research. When pooled together, evidence suggested a reduction for in-hospital all-cause mortality. However, the evidence was at serious-critical risk of bias, and the only study at moderate risk of bias suggested an increase in in-hospital all-cause mortality in those people given a filter. In people with VTE and cancer, where the filters were placed specifically because the person had cancer, evidence was conflicting. The only available RCT could not differentiate any of the outcomes of interest to this review. Some of the cohort studies showed a benefit for filters and others showed a harm. Further evidence is needed to clarify the effectiveness of filters in this group of people.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well-defined population available that a high quality prospective cohort study should be possible. A high quality RCT may be less feasible as there are a likely to be limited number of people in each of the specific population subgroups that are candidates for IVC filters.

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