Impact of Pulmonary Embolism Response Teams on Acute Pulmonary Embolism, a systematic review and meta-analysis

<u>**Supplemental Methods**</u>
<u>**Search strategy**</u>
Search Methods
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11/9/2020; revised 1/13/2021

Search Methods for Identification of Studies:
To identify studies to include or consider for this systematic review, the review team worked with a medical librarian to develop detailed search strategies for each database. The search was developed for PubMed (NLM) and was translated to Embase (Elsevier), Web of Science (Clarivate Analytics) and CINAHL (EbscoHost) using a combination of keywords and subject headings. A grey literature search included World Wide Science and MedRxiv. The search was restricted to human studies and by the year 2009 to Present. The final search was completed on November 9, 2020.

PubMed (NLM) *from 2009 to 11/9/2020* (420 Results)
Embase (Elsevier) *from 2009 to 11/9/2020* (748 Results)
Web of Science (Clarivate Analytics) *from 2009 to 11/9/2020* (503 Results)
CINAHL (EbscoHost) *from 2009 to 11/9/2020* (123 Results)

The search resulted in 2,119 studies (325 from grey literature sources). 382 duplicate studies were found and omitted using Endnote X.7 for the deduplication of records and an additional 192 duplicate records were later found using Rayyan. In total 1,545 references were eligible to screen. Studies were screened by title and abstract by two blinded and independent reviewers using Rayyan. If a tiebreaker was needed, a third reviewer was called in. This process was repeated for full text article screening and selection.

PubMed (NLM)

(PERT[tiab] OR "pulmonary embolism response team*"[tiab] OR "PE response team*"[tiab] OR "Patient Care Team"[Mesh] OR "patient care team*"[tiab] OR "response team*"[tiab] OR "multidisciplinary team*"[tiab]) AND (PE[tiab] OR "pulmonary embolism*"[tiab] OR "fibrinolytic therap*"[tiab] OR 'lung embolism*[tiab] OR DVT[tiab] OR VTE[tiab] OR "deep vein thrombos*"[tiab] OR "Venous thromboembolism*"[tiab] OR phlebothrombos*[tiab] OR

"Endovascular Procedures"[Mesh] OR "endovascular procedur*"[tiab] OR "Pulmonary Embolism"[Mesh] OR thrombo*[tiab] OR "thrombolytic therap*"[tiab] OR "Thrombolytic Therapy"[Mesh] OR "Embolectomy"[Mesh] OR embolectom*[tiab]) AND ((longitudinal*[tiab] OR "observational stud*"[tiab] OR survey*[tiab] OR retrospectiv*[tiab] OR cohort*[tiab] OR "cohort studies"[mesh] OR "longitudinal studies"[mesh] OR "follow-up studies"[mesh] OR "prospective studies"[mesh] OR "retrospective studies"[mesh] OR prospectiv*[tiab] OR retrospectiv*[tiab] OR analysis*[tiab])) NOT ((animals[MeSH Terms]) NOT ((animals[MeSH Terms]) AND (humans[MeSH Terms]))) 2009/01/01:2030/01/01[dp]

Embase (Elsevier)

(pert:ti,ab OR 'pulmonary embolism response team'/exp OR 'pe response team*':ti,ab OR 'pulmonary embolism response team*':ti,ab OR (('patient car*' NEAR/3 team*):ti,ab) OR 'response team*':ti,ab OR 'multidisciplinary team*':ti,ab) AND (pe:ti,ab OR 'pulmonary embolism*':ti,ab OR dvt:ti,ab OR vte:ti,ab OR 'deep vein thrombos*':ti,ab OR 'venous thromboembolism*':ti,ab OR phlebothrombos*:ti,ab OR 'endovascular surgery'/exp OR ((endovascular NEAR/3 surger*):ti,ab) OR 'endovascular procedur*':ti,ab OR 'lung embolism'/exp OR ((lung NEAR/3 embolism*):ti,ab) OR thrombo*:ti,ab OR 'thrombolytic therap*':ti,ab OR 'fibrinolytic therap*':ti,ab OR 'fibrinolytic therapy'/exp OR 'embolectomy'/exp OR embolectom*:ti,ab) AND (longitudinal*:ti,ab OR 'observational stud*':ti,ab OR survey*:ti,ab OR cohort*:ti,ab OR 'cohort analysis'/exp OR 'longitudinal study'/exp OR 'follow up'/exp OR 'prospective study'/exp OR 'retrospective study'/exp OR prospectiv*:ti,ab OR retrospectiv*:ti,ab OR analysis*:ti,ab) NOT ([animals]/lim NOT [humans]/lim) AND [2009-2020]/py

CINAHL (EbscoHost)

S1	TI(PERT OR "pulmonary embolism response team*" OR "patient care team*" OR "response team*" OR "multidisciplinary team*") OR AB(PERT OR "pulmonary embolism response team*" OR "patient care team*" OR "response team*" OR "multidisciplinary team*") OR (MH "Electronic Health Records+")
S2	TI(PE OR "pulmonary embolism*" OR DVT OR VTE OR "deep vein thrombos*" OR "Venous thromboembolism*" OR phlebothrombos* OR "endovascular procedur*" OR thrombo* OR "thrombolytic therap*" OR embolectom) OR AB(PE OR "pulmonary embolism*" OR DVT OR VTE OR "deep vein thrombos*" OR "Venous thromboembolism*" OR phlebothrombos* OR "endovascular procedur*" OR thrombo* OR "thrombolytic therap*" OR embolectom) OR ((MH "Endovascular Procedures+" OR MM "Pulmonary Embolism" OR MM "Thrombolytic Therapy" OR MM "Embolectomy"))

S3	TI((longitudinal* OR "observational stud*" OR survey* OR retrospectiv* OR cohort* OR prospectiv* OR retrospectiv* OR analysis*) OR AB((longitudinal* OR "observational stud*" OR survey* OR retrospectiv* OR cohort* OR prospectiv* OR retrospectiv* OR analysis*) OR (MH "Prospective Studies+" OR MM "Retrospective Panel Studies"))
S4	S1 AND S2 AND S3
	Limiters - Published Date: 20090101-20201231

Web of Science (Clarivate Analytics)

TS=(PERT OR 'pulmonary embolism response team*' OR 'patient care team*' OR 'response team*' OR 'multidisciplinary team*') AND TS=(PE OR 'pulmonary embolism*' OR DVT OR VTE OR 'deep vein thrombos*' OR 'Venous thromboembolism*' OR phlebothrombos* OR 'endovascular procedur*' OR thrombo* OR 'thrombolytic therap*' OR embolectom*) AND TS=(longitudinal* OR 'observational stud*' OR survey* OR retrospectiv* OR cohort* OR prospectiv* OR retrospectiv* OR analysis*)

Timespan=2009-2020

WorldWideScience.org

"pulmonary embolism response team"

MedRxiv

"pulmonary embolism response team"

Bias assessment

Supplemental Table 1. New Castle Ottawa Scale for cohort studies

Study	Selection	Comparability	Outcome	Total
Annabathula et al.	4	1	3	8
Carroll et al	4	2	3	9
Chaudhury et al.	4	0	3	7
Jen et al.	4	2	3	9
Kwok et al.	4	0	3	7
Myc et al.	4	1	3	8
Melamed et al.	4	0	2	6
Wright et al.	4	1	3	8
Xenos et al.	4	2	3	9

Supplemental Table2. IHE for case control. Checklist scores.

Study	Yes	No	Partial or Unclear
Kabrhel et al.	15	3	2
Khaing et al.	16	2	2
Mahar et al.	14	2	4
Romano et al.	15	2	3
Sista et al.	16	2	2
Szmyt et al.	15	2	3
Wiske et al.	13	2	5

<u>**Forms used for Bias assessment**</u>
NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE
      COHORT STUDIES

<u>Note</u>: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

Selection
1) <u>Representativeness of the exposed cohort</u>
    a) truly representative of the average **_Inpatient PE patients** (describe) in the community
    b) somewhat representative of the average __ **Inpatient PE patients_** in the community
    c) selected group of users eg nurses, volunteers
    d) no description of the derivation of the cohort
2) <u>Selection of the non exposed cohort</u>
    a) drawn from the same community as the exposed cohort
    b) drawn from a different source
    c) no description of the derivation of the non exposed cohort
3) <u>Ascertainment of exposure</u>
    a) secure record (eg surgical records)
    b) structured interview
    c) written self report
    d) no description
4) <u>Demonstration that outcome of interest was not present at start of study</u>
    a) yes
    b) no
Comparability
1) <u>Comparability of cohorts on the basis of the design or analysis</u>
    a) study controls for **_PE severity_** (select the most important factor)
    b) study controls for any additional factor   (This criteria could be modified to indicate specific control for a second important factor.)**Baseline patient characteristics and comorbidities**
Outcome
1) <u>Assessment of outcome</u>
    a) independent blind assessment ✸
    b) record linkage ✸
    c) self report
    d) no description
2) <u>Was follow-up long enough for outcomes to occur</u>
    a) yes (select an adequate follow up period for outcome of interest) ✸
    b) no
3) <u>Adequacy of follow up of cohorts</u>
    a) complete follow up - all subjects accounted for ✸
    b) subjects lost to follow up unlikely to introduce bias - small number lost - > ___ % (select an   adequate %) follow up, or description provided of those lost) ✸
    c) follow up rate < ___% (select an adequate %) and no description of those lost
    d) no statement

Reference: GA Wells, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Available on:
http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp

Quality Appraisal Checklist for Case Series Studies*

Study objective		
1. **Was the hypothesis/aim/objective of the study clearly stated?**	Yes	☐
	Partial	☐
	No	☐
Study design		
2. **Was the study conducted prospectively?**	Yes	☐
	Unclear	☐
	No	☐
3. **Were the cases collected in more than one centre?**	Yes	☐
	Unclear	☐
	No	☐
4. **Were patients recruited consecutively?**	Yes	☐
	Unclear	☐
	No	☐
Study population		
5. **Were the characteristics of the patients included in the study described?**	Yes	☐
	Partial	☐
	No	☐
6. **Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?**	Yes	☐
	Partial	☐
	No	☐
7. **Did patients enter the study at a similar point in the disease?**	Yes	☐
	Unclear	☐
	No	☐
Intervention and co-intervention		
8. **Was the intervention of interest clearly described?**	Yes	☐
	Partial	☐

		No	☐
9.	**Were additional interventions (co-interventions) clearly described?**	Yes	☐
		Partial	☐
		No	☐

Outcome measure			
10.	**Were relevant outcome measures established a priori?**	Yes	☐
		Partial	☐
		No	☐
11.	**Were outcome assessors blinded to the intervention that patients received?**	Yes	☐
		Unclear	☐
		No	☐
12.	**Were the relevant outcomes measured using appropriate objective/subjective methods?**	Yes	☐
		Partial	☐
		No	☐
13.	**Were the relevant outcome measures made before and after the intervention?**	Yes	☐
		Unclear	☐
		No	☐
Statistical analysis			
14.	**Were the statistical tests used to assess the relevant outcomes appropriate?**	Yes	☐
		Unclear	☐
		No	☐
Results and conclusions			
15.	**Was follow-up long enough for important events and outcomes to occur?**	Yes	☐
		Unclear	☐
		No	☐
16.	**Were losses to follow-up reported?**	Yes	☐
		Unclear	☐
		No	☐
17.	**Did the study provided estimates of random variability in the data analysis of relevant outcomes?**	Yes	☐
		Partial	☐
		No	☐

18.	Were the adverse events reported?	Yes	☐
		Partial	☐
		No	☐
19.	Were the conclusions of the study supported by results?	Yes	☐
		Unclear	☐
		No	☐
Competing interests and sources of support			
20.	**Were both competing interests and sources of support for the study reported?**	Yes	☐
		Partial	☐
		No	☐

*Note: Assessor(s) may decide to remove from the checklist the items that are not applicable to their project.
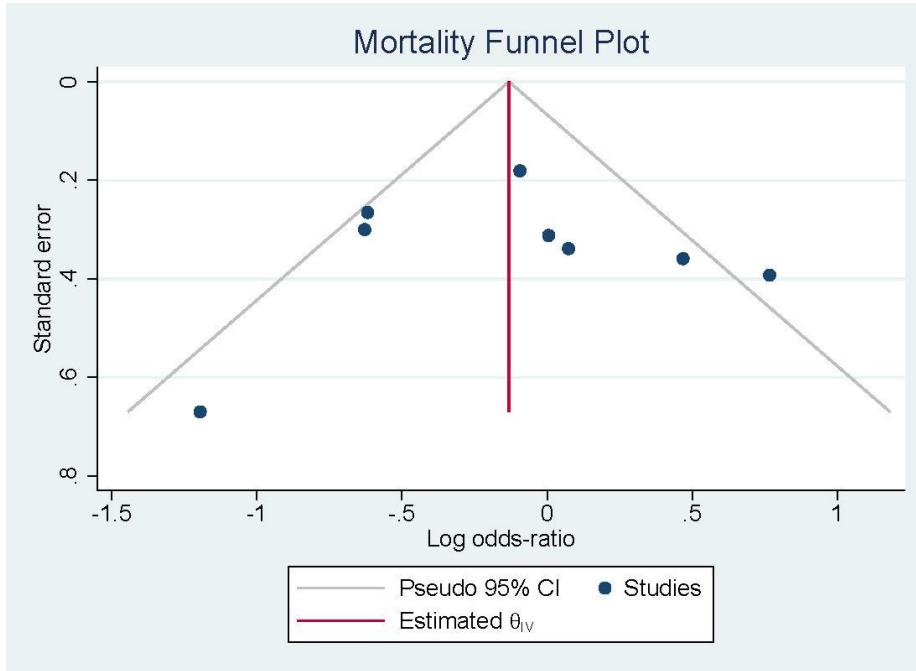
Reference:

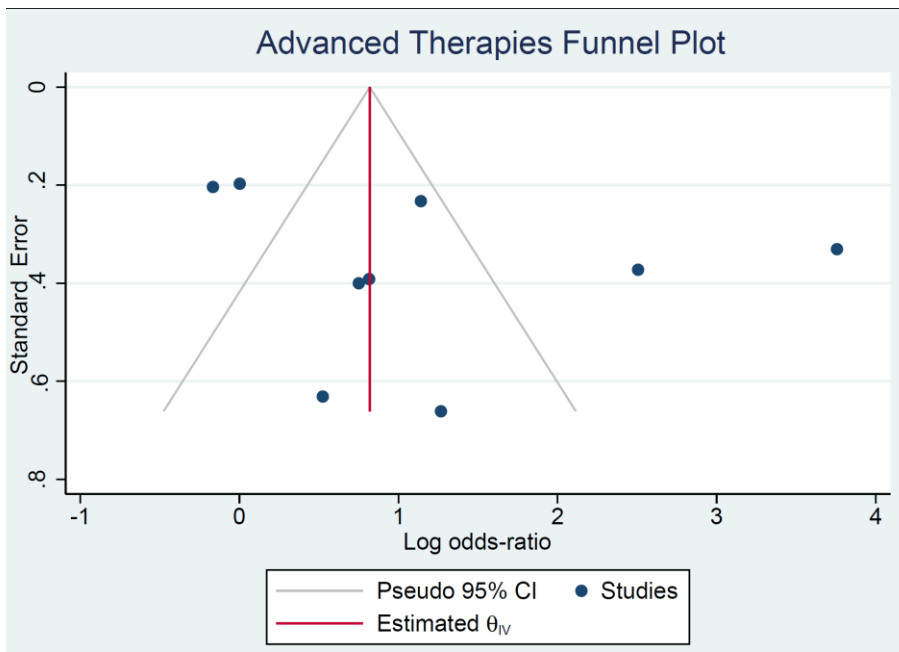Institute of Health Economics (IHE). Quality Appraisal of Case Series Studies Checklist. Edmonton (AB): Institute of Health Economics; 2014. Available from: http://www.ihe.ca/research-programs/rmd/cssqac/cssqac-about

Supplemental Results
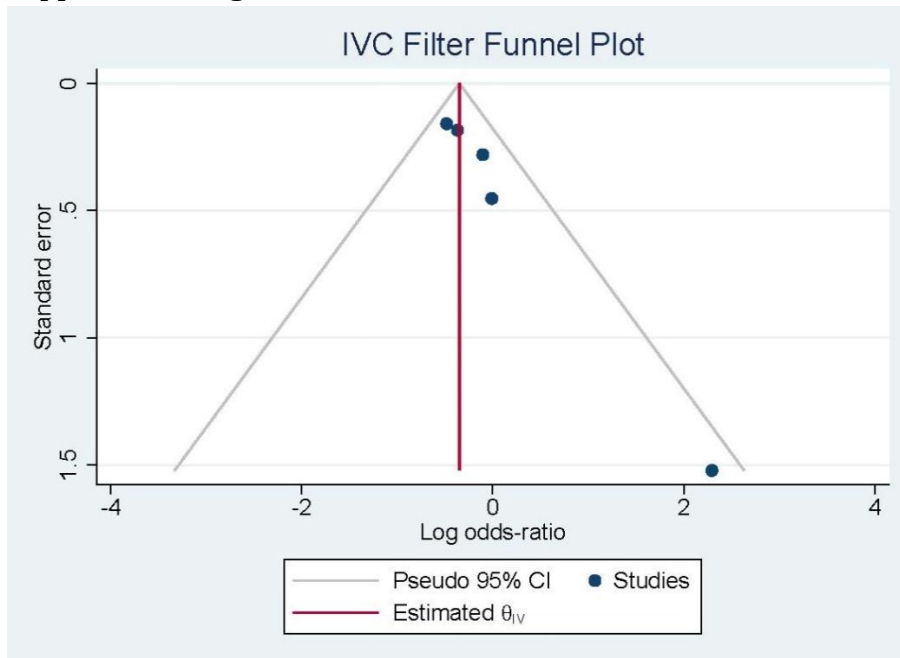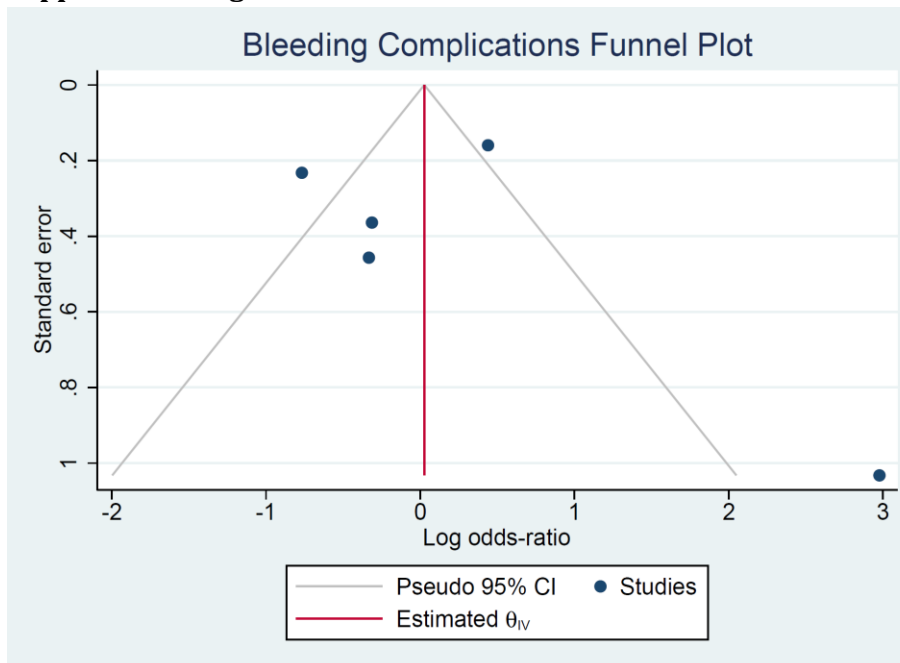
Funnel Plots
Supplemental-Figure A

Supplemental-Figure B

Supplemental-Figure C

Supplemental-Figure D

Table A. PE severity by group

Study	PERT				Control			
	n	High Risk	Intermediate Risk	Low risk	n	High Risk	Intermediate Risk	Low risk
Carroll et al., 2020 [6]	1158	44 (3.8%)	571 (49.3%)	532 (45.9%)	884	42 (4.8%)	296 (33.9%)	538 (60.9%)
Jen et al., 2019 [13].	167	20 (12.0%)	100 (59.9%)	47 (28.1%)	154	13 (8.4%)	78 (50.6%)	63 (40.9%)
Kabrhel et al., 2016 [14]	314	80 (25.5%)	143 (45.5%)	91 (28.29%)	n/a	n/a	n/a	n/a
Khaing et al., 2020 [15]	52	3 (5.8%)	49 (94.2%)	0	n/a	n/a	n/a	n/a
Kwok et al., 2020 [16]	60	3 (5%)	46 (76.7%)	11 (18.3%)	81	0 (0%)	59 (72.8%)	22 (27.2%)
Mahar et al., 2018 [17]	118	23 (19.5%)	80 (67.8%)	15 (12.7%)	n/a	n/a	n/a	n/a
Wright et al., 2019 [24]	146	28 (19.2%)	118 (80.8%)	0	159	43 (27%)	116 (73%)	0 (0%)
Xenos et al., 2019 [25]	77	10 (13.0%)	67 (87.0%)	0	n/a	n/a	n/a	n/a
Total[a]	2092	224 (10.7%)	1160 (55.5%)	671 (32.1%)	1124	88 (7.8%)	458 (40.7%)	549 (48.8%)

Total patients	High Risk	Intermediate Risk	Low risk					
3216	312 (9.7%)	1618 (50.3%)	1220 (37.9%)					

PERT: pulmonary embolism response team
[a] Reported classification n is < than total n for each group. Post Pert 11 cases are not classified. Control group 8 cases are not classified