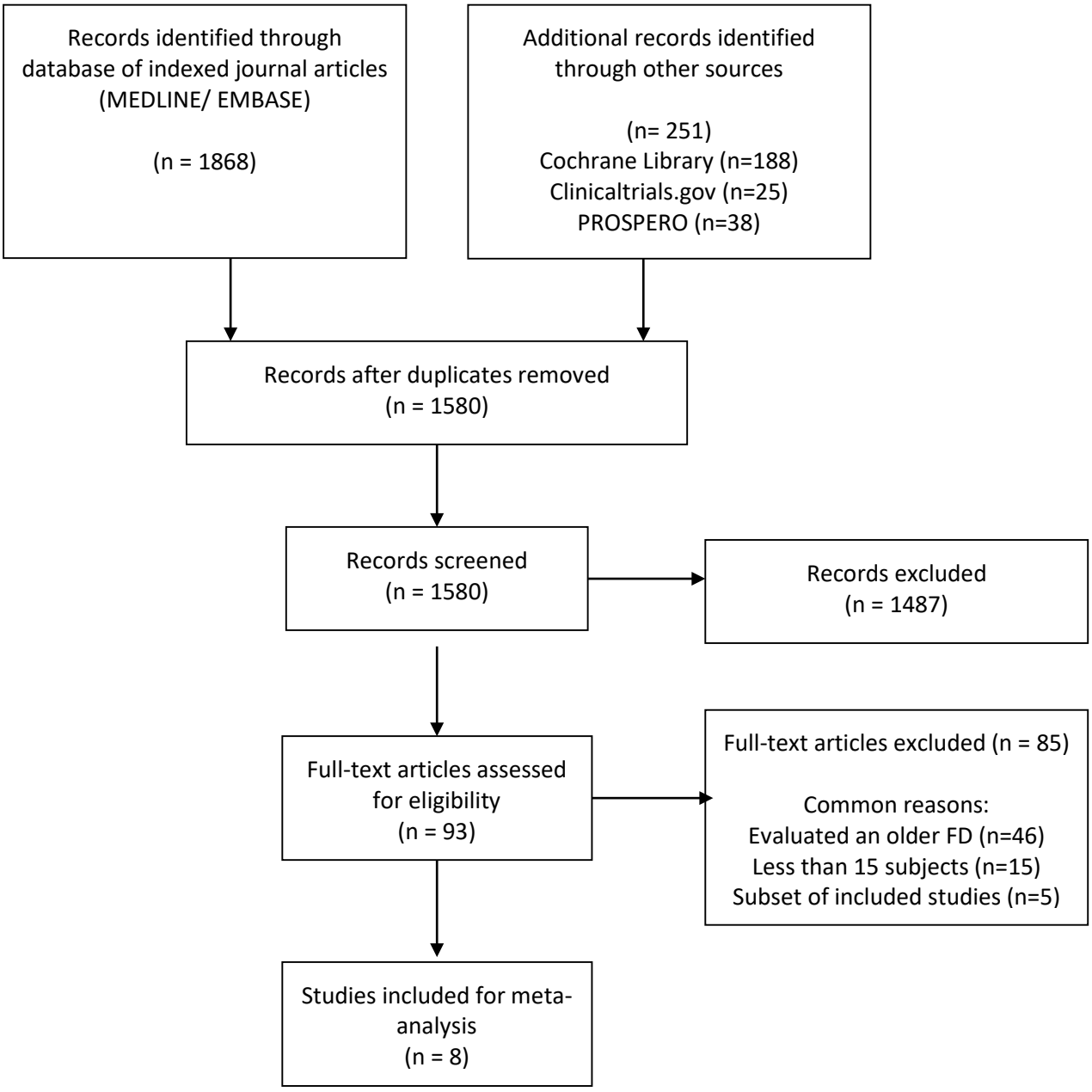
Table A. Summary of included studies

Study, Year and Design	FD type and number	Patients	Aneurysms	Age (mean)	Females (%)	Ruptured Aneurysms (%)	Posterior Circulation Aneurysms (%)	Sac size (mean, mm)	Follow up (mean, months)	Coil assisted (%)	Balloon angioplasty (%)	Technical success (%)	Mortality (%)	Morbidity (%)	Ischaemic event rate (%)	Serious ischaemic event rate (%)	Aneurysm occlusion at 6 months (%)	Aneurysm occlusion at 12 months (%)	Study quality by NIH tool
Daglioglu et al. [15] **2020** **Retrospective**	DED 180	146	182	51.5	65.8	25.3	6.6	8.3	7.0	21.4	NA	98.9	2.7	5.5	4.1	4.1	78.8	NA	Fair
Goertz et al. [16-19] ***2019*** **Retrospective**	DED 63	59	59	52.6	81.4	16.9	15.3	8.1	12.0	20.3	10.2	100	0	10.2	8.5	1.7	70.5	82.8	Fair
Akgul et al. [23] **2016** **Retrospective**	DED 26	24	34	51.4	58.3	2.9	8.8	9.5	7.4	47.1	26.5	100	4.2	8.4	29.2	4.2	77.8	NA	Good
Trivelato et al. [21] ***2019*** **Prospective**	DED 186	146	183	55.3	82.9	3.3	9.3	6.7	9.1	6.0	16.9	100	1.4	6.2	5.5	2.1	80.7	89.2	Good
Martinez-Galdamez et al. [13-14] ***2019*** **Prospective**	SPED 54	50	50	53	82.0	0.0	6.0	7.7	12.0	14.0	18.0	98.1	0.0	10.0	6.0	0.0	76.3	81.8	Good
SCOPE AUS [20] ***2019*** **Retrospective**	SPED 344	294	318	NA	72.4	6.7	10.4	7.5	5.6	NA	NA	98.3	1.4	5.8	10.2	1.4	90.0	NA	Good
Trivelato et al. [22] ***2019*** **Prospective**	SPED 188	151	182	52.7	79.5	3.8	6.6	7.0	5.0	12.9	9.9	100	0.7	6.0	4.6	4.0	79.7	85.3	Good
Atasoy et al. [24] ***2019*** **Retrospective**	SPED 45	41	52	56	68.3	0.0	11.5	9.0	17.2	NA	NA	97.8	2.4	4.9	2.4	0.00	78.8	82.7	Good

Table B. Current and previous meta-analyses on flow diverters treating cerebral aneurysms

	Examining all types of aneurysms					Examining a specific type of aneurysm					
Meta-analysis Year	**Li 2020**	**Brinjikji[4] 2013**	**Briganti[5] 2015**	**Ye[6] 2016**	**Zhou[3] 2017**	**Cagnazzo[31] 2018**	**Cagnazzo[30] 2018**	**Zhu[32] 2018**	**Kiyofuji[33] 2018**	**Bhatia[28] 2019**	**Fiorella[27] 2020**
Flow diverters	SPED, DED	PED, SILK	PED, SILK, SURPASS	PED, SILK, FRED, SURPASS	PED, FPED, SILK, FRED, SURPASS, Tubridge, WEB	PED, SILK, FRED, SURPASS	/	PED, SILK, FRED, Enterprise	/	FPED	PED, SURPASS, DED, FRED, SPED, SILK
Comments	Surface modified flow diverters	Early data on older flow diverters	Early data on older flow diverters	Large number of subjects	Focused on complications	Acutely ruptured aneurysms	Giant aneuryms	Blister like aneurysms	Non-saccular posterior circulation aneurysms	Peri-operative outcomes of FPED for unruptured aneurysms	Unruptured small/ medium-sized aneurysms of the ICA
Patients/ Aneurysms	911/1060	1451/1654	1483/1704	2508/2826	3125/3427	20/223	/	-/165	129/131	879/901	2614/-
Follow Up Length (Months)	8.36	/	9	6.3	/	9.6	26	3-24	11.25	1	/
Technical Success (%)	99.6	/	91.7	/	90.6	/	/	100	/	99.3	/
Aneurysm Occlusion (6 months, %)	80.5	76	74.5	77.9	/	88.9 (9.6 months)	/	72 (on last FU)	/	/	/
Aneurysm Occlusion (12 months, %)	85.6	/	89.6	/	/	/	72	/	52	/	74.6%
Mortality Rate (%)	0.7	4	3.4	3.8	2.8	4.5	9% (grouped)	3	21	0.8	/
Morbidity Rate (%)	6.0	5 (permanent)	3.5 (permanent)	/	17 (overall) 3.7 (permanent)	17.8	15	26	26	10.1	7.8%
Total Ischaemia Rate (%)	6.7	/	/	9.8	/	/	30	/	23	/	/
Serious Ischaemia Rate (%)	1.8	6	4.1	5.5	7.5	8	/	12	/	0.6	/

Appendix 1: PRISMA flowchart, detailed search method and results



PRISMA Flowchart

Search Strategy

1. MEDLINE & EMBASE

Search date:
26th December 2019

Search Engine:
OvidSP

Databases:
Embase 1974 to present
Medline (Ovid MEDLINE® Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE®) 1946 to present

Parameters:
Advanced Search
Search keywords are for 'All fields'
CheckTag: "Human"
Age Group: All
Publication Year: 2014 – 2020 (to include preprints)
No limit in language

Search Keywords
"Intracranial Aneurysm"
"Cerebral Aneurysm"
"Brain aneurysm"
"Flow diver*"
"Derivo"
"DED"
"Pipeline shield"
"SPED"
"PED"
"P64"
"p48"

Search Syntax:

1. "Intracranial aneurysm".mp. [mp=tx, bt, ti, ab, ct, bo, hw, tn, ot, dm, mf, dv, kw, fx, dq, nm, kf, ox, px, rx, ui, sy]
2. limit 1 to humans
3. limit 2 to yr="2014 -2020"
4. cerebral aneurysm.mp. [mp=tx, bt, ti, ab, ct, bo, hw, tn, ot, dm, mf, dv, kw, fx, dq, nm, kf, ox, px, rx, ui, sy]
5. limit 3 to humans
6. limit 5 to yr="2014 -2020"
7. brain aneurysm.mp. [mp=tx, bt, ti, ab, ct, bo, hw, tn, ot, dm, mf, dv, kw, fx, dq, nm, kf, ox, px, rx, ui, sy]
8. limit 7 to humans
9. limit 8 to yr="2014 -2020"
10. 3 or 6 or 9
11. flow diver*.mp. [mp=tx, bt, ti, ab, ct, bo, hw, tn, ot, dm, mf, dv, kw, fx, dq, nm, kf, ox, px, rx, ui, sy]
12. limit 11 to humans
13. limit 12 to yr="2014 -2020"
14. (Derivo or DED).mp. [mp=tx, bt, ti, ab, ct, bo, hw, tn, ot, dm, mf, dv, kw, fx, dq, nm, kf, ox, px, rx, ui, sy]
15. limit 14 to humans
16. limit 15 to yr="2014-2020"
17. ("Pipeline" or "SPED" or "PED").mp. [mp=tx, bt, ti, ab, ct, bo, hw, tn, ot, dm, mf, dv, kw, fx, dq, nm, kf, ox, px, rx, ui, sy]
18. limit 17 to humans
19. limit 18 to yr="2014 -2020"
20. p64.mp. [mp=tx, bt, ti, ab, ct, bo, hw, tn, ot, dm, mf, dv, kw, fx, dq, nm, kf, ox, px, rx, ui, sy]
21. limit 20 to humans
22. limit 21 to yr="2014 -2020"
23. p48mw.mp. [mp=tx, bt, ti, ab, ct, bo, hw, tn, ot, dm, mf, dv, kw, fx, dq, nm, kf, ox, px, rx, ui, sy]
24. limit 23 to humans
25. limit 24 to yr="2014 - 2020"
26. 13 or 16 or 19 or 22 or 25
27. 10 and 26

Results:
1868 results generated
532 duplicates removed
1336 eligible for title screening

2. Cochrane Library search

Search date:
26th December 2019

Databases:
Cochrane Central Register of Controlled Trials (CENTRAL)
Cochrane Database of Systematic Reviews (CDSR)

Parameters:
Advanced search
Search fields: Title Abstract Keyword

Search syntax:
Aneurysm OR flow diver* OR pipeline OR derive OR P64 OR P48

Result:
188 titles generated.
All screened and 0 found relevant

3. Clinicaltrials.gov search

Search date:
26th December 2019

Parameters:
Advanced search
Under intervention/treatment

Search syntax and yield:
Pipeline: 25 results
Derivo: 0
P64: 0
P48: 0

Results:
3 records found relevant.
Full text screened and 0 additional study included.

4. PROSPERO

Search date:
26th December 2019

Search syntax and yield:

1. Pipeline
28 titles yielded
4 relevant and 4 proceeded to full text screening

2. Flow diverter
6 results yielded
4 duplicates and 2 proceeded to full text screening

3. Derivo
1 result yielded - duplicate

4. P64
2 results yielded - duplicate

5. P48
1 result yielded – irrelevant

5. Manufacturer websites

The following manufacturer website were browsed and no additional eligible study on their products were found.

- Medtronic (www.medtronic.com)
- Acandis (www.acandis.com)
- Phenox (www.phenox.net)

6. Related journal, society and conference websites

Recent issues and events from the following major interventional neuroradiology journals, organization and conference website were browsed and no additional eligible study were found.

- Interventional Neuroradiology (https://journals.sagepub.com/home/ine)
- Journal of Neurointerventional Surgery (https://jnis.bmj.com/)
- Neuroradiology (https://www.springer.com/journal/234)
- Clinical neuroradiology (https://link.springer.com/journal/62)
- American Journal of Neuroradiology (https://www.ajnr.org)
- WFITN (https://www.wfitn.org)
- ESMINT (https:///esmint.eu)
- Society of NeuroInterventional Surgery (https://snisonline.org)

Appendix 2. Risk of bias assessment with NIH tool for Case Series Studies

	Daglioglu 2019 [15] (DED)	Goertz 2019 [16-19] (DED)	Akgul 2019 [23] (DED)	Trivelato 2019 [21] (DED)	Martinez-Galdamez 2019 [13-14](SPED)	SCOPE AUS 2019 [20] (SPED)	Trivelato 2019 [22] (SPED)	Atasoy 2019 [24] (SPED)
Clear study question	✓	✓	✓	✓	✓	✓	✓	✓
Appropriate study population and case definition	✓	✓	✓	✓	✓	✓	✓	✓
Consecutive cases	NR	✓	NR	✓	NR	✓	✓	✓
Comparable subjects	✓	✓	✓	✓	✓	✓	✓	✓
Clear depiction of intervention	✓	✓	✓	✓	✓	✓	✓	✓
Appropriate outcome measurements	✓	✗	✓	✓	✓	✓	✓	✓
Adequate follow up	✗	✗	✗	✗	✓	✗	✗	✓
Sound statistical methods	✗	✓	✓	✓	✓	✓	✓	✓
Good description of results	✗	✓	✓	✓	✓	✓	✓	✓
Overall grading	Fair	Fair	Good	Good	Good	Good	Good	Good

Appendix 3. Detailed summary of unsuccessful deployments, mortality and morbidity

Table 1. Summary of technically challenges and unsuccessful deployments

Number	Study	Details	Solution
Unsuccessful deployments (6)			
1-2 (2)	Daglioglu (DED)	Inability to cannulate the target arterial segment with the DED. Deployment not actually attempted.	Not mentioned but commented that Headway 27 and XT 27 microcatheters were most suitable for delivery overall.
3-5 (3)	Martinez-Galdamez (SPED)	Commented that 3 SPEDS did not fully deploy and were therefore not implanted	Not mentioned.
6 (1)	Atasoy (SPED)	Unable to deploy SPED in an a patient with a wide neck saccular M1 aneurysm as the SPED would not travel through the Marksman/Navien catheters through a tourtuous ICA	Treated eventually with Balt Baby Leo stent.
Technical challenges (13)			
1 (1)	Akgul (DED)	Fish mouthing of a DED	Placement of an additional DED
2-5 (4)	Trivelato (DED)	Improper proximal DED expansion in 4 cases. Commented that entering the device with a balloon was challenging.	2 solved with balloon angioplasty and 2 with device removal and substitution
6-11 (6)	SCOPE AUS (SPED)	Commented to have unsuccessful initial deployments.	No further details.
12-13 (2)	Trivelato (SPED)	Improper SPED expansion in 2 cases	No further information.

Table 2. Summary of mortality (13)

Number	Study	Details
1	Daglioglu (DED)	Perforation of aneurysm in DED-assisted coiling
2-4 (3)	Daglioglu (DED)	Unspecified cause of death. Patient noted to have mRS 6 (exitus) on follow up.
5	Akgul (DED)	Giant ICA terminus aneurysm treated with DED without coiling, DSA showing stasis. Persistent headache post procedure with CT showing peri-aneurysmal oedema, treated with dexamethasone. Aneurysm ruptured 6 months post procedure and patient died.
6	Trivelato (DED)	Incidental paraophthalmic ICA aneurysm treated with DED, thrombosis 4 days afterwards (commented related to self-discontinuation of antiplatelets) and succumbed.
7	Trivelato (DED)	Ruptured giant fusiform basilar trunk aneurysm treated with DED, died 5 days postoperatively due to rebleed.
8	SCOPE AUS (SPED)	MCA aneurysm treated with SPED. Fatal delayed parenchymal haemorrhage.
9	SCOPE AUS (SPED)	Paraclinoid ICA aneurysm treated with SPED. Fatal delayed parenchymal haemorrhage.
10	SCOPE AUS (SPED)	PICA aneurysm treated with SPED. Fatal recurrent subarachnoid haemorrhage.
11	SCOPE AUS (SPED)	Paraclinoid ICA aneurysm treated with SPED. Fatal recurrent subarachnoid haemorrhage.
12	Trivelato (SPED)	Unspecified death occurring in the SPED series
13	Atasoy (SPED)	Giant basilar tip aneurysm (27mm), previous coiling with recurrent 10mm sac. Treated with SPED and adjunctive coiling. Developed acute subdural hematoma 15 days post procedure and died.

Table 3. Summary of morbidity and ischaemic complications.

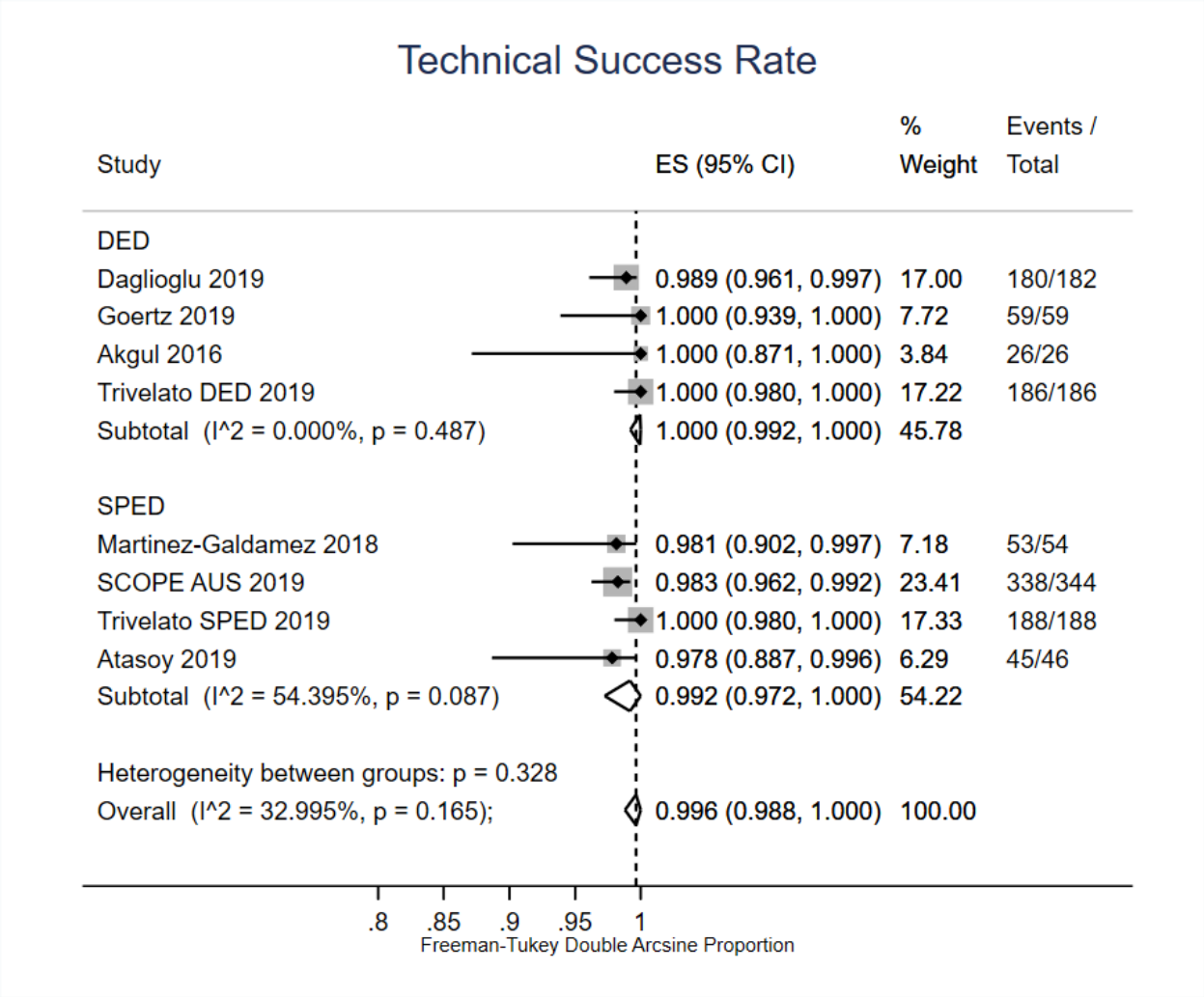
Number	Event	Details	Ischaemia related
Daglioglu – DED (8 morbidities, 6 ischaemia, 6 serious ischaemia)			
1	Massive cerebral infarction	Occlusion of DED. Considered serious ischaemic event.	Yes
2-6 (5)	Thromboembolic infarction	DED placed in 1 MCA, 3 ICA, 1 BA. Commented to be symptomatic with no further information. Considered serious ischaemic event.	Yes
7	Retroperitoneal haematoma	Did not require surgical intervention. Considered non-ischaemic morbidity.	No
8	Small intracranial haemorrhage	Commented to have no residual symptom and attributed to antiplatelet therapy. Considered non-ischaemic morbidity.	No
Goertz - DED (6 morbidities, 5 ischaemia, 1 serious ischaemia)			
1	Thromboembolic infarction	Occurred during procedure and treated with IV tirofiban. Discharged with mild motor aphasia (mRS1, NIHSS 1), but was free of symptoms 1 year later. Considered non-serious ischaemic event.	Yes
2	Thromboembolic infarction	Ruptured ophthalmic ICA aneurysm treated with DED. Right hemiparesis and motor aphasia 4 days post operatively. Instent thrombosis noted treated by thrombectomy. Persistent hemiparesis (mRS1) at 1 year follow up. Considered serious ischaemic event.	Yes
3-5	Thromboembolic event	No further information provided. Considered ischaemic morbidity.	Yes
6	Intracranial haemorrhage	No further information provided. Considered non-ischaemic morbidity.	No
Akgul - DED (2 morbidities, 7 ischaemia, 1 serious ischaemia)			
1	Thromboembolic infarct	Right hemiparesis directly after procedure due to a small cortical infarct treated with tirofiban. No residual deficit. Considered non-serious ischaemic morbidity.	Yes
2	Ischaemic stroke due to stent occlusion	Right hemiplegia and aphasia 3 days after procedure, found to have stent occlusion and treated with thrombectomy, with mild residual deficit. Later found to have clopidogrel insensitivity and the second APT was switched to ticlopidine. Considered serious ischaemic morbidity.	Yes
3-7 (5)	Thromboembolic infarct	Asymptomatic and only seen on DWI MRI. Considered non-serious ischaemic event.	Yes
Trivelato – DED (9 morbidities, 8 ischaemia, 3 serious ischaemia)			
1-2 (2)	Major ischaemic stroke	No further information. Treated as serious ischaemic event.	Yes
3-4 (2)	Transient ischaemic attack (TIA)	No further information. Treated as non-serious ischaemic event.	Yes
5	Intracranial haemorrhage	Commented to be contralateral to aneurysms. No further information. Considered a non-ischaemic morbidity.	No
6	Increased mass effect	No further information. Considered a non-ischaemic morbidity.	No
7-10 (4)	Thromboembolic events in 4 patients	Occurred during intervention and treated by IA abciximab. Resulted in 1 ischaemic stroke (serious) and 3 asymptomatic patients	Yes

11	Intracranial haemorrhage	Due to vessel perforation during exchange maneuverer. Commented to be asymptomatic. Not considered a morbidity.	No
12-13 (2)	Retroperitoneal haemorrhage in 2 patients	No further information. Considered non-ischaemic morbidities.	No
Martinez-Galdamez – SPED (5 morbidities, 3 ischaemia, 0 serious ischaemia)			
1	Headache ? due to mass effect	Unruptured giant aneurysm (29mm) treated with SPED and readmitted 4 days later for headache with no neurological deficits. Symptoms resolved with medical treatment. Considered a non-ischaemic morbidity.	No
2	Thromboembolic infarct	Previously ruptured 4.5mm aneurysm treated with SPED. Diploplia 2 days post procedure and imaging showed multifocal infarcts and patent SPED, likely thrombo-embolism. Considered a serious ischaemic morbidity.	Yes
3	Retroperitoneal haematoma	High femoral puncture with extravasation and hypotensive shock requiring surgical intervention. No permanent sequale. Considered a non-ischaemic morbidity.	No
4	Left ICA thrombosis with collateral formation	Asymptomatic patient. Noted 63 days post procedure during reassessment DSA. Antiplatelet assay showed suboptimal platelet inhibition. Continued on DAPT. Considered a non-serious ischaemic event.	Yes
11	Carotid dissection	Considered non-serious and no further details given. Not considered morbidity.	No
12	Groin haematoma	Considered non-serious and no further details given. Considered non-ischaemic morbidity.	No
13	Cerebral infarction	Considered non-serious and no further details given. Considered ischaemic morbidity.	Yes
14-15	Nausea in 2 cases	Considered non-serious and no further details given. Not considered morbidity as minor symptoms.	No
SCOPE AUS (17 morbidities, 30 ischaemia, 4 serious ischaemia)			
1	Cerebral infarction	Basilar/PCA aneurysm with pontine infarct leaving permanent ischaemic deficit. Considered serious ischaemic morbidity.	Yes
2	Cerebral infarction	MCA aneurysm with lenticulostriate infarct leaving permanent ischaemic deficit. Considered serious ischaemic morbidity.	Yes
3	Cerebral infarction	MCA aneurysm with distal territory infarct leaving permanent ischaemic deficit. Considered serious ischaemic morbidity.	Yes
4	Cerebral infarction	Basilar dissection with PCA territory infarct leaving permanent ischaemic deficit. Considered serious ischaemic morbidity.	Yes
5-17 (13)	Transient ischaemic symptoms in 13 cases	Classified as non-serious ischaemic morbidity.	Yes
18-30 (13)	MRI showing infarct in 13 patients	Commented to be asymptomatic. Considered an ischaemic event but not morbidity.	Yes
Trivelato – SPED (9 morbidities, 7 ischaemia, 6 serious ischaemia)			
1-2 (2)	Ischaemic stroke	Commented to be disabling. Classified as serious ischaemic morbidity	Yes
3-5 (3)	Minor ischaemic stroke	No further information. Classified as serious ischaemic morbidity	Yes
6	TIA	No further information. Classified as non-serious ischaemic morbidity	Yes
7	Cerebral haemorrhage	Symptomatic. No further information. Considered a non-ischaemic morbidity.	No

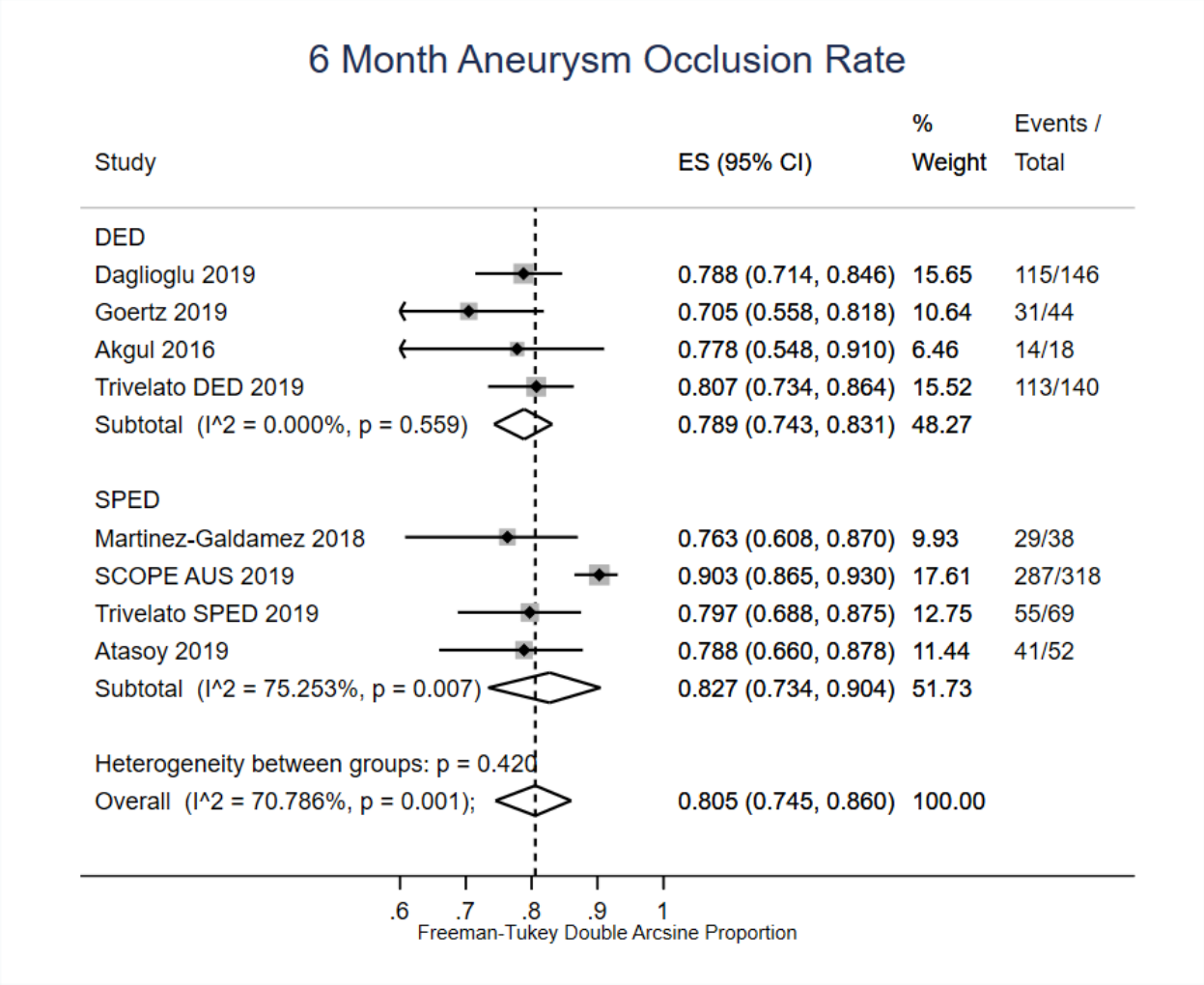
8	Increase in mass effect	Symptomatic. No further information. Considered a non-ischaemic morbidity.	No
9	Retinal ischaemia	Symptomatic. No further information. Classified as serious ischaemic morbidity	Yes
10-13 (4)	Dissection of cervical vessels in 4 patients	No further information. Assumed as asymptomatic as they were considered to have reached the primary safety endpoint in study. Not considered morbidity.	No
14-16 (3)	Thromboembolism in 3 cases	No further information. Assumed as asymptomatic as they were considered to have reached the primary safety endpoint in study. Considered non-serious ischaemic events.	Yes
17-18 (2)	Vessel perforation in 2 cases	No further information. Assumed as asymptomatic as they were considered to have reached the primary safety endpoint in study. Not considered morbidity.	No
Atasoy – SPED (2 morbidities, 1 ischaemia, 0 serious ischaemia)			
1	Intracranial haemorrhage with headache	Giant right cavernous ICA aneurysm (28mm) treated with 2 SPEDs. Developed 3rd nerve palsy day 7 post procedure with CT showing thrombosed aneurysm and small remote ICH. Headache resolved. No further details regarding 3rd nerve palsy. Considered a non-ischaemic morbidity.	No
2	TIA	Temporary left sided facial droop and slurred speech 6 days after right ICA SPED deployment. CT, MR and MRA were normal. Also known to have atrial fibrillation. Considered non-serious ischaemic morbidity.	Yes

Appendix 4. Forest Plots of 7 meta-analyzed outcomes

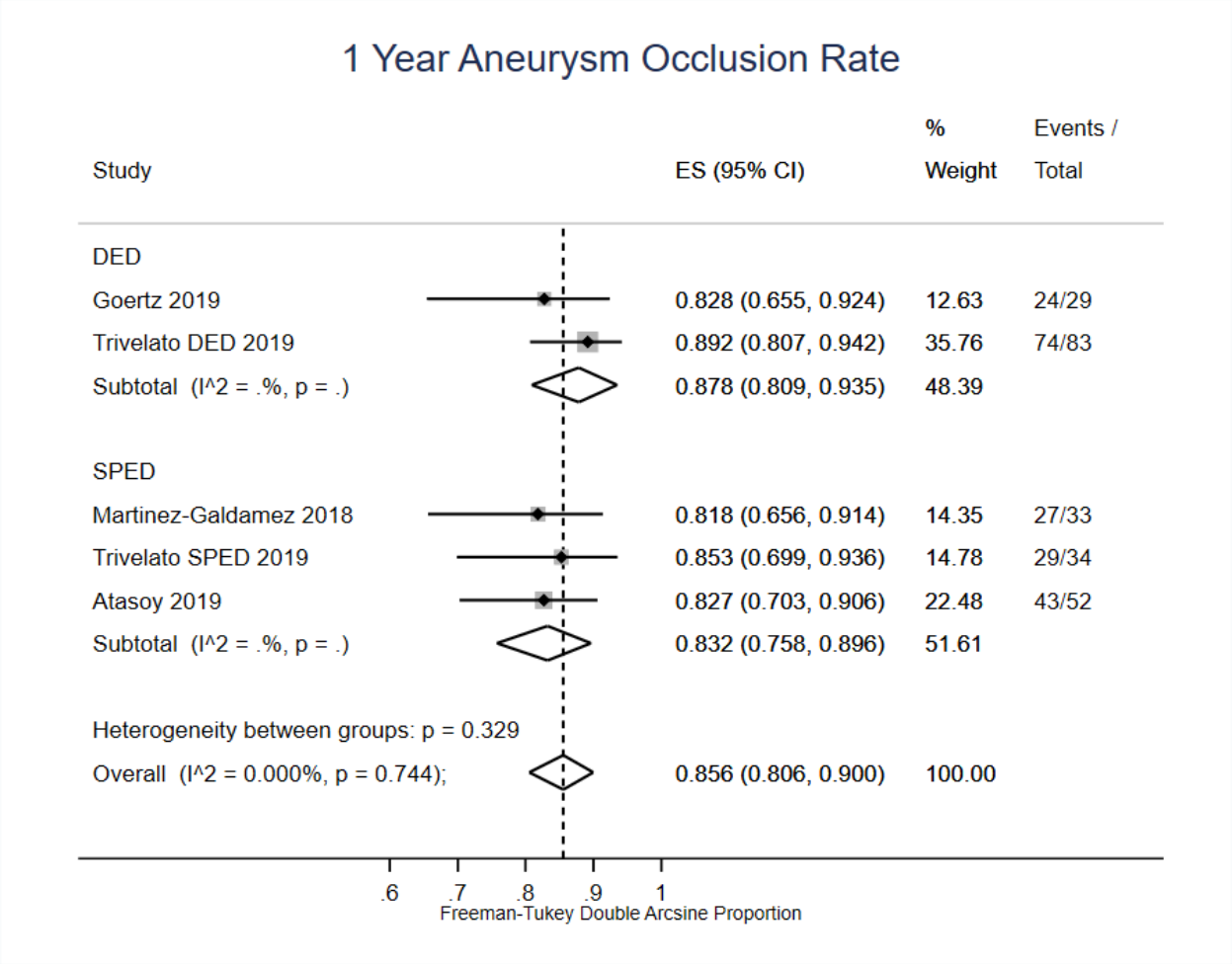
Efficacy outcome 1: Technical Success Rate



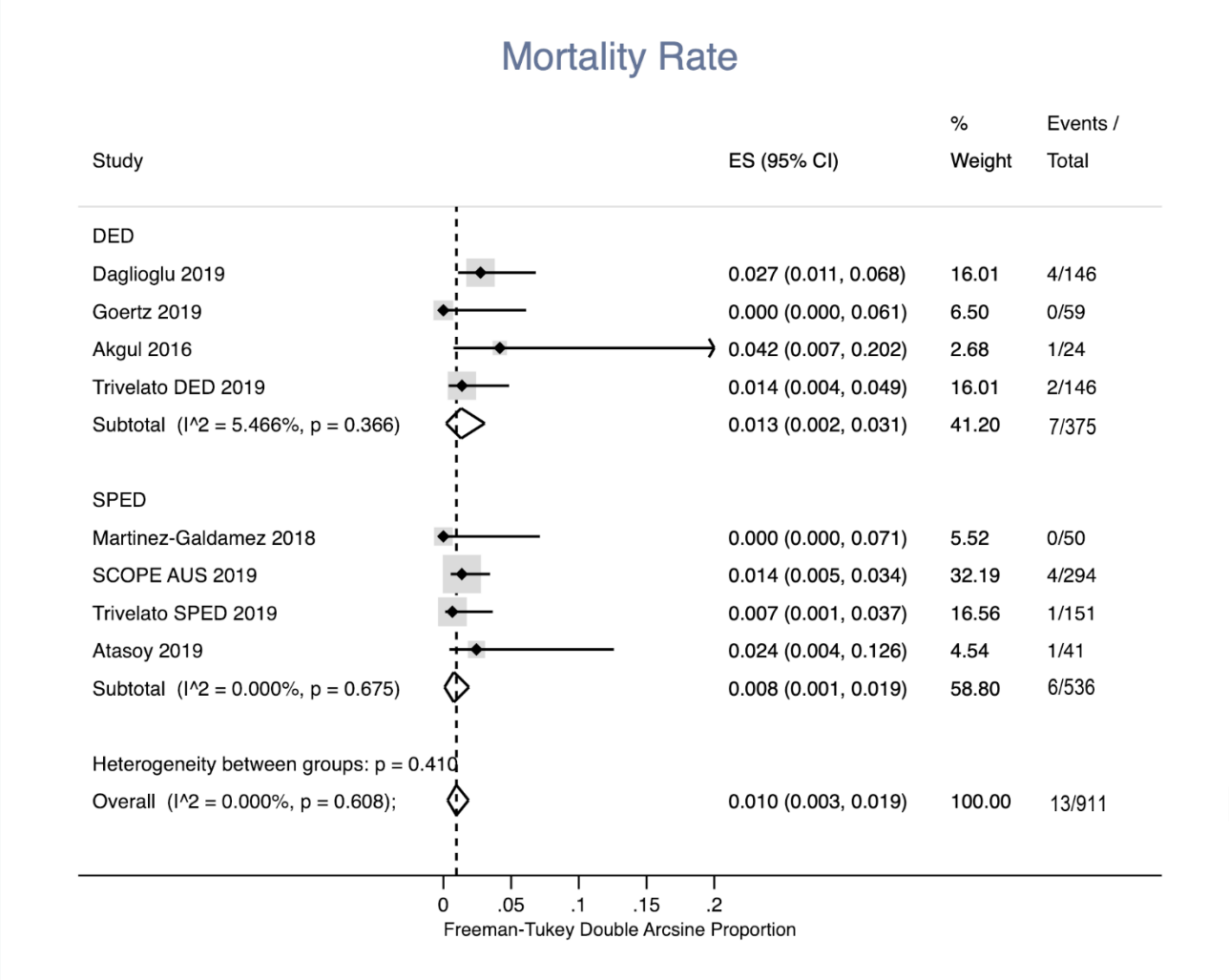
Efficacy outcome 2: 6 Month Aneurysm Occlusion Rate



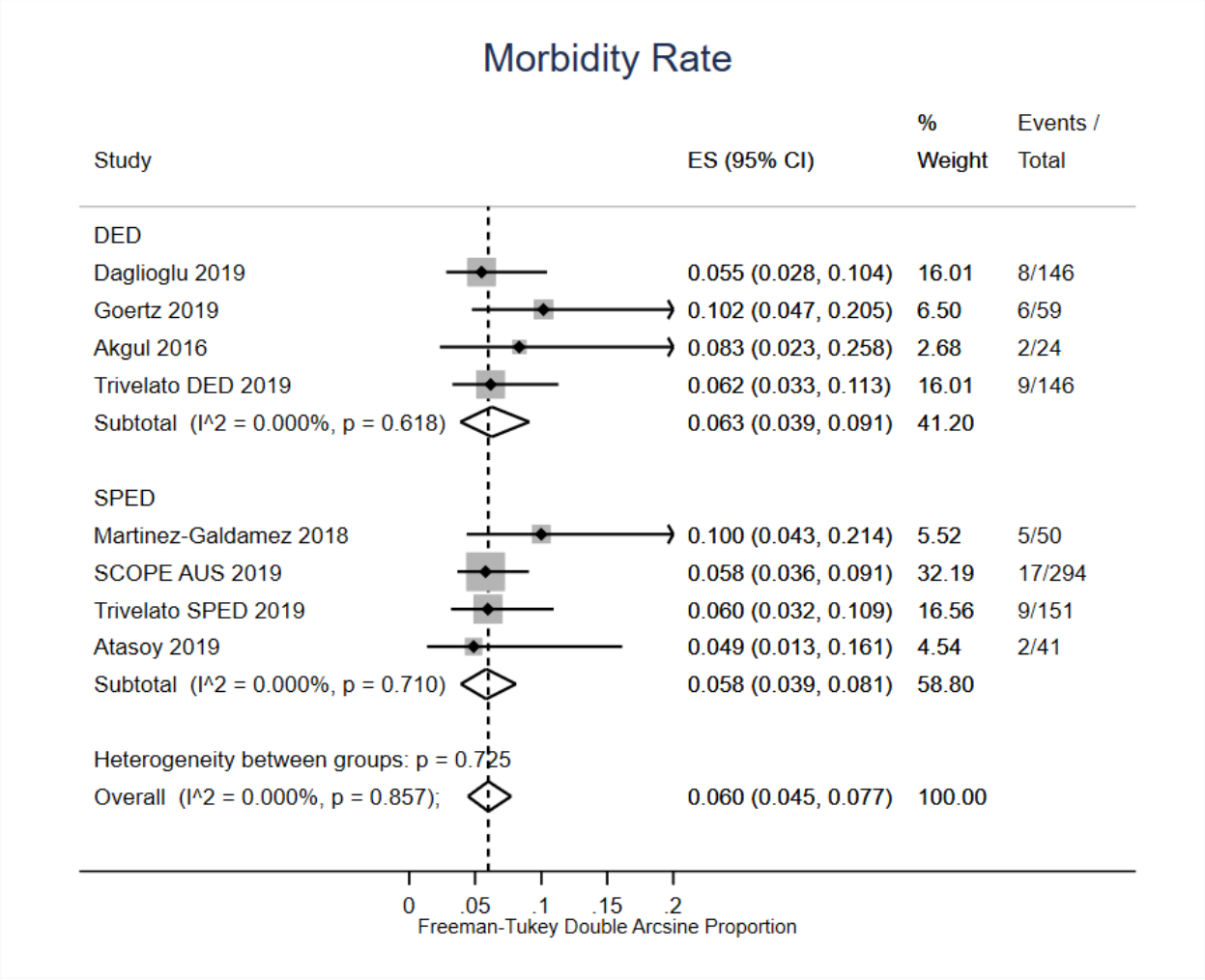
Efficacy outcome 3: 1 Year Aneurysm Occlusion Rate



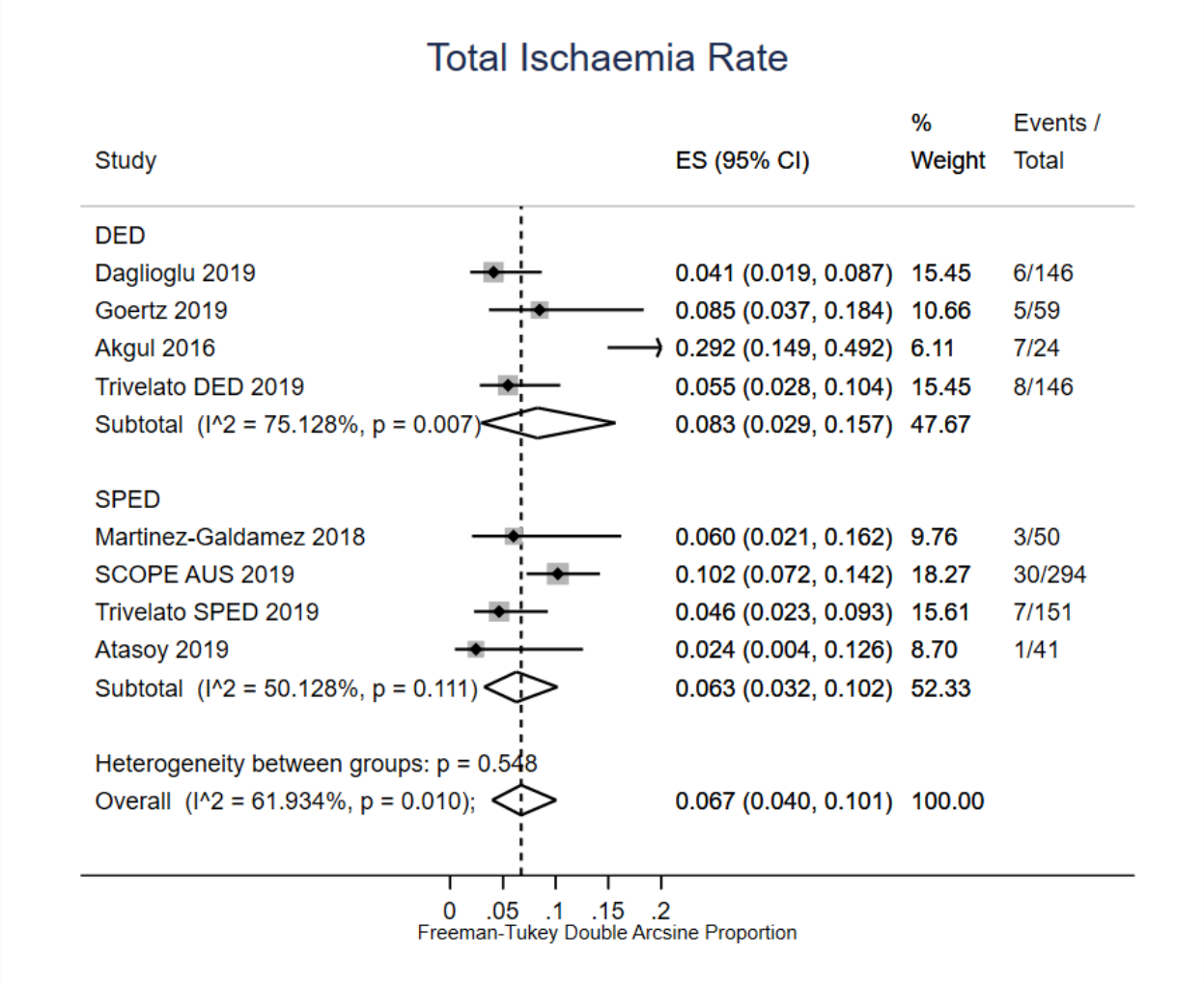
Safety outcome 1: Mortality Rate



Safety outcome 2: Morbidity Rate



Safety outcome 3: Total Ischaemia Rate



Safety outcome 4: Serious Ischaemia Rate