

## Supplementary data

**Table 1.** Main characteristics of studies included in the study.

Study year	Study design	Country	Sample size	Key endpoints	Secondary end-points	Follow-up (months)
Qin 2001	Prospective cohort	USA Cleveland	51	PC, PD	LVOTO, IVSd LVEDD, LA	3
Firoozi 2002	Prospective cohort	UK	44	All-cause mortality SCD, CV mortality PC	NYHA, Angina LVOTO, LVEDD LA size	32.2
Jing 2004	Prospective cohort	China	54	All-cause mortality		24
Ralph-Edwards 2005	Prospective cohort	Canada	102	All-cause mortality SCD, CV mortality	LVEDD, IVSd LA size	24.3
Vural 2007	Prospective cohort	Turkey	40	All-cause mortality Reintervention PC	NYHA, Angina LVOTO, LVEDD IVSd, LA size	13.12
Ball 2011	Prospective cohort	Canada	372	All-cause mortality	IVSd, LA size	60
Sorajja 2012	Retrospective cohort	USA Mayo Clinic	354	All-cause mortality SCD, CV mortality PC, Stroke	Angina, LVOTO LVEDD, LA size	68.4
Knyshev 2013	Prospective cohort	Ukraine	42	All-cause mortality	LVOTO, NYHA	31.9

Steggerda 2014	Prospective cohort	Netherlands	263	All-cause mortality SCD, CV mortality Reintervention, PCI	IVSd	60
Samardhi 2014	Prospective cohort	Australia	70	All-cause mortality Reintervention PC, PD	NYHA, Angina LVOTO, IVSd LA size	43
Vriesendorp 2014	Prospective cohort	Netherlands & Belgium	574	All-cause mortality SCD, CV mortality PC	LVOTO, IVSd	91.2
Sedehi 2015	Prospective cohort	USA Stanford	223	All-cause mortality PD	NYHA LVOTO, IVSd	120
Yang 2016	Prospective cohort	China	59	All-cause mortality SCD, CV mortality Reintervention	Angina, LVOTO LVEDD, IVSd LA size	36
Finocchiaro 2016	RCTs	USA Stanford	40		LVOTO, IVSd LVEDD, LA size	12
Cavigli 2018	Prospective cohort	Italy	126	All-cause mortality SCD, CV mortality Reintervention, PD	Angina LVOTO, IVSd LA size	60
Guo 2018	RCTs	China	226	All-cause mortality Reintervention, PD PC	Angina LVOTO, IVSd LA size	41.2
Hoedemakers 2019	Retrospective	Belgium	77	All-cause mortality SCD, CV mortality PD	LVOTO, IVSd LA size	84

Nguyen 2019	Prospective cohort	USA	503	All-cause mortality PC, Reintervention	LVOTO, IVSd LA size	31.2
Kimmelstiel 2019	Prospective cohort	USA Boston	477	All-cause mortality PC, Reintervention	LVOT, IVSd	48
Shimada 2019	Prospective cohort	USA California Florida	850		PC, PP	76.8

Abbreviation: CV: cardio-vascular; SCD: sudden cardiac death; PC: peri-procedural complication; PD: pacemaker dependence; LVOTO: left ventricle outflow tract obstruction; IVSd: interventricular septal in diastole; LA: left atrium; LVEDD: left ventricle end-diastolic dimension.

**Table S2. Main characteristics of patients enrolled among trials included in the study**

Study (year)	Arms of treatment	Number of patients	Age (year)	Female (%)	Mean hospital Stay (days)	LVOTO mmHg	NYHA class (mean)
Qin 2001	ASA	25	63 ± 14	72	5.6 ± 2.3	64 ± 39	3.5 ± 0.5
	SM	26	48 ± 13	39	8.1 ± 3.5	62 ± 43	3.3 ± 0.5
Firoozi 2002	ASA	20	49 ± 13	40	NR	83 ± 23	2.3 ± 0.5
	SM	24	38 ± 16	46	NR	91 ± 18	2.4 ± 0.6
Jing 2004	ASA	43	36 ± 11		NR	NR	NR
	SM	11	45 ± 14		NR	NR	NR
Ralph-Edwards 2005	ASA	54	59 ± 15	52	7 days	74 ± 36	NR
	SM	48	46 ± 17	38	8 days	64 ± 27	NR
Vural 2007	ASA	24	25 ± 7.3	42	4.3 ± 0.9	65 ± 60	NR
	SM	16	24 ± 6.6	44	6.5 ± 1.8	72.5 ± 20	NR

Ball 2011	ASA	85	57 ± 16	50	NR	NR	NR
	SM	287	47 ± 15	40	NR	NR	NR
Sorajja 2012	ASA	177	63 ± 13	58	NR	70 ± 40.	NR
	SM	177	62 ± 12	58	NR	67 ± 40.	NR
Knyshov 2013	ASA	14	34 ± 8.5	43	NR	97.5 ± 8.9	2.14 ± 0.53
	SM	28	29.1 ± 16.1	54	NR	113.3 ± 14.9	2 ± 0.86
Steggerda 2014	ASA	161	59 ± 14	48	5 ± 3	NR	NR
	SM	102	56 ± 16	54	9 ± 6	NR	NR
Samardhi 2014	ASA	47	57 ± 14.7	45	NR	74.0 ± 20	NR
	SM	23	47 ± 20.6	56.5	NR	75.5 ± 18	NR
Vriesendorp 2014	ASA	321	58 ± 14	45	NR	102 ± 52	NR
	SM	253	52 ± 16	46	NR	92 ± 39	NR
Sedehi 2015	ASA	52	57.3 ± 12.9	44	NR	67.1 ± 26.9	2.99 ± 0.35
	SM	171	48.0 ± 17.1	51	NR	67.4 ± 43.4	2.74 ± 0.65
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Yang 2016	ASA	22	45.5 ± 8.1	20	NR	79.7 ± 21.2	NR
	SM	37	44.6 ± 9.5	33	NR	69.0 ± 23.9	NR
Finocchiaro 2016	ASA	9	54 ± 14	45	NR	48 ± 32	NR
	SM	31	50 ± 12	42	NR	59 ± 32	NR
Cavigli 2018	ASA	55	49 ± 14	58	NR	70 ± 33	NR
	SM	71	42 ± 16	38	NR	52 ± 31	NR
Guo 2018	ASA	68	52.59 ± 10.54	37	NR	70.30 ± 44.79	NR
	SM	158	49.20 ± 12.30	51	NR	74.58 ± 45.52	NR
Hoedemakers 2019	ASA	25	61.18 ± 20.8	68	6.0 ± 3	45.00 ± 20	NR
	SM	52	54.49 ± 26.1	54	3.0 ± 3	64.00 ± 30	NR
Nguyen 2019	ASA	167	65 ± 14	56	NR	65.0 ± 19	NR
	SM	334	64 ± 13	54	5.8 ± 5.6	60.0 ± 17	NR

Kimmelstiel 2019	ASA	99	66.3 ± 11.9	63	6.4 ± 3.3	65.7 ± 40.7	NR
	SM	378	52.7 ± 14.7	42	NR	58.0 ± 41.8	NR
Shimada 2019	ASA	393	61 ± 15	NR	5.1 ± 2.7	NR	NR
	SM	457	61 ± 15	NR	7.8 ± 4.6	NR	NR

Abbreviations: ASA: Alcohol septal ablation; SM: septal myectomy; LVOTO: left ventricle outflow tract obstruction; NR: non reported

**Table S3.** Assessment of risk of bias in the included studies using Cochrane criteria for CTs

Study (trial) year	Sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective outcome reporting	Other bias
Finocchiaro 2016	L	L	U	L	L	L	L
Guo 2018	L	L	U	U	L	L	L

*Legend: L: low risk of bias; H: high risk of bias; U: unclear risk of bias.*

**Table S4.** Assessment of risk of bias in the included studies using Newcastle-Ottawa Quality Assessment Scale (NOS) for cohort studies.

Study, year	Selection				Comparability	Exposure			Quality
	1	2	3	4		1	2	3	
Qin 2001	a)	a)	b)	a)	a)	b)	a)	b)	Good
Firoozi 2002	a)	a)	a)	a)	b)	a)	a)	a)	Good
Jing 2004	a)	b)	b)	a)	b)	a)	b)	b)	Good
Ralph-Edwards 2005	a)	a)	a)	a)	a)	b)	a)	b)	Good
Vural 2007	b)	a)	b)	b)	a)	a)	a)	b)	Good
Ball 2011	a)	b)	b)	a)	b)	b)	a)	b)	Good
Sorajja 2012	a)	a)	a)	a)	a)	a)	a)	a)	Good
Knyshev 2013	b)	a)	b)	b)	b)	d)	b)	a)	Fair
Steggerda 2014	a)	a)	b)	b)	a)	a)	b)	a)	Good
Samardhi 2014	b)	b)	a)	b)	a)	a)	b)	b)	Fair
Vriesendorp 2014	a)	a)	b)	a)	a)	a)	b)	a)	Good

Sedehi 2015	c)	b)	b)	b)	a)	b)	a)	b)	Fair
Yang 2016	b)	a)	b)	b)	b)	b)	a)	b)	Fair
Cavigli 2018	b)	a)	b)	b)	a)	a)	b)	b)	Good
Hoedemakers 2019	a)	b)	a)	a)	b)	a)	b)	a)	Good
Nguyen 2019	b)	b)	a)	a)	a)	a)	b)	b)	Good
Kimmelstiel 2019	b)	b)	a)	a)	b)	a)	b)	b)	Good
Shimada 2019	b)	b)	a)	a)	a)	a)	b)	b)	Good

Legend: NOS: Selection- 1: a),b) one star, c), d) no star; Selection- 2: a) one star, b, c) no star; Selection- 3: a), b) one star, c), d), e) no star, Selection- 4: a) one star, b) no star;

Comparability: a), b) one star, c) no star; Exposure-1: a),b) one star, c), d), e) no star; Exposure-2: a) one star, b) no star; Exposure-2: a),b) one star, c), d), no star.

**Good quality:** 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain

**Fair quality:** 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain

**Poor quality:** 0 or 1 star in selection domain OR 0 stars in comparability domain OR 0 or 1 stars in outcome/exposure domain

Figure S1. Flow chart of study section

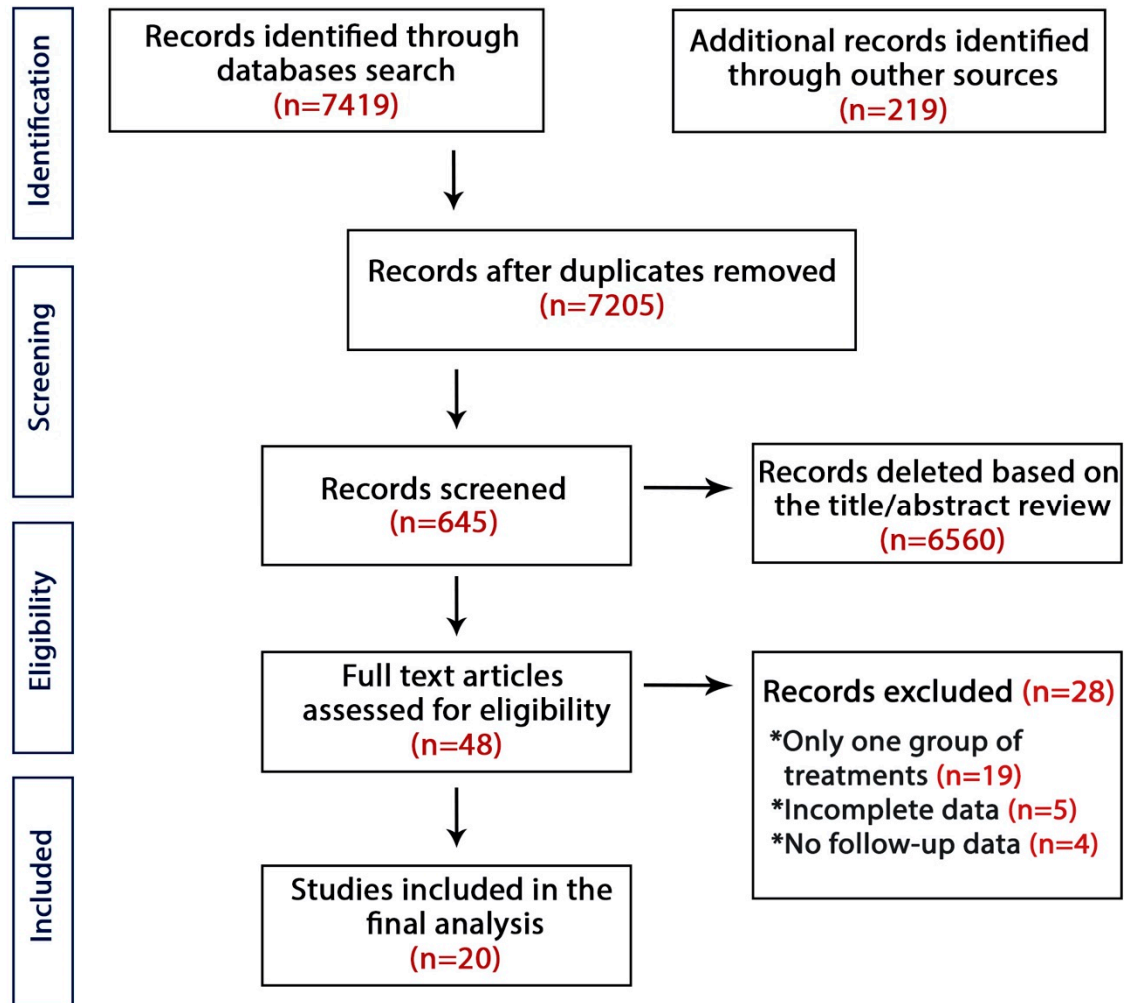
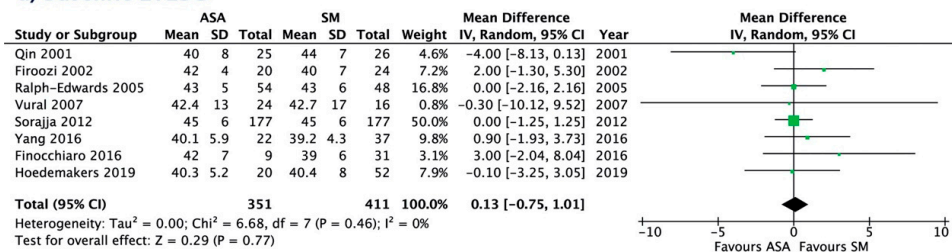
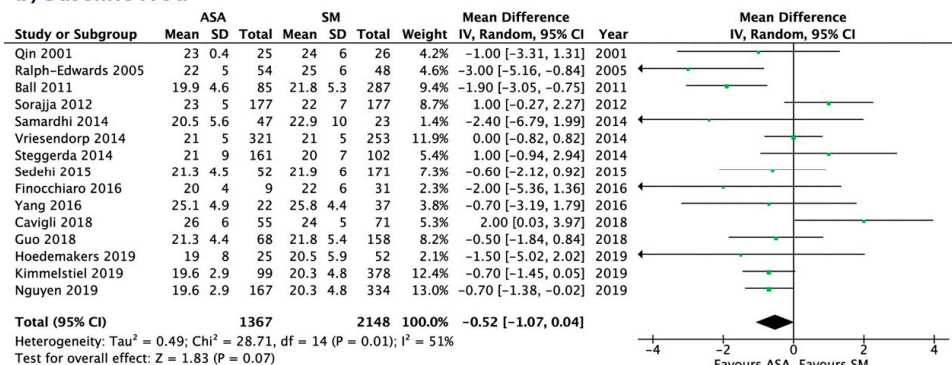


Figure S2. Baseline LV dimensions and function difference: comparison between ASA vs. SM

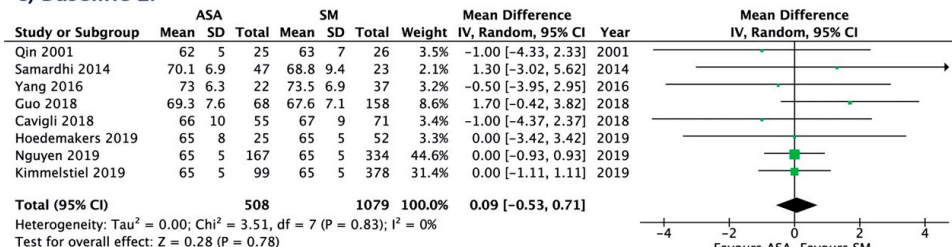
a) Baseline LVEDD



b) Baseline IVSd



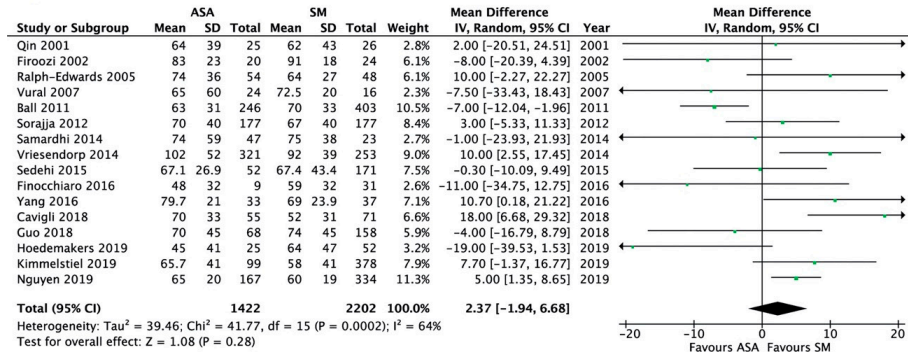
c) Baseline EF



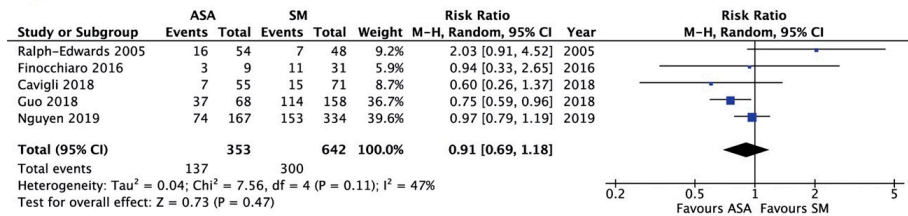
LVEDD: left ventricle end-diastolic dimension; IVSd: interventricular septum in diastole; EF: ejection fraction

Figure S3. Baseline LVOTO, MR & LA size: comparison between ASA vs. SM.

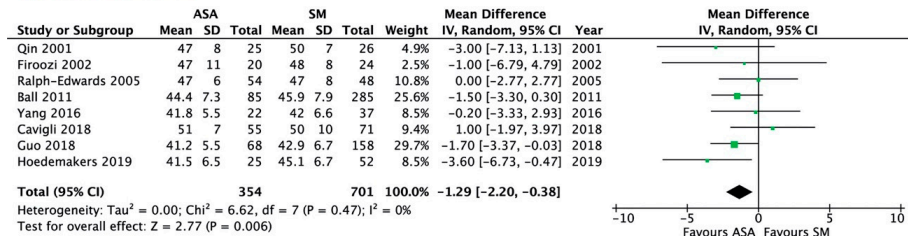
a) Baseline LVOTO



b) Baseline MR



c) Baseline LA size



LVOTO: left ventricle outflow tract obstruction; MR: mitral regurgitation; LA: left atrium

Figure S4. NYHA class mean change between ASA vs. SM

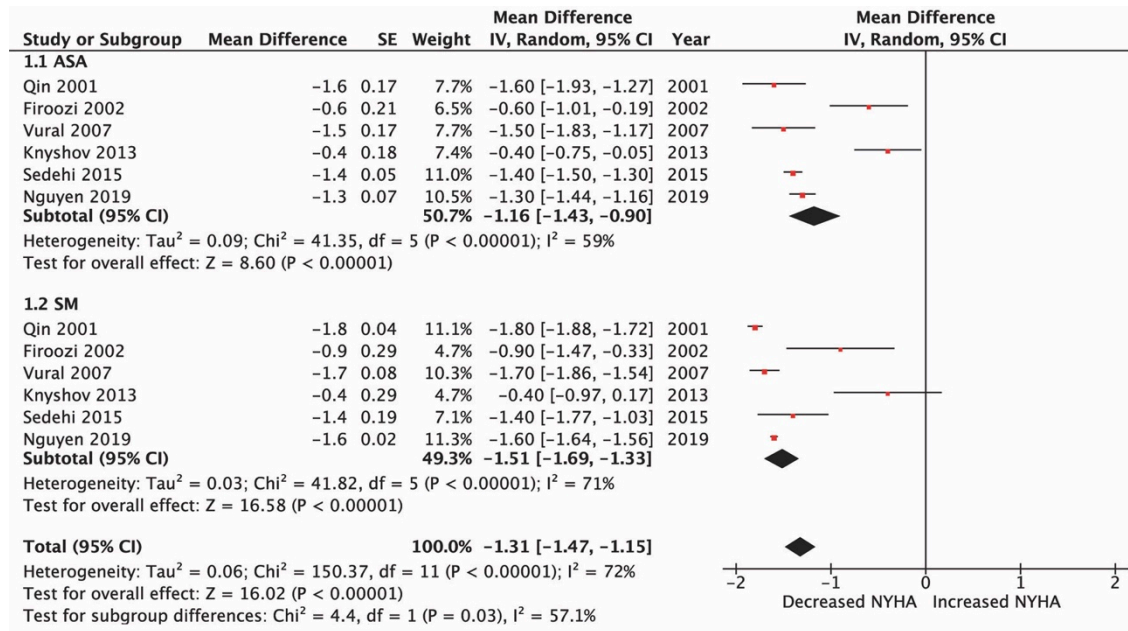
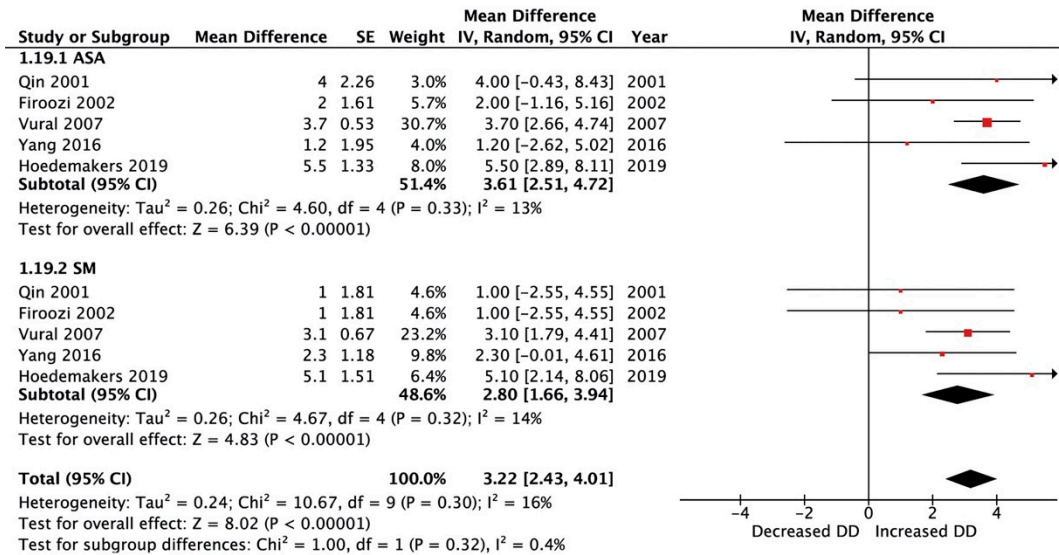
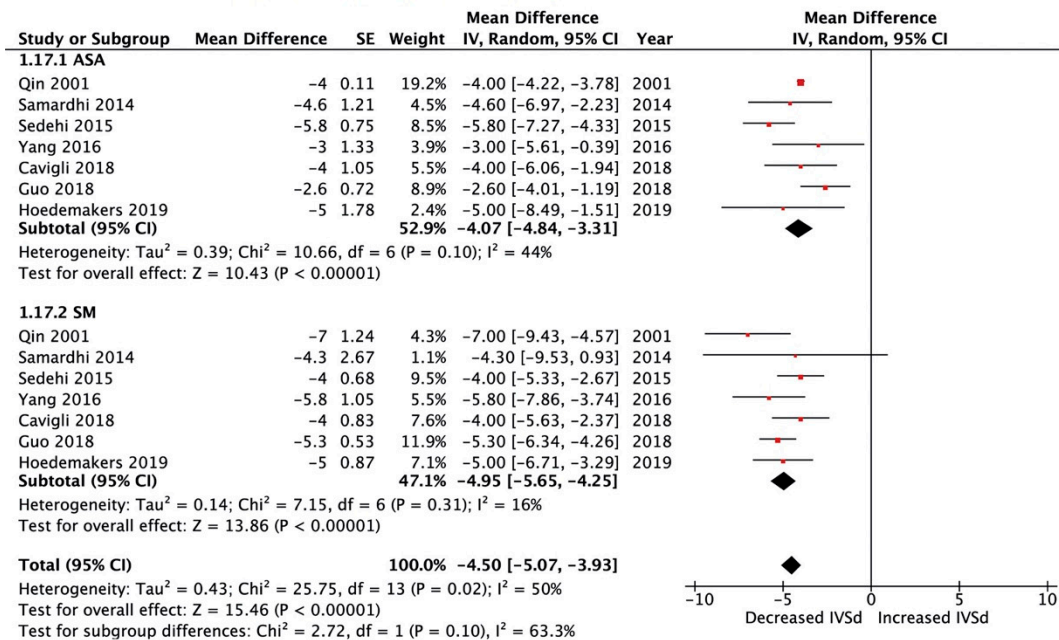


Figure S5. LV dimensions mean change; a) LVEDD; b) IVSd

a) LVEDD mean change; a) ASA group; b) SM group

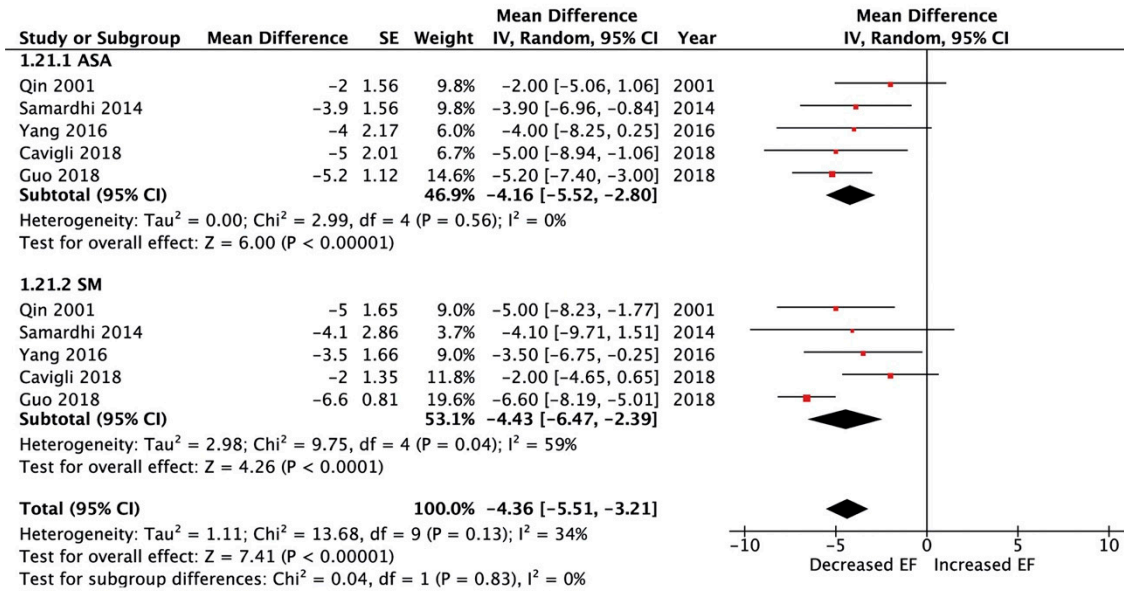


b) IVSd mean change; a) ASA group; b) SM group

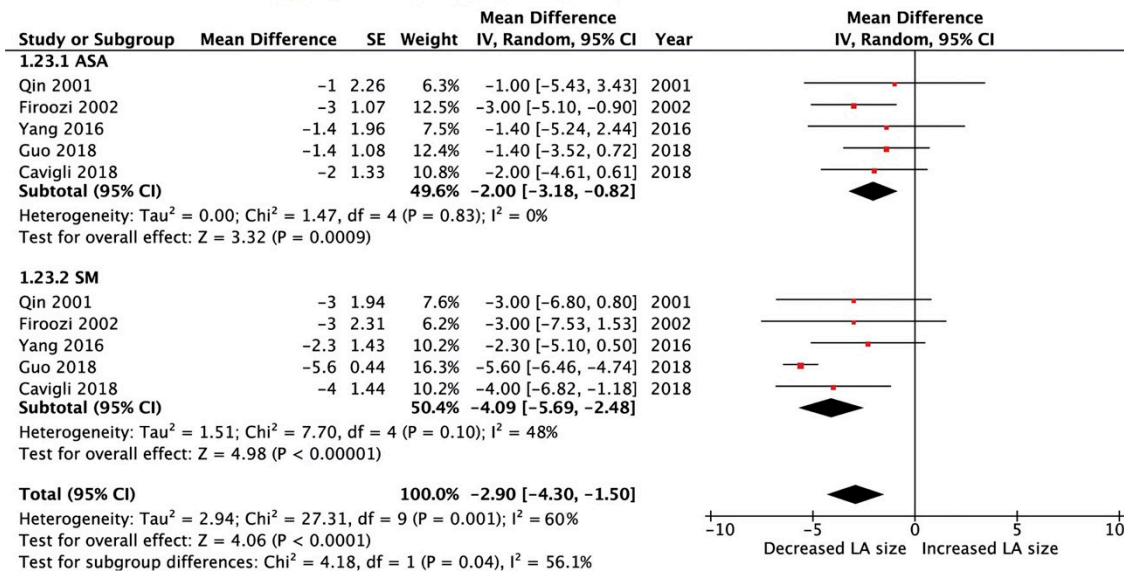


*Figure S6. LV systolic function and LA size mean change; a) LVEF; b) LA size*

a) LVEF mean change; a) ASA group; b) SM group

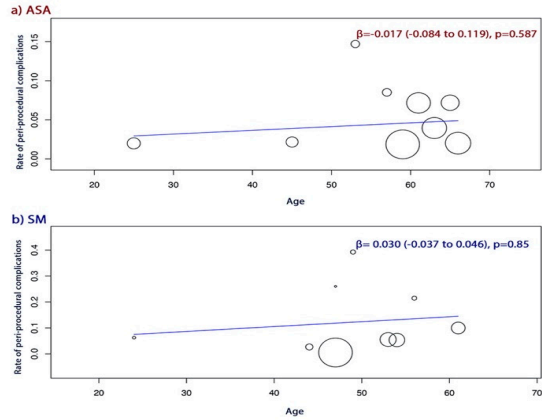


b) LA size mean change; a) ASA group; b) SM group

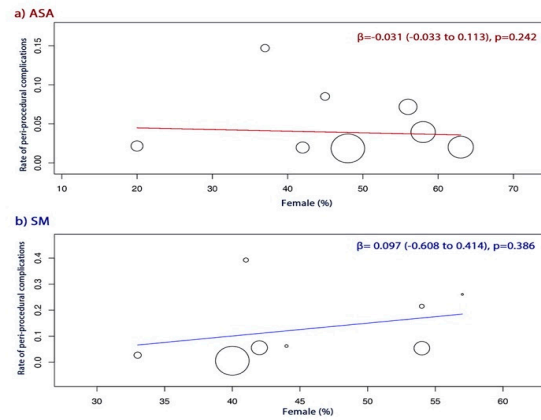


**Figure S7. Meta-regression for interaction of age, female gender, LVOT and IVSd with peri-procedural complications; a) Age; b) Female; c) LVOT mean reduction; d) IVSd mean reduction.**

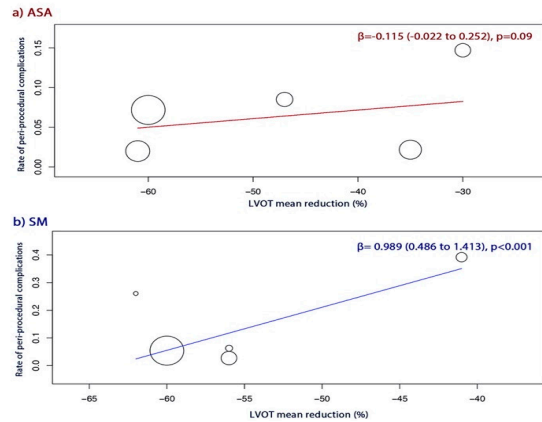
**A) Interaction of age with peri-procedural complications**



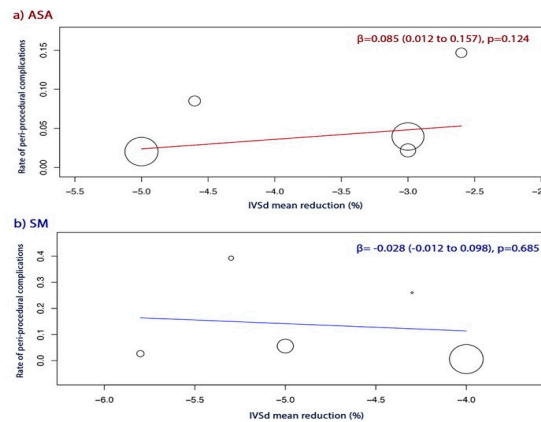
**B) Interaction of female with peri-procedural complications**



**C) Interaction of LVOT mean reduction with peri-procedural complications**

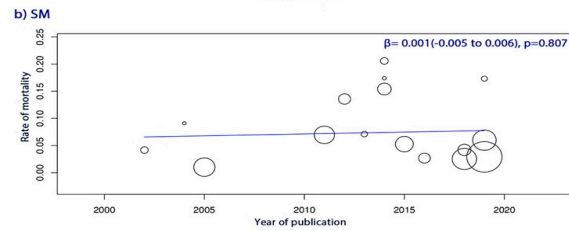
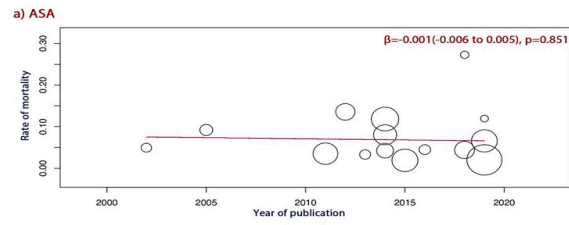


**D) Interaction of IVSd mean reduction with peri-procedural complications**

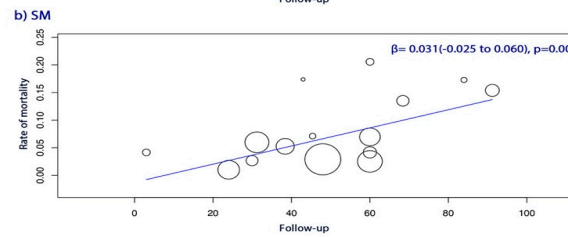
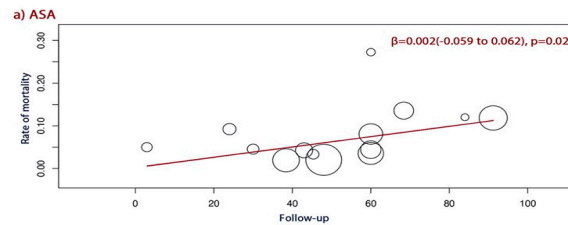


**Figure S8. Meta-regression for interaction of year of publication, follow-up, age and female with all-cause mortality; a) Year of publication; b) follow-up; c) age; d) Female gender**

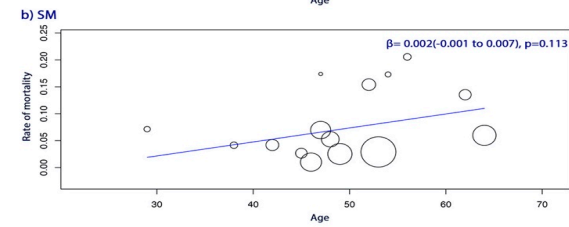
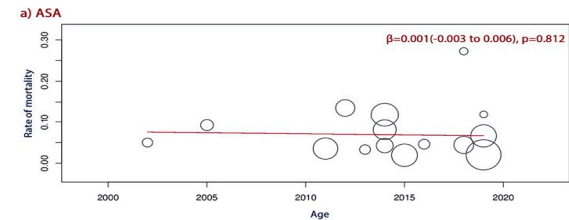
**A) Interaction of year of publication with all-cause mortality**



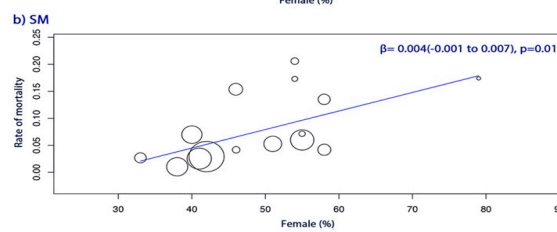
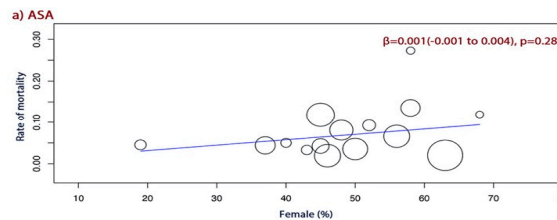
**B) Interaction of follow-up with all-cause mortality**



**C) Interaction of age with all-cause mortality**

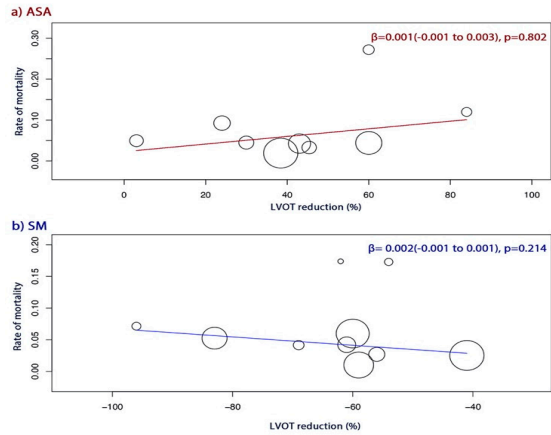


**D) Interaction of gender with all-cause mortality**

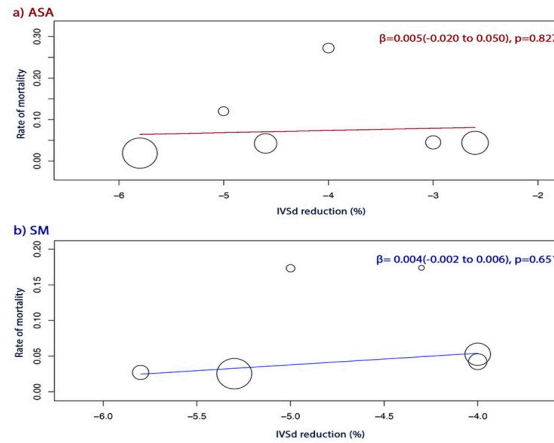


**Figure S9. Meta-regression for interaction of LVOT, IVSd and LA size with all-cause mortality; a) LVOT; b) IVSd; c) LA size;**

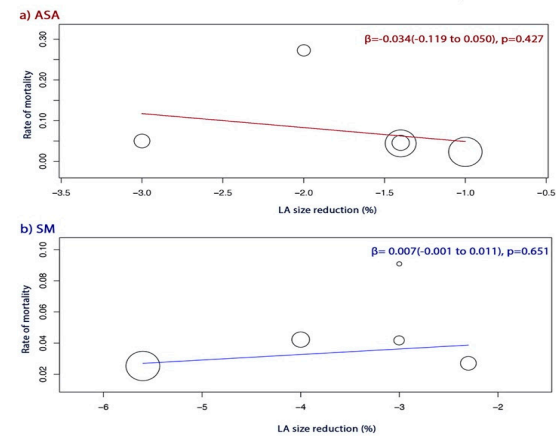
**A) Interaction of LVOT with all-cause mortality**



**B) Interaction of IVSd with all-cause mortality**

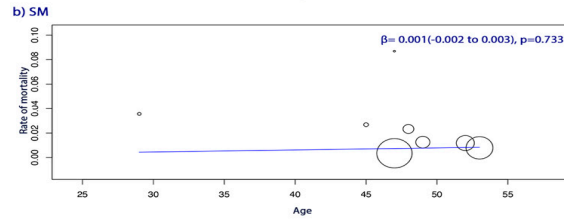
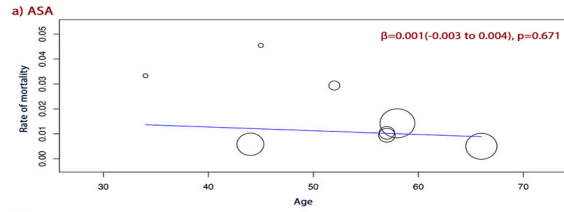


**C) Interaction of LA size with all-cause mortality**

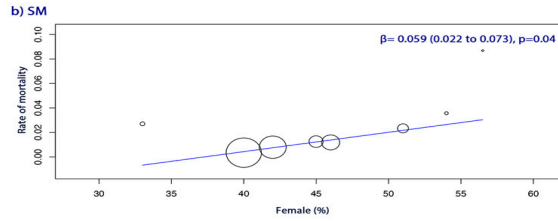
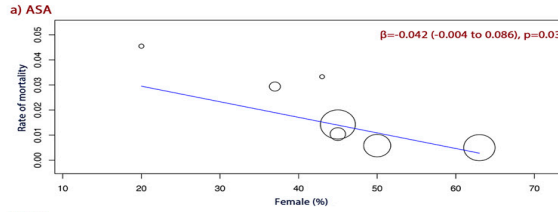


**Figure S10. Meta-regression for interaction of age, female gender, LVOT and IVSd with short-term mortality; a) Age; b) Female; c) LVOT mean reduction; d) IVSd mean reduction.**

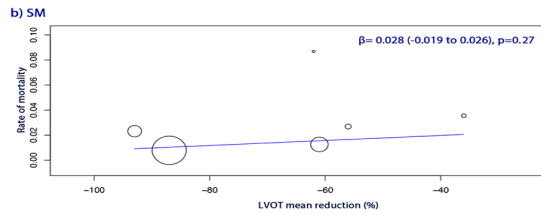
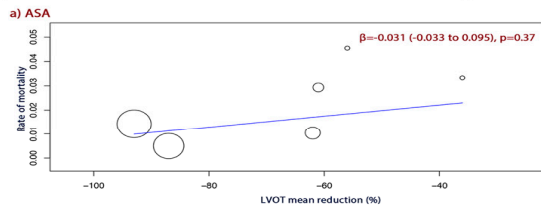
**A) Interaction of age with short-term mortality**



**B) Interaction of female with short-term mortality**



**C) Interaction of LVOT mean reduction with short-term mortality**



**D) Interaction of IVSd mean reduction with short-term mortality**

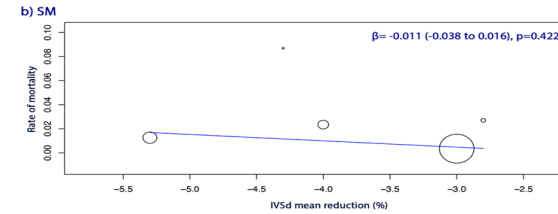
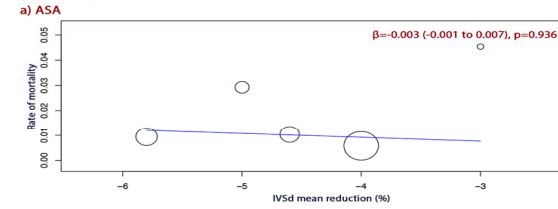


Figure S11. Meta-regression for interaction of age, female gender, LVOT and IVSd with NYHA class; a) Age; b) Female; c) LVOT mean reduction; d) IVSd mean reduction.

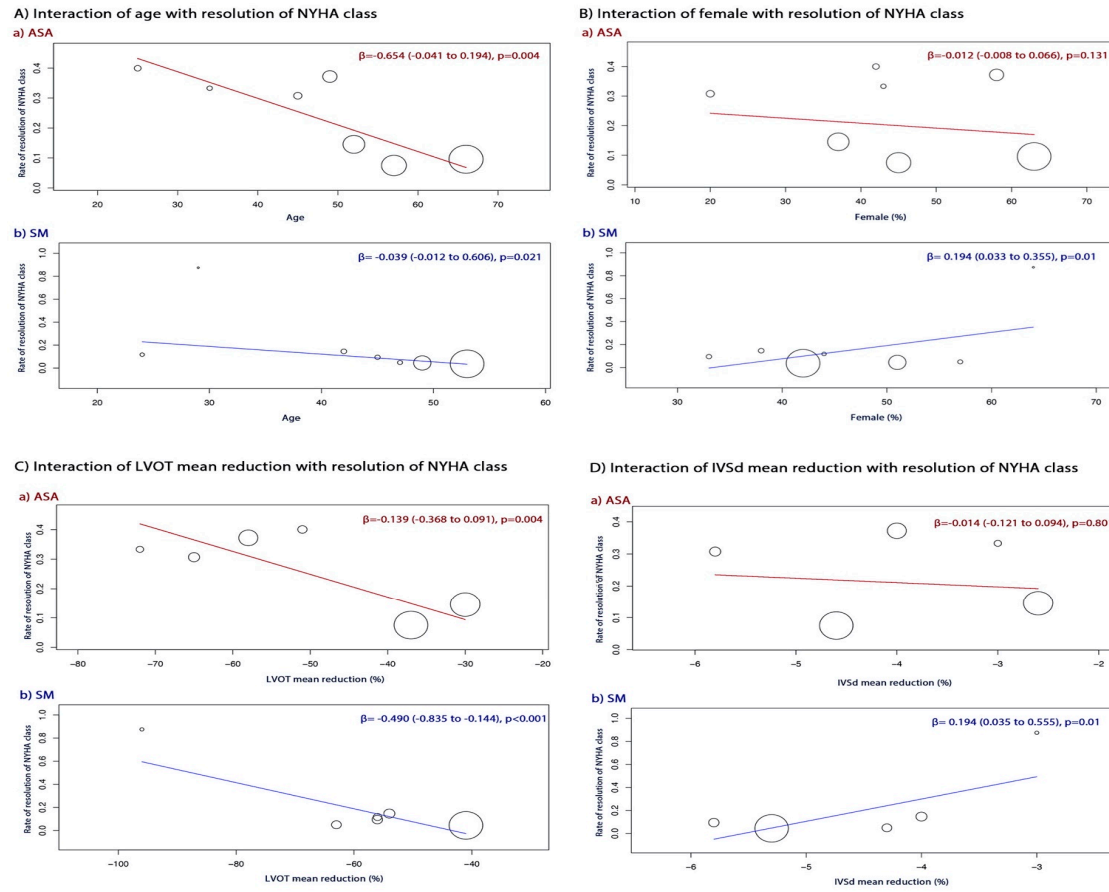
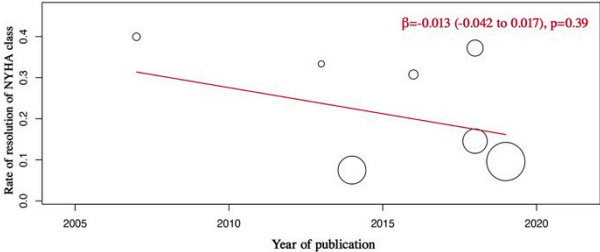


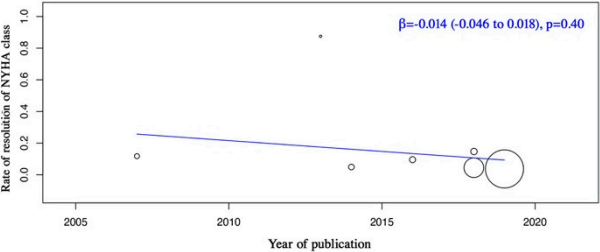
Figure S12. Meta-regression for interaction of year of publication with clinical symptoms A) NYHA class; B) Angina

A) Interaction of year of publication with resolution of NYHA class

a) ASA

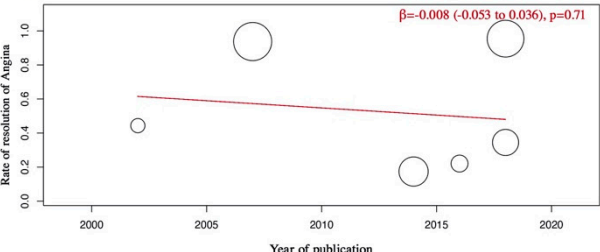


b) SM



B) Interaction of year of publication with resolution of angina

a) ASA



b) SM

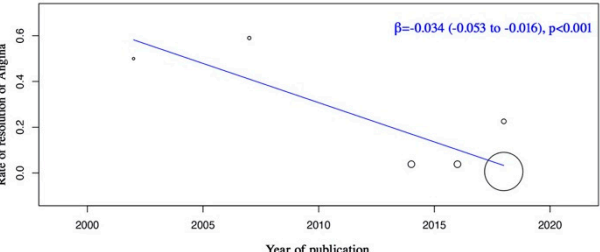


Figure S13. Meta-regression for interaction of age, female gender, LVOT and IVSd with Angina; a) Age; b) Female; c) LVOT mean reduction; d) IVSd mean reduction.

