
SUPPLEMENTAL MATERIAL

Literature search strategy**Embase 1974 to 2015 September 17**

1. exp aorta valve/
2. exp aorta valve stenosis/
3. exp mitral valve/
4. exp mitral valve stenosis/
5. exp mitral valve regurgitation/
6. valvular heart disease/
7. (left adj2 valv*).af.
8. (native adj2 valve*).af.
9. (mitral adj2 valve*).af.
10. (aortic adj2 valve*).af.
11. or/1-10
12. exp pregnancy/
13. exp pregnancy complication/
14. exp pregnancy outcome/
15. exp Apgar score/
16. exp birth weight/
17. exp crown rump length/
18. (exp body weight/ or ((body adj2 weight) or (body adj2 length)).mp.) and infant/
19. crown-rump.tw.
20. (birth weight or birthweight).tw.
21. (apgar adj2 score*).tw.
22. (fetal* adj2 outcome).tw.
23. (obstetric* adj2 (complication* or outcome*)).tw.
24. pregnan*.tw.
25. or/12-24
26. 11 and 25
27. (exp animals/ or exp animal experimentation/ or nonhuman/) not ((exp animals/ or exp animal experimentation/ or nonhuman/) and exp human/)
28. 26 not 27
29. limit 28 to (book or book series or conference abstract or conference paper or conference proceeding or "conference review" or letter or note or short survey or trade journal)
30. 28 not 29
31. limit 30 to yr="1985 -Current"

MEDLINE(R) 1946 to Present September 17, 2015

1. exp Pregnancy/
2. Pregnancy Complications/
3. exp Pregnancy Outcome/
4. exp Apgar Score/
5. exp Birth Weight/

6. exp crown-rump length/
7. pregnan*.tw.
8. (obstetric* adj2 outcome*).tw.
9. (fet* adj2 outcome*).tw.
10. (apgar adj2 score*).tw.
11. (birthweight or birth weight).tw.
12. crown-rump*.tw.
13. (exp Body Weight/ or ((body adj2 weight) or (body adj2 length)).mp.) and infant/
14. or/1-13
15. exp Aortic Valve/
16. exp Aortic Valve Stenosis/
17. exp Mitral Valve/
18. exp mitral valve stenosis/
19. exp mitral valve insufficiency/
20. Heart Valve Diseases/
21. (left adj2 valv*).af.
22. (native adj2 valve*).af.
23. (mitral adj2 valv*).af.
24. (aortic adj2 valv*).af.
25. or/15-24
26. 14 and 25
27. animals/ not (animals/ and humans/)
28. 26 not 27
29. limit 28 to yr="1985 -Current"

Supplementary Table 1: Description of Excluded Studies

Number	Name	Year	Country	Reason for exclusion	Notes
1	Abdi	2012	Iran	All patients underwent intervention	Case series of PMBV
2	Abid	1990	Tunisia	All patients underwent intervention	Case series of closed mitral commissurotomy
3	Abouziad	2001	USA	All patients underwent intervention	Case series of PMBV
4	Aggarwal	2004	India	All patients underwent intervention	Case series of closed mitral commissurotomy
5	Aka	2015	Turkey	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
6	Akhter	2011	Bangladesh	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
7	Ali Oto	1997	Turkey	Less than 5 cases	
8	Arnoni	2003	Brazil	All patients underwent intervention	Case series of cardiac surgery in pregnancy
9	Aroni	2003	Brazil	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
10	Arora	2002	India	All patients underwent intervention	Case series of PMBV
11	Bachowski	1996	Poland	Less than 5 cases	
12	Banning	1993	UK	Less than 5 cases	
13	Ben Farhat	1997	Tunisia	Duplicate Data	Duplicate data/overlap to Ben Farhat 1997, Gamra 2007
14	Ben Farhat	1995	Tunisia	Duplicate Data	Duplicate data/overlap to Ben Farhat 1997
15	Bernard	1991	France	Not population of interest	Non-pregnant patients
16	Bhatla	2003	India	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion

17	Birincioglu	1999	Turkey	All patients underwent intervention	Case series of closed mitral commissurotomy and mitral valve replacement.
18	Birincioglu	2014	Turkey	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
19	Biswas	2003	India	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
20	Borges	2011	Brazil	No outcome of interest	Structural changes in cardiac chambers with mitral regurgitation in pregnancy. No outcome data.
21	Borna	2006	Iran	Not population of interest	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
22	Chen	2011	Taiwan	Not lesion of interest	Study describes pregnancy in mitral valve prolapse but does not quantify mitral regurgitation
23	Chia	1994	Singapore	Not lesion of interest	Study describes pregnancy in mitral valve prolapse but does not quantify mitral regurgitation
24	Chia	1996	Singapore	Not population of interest	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
25	Chmielak	2011	Poland	All patients underwent intervention	Case series of PMBV
26	Cornette	2013	Netherlands	Not population of interest	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
27	Dawson	2012	USA	Less than 5 cases	
28	Del Castillo	1992	Brazil	All patients underwent intervention	Case series of PMBV
29	DeSouza	2001	Brazil	All patients underwent intervention	Case series of PMBV and open mitral commissurotomy
30	Devabhaktuni	2010	India	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion

31	Dob	2001	UK	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
32	Dommissie	1996	South Africa	All patients underwent intervention	Case series of PMBV
33	Doshi	2010	India	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
34	Drenthen	2010	ZAHARA	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
35	Elassy	2014	Egypt	Less than 5 cases	
36	Esteves	2006	Brazil	All patients underwent intervention	Case series of PMBV
37	Esteves	1991	Brazil	Duplicate Data	Duplicate data/overlap to Esteves 2006
38	Faiz	2003	Saudi Arabia	Insufficient data obtained	Did not grade valve severity or separate outcomes based on valve lesion
39	Farhat	1992	Tunisia	Duplicate Data	Duplicate data/overlap to Ben Farhat 1997 , Gamra 2006
40	Fawzy	2001	Saudi Arabia	All patients underwent intervention	Case series of PMBV
41	Fawzy	1996	Saudi Arabia	All patients underwent intervention	Case series of PMBV but no pregnancy outcomes recorded.
42	Gamra	2006	Tunisia	All patients underwent intervention	Case series of PMBV
43	Goon	1987	Malaysia	All patients underwent intervention	Case series of closed mitral commissurotomy
44	Gulraze	2014	Saudi Arabia	Duplicate Data	Duplicate data/overlap to Fawzy 2001
45	Gupta	1998	India	All patients underwent intervention	Case series of PMBV
46	Haththotuwa	2009	Sri Lanka	Not population of interest	Data reported a series of maternal deaths
47	Hiralal	2012	India	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion

48	Hosseinzadeh	2018	Iran	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
49	Hsieh	1993	Taiwan	Insufficient data obtained	Only evaluated rheumatic heart disease and mitral valve prolapse but did not specify lesion or severity.
50	Imani	2013	Iran	Not population of interest	Did not grade valve severity or separate outcomes based on valve lesion
51	Iskan	2006	Turkey	All patients underwent intervention	Case series of cardiac surgery in pregnancy
52	Isogal	2018	Japan	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
53	Jahangiri	2003	UK	Not lesion of interest	Case series of re-do aortic valve replacement and ascending aorta replacement
54	Jain	2013	India	Insufficient data obtained	Did not grade valve severity or separate outcomes based on valve lesion
55	John	2011	USA	Less than 5 cases	
56	Joshi	2015	India	All patients underwent intervention	Case series of PMBV
57	Karabulut	2010	Iran	Not population of interest	Data on maternal deaths in pregnancy not representative population of valvular heart disease in pregnancy
58	Karla	1994	India	All patients underwent intervention	Case series of PMBV
59	Khursheed	2015	India	Insufficient data obtained	Did not grade valve severity or separate outcomes based on valve lesion
60	Kinsara	2002	Saudi Arabia	All patients underwent intervention	Case series of PMBV
61	Konar	2012	India	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
62	Koregol	2009	India	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion

63	Kotrolou-Sotriopoulou	2015	USA	Insufficient data obtained	Data grouped. Outcome not specifically linked to lesion
64	Kuczkowski	2004	USA	Less than 5 cases	
65	Langford	2009	UK	Less than 5 cases	
66	Lao	1993	Canada	Duplicate Data	Duplicate data/overlap to Silversides 2003
67	Lao	1993	Canada	Less than 5 cases	
68	Lerman	2013	Israel	Not lesion of interest	Discussed mitral valve prolapse and mitral regurgitation but did not quantify regurgitation or isolate outcomes
69	Lesniak	1999	Poland	Duplicate Data	Duplicate data/overlap to Lesniak-Sobelga 2004
70	Lewis	2002	UK	Insufficient data obtained	Did not separate outcomes based on severity of valve lesion.
71	Liu	2012	China	Insufficient data obtained	Mixed population of heart disease. Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
72	Liu	2010	China	Insufficient data obtained	Mixed population of heart disease. Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
73	Lung	1993	France	All patients underwent intervention	Case series of PMBV
74	Lung	2000	France	Less than 5 cases	
75	Madazili	2010	Turkey	Insufficient data obtained	Mixed population of heart disease. Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
76	Mahoori	2007	Iran	All patients underwent intervention	Case series of cardiac surgery in pregnancy
77	Malhorta	2004	India	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
78	Malhotra	2006	UK	Insufficient data obtained	Pooled data on maternal deaths. No specific outcomes for specific valve lesions.

					Reported total 8 cases of valvular heart disease.
79	Malhotra	2003	India	Insufficient data obtained	Did not grade valve severity or separate outcomes based on valve lesion
80	Mangione	2000	Brazil	All patients underwent intervention	Case series of PMBV
81	Mangione	1989	Brazil	Duplicate Data	Duplicate data/overlap to Mangione 2000
82	Martinez-Reding	1998	Mexico	All patients underwent intervention	Case series of PMBV
83	Matorras	1986	Spain	Insufficient data obtained	Patients with mitral stenosis who underwent intervention. Did not quantify severity of valve disease.
84	McCredie	1998	Australia	Not population of interest	Outcomes of pregnancies not provided.
85	McKeller	2011	USA	No outcome of interest	Evaluated patients with bicuspid aortic valve in pregnancy and lifetime dissection risk. Did not quantify valve severity.
86	Merz	2011	Germany	Insufficient data obtained	Data grouped. Outcome not specifically linked to lesion
87	Meyer	1994	USA	Insufficient data obtained	Data grouped. Outcome not specifically linked to lesion
88	Mishra	2001	India	All patients underwent intervention	Case series of PMBV with no outcome data
89	Motiang	2017	South Africa	Not population of interest	Only included obstetric cases admitted to ICU. Not specifically valvular heart disease.
90	Nercolini	2002	Brazil	All patients underwent intervention	Case series of PMBV
91	Ngan	1999	China	Less than 5 cases	
92	Nqayana	2008	South Africa	Insufficient data obtained	Did not grade valve severity or separate outcomes based on valve lesion
93	Oliveria	1996	Brazil	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
94	Ordenoglu	1995	Turkey	Less than 5 cases	

95	Orme	2003	UK	Less than 5 cases	
96	Oto	1997	Turkey	Less than 5 cases	
97	Patel	1993	South Africa	All patients underwent intervention	Case series of PMBV
98	Patel	2015	USA	Insufficient data obtained	Retrospective review of stillbirths. Does not breakdown type of maternal valve disease.
99	Pavankumar	1988	India	All patients underwent intervention	Case series of closed mitral commissurotomy
100	Pijuan-Domenech	2015	Spain	Insufficient data obtained	Mixed population of heart disease. Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
101	Rahman	2000	Saudi Arabia	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
102	Rezk	2016	Egypt	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
103	Rezk	2016	Egypt	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
104	Rezk	2018	Egypt	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
105	Riberio	1992	Saudi Arabia	All patients underwent intervention	Case series of PMBV
106	Rooh-Hesslink	2006		No outcome of interest	Literature review
107	Roos-Hesselink	2013	ROPAC	Insufficient data obtained	Mixed population of heart disease. Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
108	Rose	1987	USA	Less than 5 cases	
109	Routray	2003	India	All patients underwent intervention	Case series of PMBV

110	Ruys	2014	ROPAC	Insufficient data obtained	Data grouped. Outcome not specifically linked to lesion
111	Ruys	2014	ROPAC	Insufficient data obtained	Data grouped. Outcome not specifically linked to lesion
112	Ruzyllo	1992	Poland	Duplicate Data	Duplicate data/overlap to Chmielak 2011
113	Salehi	2013	Iran	All patients underwent intervention	Case series of PMBV
114	Salome	2002	Portugal	Less than 5 cases	
115	Samiei	2016	Iran	No outcome of interest	Imaging outcomes. Did not link severity of lesion to outcome of interest.
116	Santacesaria	2016	Italy	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
117	Sartain	2012	Australia	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
118	Savzivand	2016	Iran	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
119	Sawhney	2002	India	All patients underwent intervention	Case series of closed mitral commisurotomy and PMBV
120	Sayeeda	2008	Bangladesh	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
121	Schoon	1997	South Africa	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
122	Senanes	1994	France	Duplicate Data	Duplicate data/overlap to Lung 1993
123	Shapiro	1985	USA	Not lesion of interest	Study describes pregnancy in mitral valve prolapse but does not report mitral regurgitation or degree
124	Sharma	2017	Nepal	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
125	Shime	1987	Canada	Insufficient data obtained	Did not grade valve severity or separate outcomes based on valve lesion

126	Sidik	2006	Israel	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
127	Sirithaweessit	2014	Thailand	Insufficient data obtained	Did not grade valve severity or separate outcomes based on valve lesion
128	Siu	1997	Canada	Duplicate Data	Duplicate data/overlap to Silversides 2003
129	Siu	2001	Canada	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
130	Sivadasanpillai	2005	India	All patients underwent intervention	Case series of PMBV
131	Soma-Pillay	2008	South Africa	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
132	Stephen	1992	Sri Lanka	All patients underwent intervention	Case series of closed mitral commisurotomy
133	Subbaiah	2013	India	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
134	Subbarao	2004	India	All patients underwent intervention	Case series of mitral commisurotomy
135	Sugishita	1986	Japan	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
136	Suntharalingam	2000	UK	Less than 5 cases	
137	Taha	2012	Egypt	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
138	Takana	1986	Japan	Insufficient data obtained	Mixed population of heart disease. Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
139	Tang	1985	China	Not lesion of interest	Reported on mitral prolapse only, no quantification of mitral regurgitation

140	Tanous	2010	Canada	Insufficient data obtained	Mixed population of heart disease. Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
141	Trehan	2005	India	No outcome of interest	Pregnant patients with MS, reported PMBV outcome but did not report obstetric or neonatal outcomes.
142	Turan	2012	Turkey	Not lesion of interest	Only mild to moderate mitral stenosis evaluated. Did not separate outcomes based on severity of valve lesion.
143	Tzemoz	2009	Canada	Duplicate Data	Duplicate data/overlap to Silversides 2003. This paper did not provide obstetric/neonatal outcomes.
144	Vosloo	1987	South Africa	All patients underwent intervention	Case series of closed mitral commissurotomy
145	Wu	2016	China	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
146	Yaghoubi	2013	Iran	Insufficient data obtained	Data grouped and severity of valve disease not provided. Outcome not specifically linked to lesion
147	Yates	2014	UK	Less than 5 cases	
148	Ziskind	1990	Israel	All patients underwent intervention	Case series of emergency cesarean section in mitral stenosis followed by open mitral commissurotomy

PMBV=percutaneous mitral balloon valvuloplasty

Supplementary Table 2: Details of outcomes in mitral stenosis

Outcome	Details
Maternal Death	<ul style="list-style-type: none"> • 1 with severe MS died at 35 weeks of pregnancy from acute heart failure • 2 with severe MS died after percutaneous mitral balloon valvuloplasty during the 2nd trimester of pregnancy <ul style="list-style-type: none"> • 1 from pulmonary edema and hypoxia • 1 from a massive cerebrovascular accident with a known history of atrial fibrillation • 1 with severe MS died from acute respiratory distress after mitral valve replacement surgery during the 2nd trimester of pregnancy • 1 with severe MS died 36 weeks post-partum due to refractory heart failure • 1 with severe MS died 2 weeks after spontaneous abortion complicated by sepsis, atrial fibrillation and cardiogenic shock • 1 with moderate MS died 2 weeks post-partum during cardiac arrest after developing severe abdominal pain and dyspnea. She had developed atrial fibrillation and was started on heparin but this was stopped due to hemorrhage of the cesarean section wound
Stillbirth	<ul style="list-style-type: none"> • 3 were related to maternal death post intervention for severe MS • 1 was attributed to delayed PMBV in severe MS • 1 was due to placental abruption in a case of severe MS • 1 occurred in the setting of persistent symptomatic severe MS. • 2 occurred in association with maternal pulmonary edema (one in moderate and one in severe MS) • 3 were attributed to fetal SGA status in mothers with moderate MS • details were unavailable for 6 (four with moderate and two with severe MS)
Neonatal Death	<ul style="list-style-type: none"> • 1 death occurred in a preterm infant due to respiratory distress (days of life at death was not reported) • 1 death occurred in an infant at day seven of life (GA at delivery was not provided) • 2 deaths were not incorporated into the analysis as the study did not clearly report maternal MS severity grade.¹⁸ <ul style="list-style-type: none"> • One infant was born prematurely at 34 weeks GA and died at one week of life from pneumonia. • 1 death occurred in an infant born at 26 weeks GA by cesarean section due to fetal distress. They were admitted to the NICU with ARDS and died within 1 week.

ARDS = acute respiratory distress syndrome, GA=gestational age, MS=mitral stenosis, NICU = neonatal intensive care unit, PMBV = percutaneous mitral balloon valvuloplasty, SGA=small for gestational age

Supplementary Table 3: Details of outcomes in aortic stenosis

Outcome	Details
Maternal Death	<ul style="list-style-type: none"> • 1 died with undiagnosed severe AS during cardiopulmonary arrest at the time of cesarean delivery • 1 died 10 days postpartum at the time of aortic valve replacement
Stillbirth	<ul style="list-style-type: none"> • 1 occurred in a mother with undiagnosed severe AS during cardiopulmonary arrest at the time of cesarean delivery <p>(2 miscarriages in mothers with moderate AS were reported before 24 weeks but the exact gestation at the time of fetal demise was not specified)</p>
Neonatal Death	<ul style="list-style-type: none"> • 1 death occurred secondary to respiratory distress in a small for gestational age infant who was delivered at 30 weeks gestational age by cesarean delivery from a mother with severe AS

AS=aortic stenosis

Supplementary Table 4: Quality Assessment of Included Studies using the Newcastle-Ottawa Scale for Observational Studies

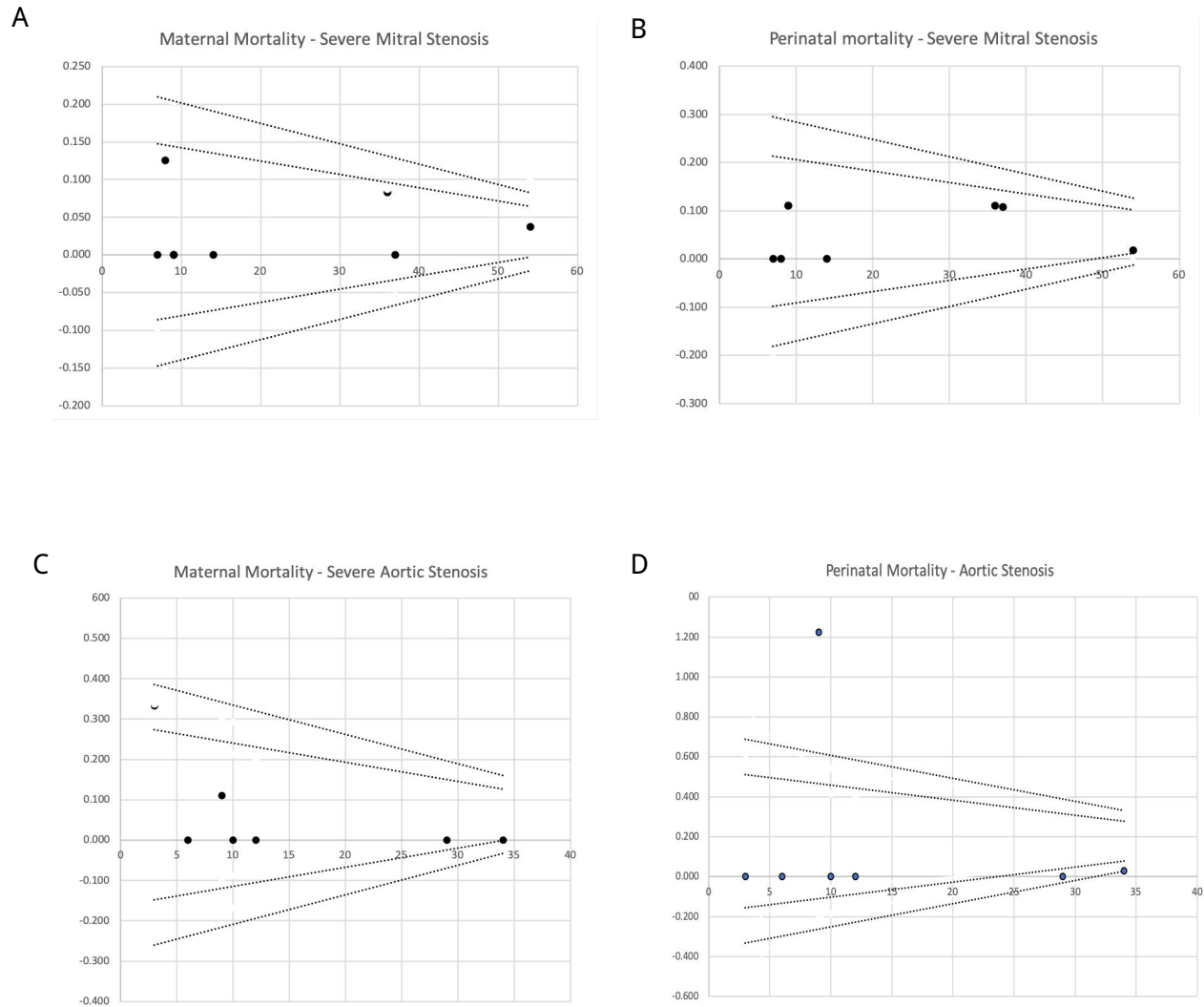
Cohort Studies

Study Name	Year published	Representativeness	Selection	Exposure	Outcome not at start	Comparability	Outcome	Follow-up length	Follow-up cohort	Score (maximum 8)
Al Kasab	1990	*		*	*		*		*	5
Clark	1985			*			*	*	*	4
Desai	2000	*		*			*		*	4
Gumrukcuoglu	2013	*		*			*		*	4
Ioscovich	2009	*		*			*		*	4
Lesniak-Sobelga	2004	*		*	*		*	*	*	6
Orwat	2016	*		*	*		*		*	5
Silversides - AS	2003	*		*	*		*	*	*	6
Silversides - MS	2003	*		*	*		*	*	*	6
Yap	2008	*		*	*		*	*	*	6
Van Hagen	2018	*		*	*		*			4

Case Control Study

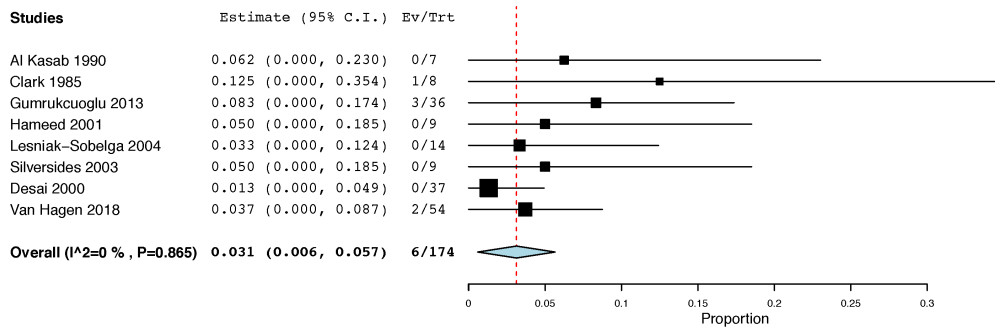
Study Name	Year published	Definition	Representativeness	Selection/Controls	Definition/Controls	Comparability	Exposure	Exposure Control	Non-Response	Score (maximum 8)
Hameed	2001		*		*		*			3

Supplementary Figures 1: Funnel plots for publication bias in severe mitral and aortic stenosis. Presented plots focused on studies describing the outcome of maternal and fetal mortality in the setting of severe mitral stenosis (A and B respectively), and maternal and fetal mortality in the setting of severe aortic stenosis (C and D respectively). No clear publication bias was identified.

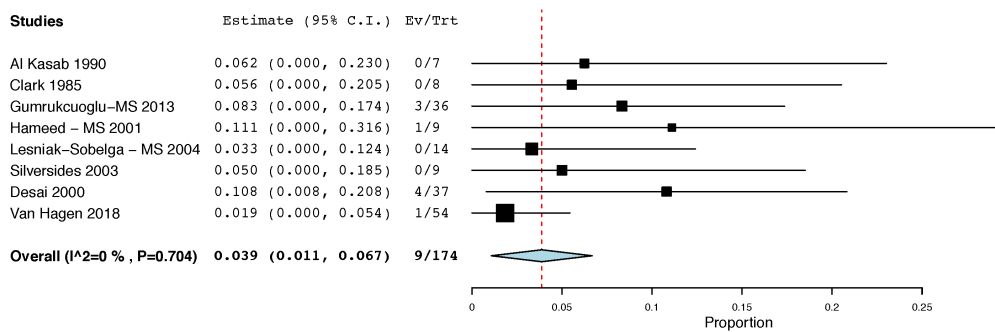


Supplementary figure 2: Forest plots for maternal and fetal death in severe mitral and aortic stenosis studies.

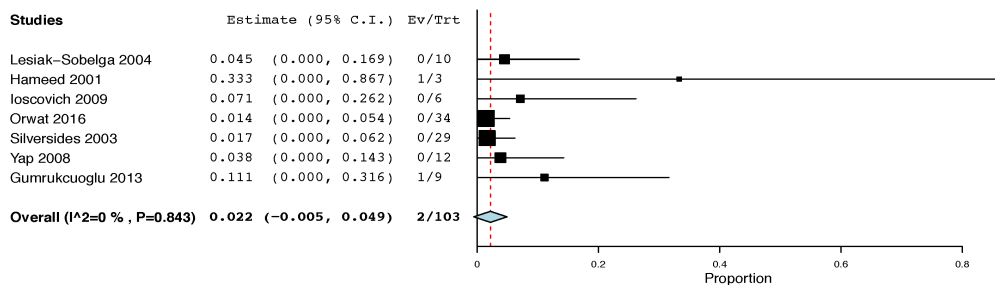
A: Forest plot for severe mitral stenosis and maternal death



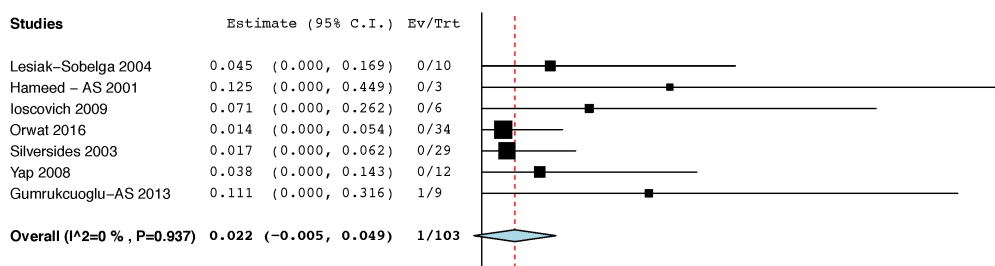
B: Forrest plot for severe mitral stenosis and fetal death



C: Forest plot for severe aortic stenosis and maternal death

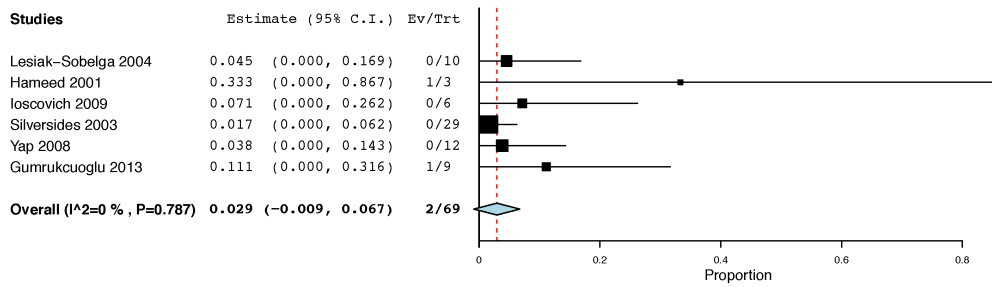


D: Forrest plot for severe aortic stenosis and fetal death



Supplementary figure 3: Forest plots for maternal and fetal death in severe aortic stenosis studies excluding Orwat ROPAC 2016 for their inclusion of prosthetic valves.

A: Forest plot for severe aortic stenosis and maternal death excluding study by Orwat et al.



B: Forest plot for severe aortic stenosis and fetal death excluding study by Orwat et al.

