

Temporal trends in characteristics and outcomes of patients undergoing percutaneous mitral valve repair: a systematic review and meta-analysis
Supplementary tables

Supplementary Table 1. Search strategy and results

Database	Search strategy – from inspection to 31/12/2021	Number of hits
Limits	Trial, Clinical Trial, Article, Human	
PubMed	MitraClip	1,669
	MitraClip AND “mitral valve”	1,487
	“transcatheter mitral valve repair”	588
	“percutaneous mitral valve repair”	500
	“edge-to-edge” AND “mitral valve”	888
	Sub-total	5,132
EMBASE	MitraClip	4,066
	MitraClip AND “mitral valve”	3,915
	“transcatheter mitral valve repair”	1,467
	“percutaneous mitral valve repair”	994
	edge-to-edge” AND “mitral valve”	958
	Sub-total	11,400
Cochrane Library	MitraClip	163
	MitraClip AND “mitral valve”	163
	“transcatheter mitral valve repair”	121
	“percutaneous mitral valve repair”	121
	“edge-to-edge” AND “mitral valve” → 49	49
	Sub-total	340
Manual search		0
Grand total		16,872
Duplicates		9,117
No duplicates		7,755
Conference abstracts		1,765
Papers does not meet inclusion criteria	Irrelevant to topic, case report, reviews, societal guidelines or position statement, correspondence, editorial, letter-to-editor, commentary, animal study, landmark studies or their analyses or related studies, economic study, other devices, corrections, prediction models, surgery, in-vitro study, annuloplasty, imaging, failed MitraClip, MitraClip after failed surgery, robotic procedure, different procedure approach, published online before 2020	5,860
Full text		130
Excluded		54
Studies for sensitivity analysis		15
Included studies		61

Supplementary Table 2. Excluded studies

1.	Scandura S, Ussia GP, Capranzano P, et al. Left cardiac chambers reverse remodeling after percutaneous mitral valve repair with the MitraClip system. <i>J Am Soc Echocardiogr.</i> 2012;25(10):1099-1105. doi:10.1016/j.echo.2012.07.015
2.	Grasso C, Capodanno D, Scandura S, et al. One- and twelve-month safety and efficacy outcomes of patients undergoing edge-to-edge percutaneous mitral valve repair (from the GRASP Registry). <i>Am J Cardiol.</i> 2013;111(10):1482-1487. doi:10.1016/j.amjcard.2013.01.300
3.	Guarracino F, Ferro B, Baldassarri R, et al. Non invasive evaluation of cardiomechanics in patients undergoing MitrClip procedure. <i>Cardiovasc Ultrasound.</i> 2013;11:13. Published 2013 May 4. doi:10.1186/1476-7120-11-13
4.	Schmidt FP, von Bardeleben RS, Nikolai P, et al. Immediate effect of the MitraClip procedure on mitral ring geometry in primary and secondary mitral regurgitation. <i>Eur Heart J Cardiovasc Imaging.</i> 2013;14(9):851-857. doi:10.1093/ehjci/jes293
5.	Melisurgo G, Ajello S, Pappalardo F, et al. Afterload mismatch after MitraClip insertion for functional mitral regurgitation. <i>Am J Cardiol.</i> 2014;113(11):1844-1850. doi:10.1016/j.amjcard.2014.03.015
6.	Taramasso M, Denti P, Buzzatti N, et al. Mitraclip therapy and surgical mitral repair in patients with moderate to severe left ventricular failure causing functional mitral regurgitation: a single-centre experience. <i>Eur J Cardiothorac Surg.</i> 2012;42(6):920-926. doi:10.1093/ejcts/ezs294
7.	Vitarelli A, Mangieri E, Capotosto L, et al. Assessment of Biventricular Function by Three-Dimensional Speckle-Tracking Echocardiography in Secondary Mitral Regurgitation after Repair with the MitraClip System. <i>J Am Soc Echocardiogr.</i> 2015;28(9):1070-1082. doi:10.1016/j.echo.2015.04.005
8.	Ohno Y, Attizzani GF, Capodanno D, et al. Association of tricuspid regurgitation with clinical and echocardiographic outcomes after percutaneous mitral valve repair with the MitraClip System: 30-day and 12-month follow-up from the GRASP Registry. <i>Eur Heart J Cardiovasc Imaging.</i> 2014;15(11):1246-1255. doi:10.1093/ehjci/jeu114
9.	Bednar F, Budesinsky T, Linkova H, Kocka V. Invasive Hemodynamic Assessment of Cardiac Output State after MitraClip Therapy in Nonanaesthetized Patients with Functional Mitral Regurgitation. <i>Biomed Res Int.</i> 2016;2016:6296972. doi:10.1155/2016/6296972
10.	De Bonis M, Taramasso M, Lapenna E, et al. MitraClip therapy and surgical edge-to-edge repair in patients with severe left ventricular dysfunction and secondary mitral regurgitation: mid-term results of a single-centre experience†. <i>Eur J Cardiothorac Surg.</i> 2016;49(1):255-262. doi:10.1093/ejcts/ezv043
11.	De Bonis M, Lapenna E, Buzzatti N, et al. Optimal results immediately after MitraClip therapy or surgical edge-to-edge repair for functional mitral regurgitation: are they really stable at 4 years?. <i>Eur J Cardiothorac Surg.</i> 2016;50(3):488-494. doi:10.1093/ejcts/ezw093
12.	Giannini C, Fiorelli F, Colombo A, et al. Right ventricular evaluation to improve survival outcome in patients with severe functional mitral regurgitation and advanced heart failure undergoing MitraClip therapy. <i>Int J Cardiol.</i> 2016;223:574-580. doi:10.1016/j.ijcard.2016.08.189
13.	Hidalgo F, Mesa D, Ruiz M, et al. Effects of Mitral Annulus Remodeling Following MitraClip Procedure on Reduction of Functional Mitral Regurgitation. <i>Rev Esp Cardiol (Engl Ed).</i> 2016;69(11):1020-1025. doi:10.1016/j.rec.2016.04.003
14.	Ondrus T, Bartunek J, Vanderheyden M, et al. Minimally invasive mitral valve repair for functional mitral regurgitation in severe heart failure: MitraClip versus minimally invasive surgical approach. <i>Interact Cardiovasc Thorac Surg.</i> 2016;23(5):784-789. doi:10.1093/icvts/ivw215
15.	Schäfer U, Maisano F, Butter C, et al. Impact of Preprocedural Left Ventricular Ejection Fraction on 1-Year Outcomes After MitraClip Implantation (from the ACCESS-EU Phase I, a Prospective, Multicenter, Nonrandomized Postapproval Study of the MitraClip Therapy in Europe). <i>Am J Cardiol.</i> 2016;118(6):873-880. doi:10.1016/j.amjcard.2016.06.036
16.	Giannini C, Petronio AS, Fiorelli F, et al. Effects of levosimendan in patients with severe functional mitral regurgitation undergoing MitraClip implantation. <i>J Cardiovasc Med (Hagerstown).</i> 2017;18(9):679-686. doi:10.2459/JCM.0000000000000537
17.	Pighi M, Estevez-Loureiro R, Maisano F, et al. Immediate and 12-Month Outcomes of Ischemic Versus Nonischemic Functional Mitral Regurgitation in Patients Treated With MitraClip (from the 2011 to 2012 Pilot Sentinel Registry of Percutaneous Edge-To-Edge Mitral Valve Repair of the European Society of Cardiology). <i>Am J Cardiol.</i> 2017;119(4):630-637. doi:10.1016/j.amjcard.2016.10.049
18.	Rohm I, Poerner TC, Hamadanchi A, et al. Quantification of mitral regurgitation during percutaneous mitral valve repair: added value of simultaneous hemodynamic and 3D echocardiographic assessment. <i>Int J Cardiovasc Imaging.</i> 2017;33(10):1531-1539. doi:10.1007/s10554-017-1153-8 - No enough information
19.	Seeger J, Müller P, Gonska B, et al. Percutaneous Mitral Valve Repair With the MitraClip in Primary Compared With Secondary Mitral Valve Regurgitation Using the Mitral Valve Academic Research Consortium Criteria. <i>J Invasive Cardiol.</i> 2017;29(4):145-150.
20.	Schmidt T, Schlüter M, Thielsen T, et al. Acute Hemodynamic Changes after Mitraclip Implantation Comparing Patients with Degenerative and Functional Mitral Regurgitation. <i>Structural Heart.</i> 2017;1(3-4):188-194. ISSN 2474-8706.

21.	Schueler R, Kaplan S, Melzer C, et al. Impact of interventional edge-to-edge repair on mitral valve geometry. <i>Int J Cardiol.</i> 2017;230:468-475. doi:10.1016/j.ijcard.2016.12.081
22.	Avenatti E, Little SH, Barker CM, Nagueh SF. Changes in Left Atrial Function After Transcatheter Mitral Valve Repair. <i>Am J Cardiol.</i> 2018;122(7):1204-1209. doi:10.1016/j.amjcard.2018.06.031 - No enough information
23.	Kamperidis V, van Wijngaarden SE, van Rosendaal PJ, et al. Mitral valve repair for secondary mitral regurgitation in non-ischaemic dilated cardiomyopathy is associated with left ventricular reverse remodelling and increase of forward flow. <i>Eur Heart J Cardiovasc Imaging.</i> 2018;19(2):208-215. doi:10.1093/ehjci/jex011
24.	Mantegazza V, Pasquini A, Agati L, et al. Comprehensive Assessment of Mitral Valve Geometry and Cardiac Remodeling With 3-Dimensional Echocardiography After Percutaneous Mitral Valve Repair. <i>Am J Cardiol.</i> 2018;122(7):1195-1203. doi:10.1016/j.amjcard.2018.06.036
25.	Stolfo D, De Luca A, Morea G, et al. Predicting device failure after percutaneous repair of functional mitral regurgitation in advanced heart failure: Implications for patient selection. <i>Int J Cardiol.</i> 2018;257:182-187. doi:10.1016/j.ijcard.2018.01.009
26.	Adamo M, Godino C, Giannini C, et al. Left ventricular reverse remodelling predicts long-term outcomes in patients with functional mitral regurgitation undergoing MitraClip therapy: results from a multicentre registry. <i>Eur J Heart Fail.</i> 2019;21(2):196-204. doi:10.1002/ehf.1343
27.	Baldi C, Citro R, Silverio A, et al. Predictors of outcome in heart failure patients with severe functional mitral regurgitation undergoing MitraClip treatment. <i>Int J Cardiol.</i> 2019;284:50-58. doi:10.1016/j.ijcard.2018.10.055
28.	Buzzatti N, Denti P, Scarfò IS, et al. Mid-term outcomes (up to 5 years) of percutaneous edge-to-edge mitral repair in the real-world according to regurgitation mechanism: A single-center experience. <i>Catheter Cardiovasc Interv.</i> 2019;94(3):427-435. doi:10.1002/ccd.28029
29.	Cimino S, Maestrini V, Cantisani D, et al. Mid-term repair durability after MitraClip implantation in patients with functional mitral regurgitation. <i>J Cardiovasc Med (Hagerstown).</i> 2019;20(10):701-708. doi:10.2459/JCM.0000000000000846
30.	De Luca A, Stolfo D, Caiffa T, et al. Prognostic Value of Global Longitudinal Strain-Based Left Ventricular Contractile Reserve in Candidates for Percutaneous Correction of Functional Mitral Regurgitation: Implications for Patient Selection. <i>J Am Soc Echocardiogr.</i> 2019;32(11):1436-1443. doi:10.1016/j.echo.2019.07.006
31.	Kitamura M, Kaneko H, Schlüter M, et al. Predictive impact of previous coronary artery bypass grafting on mortality after MitraClip implantation for ischemic functional mitral regurgitation. <i>Int J Cardiol.</i> 2019;285:21-26. doi:10.1016/j.ijcard.2019.02.045
32.	Sanchis L, Freixa X, Regueiro A, Perdomo JM, Sabaté M, Sitges M. Safety and outcomes of MitraClip implantation in functional mitral regurgitation according to degree of left ventricular dysfunction. <i>Rev Esp Cardiol (Engl Ed).</i> 2020;73(7):530-535. doi:10.1016/j.rec.2019.06.002
33.	Öztürk C, Friederich M, Nickenig G, Hammerstingl C, Schueler R. Single-center five-year outcomes after interventional edge-to-edge repair of the mitral valve. <i>Cardiol J.</i> 2021;28(2):215-222. doi: 10.5603/CJ.a2019.0071. Epub 2019 Jul 17. PMID: 31313274; PMCID: PMC8078937.
34.	Utsunomiya H, Itabashi Y, Kobayashi S, et al. Comparison of mitral valve geometrical effect of percutaneous edge-to-edge repair between central and eccentric functional mitral regurgitation: clinical implications. <i>Eur Heart J Cardiovasc Imaging.</i> 2019;20(4):455-466. doi:10.1093/ehjci/jez117 – Included patients from the EVEREST II trial (n = 20) and the COAPT trial (n = 37) trials.
35.	Ikenaga H, Hayashi A, Nagaura T, et al. Relation Between Pulmonary Venous Flow and Left Atrial Pressure During Percutaneous Mitral Valve Repair With the MitraClip. <i>Am J Cardiol.</i> 2018;122(8):1379-1386. doi:10.1016/j.amjcard.2018.06.047 - Included patients from REALISM registry (a continued-access registry of EVEREST II clinical trial (n = 66) and the COAPT Failure Patients with Functional Mitral Regurgitation) trial (n = 29).
36.	Adamo M, Cani DS, Gavazzoni M, et al. Impact of disproportionate secondary mitral regurgitation in patients undergoing edge-to-edge percutaneous mitral valve repair. <i>EuroIntervention.</i> 2020;16(5):413-420. doi:10.4244/EIJ-D-19-01114
37.	Alachkar MN, Kirschfink A, Grebe J, et al. General Anesthesia Leads to Underestimation of Regurgitation Severity in Patients With Secondary Mitral Regurgitation Undergoing Transcatheter Mitral Valve Repair [published online ahead of print, 2021 Oct 20]. <i>J Cardiothorac Vasc Anesth.</i> 2021;S1053-0770(21)00942-3. doi:10.1053/j.jvca.2021.10.024
38.	Alperi A, Avanzas P, Pascual I, et al. Functional mitral regurgitation: structural modifications with percutaneous valve repair with MitraClip. <i>Ann Transl Med.</i> 2020;8(15):958. doi:10.21037/atm.2020.03.45
39.	Brugger N, Kassir M, Siontis GCM, et al. Integrative echocardiographic assessment of patients with secondary mitral regurgitation undergoing transcatheter edge-to-edge repair. <i>Catheter Cardiovasc Interv.</i> 2021;98(7):1404-1412. doi:10.1002/ccd.29916
40.	Chakravarty T, Makar M, Patel D, et al. Transcatheter Edge-to-Edge Mitral Valve Repair With the MitraClip G4 System. <i>JACC Cardiovasc Interv.</i> 2020;13(20):2402-2414. doi:10.1016/j.jcin.2020.06.053
41.	Gyoten T, Messroghli D, Schenk S, et al. Impact of preinterventional tricuspid regurgitation on outcome of MitraClip therapy in patients with severely reduced ejection fraction. <i>Open Heart.</i> 2020;7(1):e001203. Published 2020 Mar 15. doi:10.1136/openhrt-2019-001203
42.	Henández-Vaquero D, Pascual I, Almendarez M, et al. Initial experience of a MitraClip valve repair program in Spain. <i>Ann Transl Med.</i> 2020;8(15):957. doi:10.21037/atm.2020.02.121
43.	Higuchi S, Orban M, Stolz L, et al. Impact of Residual Mitral Regurgitation on Survival After Transcatheter Edge-to-Edge Repair for Secondary Mitral Regurgitation. <i>JACC Cardiovasc Interv.</i> 2021;14(11):1243-1253. doi:10.1016/j.jcin.2021.03.050 (EuroSMR Registry)

44.	Karam N, Orban M, Kalbacher D, et al. Impact of effective regurgitant orifice area on outcome of secondary mitral regurgitation transcatheter repair. <i>Clin Res Cardiol.</i> 2021;110(5):732-739. doi:10.1007/s00392-021-01807-0 (EuroSMR Registry)
45.	Karam N, Stolz L, Orban M, et al. Impact of Right Ventricular Dysfunction on Outcomes After Transcatheter Edge-to-Edge Repair for Secondary Mitral Regurgitation. <i>JACC Cardiovasc Imaging.</i> 2021;14(4):768-778. doi:10.1016/j.jcmg.2020.12.015 (EuroSMR Registry)
46.	Orban M, Karam N, Lubos E, et al. Impact of Proportionality of Secondary Mitral Regurgitation on Outcome After Transcatheter Mitral Valve Repair. <i>JACC Cardiovasc Imaging.</i> 2021;14(4):715-725. doi:10.1016/j.jcmg.2020.05.042 (EuroSMR Registry)
47.	Park SD, Orban M, Karam N, et al. Sex-Related Clinical Characteristics and Outcomes of Patients Undergoing Transcatheter Edge-to-Edge Repair for Secondary Mitral Regurgitation. <i>JACC Cardiovasc Interv.</i> 2021;14(8):819-827. doi:10.1016/j.jcin.2020.12.042 (EuroSMR Registry)
48.	Ooms JF, Geleijnse ML, Spitzer E, et al. Transcatheter mitral valve repair in proportionate and disproportionate functional mitral regurgitation-insights from a small cohort study. <i>Neth Heart J.</i> 2021;29(7-8):359-364. doi:10.1007/s12471-021-01583-6
49.	Osteresch R, Diehl K, Schmucker J, et al. Prognostic Impact of the Pulmonary Artery Pulsatility Index in Patients with Chronic Heart Failure and Severe Mitral Regurgitation Undergoing Percutaneous Edge-to-Edge Repair. <i>Cardiology.</i> 2021;146(1):74-84. doi:10.1159/000510283
50.	Papadopoulos K, Ikonomidis I, Chrissoheris M, et al. MitraClip and left ventricular reverse remodelling: a strain imaging study. <i>ESC Heart Fail.</i> 2020;7(4):1409-1418. doi:10.1002/ehf2.12750
51.	Pascual I, Carrasco-Chinchilla F, Benito-Gonzalez T, et al. Transcatheter Mitral Repair for Functional Mitral Regurgitation According to Left Ventricular Function: A Real-Life Propensity-Score Matched Study. <i>J Clin Med.</i> 2020;9(6):1792. Published 2020 Jun 9. doi:10.3390/jcm9061792
52.	Scisło P, Rdzanek A, Pietrasik A, Kochman J, Opolski G. The function of the heart after successful transcatheter mitral valve repair due to severe functional regurgitation. <i>Pol Arch Intern Med.</i> 2021;131(7-8):686-692. doi:10.20452/pamw.16000
53.	Stolfo D, Castrichini M, Biagini E, et al. Modifications of medical treatment and outcome after percutaneous correction of secondary mitral regurgitation. <i>ESC Heart Fail.</i> 2020;7(4):1753-1763. doi:10.1002/ehf2.12737
54.	Vignati C, De Martino F, Muratori M, et al. Rest and exercise oxygen uptake and cardiac output changes 6 months after successful transcatheter mitral valve repair. <i>ESC Heart Fail.</i> 2021;8(6):4915-4924. doi:10.1002/ehf2.13518

Supplementary Table 3. Studies for sensitivity analysis and the included studies

		Studies with prolonged recruitment periods that overlap with the two 5-year periods
1.	Reichart et al 2020	Reichart D, Kalbacher D, Rübsamen N, et al. The impact of residual mitral regurgitation after MitraClip therapy in functional mitral regurgitation. <i>Eur J Heart Fail.</i> 2020;22(10):1840-1848. doi:10.1002/ehf.1774
2.	Godino et al 2018	Godino C, Scotti A, Taramasso M, et al. Two-year cardiac mortality after MitraClip treatment of functional mitral regurgitation in ischemic and non-ischemic dilated cardiomyopathy. <i>Int J Cardiol.</i> 2018;269:33-39. doi:10.1016/j.ijcard.2018.06.041
3.	Godino et al 2021	Godino C, Sisinni A, Pivato CA, et al. Prognostic Value of Pre-operative Atrial Fibrillation in Patients With Secondary Mitral Regurgitation Undergoing MitraClip Implantation. <i>Am J Cardiol.</i> 2021;143:51-59. doi:10.1016/j.amjcard.2020.12.043
4.	Hagnäs et al 2021	Hagnäs MJ, Grasso C, Di Salvo ME, et al. Impact of Post-Procedural Change in Left Ventricle Systolic Function on Survival after Percutaneous Edge-to-Edge Mitral Valve Repair. <i>J Clin Med.</i> 2021;10(20):4748. Published 2021 Oct 16. doi:10.3390/jcm10204748
5.	Koell et al 2021	*Koell B, Orban M, Weimann J, et al. Outcomes Stratified by Adapted Inclusion Criteria After Mitral Edge-to-Edge Repair. <i>J Am Coll Cardiol.</i> 2021;78(24):2408-2421. doi:10.1016/j.jacc.2021.10.011
6.	Kortlandt et al 2019	Kortlandt F, Velu J, Schurer R, et al. Impact of mitral valve treatment choice on mortality according to aetiology. <i>EuroIntervention.</i> 2019;14(17):1733-1739. doi:10.4244/EIJ-D-18-00874
7.	Kitamura et al 2019 (Clin Res Cardiol)	Kitamura M, Kaneko H, Schlüter M, et al. Predictors of mortality in ischaemic versus non-ischaemic functional mitral regurgitation after successful transcatheter mitral valve repair using MitraClip: results from two high-volume centres. <i>Clin Res Cardiol.</i> 2019;108(3):264-272. doi:10.1007/s00392-018-1352-x
8.	Adamo et al 2021 (JACC cardiovasc interv)	Adamo M, Fiorelli F, Melica B, et al. COAPT-Like Profile Predicts Long-Term Outcomes in Patients With Secondary Mitral Regurgitation Undergoing MitraClip Implantation. <i>JACC Cardiovasc Interv.</i> 2021;14(1):15-25. doi:10.1016/j.jcin.2020.09.050
9.	Adamo et al 2020 (Am J Cardiol)	Adamo M, Gavazzoni M, Castiello A, et al. Prognostic Impact of Heart Failure History in Patients with Secondary Mitral Regurgitation Treated by MitraClip. <i>Am J Cardiol.</i> 2020;135:120-127. doi:10.1016/j.amjcard.2020.08.037
10.	Ooms et al 2022	Ooms JF, Bouwmeester S, Debonnaire P, et al. Transcatheter Edge-to-Edge Repair in Proportionate Versus Disproportionate Functional Mitral Regurgitation. <i>J Am Soc Echocardiogr.</i> 2022;35(1):105-115.e8. doi:10.1016/j.echo.2021.08.002
11.	Claeys et al 2021	Claeys MJ, Debonnaire P, Bracke V, et al. Clinical and Hemodynamic Effects of Percutaneous Edge-to-Edge Mitral Valve Repair in Atrial Versus Ventricular Functional Mitral Regurgitation. <i>Am J Cardiol.</i> 2021;161:70-75. doi:10.1016/j.amjcard.2021.08.062
12.	Sugiura et al 2021	Sugiura A, Weber M, Tabata N, et al. Association of heart failure duration with clinical outcomes after transcatheter mitral valve repair for functional mitral regurgitation. <i>Catheter Cardiovasc Interv.</i> 2021;98(3):E412-E419. doi:10.1002/ccd.29390
13.	Sürder et al 2020	Sürder D, Klersy C, Corti R, et al. Impact of mitral regurgitation aetiology on MitraClip outcomes: the MitraSwiss registry. <i>EuroIntervention.</i> 2020;16(2):e112-e120. Published 2020 Jun 12. doi:10.4244/EIJ-D-19-00718
14.	Hirasawa et al 2021	Hirasawa K, Namazi F, Milhorini Pio S, et al. Insufficient Mitral Leaflet Remodeling in Relation to Annular Dilation and Risk of Residual Mitral Regurgitation After MitraClip Implantation. <i>JACC Cardiovasc Imaging.</i> 2021;14(4):756-765. doi:10.1016/j.jcmg.2020.08.019
15.	Caiffa et al 2021	Caiffa T, De Luca A, Biagini E, et al. Impact on clinical outcomes of right ventricular response to percutaneous correction of secondary mitral regurgitation. <i>Eur J Heart Fail.</i> 2021;23(10):1765-1774. doi:10.1002/ehf.2316
		Included studies
1.	Altiok et al 2012	Altiok E, Hamada S, Brehmer K, et al. Analysis of procedural effects of percutaneous edge-to-edge mitral valve repair by 2D and 3D echocardiography. <i>Circ Cardiovasc Imaging.</i> 2012;5(6):748-755. doi:10.1161/CIRCIMAGING.112.974691
2.	Conradi et al 2013	Conradi L, Treede H, Rudolph V, et al. Surgical or percutaneous mitral valve repair for secondary mitral regurgitation: comparison of patient characteristics and clinical outcomes. <i>Eur J Cardiothorac Surg.</i> 2013;44(3):490-496. doi:10.1093/ejcts/ezt036
3.	Rudolph et al 2013	Rudolph V, Lubos E, Schlüter M, et al. Aetiology of mitral regurgitation differentially affects 2-year adverse outcomes after MitraClip therapy in high-risk patients. <i>Eur J Heart Fail.</i> 2013;15(7):796-807. doi:10.1093/eurjhf/hft021

4.	Godino et al 2016	Godino C, Salerno A, Cera M, et al. Impact and evolution of right ventricular dysfunction after successful MitraClip implantation in patients with functional mitral regurgitation. <i>Int J Cardiol Heart Vasc.</i> 2016;11:90-98. Published 2016 May 9. doi:10.1016/j.ijcha.2016.05.017
5.	Taramasso et al 2014	Taramasso M, Maisano F, Latib A, et al. Clinical outcomes of MitraClip for the treatment of functional mitral regurgitation. <i>EuroIntervention.</i> 2014;10(6):746-752. doi:10.4244/EIJV10I6A128
6.	Capodanno et al 2015	Capodanno D, Adamo M, Barbanti M, et al. Predictors of clinical outcomes after edge-to-edge percutaneous mitral valve repair. <i>Am Heart J.</i> 2015;170(1):187-195. doi:10.1016/j.ahj.2015.04.010
7.	Toggweiler et al 2014	Toggweiler S, Zuber M, Sürder D, et al. Two-year outcomes after percutaneous mitral valve repair with the MitraClip system: durability of the procedure and predictors of outcome. <i>Open Heart.</i> 2014;1(1):e000056. Published 2014 Apr 8. doi:10.1136/openhrt-2014-000056
8.	Buck et al 2021	Buck T, Eiswirth N, Farah A, et al. Recurrence of Functional Versus Organic Mitral Regurgitation After Transcatheter Mitral Valve Repair: Implications from Three-Dimensional Echocardiographic Analysis of Mitral Valve Geometry and Left Ventricular Dilation for a Point of No Return. <i>J Am Soc Echocardiogr.</i> 2021;34(7):744-756. doi:10.1016/j.echo.2021.02.017
9.	Kaneko et al 2016	Kaneko H, Neuss M, Weissenborn J, Butter C. Prognostic Significance of Right Ventricular Dysfunction in Patients With Functional Mitral Regurgitation Undergoing MitraClip. <i>Am J Cardiol.</i> 2016;118(11):1717-1722. doi:10.1016/j.amjcard.2016.08.054
10.	Maisano et al 2013	Maisano F, Franzen O, Baldus S, et al. Percutaneous mitral valve interventions in the real world: early and 1-year results from the ACCESS-EU, a prospective, multicenter, nonrandomized post-approval study of the MitraClip therapy in Europe. <i>J Am Coll Cardiol.</i> 2013;62(12):1052-1061. doi:10.1016/j.jacc.2013.02.094
11.	Braun et al 2014	Braun D, Lesevic H, Orban M, et al. Percutaneous edge-to-edge repair of the mitral valve in patients with degenerative versus functional mitral regurgitation. <i>Catheter Cardiovasc Interv.</i> 2014;84(1):137-146. doi:10.1002/ccd.25331
12.	Orban et al 2017	Orban M, Orban M, Lesevic H, et al. Predictors for long-term survival after transcatheter edge-to-edge mitral valve repair. <i>J Interv Cardiol.</i> 2017;30(3):226-233. doi:10.1111/joic.12376
13.	Giannini et al 2014	Giannini C, Petronio AS, De Carlo M, et al. Integrated reverse left and right ventricular remodelling after MitraClip implantation in functional mitral regurgitation: an echocardiographic study. <i>Eur Heart J Cardiovasc Imaging.</i> 2014;15(1):95-103. doi:10.1093/ehjci/jet141
14.	Giannini et al 2016 (Am J Cardiol)	Giannini C, Fiorelli F, De Carlo M, et al. Comparison of Percutaneous Mitral Valve Repair Versus Conservative Treatment in Severe Functional Mitral Regurgitation. <i>Am J Cardiol.</i> 2016;117(2):271-277. doi:10.1016/j.amjcard.2015.10.044
15.	Gripari et al 2016	Gripari P, Tamborini G, Bottari V, et al. Three-Dimensional Transthoracic Echocardiography in the Comprehensive Evaluation of Right and Left Heart Chamber Remodeling Following Percutaneous Mitral Valve Repair. <i>J Am Soc Echocardiogr.</i> 2016;29(10):946-954. doi:10.1016/j.echo.2016.06.009
16.	Schueler et al 2014	Schueler R, Momcilovic D, Weber M, et al. Acute changes of mitral valve geometry during interventional edge-to-edge repair with the MitraClip system are associated with midterm outcomes in patients with functional valve disease: preliminary results from a prospective single-center study. <i>Circ Cardiovasc Interv.</i> 2014;7(3):390-399. doi:10.1161/CIRCINTERVENTIONS.113.001098
17.	Palmiero et al 2017	Palmiero G, Ascione L, Briguori C, et al. The mitral-to-aortic flow-velocity integral ratio in the real world echocardiographic evaluation of functional mitral regurgitation before and after percutaneous repair. <i>J Interv Cardiol.</i> 2017;30(4):368-373. doi:10.1111/joic.12401
18.	Hellhammer et al 2021	Hellhammer K, Haurand JM, Spieker M, et al. Predictors of functional mitral regurgitation recurrence after percutaneous mitral valve repair. <i>Heart Vessels.</i> 2021;36(10):1574-1583. doi:10.1007/s00380-021-01828-9
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31.	Benito-González et al 2021	Benito-González T, Carrasco-Chinchilla F, Estévez-Loureiro R, et al. Clinical and echocardiographic outcomes of transcatheter mitral valve repair in atrial functional mitral regurgitation. <i>Int J Cardiol.</i> 2021;345:29-35. doi:10.1016/j.ijcard.2021.09.056
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51.	Debonnaire et al 2020	Debonnaire P, Heyning CMV, Haddad ME, et al. Left Ventricular End-Systolic Dimension and Outcome in Patients With Heart Failure Undergoing Percutaneous MitraClip Valve Repair for Secondary Mitral Regurgitation. <i>Am J Cardiol.</i> 2020;126:56-65. doi:10.1016/j.amjcard.2020.03.045
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53.	Osteresch et al 2021	Osteresch R, Diehl K, Dierks P, et al. Influence of the ratio of mean arterial pressure to right atrial pressure on outcome after successful percutaneous edge-to-edge repair for severe mitral valve regurgitation. <i>Int J Cardiol Heart Vasc.</i> 2021;37:100903. Published 2021 Nov 5. doi:10.1016/j.ijcha.2021.100903
54.	Krawczyk-Ożóg et al 2018	Krawczyk-Ożóg A, Siudak Z, Sorysz D, et al. Comparison of clinical and echocardiographic outcomes and quality of life in patients with severe mitral regurgitation treated by MitraClip implantation or treated conservatively. <i>Postepy Kardiol Interwencyjne.</i> 2018;14(3):291-298. doi:10.5114/aic.2018.78334
55.	Bedogni et al 2021	Bedogni F, Popolo Rubbio A, Grasso C, et al. Italian Society of Interventional Cardiology (Glse) registry Of Transcatheter treatment of mitral valve regurgitaTiOn (GIOTTO): impact of valve disease aetiology and residual mitral regurgitation after MitraClip implantation. <i>Eur J Heart Fail.</i> 2021;23(8):1364-1376. doi:10.1002/ehj.2159
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59.	Matsumoto et al 2021	Matsumoto T, Kubo S, Izumo M, Mizuno S, Shirai S; MitraClip Japan PMS Investigators. MitraClip Treatment of Moderate-to-Severe and Severe Mitral Regurgitation in High Surgical Risk Patients - Real-World 1-Year Outcomes From Japan [published online ahead of print, 2021 Oct 29]. <i>Circ J.</i> 2021;10.1253/circj.CJ-21-0309. doi:10.1253/circj.CJ-21-0309
60.	Tusa et al 2021	Tusa MB, Barletta M, Popolo Rubbio A, et al. Acute changes in mitral valve geometry after percutaneous valve repair with MitraClip XT _R by three-dimensional echocardiography. <i>Echocardiography.</i> 2021;38(11):1913-1923. doi:10.1111/echo.15238
61.	Tanaka et al 2021	Tanaka S, Imamura T, Ushijima R, Fukuda N, Ueno H, Kinugawa K. Risk Stratification of Percutaneous Edge-to-Edge Repair by MitraClip in Patients with Mitral Regurgitation. <i>Int Heart J.</i> 2021;62(1):112-118. doi:10.1536/ihj.20-437

Supplementary Table 4. Landmark trials general characteristics

Landmark study	Year of publication/ Online publication	Recruitment period	Country	Number of sites	Sample size	Device group size	Comments/Device
COAPT 2018	2018	December 27, 2012, to June 23, 2017	Canada and the United States	78	614	302/614 (49%)	RCT MitraClip® System (Abbott Vascular)
MITRA-FR 2018	2018	From December 2013 to March 2017	France	37	307	152/307 (49.5%)	RCT MitraClip® System (Abbott Vascular)
EVEREST program (Secondary MR patients only)	2019	August 2005 to December 2013	North America	37	616	616/616 (100%)	RCT and related registries MitraClip® System (Abbott Vascular)

Supplementary Table 5. Study general characteristics

	Observational study	Online publication	Recruitment period	Recruitment duration (years)	Country	Number of sites	Sample size	FMR/SMR subgroup or in device group	Study objective/ Comments/inclusion in which analysis
First 5-year period									
1.	Altiok et al 2012	2012	Assumed 2008 (approval of MitraClip®)	-	Germany University Hospital RWTH Aachen	1	39	39/39 (100%)	MitraClip® (Abbott Vascular Structural Heart, Menlo Park, CA)
2.	Conradi et al 2013	2013	MitraClip 2008	?2	Germany University Heart Center Hamburg	1	171	95/171 (55.5%)	Device: not specified
3.	Rudolph et al 2013	2013	September 2008 to December 2011	3	Germany University Heart Centre Cologne	1	230	153/230 (66.5%)	Prospective registry Device: not specified
4.	Godino et al 2016	2016	October 2008 to July 2014	6	Italy San Raffaele Scientific Institute, Milan EMO-GVM Centro Cuore Columbus, Milan	2	60	60/60 (100%)	Device: not specified
5.	Taramasso et al 2014	2015	October 2008 to October 2013	5	Italy Ferrarotto Hospital, University of Catania, Catania Spedali Civili, Brescia AOU Pisana, Pisa St. Ambrogio Clinical Institute, Milan	4	240	240/304 (79.0%)	GRASP-IT registry Device: not specified
6.	Capodanno et al 2015	2015	October 2008 to October 2013	5	Italy	4	240	240/304 (79.0%)	GRASP-IT registry Device: not specified

	Observational study	Online publication	Recruitment period	Recruitment duration (years)	Country	Number of sites	Sample size	FMR/SMR subgroup or in device group	Study objective/ Comments/inclusion in which analysis
					Ferrarotto Hospital, University of Catania, Catania Spedali Civili, Brescia AOU Pisana, Pisa St. Ambrogio Clinical Institute, Milan				
7.	Toggweiler et al 2014	2014	February 2009 to March 2011	2	Switzerland Cantonal Hospital Lucerne Cardiocentro Ticino University Hospital Zurich	3	74	46/74 (62.2%)	MitraSwiss registry Device: not specified
8.	Buck et al 2021	2021	March 2009 to February 2014	5	Germany Klinikum Westfalen, Heart Center Westfalen University Clinic Essen, West-German Heart and Vascular Center	1	61	45/61 (73.8%)	MitraClip® (Abbott Laboratories, Abbott Park, IL)
9.	Kaneko et al 2016	2016	March 2009	-	Germany Heart Center Brandenburg	1	117	117/117 (100%)	Device: not specified
10.	Maisano et al 2013	2013	April 2009 to April 2011	2	Europe	14	567	393/510 (77.1%)	ACCESS-EU registry (Phase I) MitraClip® (Abbott Vascular, Inc., Santa Clara, California)
11.	Braun et al 2014	2013	June 2009 to January 2012	2.5	Germany Translation: TU stands for Technische Universität (Technical University) The centre is The German Heart Centre in Munich The clinic of Heart and Circulatory disease in adult age	1	119	47/119 (39.5%)	Device: not specified
12.	Orban et al 2017	2017	August 2009 to April 2011	1.5	Germany German Heart Center, Technische Universität of Munich, Munich University Hospital of the Ludwig-Maximilians University, Munich	2	126	51/126 (40.5%)	Device: not specified
13.	Giannini et al 2014	2013	November 2009 to August 2012	2.5	Italy University of Pisa	1	35	35/35 (100%)	Device: not specified
14.	Giannini et al 2016 (Am J Cardiol)	2015	December 2009 to February 2015	5	Italy Azienda Ospedaliero-Universitaria Pisana, Pisa	1	120	60/120 (50.0%)	Device: not specified
15.	Gripari et al 2016	2016	2010 to 2015	5	Italy Centro Cardiologico Monzino, IRCCS, Milan	1	58	26/58 (44.8%)	Device: not specified

	Observational study	Online publication	Recruitment period	Recruitment duration (years)	Country	Number of sites	Sample size	FMR/SMR subgroup or in device group	Study objective/ Comments/inclusion in which analysis
16.	Schueler et al 2014	2014	June 2010 to May 2013	3	Germany Heart Centre Bonn, University Hospital Bonn	1	107	71/107 (66.3%)	Device: not specified
17.	Palmiero et al 2017	2017	June 2010 to December 2014	4.5	Italy ARON Ospedali, dei Colli, Monaldi Hospital, Naples	1	25	25/25 (100%)	Device: not specified
18.	Hellhammer et al 2021	2021	August 2010 to May 2019	9 Small number of pts after 2013	Germany Heart Center Düsseldorf	1	220	220/220 (100%)	MitraClip® system (Abbott Vascular GmbH, Santa Clara, California, USA); 1 st and 2 nd generations
19.	Adamo et al 2016	2016	October 2010 to July 2015	5	Italy Spedali Civili, Brescia	1	62	62/62 (100%)	Device: not specified
20.	Alessandrini et al 2017	2017	December 2010 to February 2014	3	Germany Asklepios Klinik St. Georg, Hamburg	1	97	97/97 (100%)	Device: not specified
21.	Azzalini et al 2016	2016	December 2010 to January 2015	4	Canada Universite De Montreal, Montreal	1	77	77/77 (100%)	Device: not specified
22.	Nickenig et al 2014	2014	January 2011 to December 2012	2	Europe (8 countries)	25	628	452/628 (72.0%)	Pilot - TCVT registry of EORP (ESC) Device: not specified
23.	Tay et al 2016	2015	February 2011 to Mar 2014	3	Asia-Pacific countries (Australia, China, Indonesia, Malaysia and Singapore)	8	163	88/163 (54.0%)	MitraClip Asia-Pacific (MARS) Registry Device: not specified
24.	Herbrand et al 2017	2017	October 2011 to May 2013	1.5	Germany University Hospital Duesseldorf, Duesseldorf	1	45	45/45 (100%)	Device: not specified
25.	Barth et al 2017	2017	October 2011 to December 2016	5	Germany Cardiovascular Center, Bad Neustadt	1	75	75/75 (100%)	Device: not specified
26.	Al Amri et al 2016	2015	January 2012 to July 2014	2.5	The Netherlands Leiden University Medical Centre, Leiden	1	42	42/42 (100%)	MitraClip® (Abbott Vascular Structural Heart, Menlo Park, CA, USA)
27.	Citro et al 2017	2017	March 2012 to January 2015	3	Italy University Hospital 'San Giovanni di Dio e Ruggi d'Aragona', Salerno	1	41	41/41 (100%)	Device: not specified
28.	Hubert et al 2019	2019	August 2012 to September 2016	5	France University Hospital of Rennes	1	56	37/56 (66.0%)	Device: not specified
29.	Ussia et al 2016	2015	November 2012 to September 2014	2	Italy Tor Vergata University of Rome, Rome	1	46	46/46 (100%)	Device: not specified

	Observational study	Online publication	Recruitment period	Recruitment duration (years)	Country	Number of sites	Sample size	FMR/SMR subgroup or in device group	Study objective/ Comments/inclusion in which analysis
30.	El-Shurafa et al 2021	2021	February 2012 to December 2018	7	Kingdom of Saudi Arabia Prince Sultan Cardiac Center	1	111	88/111 (79.3%)	MitraClip® system (Abbott Vascular, Menlo Park, California, USA)
31.	Benito-González et al 2021	2021	June 2012 to July 2020	8	Spain	24	672	672/672 (100%)	Spanish MitraClip® registry MitraClip® (Abbott; Menlo Park, CA, USA)
32.	Kłapyta et al 2018	2018	May 2012 to December 2017	5.5	Poland Institute of Cardiology, Warsaw	1	53	53/53 (100%)	Device: not specified
33.	Okuno et al 2021	2021	2012 to 2018	6	Switzerland Bern University Hospital	2	421	199/421 (47.3%)	MitraClip® NT _R and XT _R MitraClip® vs. surgery
34.	Chan et al 2021	2021	2012 to 2018	6	Canada University of Ottawa, Ottawa	1	175	175/175 (100%)	MitraClip® NT/NTR (Abbott)
35.	Renker et al 2021	2021	2012 to 2018	6	Germany Justus-Liebig-University Giessen University Hospital Frankfurt/Main	2	30	30/30 (100%)	Device: not specified
36.	Pascual et al 2020 (1)	2019	June 2012 to July 2018	6	Spain	16	558	364/558 (65.2%)	Spanish MitraClip registry
Second 5-year period									
37.	Weber et al 2019	2019	2013 to 2018	5	Europe University Hospital Bonn, Bonn University Hospital Zurich, Zurich University of Cologne, Cologne Asklepios Klinik St. Georg, Hamburg Ospedale San Raffaele, Milan	5	186	93/186 (50.0%)	Device: not specified
38.	Nikendei et al 2016	2015	January 2013 to April 2014	1.5	Germany University Hospital Heidelberg, Heidelberg	1	24	24/24 (100%)	MitraClip® (Abbott Vascular, Santa Clara, CA)
39.	Gyoten et al 2020 (ESC HF)	2020	January 2013 to December 2017	5	Germany Sana-Herzzentrum Cottbus	1	132	85/132 (64.4%)	Device: not specified MitraClip® vs. surgery
40.	Osteresch et al 2018	2018	March 2013 to April 2015	2	Germany Institut für Herz- und Kreislaufforschung am Klinikum Links der Weser Bremen (BIHKF), Bremen	1	130	130/130 (100%)	Device: not specified

	Observational study	Online publication	Recruitment period	Recruitment duration (years)	Country	Number of sites	Sample size	FMR/SMR subgroup or in device group	Study objective/ Comments/inclusion in which analysis
41.	Noack et al 2019	2018	April 2013 to May 2014	1	Germany Heart Center University Leipzig, Leipzig	1	28	28/28 (100%)	MitraClip® (Abbott Vascular Structural Heart, Menlo Park, CA)
42.	Berardini et al 2017	2016	June 2013 to April 2015	2	Italy University Hospital St. Orsola-Malpighi of Bologna University Hospital of Trieste University Hospital of Pavia	3	75	75/75 (100%)	MitraClip® (Abbott, Abbott Park, IL, USA)
43.	Stolz et al 2021	2021	July 2013 to March 2019	5.5	Germany Universitat Munchen, Munich	1	178	178/178 (100%)	MitraClip® (Abbott, Santa Clara, California, USA) NT, NT _R or XT _R
44.	Terhoeven et al 2019	2019	2014 to 2016	2	Germany University of Heidelberg, Heidelberg	1	40	40/40 (100%)	Device: not specified
45.	Spieker et al 2021	2021	2014 to 2018 Included in the temporal trend	4	Germany University Hospital Duesseldorf	1	29	29/29 (100%)	Assessment by sequential CMR Device: not specified
46.	Öztürk et al 2020	2020	February 2014 to November 2015	1.5	Germany Heart Center Bonn, University of Bonn	1	50	50/50 (100%)	Device: not specified
47.	Patzelt et al 2019	2019	May 2014 to February 2017	3	Germany University Hospital of the University of Tübingen	1	255	151/255 (59.2%)	MitraClip® NT system
48.	Iliadis et al 2020	2020	May 2014 to December 2017	3.5	Germany University Hospital Cologne	1	122	122/122 (100%)	Device: not stated
49.	Cimino et al 2019	2018	June 2014 to July 2017	3	Italy Sapienza University of Rome, Rome	1	45	45/45 (100%)	MitraClip® (Abbott Vascular, Santa Clara, CA, USA)
50.	Benák et al 2018	2018	From 2014 to “not stated”	-	Czech Republic Institute for Clinical and Experimental Medicine, Prague	1	30	30/30 (100%)	MitraClip® (Abbott Vascular-Structural Heart, Menlo Park, California, USA)
51.	Debonnaire et al 2020 Belgian MitraClip® registry	2020	Recruitment started in 2015 (NCT02506387)	~5	Belgium Sint-Jan Hospital Bruges and University Hospital Antwerp	2	107	107/107 (100%)	Belgian MitraClip® Registry Device: not specified

	Observational study	Online publication	Recruitment period	Recruitment duration (years)	Country	Number of sites	Sample size	FMR/SMR subgroup or in device group	Study objective/ Comments/inclusion in which analysis
52.	Pascual et al 2020 (2)	2020	October 2015 to October 2019	4	Spain Hospital Universitario Central de Asturias University of Oviedo Hospital Alvaro Cunqueiro University Hospital of León	2	119	119/119 (100%)	Device: not specified XT _R clips: 52/119 (43.7%)
53.	Osteresch et al 2021	2021	November 2015 to November 2018	3	Germany Bremen Heart Centre	1	145	145/145 (100%)	Registry of BIHKF Device: not specified
54.	Krawczyk-Ożóg et al 2018	2018	January 2016 to January 2017	1	Poland University Hospital in Krakow	1	33	10/33 (30.3%)	Device: not specified
55.	Bedogni et al 2021	2021	January 2016 to March 2020	4	Italy	20	1659	986/1659 (59.4%)	From GIOTTO registry MitraClip® NT, NT _R , XT _R
56.	Frea et al 2021	2020	June 2016 to June 2018	2	Italy Città della Salute e della Scienza	1	58	58/58 (100%)	Device: not specified
57.	Shim et al 2020	2020	January 2017 to December 2019	3	United States Brigham and Women's Hospital, Harvard Medical School	1	40	40/40 (100%)	MitraClip® NT, NT _R or XT _R
58.	Kassar et al 2022	2021	March 2017 to December 2019	3	Switzerland Bern University Hospital	1	116	61/116 (52.5%)	MitraClip® (Abbott Vascular, Abbott Park, IL) NT _R or XT _R
59.	Matsumoto et al 2021	2021	April 2018 to January 2019	1	Japan Sendai Kousei Hospital, Sendai Shonan Kamakura General Hospital, Kamakura	40	500	358/500 (71.6%)	MitraClip Japan PMS MitraClip® NT System
60.	Tusa et al 2021	2021	April 2018 to February 2020	2	Italy IRCCS Policlinico San Donato	1	59	33/59 (56.0%)	Third generation MitraClip® XT _R
61.	Tanaka et al 2021	2021	September 2018 to October 2019	1	Japan University of Toyama	1	25	21/25 (84.0%)	Device: not specified
Studies with long recruitment periods that overlap with the two 5-year periods									
1.	Reichart et al 2020	2020	September 2008 to December 2017	9	Germany University Heart & Vascular Center	1	458	458/458 (100%)	Device: not specified
2.	Godino et al 2018	2018	October 2008 to December 2016	8	Italy, Switzerland San Raffaele Hospital of Milan Spedali Civili of Brescia	4	314	314/314 (100%)	Device: not specified

	Observational study	Online publication	Recruitment period	Recruitment duration (years)	Country	Number of sites	Sample size	FMR/SMR subgroup or in device group	Study objective/ Comments/inclusion in which analysis
					EMO-GVM Centro Cuore Columbus of Milan University Heart Center of Zurich				
3.	Godino et al 2021	2020	October 2008 to May 2018	9.5	Italy and Switzerland Spedali Civili of Brescia University Heart Center of Zurich San Raffaele Hospital of Milan	3	605	605/605 (100%)	MiZüBr registry Device: not specified
4.	Hagnäs et al 2021	2021	October 2008 to December 2019	11	Italy A.O.U. "Policlinico-Vittorio Emanuele", University of Catania, Catania	1	399	399/399 (100%)	GRASP registry MitraClip® (Abbot Vascular)
5.	Koell et al 2021 EuroSMR registry	2021	November 2008 to September 2019	11	European countries	11	1867	1867/1867 (100%)	EuroSMR registry Influence of COPAT and MITRA-FR criteria on outcomes
6.	Kortlandt et al 2019	2018	January 2009 to April 2016	7	The Netherlands St. Antonius Hospital, Nieuwegein, Academic Medical Center, Amsterdam University Medical Center, Groningen Amphia Hospital, Breda	4	688	365/688 (53.0%)	MitraClip® (Abbott Vascular, Santa Clara, CA, USA)
7.	Kitamura et al 2019 (Clin Res Cardiol)	2018	September 2009 to June 2016	7	Germany Asklepios Klinik St. Georg, Hamburg Brandenburg Heart Centre, Bernau	2	575	575/575 (100%)	Device: not specified
8.	Adamo et al 2021 (JACC Cardiovasc Interv)	2020	December 2009 to November 2019	10	Italy and Portugal Spedali Civili di Brescia, University Hospital of Pisa Centro Hospitalar Vila Nova de Gaia/Espinho	3	304	304/304 (100%)	Device: not specified
9.	Adamo et al 2020 (Am J Cardiol)	2020	October 2010 to October 2018	8	Italy, Spain, and Switzerland Civil Hospitals of Brescia University Hospital of Zurich Hospital of Leon Hospital Puerta de Hierro-Majadahonda of Madrid	4	186	186/186 (100%)	Device: not specified
10.	Ooms et al 2022	2021	2011 to 2019	8	Belgium and the Netherlands Erasmus University Medical Center Catharina Hospital Sint-Jan Hospital University Hospital Antwerp University Hospital Leuven	6	241	241/241 (100%)	MitraClip® (Abbott Vascular, Santa Clara, CA)

	Observational study	Online publication	Recruitment period	Recruitment duration (years)	Country	Number of sites	Sample size	FMR/SMR subgroup or in device group	Study objective/ Comments/inclusion in which analysis
					St. Antonius Hospital				
11.	Claeys et al 2021	2021	2011 to 2019	8	Belgium	7	359	359/359 (100%)	Belgian MitraClip® registry Device: not specified
12.	Sugiura et al 2021	2020	January 2011 to March 2019	8	Germany Heart Center Bonn, University of Bonn	1	208	208/208 (100%)	Device: not specified
13.	Sürder et al 2020	2020	September 2011 to December 2018	7	Switzerland	10	1212	560/1212 (46.2%)	MitraSwiss registry MitraClip® NT/NT _R
14.	Hirasawa et al 2021	2020	January 2012 to March 2019	7	The Netherlands Leiden University Medical Center	1	119	119/119 (100%)	Device: not specified
15.	Caiffa et al 2021	2021	April 2012 to September 2020	8.5	Italy University Hospital of Trieste University Hospital St. Orsola-Malpighi of Bologna IRCCS Policlinico San Donato Spedali Civili of Brescia	4	221	221/221 (100%)	MitraClip® System (Abbott Vascular, Santa Clara, CA, USA)

Sensitivity analysis – Studies with long recruitment periods that overlap with the two 5-year periods

Supplementary Table 6. Sensitivity analysis – Baseline characteristics

Variable	Pooled real-life variables	EVEREST program, Mean±SD or % (Population size)	EVEREST vs. Pooled variable, MD or OR (95%CI)	COAPT trial, Mean±SD or % (Population size)	COAPT vs. Pooled variable, MD or OR (95%CI)	MITRA-FR trial, Mean±SD, or % (Population size)	MITRA-FR vs. Pooled variable, MD or OR (95%CI)
Age (Year)	73.38±0.24; Q=1.55	73.3±10.5 (n=616)	-0.10 (-0.93, 0.73)	71.7±11.8 (n=302)	-0.17 (-3.03, -0.37)	70.1±10.1 (n=152)	-3.30 (-4.91, -1.69)
Male	68.4% (65.2-71.5); I ² =84%	364/616 (59.1%)	0.66 (0.56-0.78)	201/302 (66.6%)	0.91 (0.71-1.16)	120/152 (78.9%)	1.71 (1.16-2.54)
Diabetes mellitus	31.2% (27.6-34.9); I ² =90%	239/616 (38.8%)	1.37 (1.16-1.63)	106/302 (35.1%)	1.17 (0.92-1.49)	50/152 (32.9%)	1.06 (0.75-1.49)
Prior myocardial infarction	44.7% (38.3-51.2); I ² =96%	334/602 (55.5%)	1.89 (1.59-2.24)	156/302 (51.7%)	1.62 (1.28-2.04)	75/152 (49.3%)	1.47 (1.07-2.04)
Non-ischemic etiology	39.5 (31.5-47.9); I ² =92%	407/615 (66.2%)	2.85 (2.35-3.46)	118/302 (39.1%)	0.94 (0.73-1.20)	57/152 (37.5%)	0.87 (0.62-1.23)
Atrial fibrillation	49.9% (40.6-59.1); I ² =100%	359/552 (65.0%)	3.54 (2.96-4.24)	173/302 (57.3%)	2.55 (2.02-3.22)	49/142 (34.5%)	1.00 (0.71-1.42)
Renal insufficiency	54.8% (42.9-66.5); I ² =99%	163/616 (26.5%)	0.27 (0.22-0.32)	214/299 (71.6%)	1.87 (1.45-2.42)	22/152 (14.5%)	0.13 (0.08-0.20)
Prior percutaneous coronary intervention	41.5% (37.1-46.1); I ² =92%	292/615 (47.5%)	1.39 (1.17-1.64)	130/302 (43.0%)	1.16 (0.92-1.47)	71/152 (46.7%)	1.35 (0.97-1.86)
ACEI/ARB	62.4% (51.2-73.0); I ² =97%	390/616 (63.3%)	1.17 (0.97-1.40)	204/302 (71.9%)	1.41 (1.09-1.82)	111/152 (82.2%)	1.83 (1.27-2.64)
Beta-blocker	77.3% (72.0-82.3); I ² =93%	491/616 (79.7%)	1.29 (1.05-1.59)	275/302 (91.1%)	3.35 (2.24-5.00)	134/152 (88.2%)	2.45 (1.49-4.02)
Diuretics	90.4% (85.7-94.2); I ² =96%	543/616 (88.1%)	1.32 (1.02-1.71)	270/302 (89.4%)	1.50 (1.03-2.18)	151/152 (99.3%)	26.78 (3.74-191.74)
Oral anticoagulation agents	44.0% (40.8-47.2); I ² =0%	253/616 (41.1%)	0.89 (0.72-1.09)	140/302 (46.4%)	1.10 (0.85-1.43)	93/152 (61.2%)	2.01 (1.41-2.86)
ICD device	38.3% (27.3-50.0); I ² =98%	170/600 (28.3%)	0.89 (0.74-1.07)	91/302 (30.1%)	0.97 (0.75-1.25)	48/151 (31.8%)	1.05 (0.74-1.48)
Any cardiac device	47.4% (36.3-58.6); I ² =98%	170/600 (28.3%)	0.43 (0.36-0.51)	206/302 (68.1%)	2.32 (1.81-2.97)	94/151 (62.3%)	1.78 (1.28-2.49)

Abbreviations: 95%CI, 95% confidence interval; ACEI/ARB, angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers; ICD, implantable cardioverter-defibrillator; MD, mean difference; OR, odds ratio; SD, standard deviation.

Supplementary Table 7. Sensitivity analysis – Hospital presentation and echocardiographic parameters

Variable	Pooled real-life variables	EVEREST program, Mean±SD or % (Population size)	EVEREST vs. Pooled variable, MD or OR (95%CI)	COAPT trial, Mean±SD or % (Population size)	COAPT vs. Pooled variable, MD or OR (95%CI)	MITRA-FR trial, Mean±SD, or % (Population size)	MITRA-FR vs. Pooled variable, MD or OR (95%CI)
NYHA II	13.8% (10.9-17.0); I ² =90%	107/615 (17.4%)	1.27 (1.01-1.58)	129/302 (42.7%)	4.48 (3.52-5.70)	56/152 (36.8%)	3.51 (2.50-4.92)
NYHA III	63.5% (59.7-67.2); I ² =85%	387/615 (62.9%)	0.98 (0.83-1.16)	154/302 (50.9%)	0.60 (0.48-0.76)	82/152 (53.9%)	0.68 (0.49-0.93)
NYHA IV	21.6% (17.9-25.6); I ² =90%	108/615 (17.6%)	0.77 (0.62-0.95)	18/302 (5.9%)	0.23 (0.14-0.37)	14/152 (9.2%)	0.36 (0.21-0.63)
NYHA III/IV	84.8% (81.0-88.1); I ² =93%	495/615 (80.5%)	0.75 (0.61-0.92)	172/302 (57.0%)	0.24 (0.19-0.30)	96/152 (63.1%)	0.31 (0.22-0.44)
MR grade 3+	30.4% (22.3-39.1); I ² =98%	355/616 (58.1%)	2.44 (2.06-2.89)	148/302 (49.0%)	1.72 (1.37-2.18)	46/123 (37.4%)	1.07 (0.74-1.55)
MR grade 4+	66.1% (57.6-74.1); I ² =98%	139/616 (22.7%)	0.19 (0.15-0.23)	154/302 (51.0%)	0.67 (0.53-0.85)	76/123 (61.8%)	1.04 (0.72-1.51)
LVEDV (ml)	186.58±1.34; Q=1.22	162.2±52.8 (558)	-24.40 (-28.78, -20.02)	194.4± 69.2 (n=302)	7.80 (-0.00, 15.60)	258.8±71.1* (n=152)	71.40 (60.10-82.70)
LVEF (%)	35.13±0.38; Q=14.4	43.2±11.7 (558)	8.10 (7.13-9.07)	31.3±9.1 (n=302)	-3.80 (-4.83, -2.77)	33.3±6.5 (n=152)	-1.80 (-2.83, -0.77)

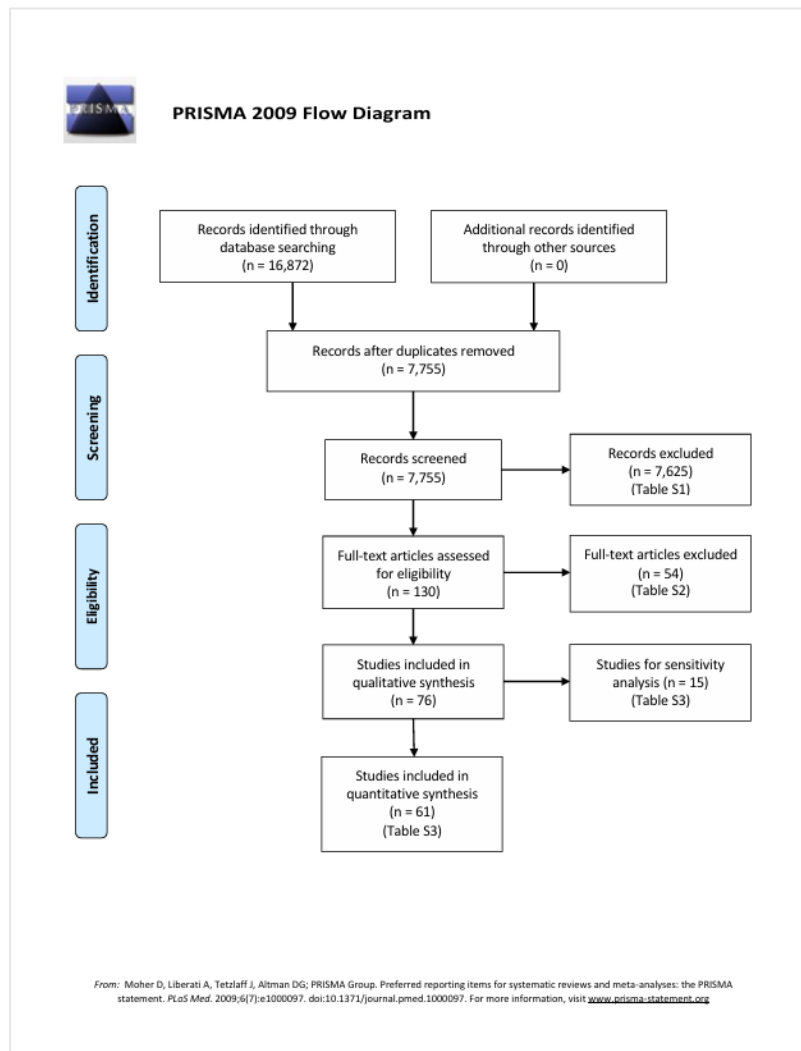
*136.2±37.4 ml/m² converted to ml using 1.9 m². Abbreviations: 95%CI, 95% confidence interval; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end-diastolic volume; MD, mean difference; MR, mitral regurgitation; NYHA, New York Heart Association; OR, odds ratio; SD, standard deviation.

Supplementary Table 8. Sensitivity analysis – Procedural and clinical outcomes

Variable	Pooled real-life variables	EVEREST program, Mean±SD or % (Population size)	EVEREST vs. Pooled variable, MD or OR (95%CI)	COAPT trial, Mean±SD or % (Population size)	COAPT vs. Pooled variable, MD or OR (95%CI)	MITRA-FR trial, Mean±SD, or % (Population size)	MITRA-FR vs. Pooled variable, MD or OR (95%CI)
One device implanted	49.1% (42.1-56.1); I ² =92%	-	-	106/293 (36.2%)	0.59 (0.46-0.76)	63/138 (45.7%)	0.87 (0.62-1.23)
Two devices implanted	44.9% (38.5-51.3); I ² =89%	-	-	157/293 (53.6%)	1.44 (1.13-1.83)	62/138 (44.9%)	1.02 (0.72-1.44)
Three or more devices implanted	6.3% (4.3-8.7); I ² =78%	-	-	24/293 (8.2%)	1.28 (0.82-2.01)	13/138 (9.4%)	1.49 (0.82-2.71)
MR grade 1+	59.1% (51.2-66.8); I ² =93%	307/589 (52.1%)	0.66 (0.55-0.78)	214/260 (82.3%)	2.82 (2.04-3.90)	54/123 (43.9%)	0.47 (0.33-0.68)
MR grade 2+	30.8% (25.0-37.0); I ² =92%	215/589 (36.5%)	1.41 (1.17-1.69)	33/260 (12.7%)	0.36 (0.25-0.52)	23/123 (18.7%)	0.56 (0.36-0.89)
MR grade ≤2+	87.7% (77.9-94.9); I ² =97%	523/589 (88.8%)	0.91 (0.69-1.19)	247/260 (95.0%)	2.17 (1.23-3.82)	115/123 (93.5%)	1.64 (0.80-3.39)
MR grade ≥3+	9.1% (6.1-12.7); I ² =90%	66/589 (11.2%)	1.35 (1.02-1.78)	13/260 (5.0%)	0.56 (0.32-0.99)	8/123 (6.25%)	0.79 (0.38-1.64)
NYHA I/II at 12 months	65.3% (34.0-90.6); I ² =100%	511/616 (83.0%)	5.17 (4.13-6.46)	171/237 (72.2%)	2.75 (2.05-3.69)	76/112 (67.8%)	2.24 (1.50-3.36)
MR grade ≤2+ at 12 months	75.1% (67.0-82.4); I ² =96%	349/413 (84.5%)	2.31 (1.75-3.04)	199/210 (94.8%)	7.65 (4.15-14.11)	79/97 (81.4%)	1.86 (1.11-3.11)
All-cause mortality within 12 months	18.6% (9.30-69.3); I ² =99%	138/616 (22.4%)	2.93 (2.38-3.61)	57/302 (19.1%)	2.36 (1.75-3.19)	37/152 (24.3%)	3.27 (2.24-4.78)

*136.2±37.4 ml/m² converted to ml using 1.9 m². Abbreviations: 95%CI, 95% confidence interval; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end-diastolic volume; MD, mean difference; MR, mitral regurgitation; NYHA, New York Heart Association; OR, odds ratio; SD, standard deviation.

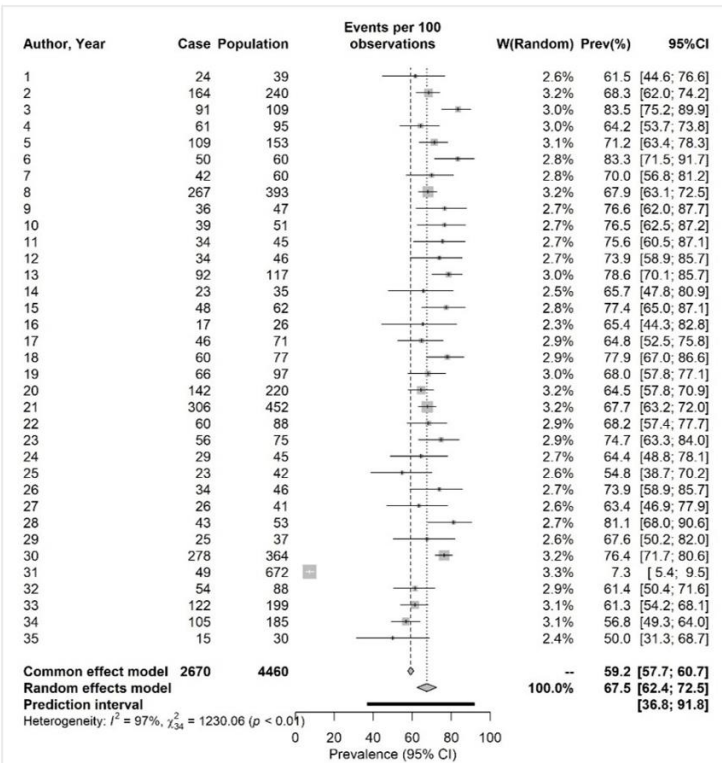
Supplementary Figures



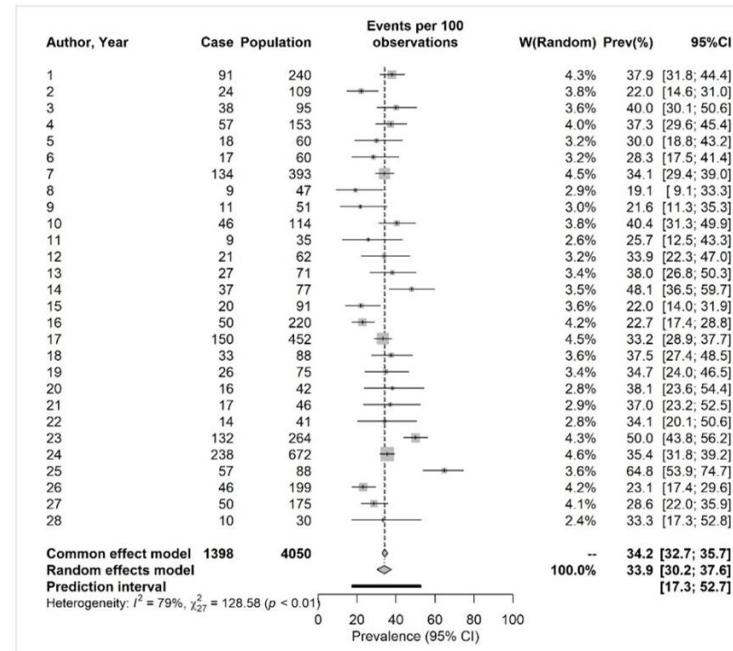
Supplementary Figure 1. PRISMA flow chart

Pooled baseline characteristics
First 5-year period

Male

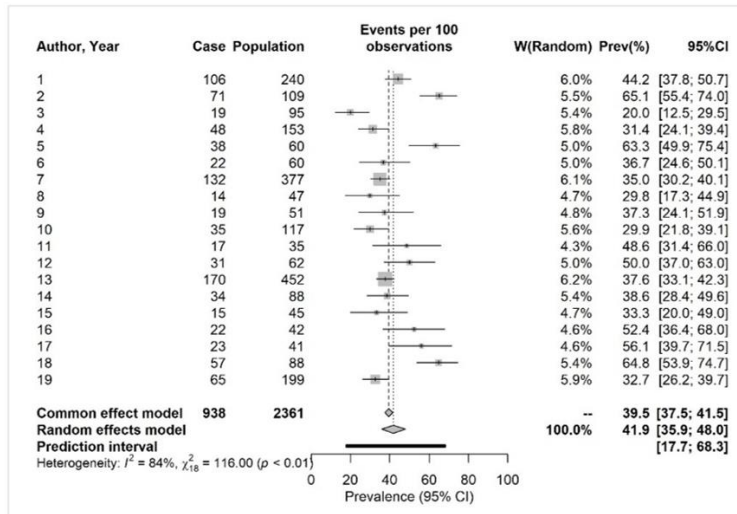


Diabetes mellitus

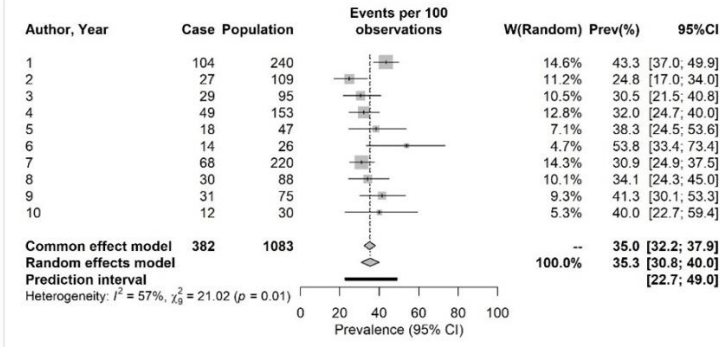


Supplementary Figure 2. Pooled male and diabetes variables – First period

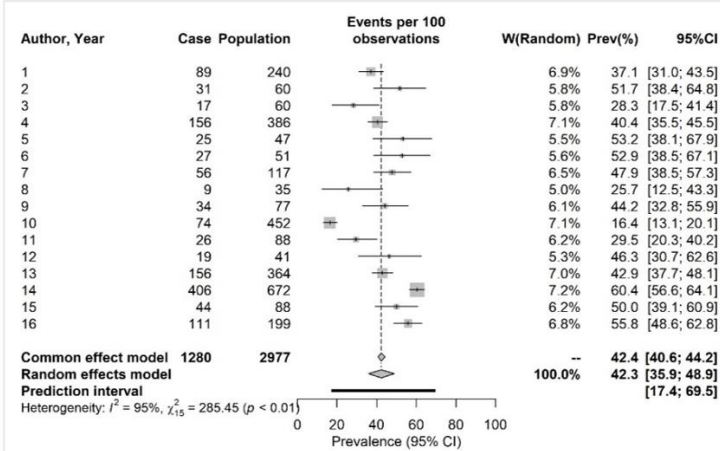
Prior MI



NICM

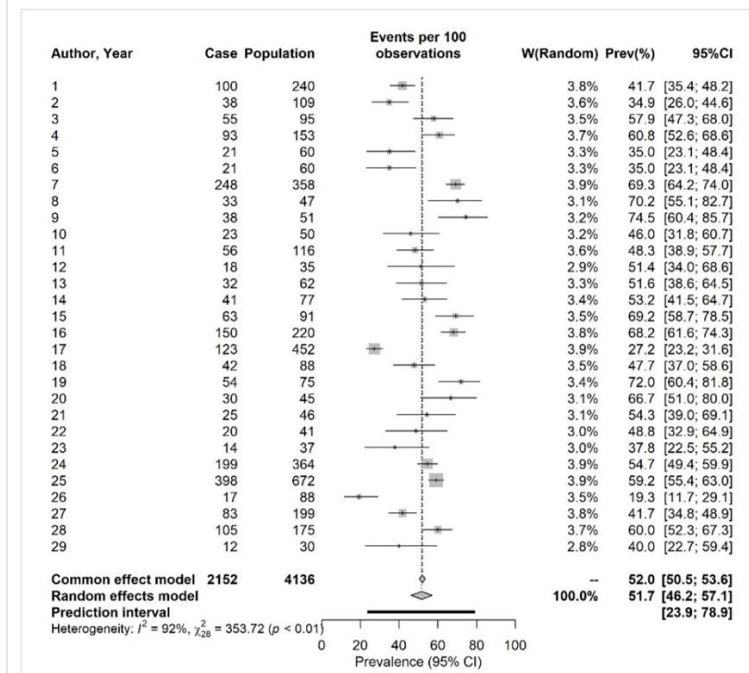


Prior PCI

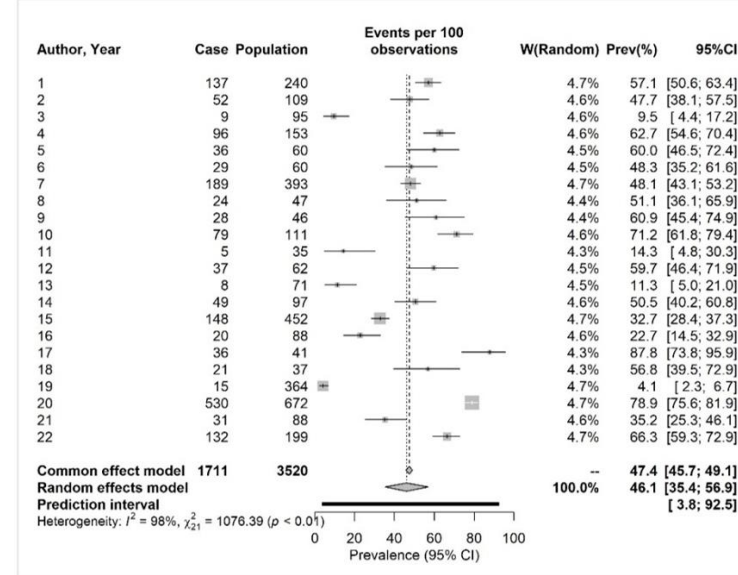


Supplementary Figure 3. Pooled NICM, prior MI, and prior PCI variables – First period

Atrial fibrillation



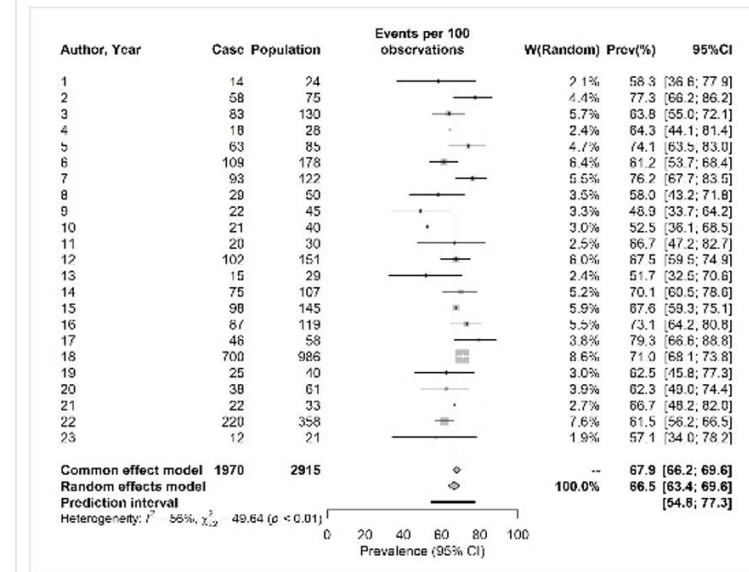
Renal insufficiency



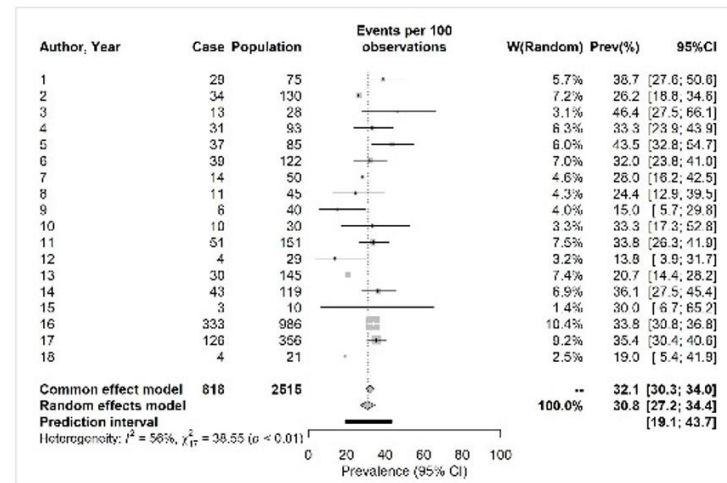
Supplementary Figure 4. Pooled atrial fibrillation and renal insufficiency variables – First period

Pooled baseline characteristics
Second 5-year period

Males

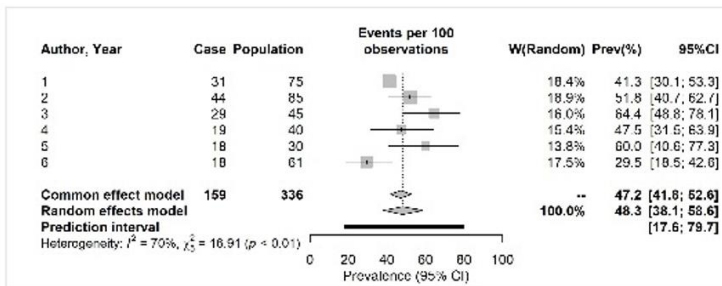


Diabetes mellitus

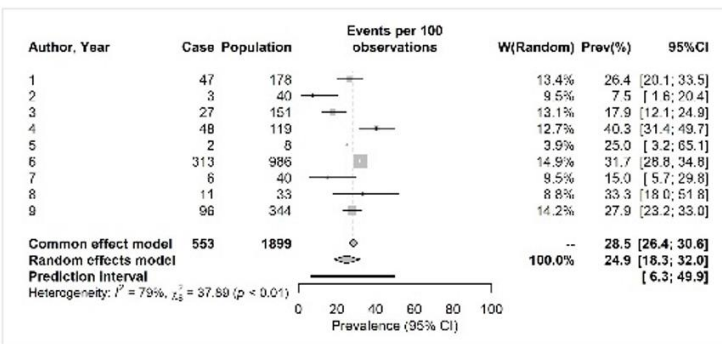


Supplementary Figure 5. Pooled male and diabetes variables – Second period

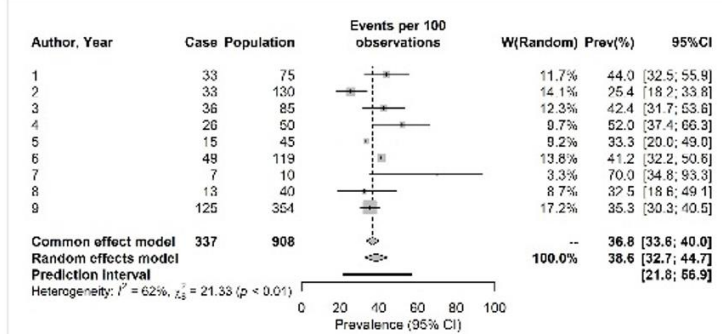
NICM



Prior MI

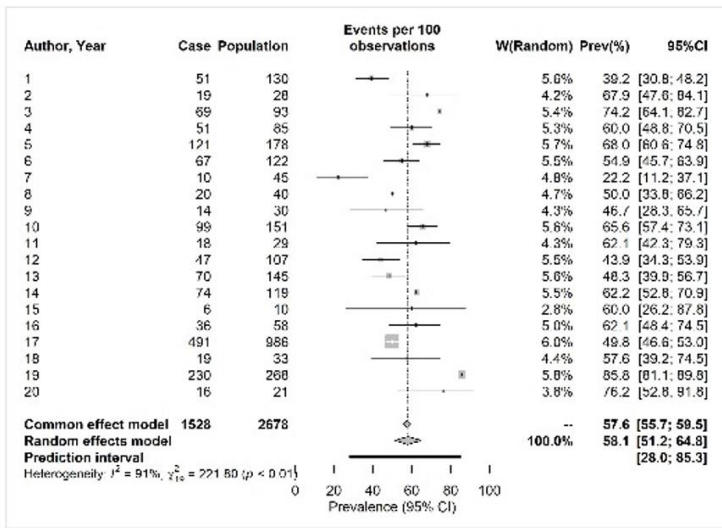


Prior PCI

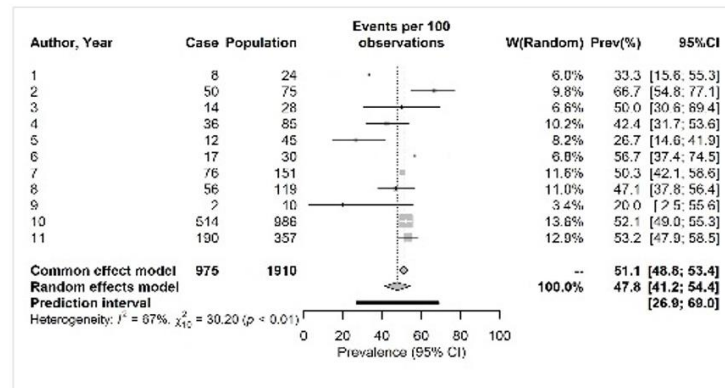


Supplementary Figure 6. Pooled NICM, prior MI, and prior PCI variables – Second period

Atrial fibrillation



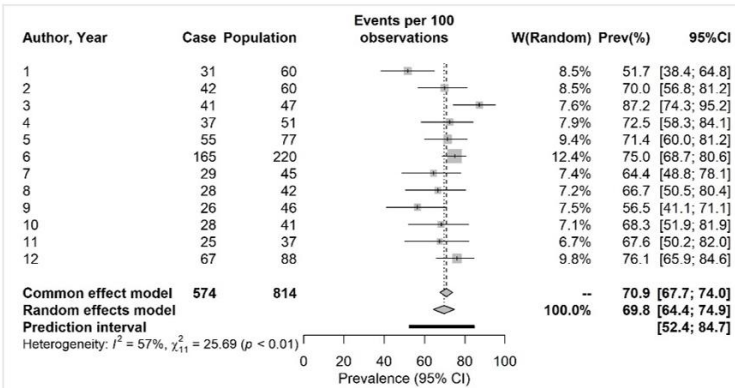
Renal insufficiency



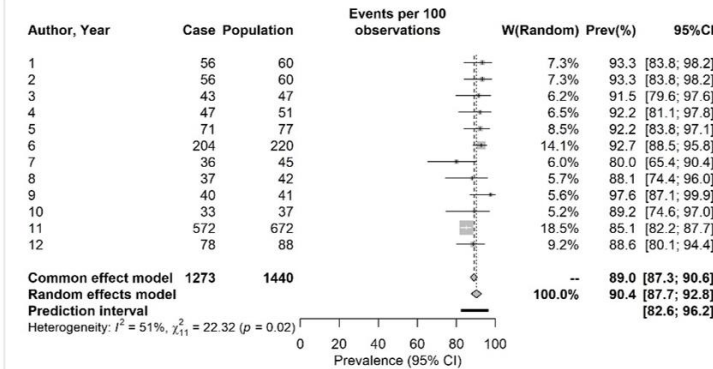
Supplementary Figure 7. Pooled atrial fibrillation and renal insufficiency variables – Second period

Pooled medical and device therapies at baseline First 5-year period

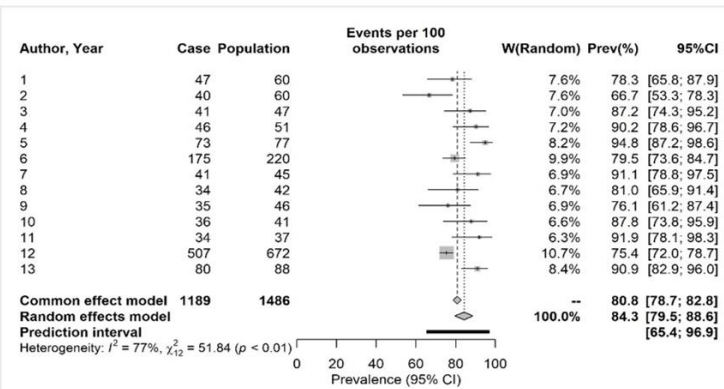
ACEI/ARB



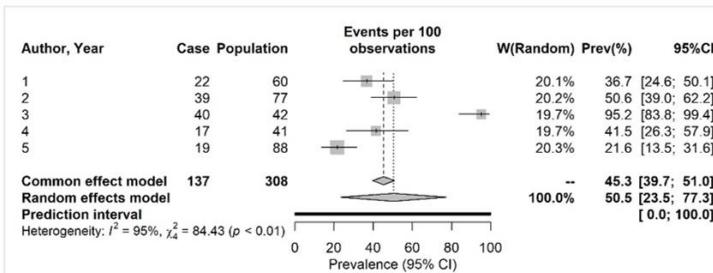
Diuretics



Beta-blockers

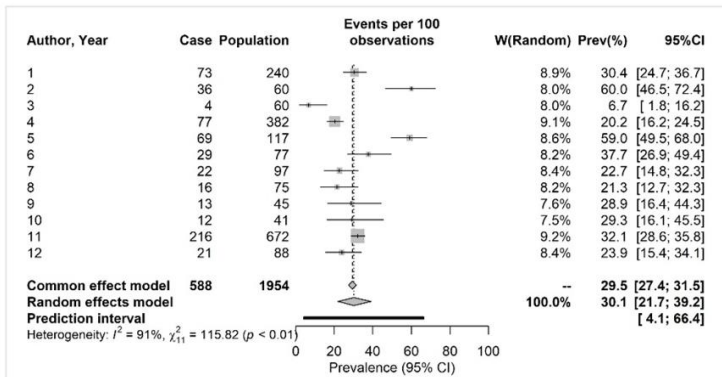


Oral anticoagulation agents

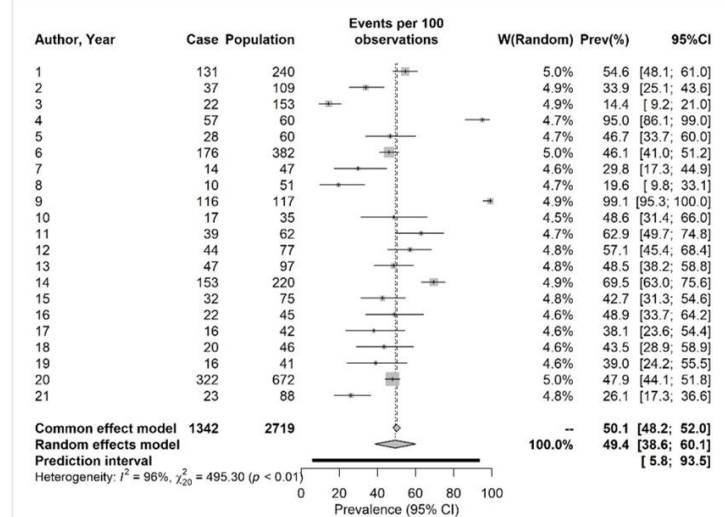


Supplementary Figure 8. Pooled medications at baseline – First period

ICD device



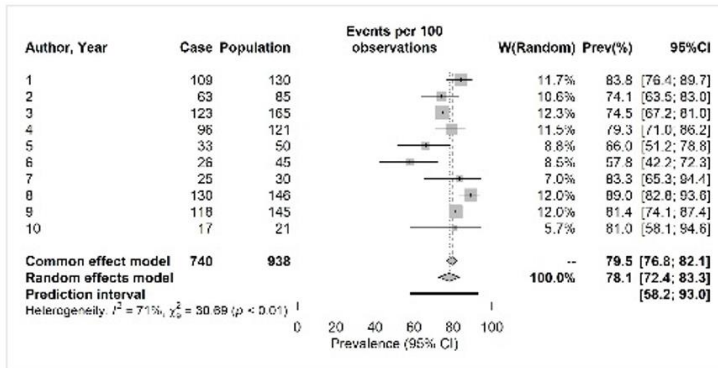
Any cardiac device



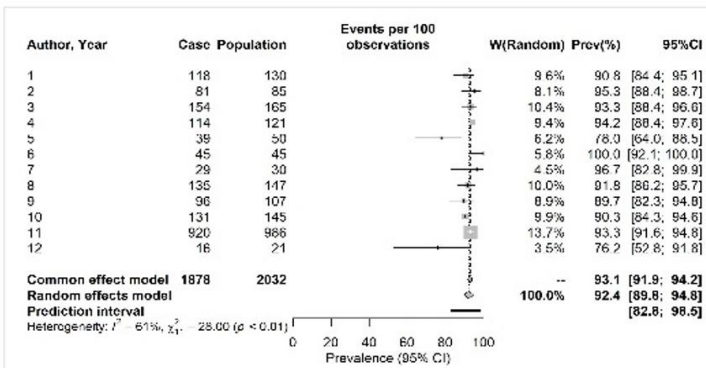
Supplementary Figure 9. Pooled implantable cardiac devices at baseline – First period

Pooled medical and device therapies at baseline Second 5-year period

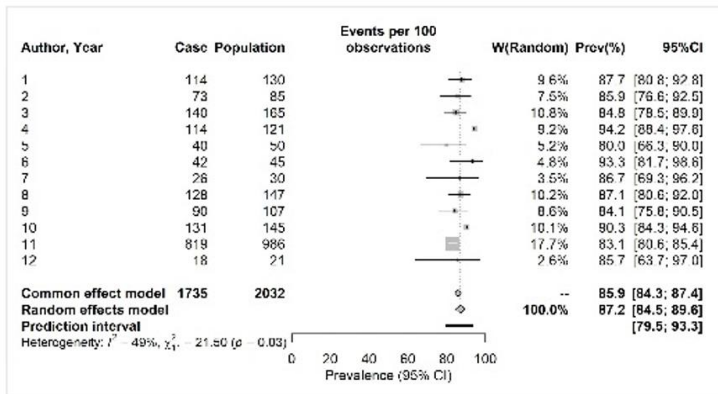
ACEI/ARB



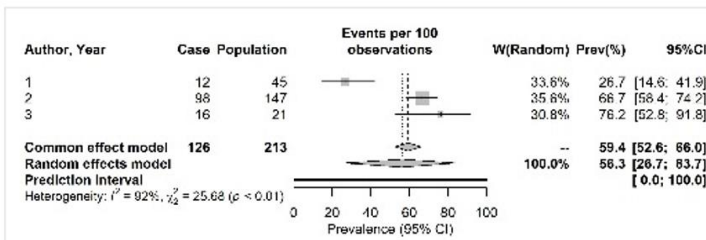
Diuretics



Beta-blockers

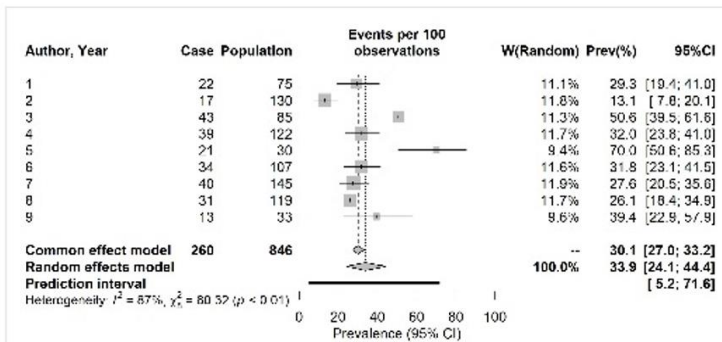


Oral anticoagulation agents

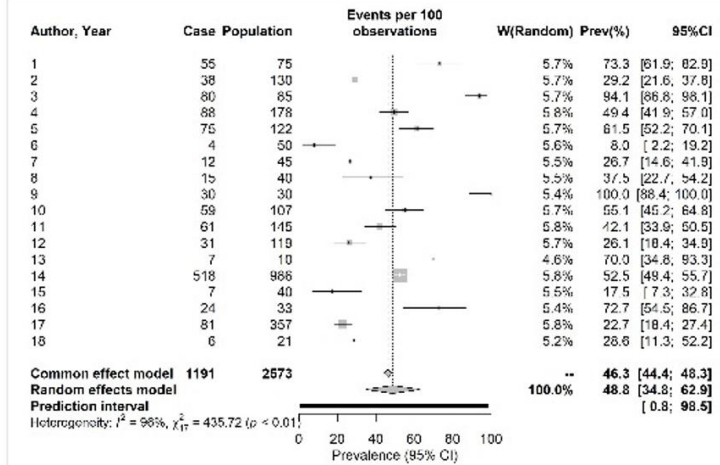


Supplementary Figure 10. Pooled medications at baseline – Second period

ICD device



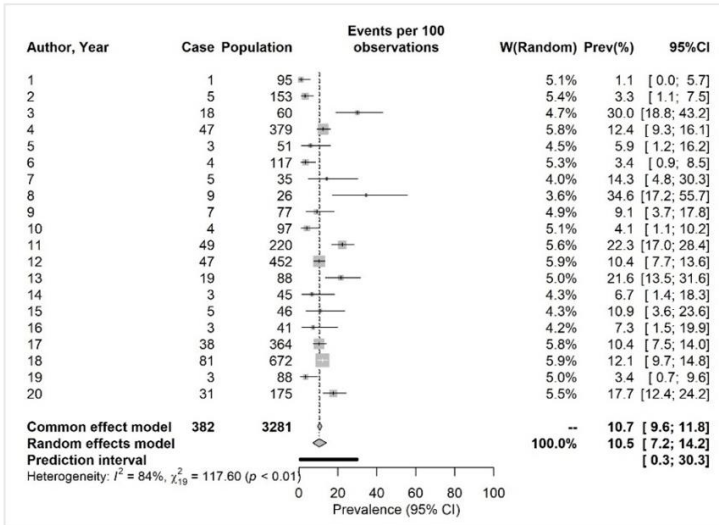
Any cardiac device



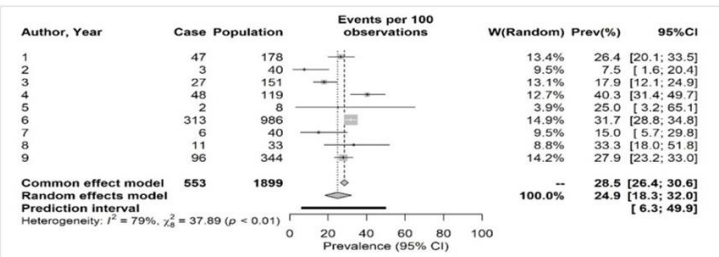
Supplementary Figure 11. Pooled implantable cardiac devices at baseline – Second period

Pooled variables at presentation to hospital First 5-year period

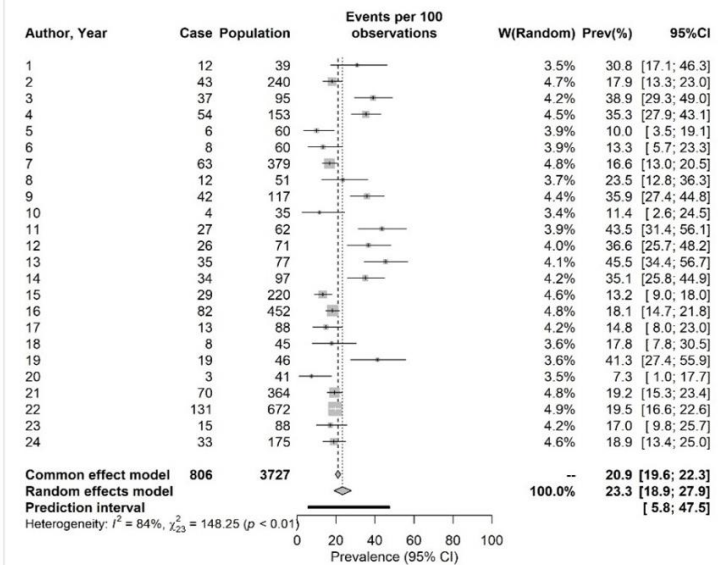
NYHA class II



NYHA class III

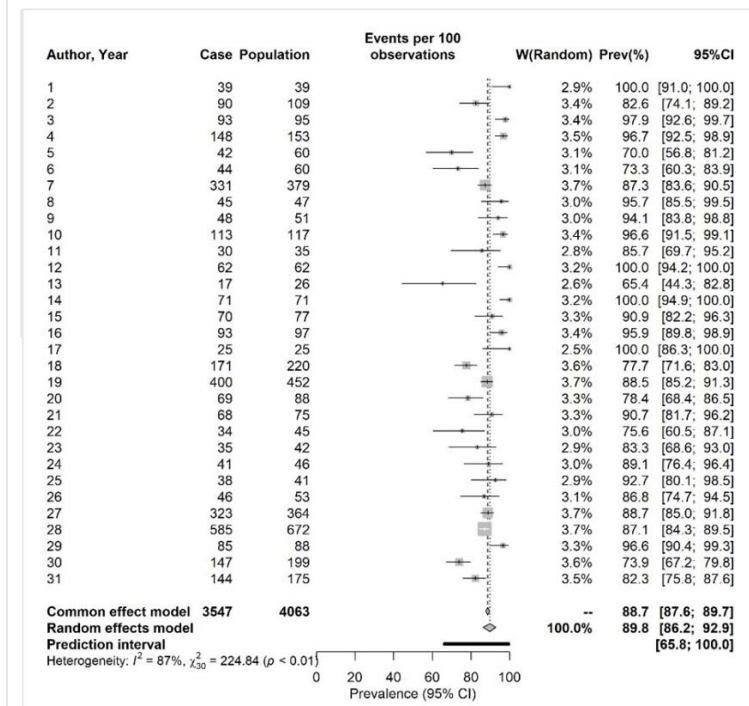


NYHA class IV

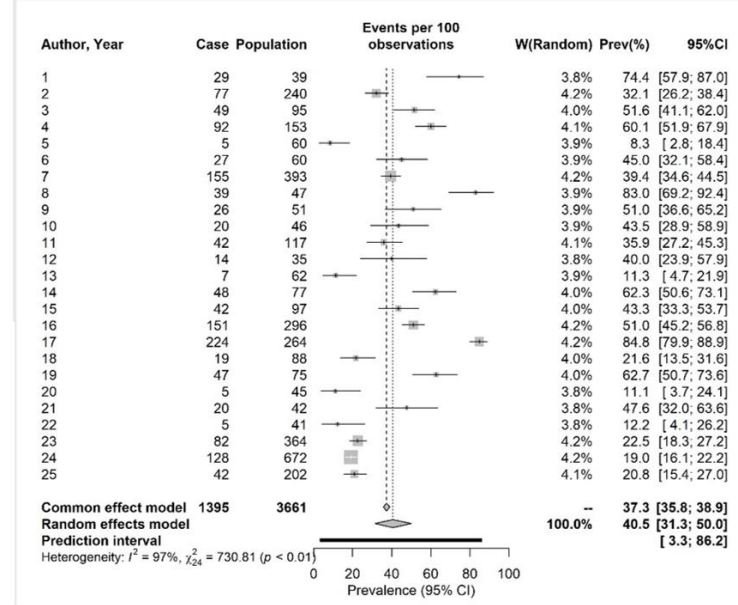


Supplementary Figure 12. Pooled NYHA class (II, III, IV) at hospital presentation – First period

NYHA class III/IV

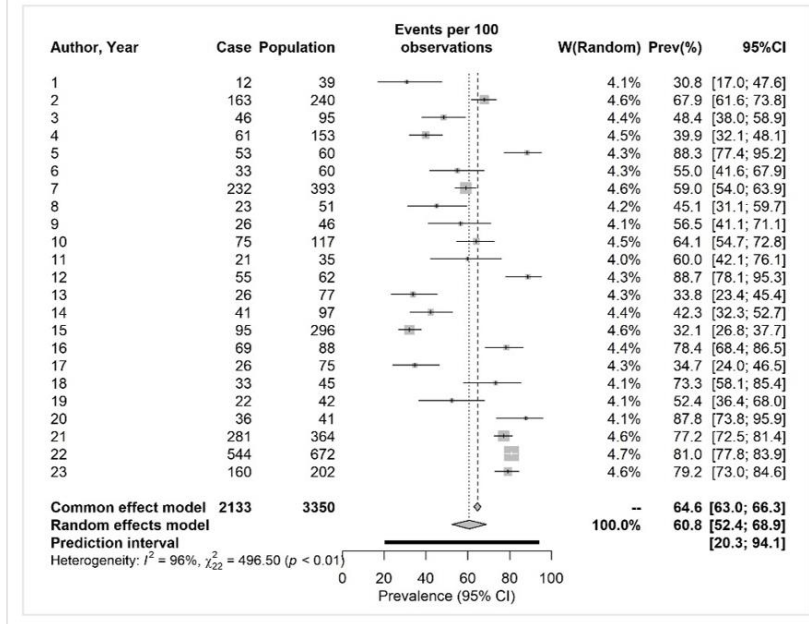


MR grade 3+



Supplementary Figure 13. Pooled NYHA class III/IV and MR grade 3+ at hospital presentation – First period

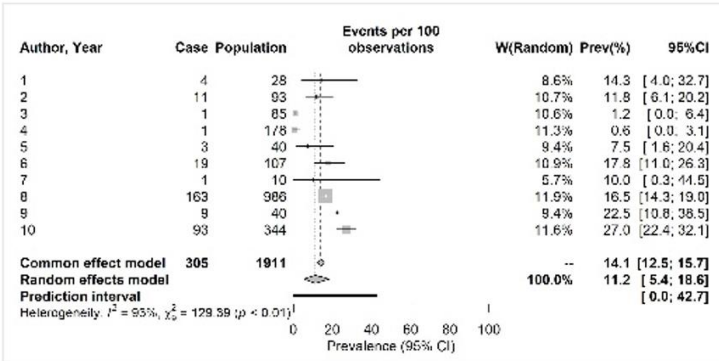
MR grade 4+



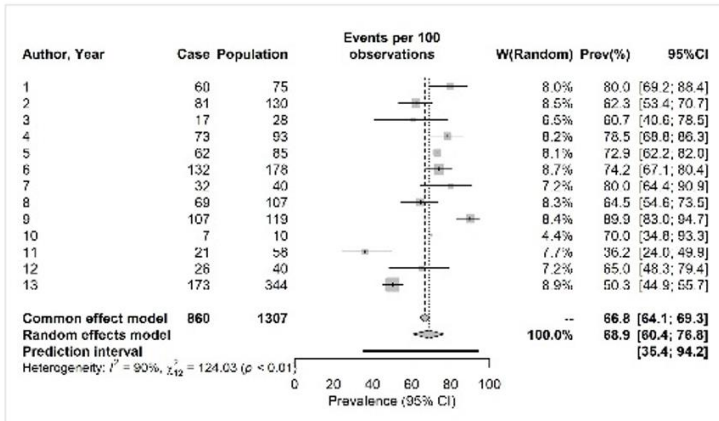
Supplementary Figure 14. Pooled MR grade 4+ at hospital presentation – First period

Pooled variables at presentation to hospital
Second 5-year period

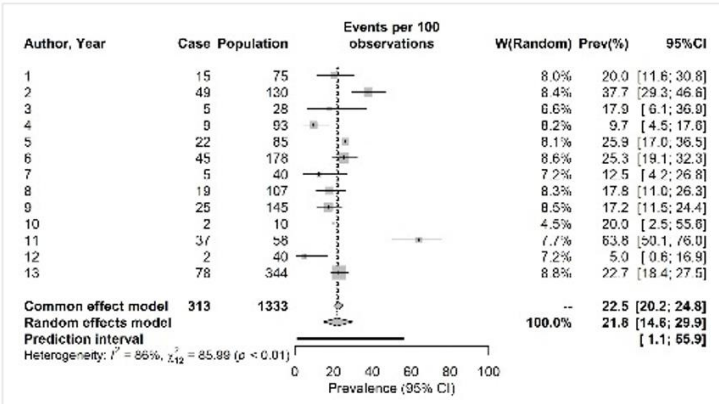
NYHA class II



NYHA class III

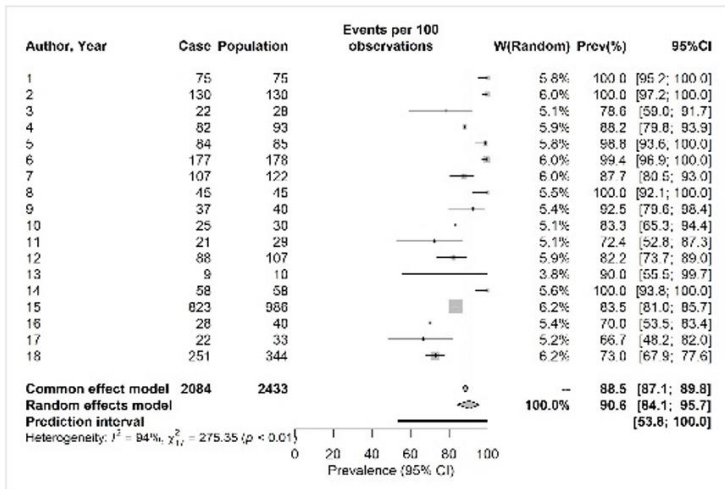


NYHA class IV

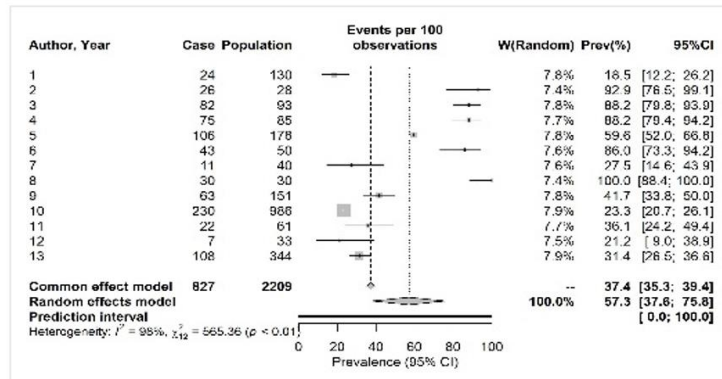


Supplementary Figure 15. Pooled NYHA class (II, III, IV) at hospital presentation – Second period

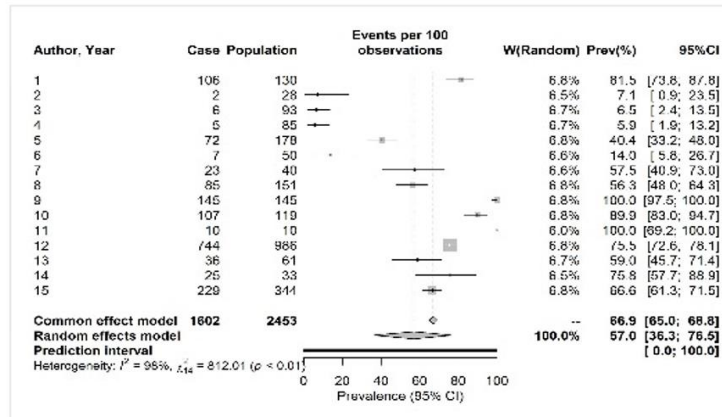
NYHA class III/IV



MR grade 3+



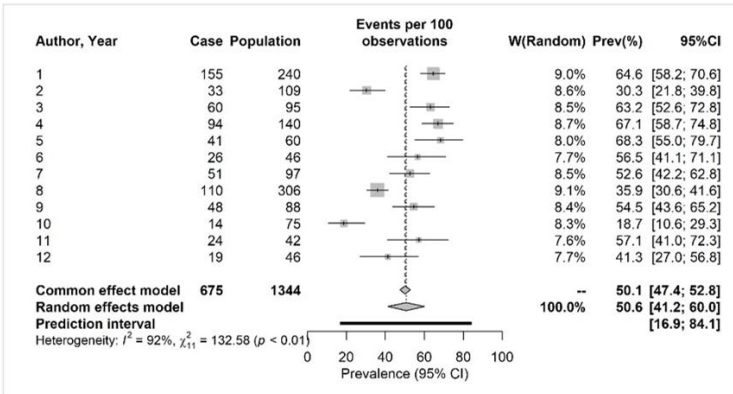
MR grade 4+



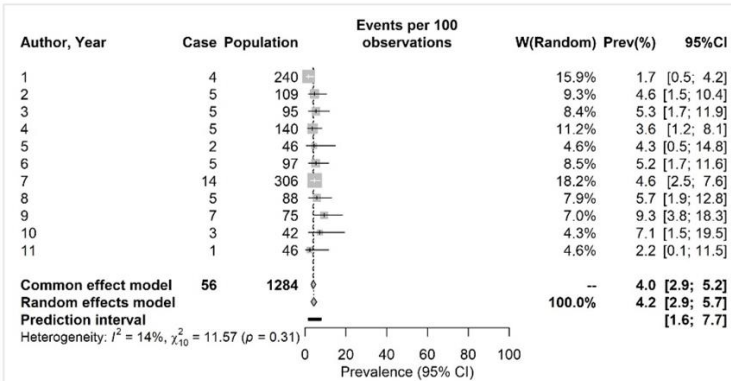
Supplementary Figure 16. Pooled NYHA class III/IV, MR grade 3+, MR grade 4+ at hospital presentation – Second period

Pooled procedural outcomes First 5-year period

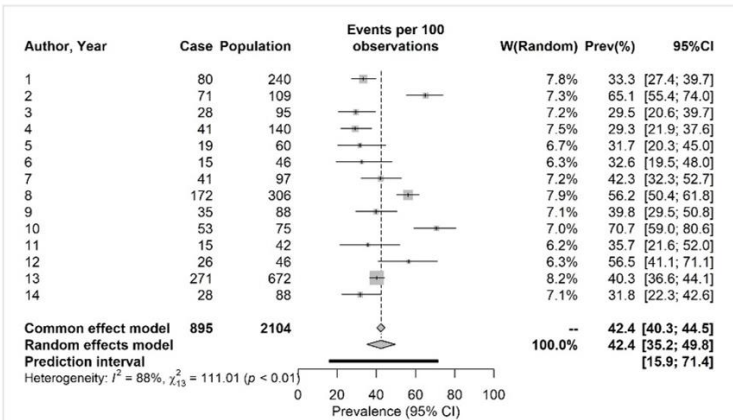
One clip implanted



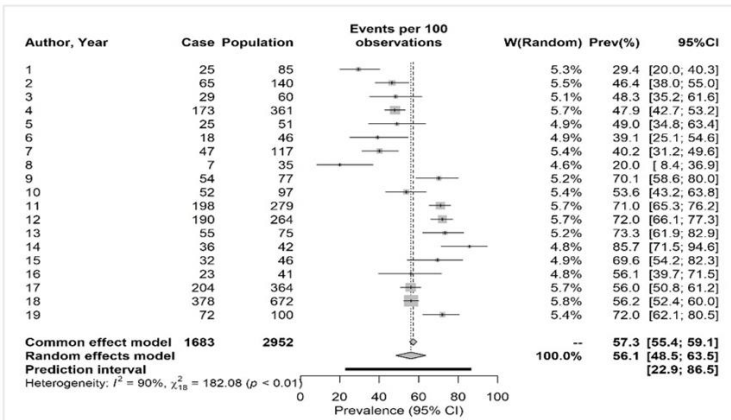
Three or more clips implanted



Two clips implanted

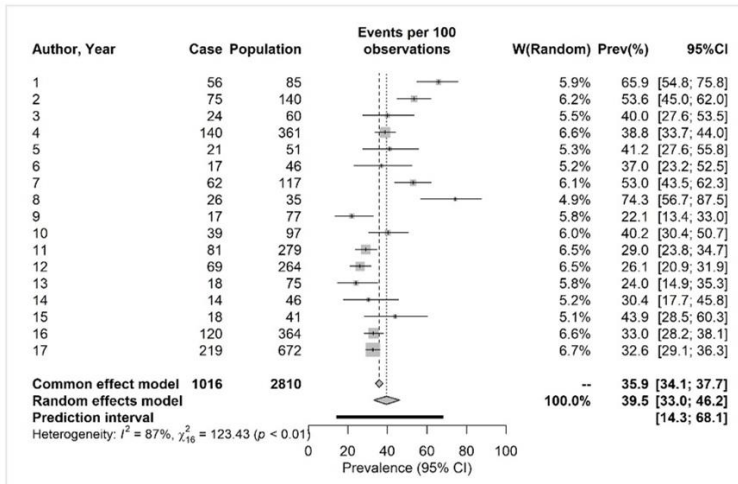


MR grade 1+

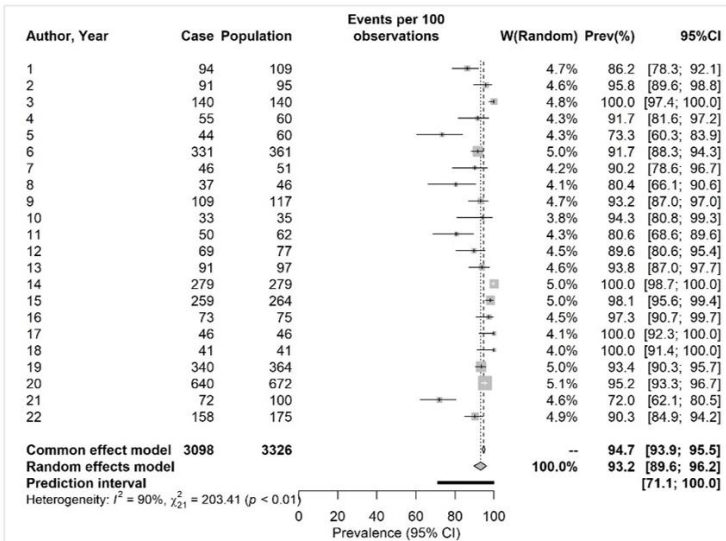


Supplementary Figure 17. Pooled implanted clips number and MR grade 1+ post procedure – First period

MR grade 2+

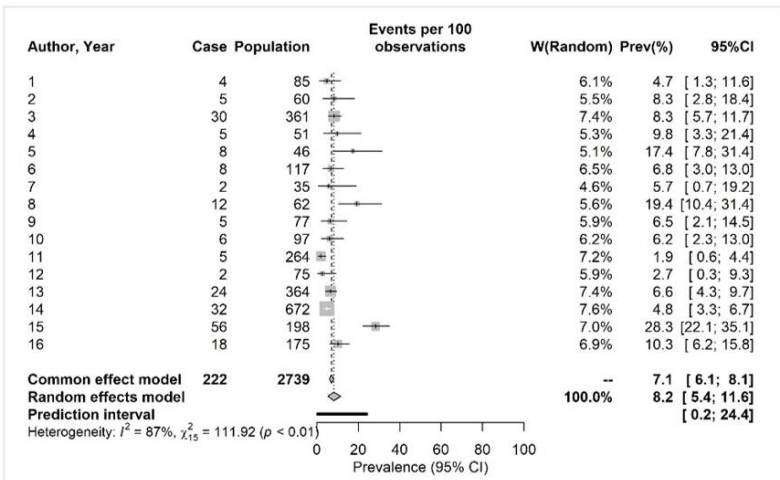


MR grade ≤2+



Supplementary Figure 18. Pooled MR grades 2+ or less post procedure – First period

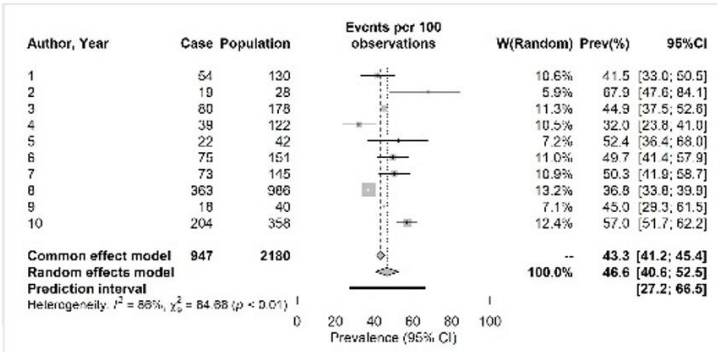
MR grade $\geq 3+$



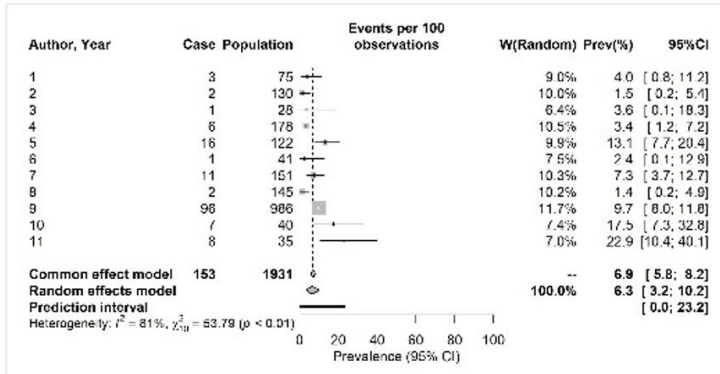
Supplementary Figure 19. Pooled MR grades 3+ or more post procedure – First period

Pooled procedural outcomes Second 5-year period

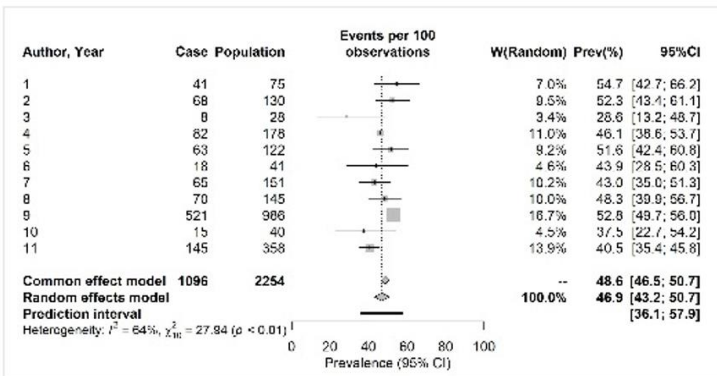
One clip implanted



Three or more clips implanted

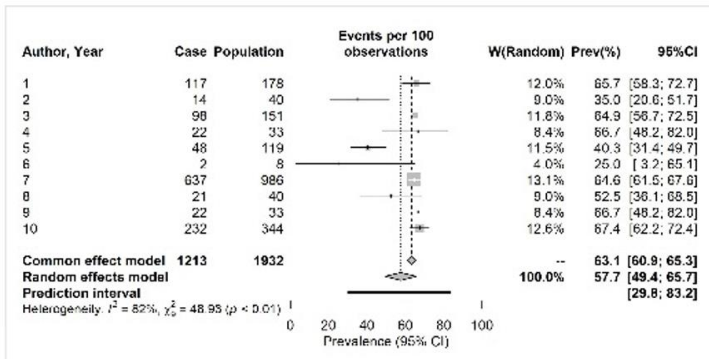


Two clips implanted

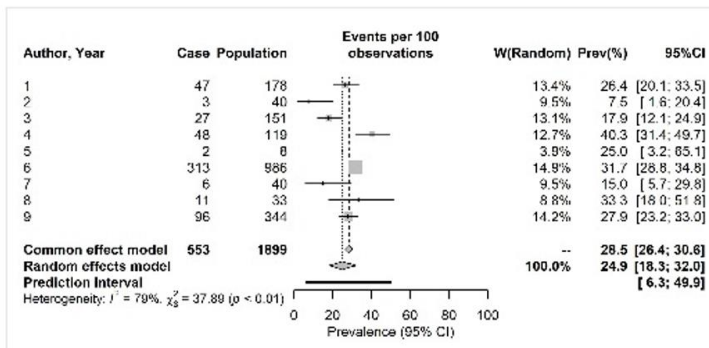


Supplementary Figure 20. Pooled implanted clips number post procedure – Second period

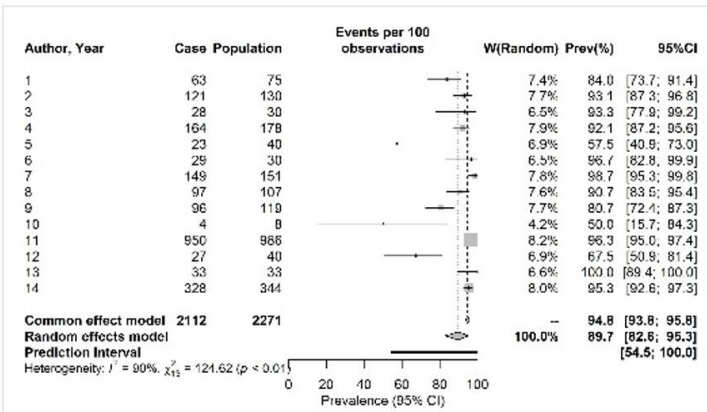
MR grade 1+



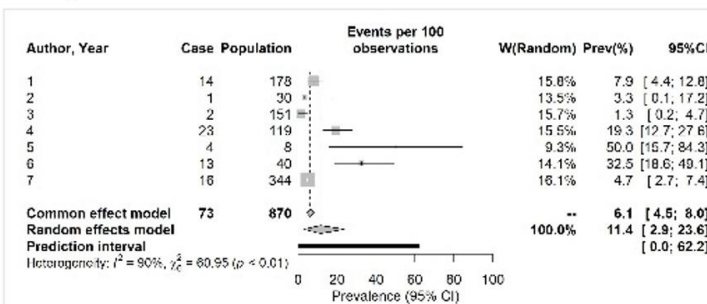
MR grade 2+



MR grade ≤2+



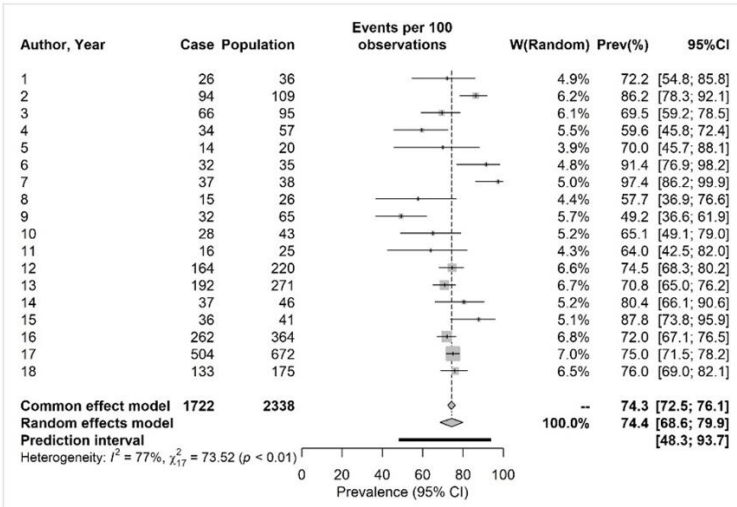
MR grade ≥3+



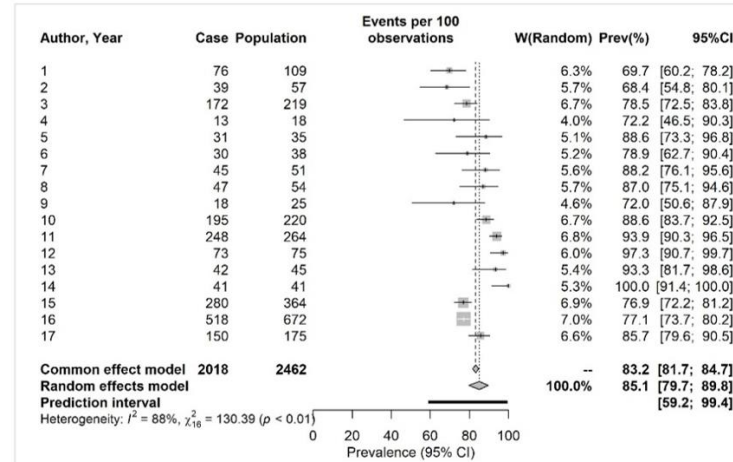
Supplementary Figure 21. Pooled MR grades post procedure – Second period

Pooled outcomes at 12-month follow-up
First 5-year period

NYHA class I/II

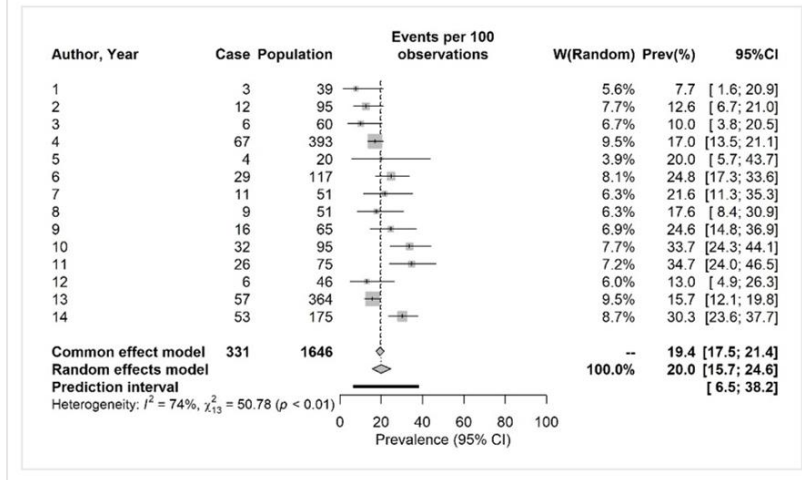


MR grade $\leq 2+$



Supplementary Figure 22. Pooled NYHA class and MR grade at 12-month follow-up – First period

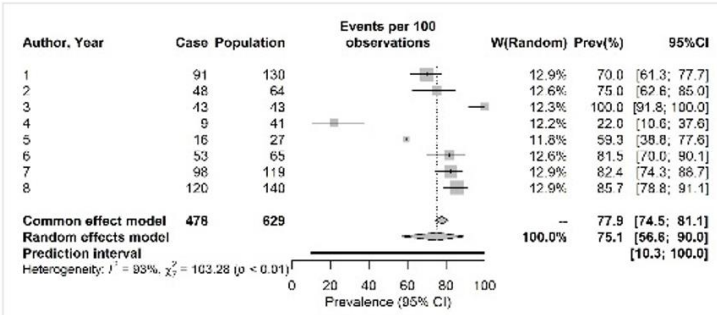
All-cause death



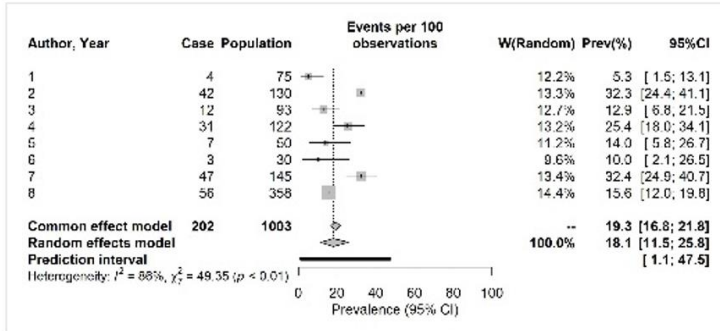
Supplementary Figure 23. Pooled all-cause death at 12-month follow-up – First period

**Pooled outcomes at 12-month follow-up
Second 5-year period**

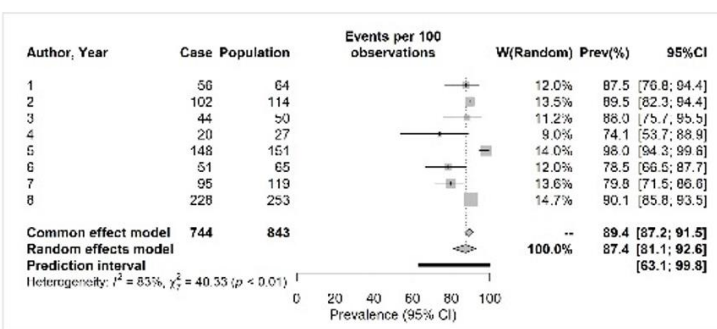
NYHA class I/II



All-cause death



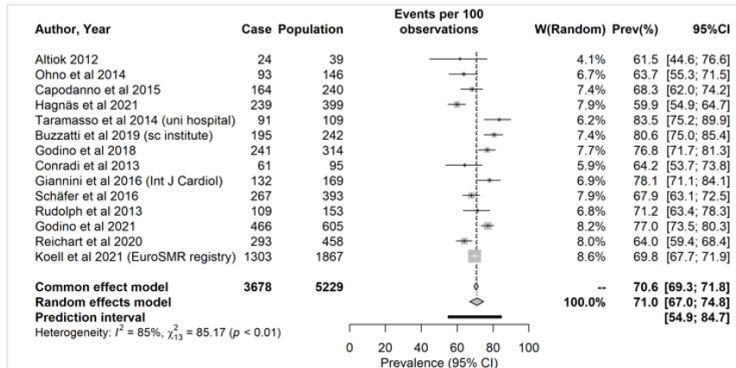
MR grade ≤2+



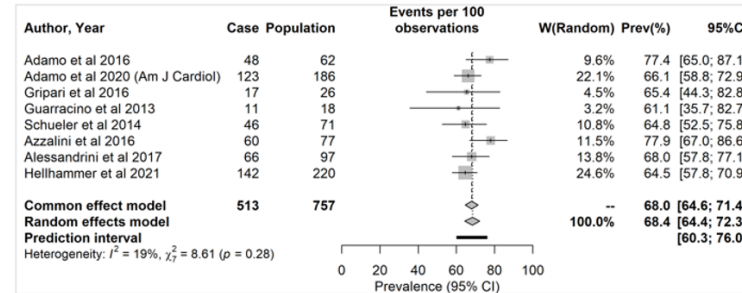
Supplementary Figure 24. Pooled outcomes at 12-month follow-up – Second period

Analysis on year-by-year basis

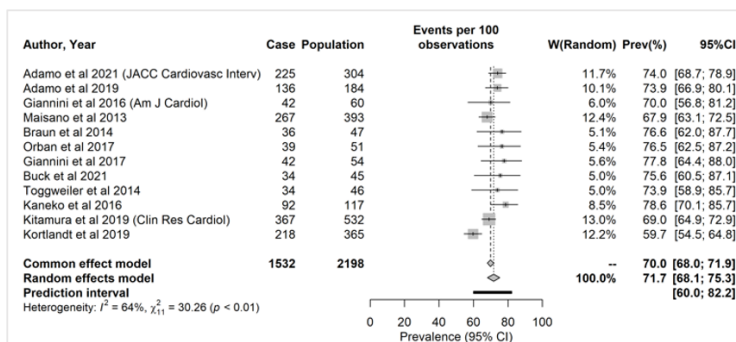
Male 2008



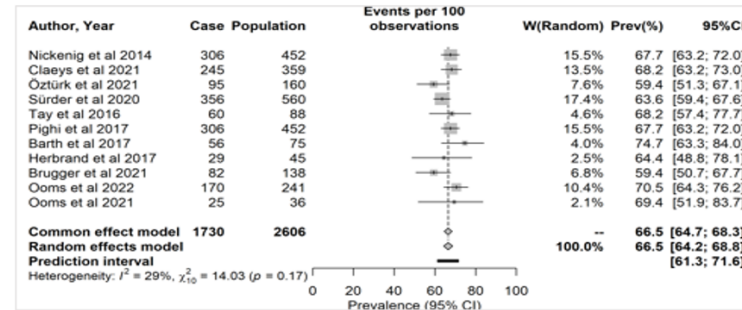
Male 2010



Male 2009

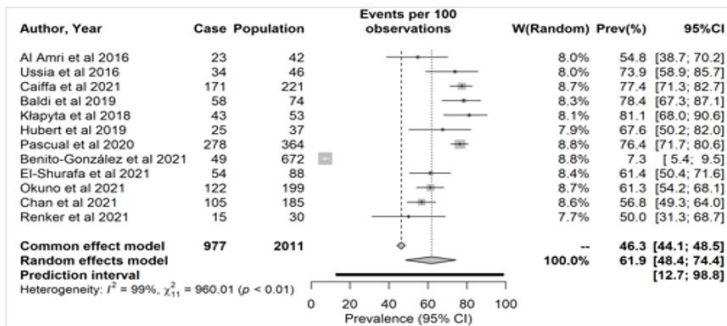


Male 2011

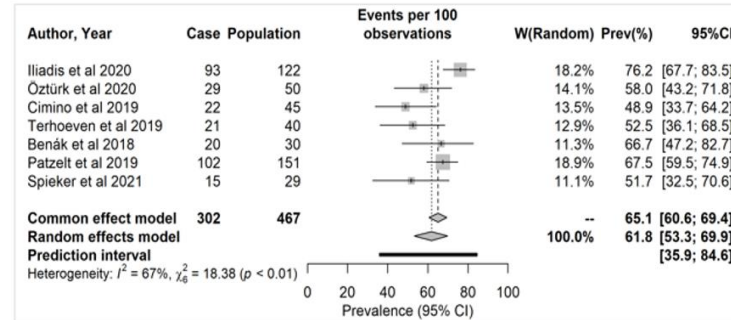


Supplementary Figure 25. Pooled male variable according to start of recruitment year 2008, 2009, 2010, 2011

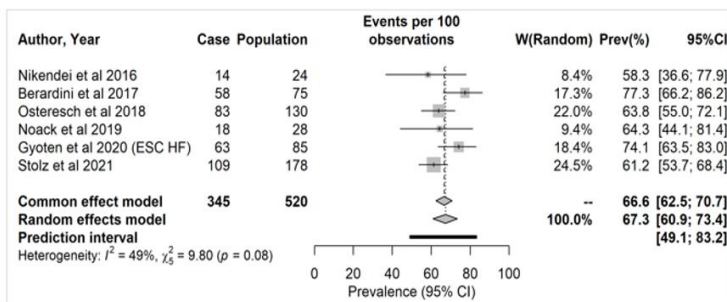
Male 2012



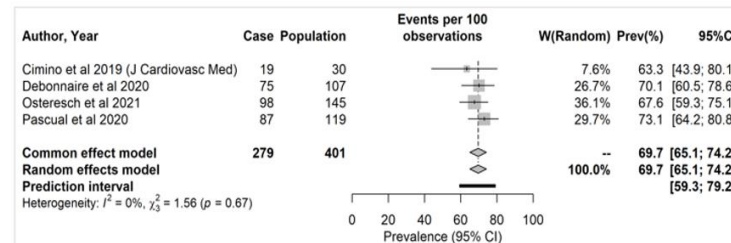
Male 2014



Male 2013

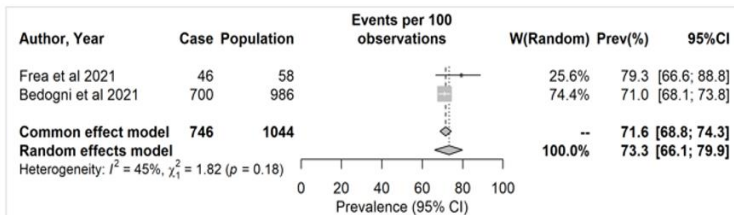


Male 2015

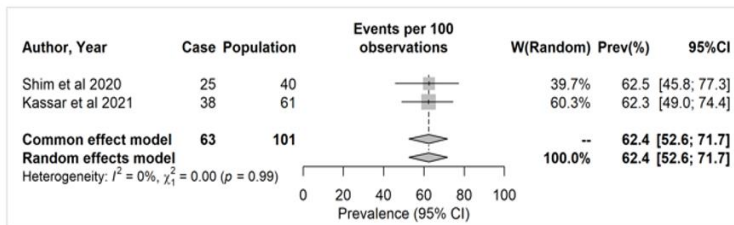


Supplementary Figure 26. Pooled male variable according to start of recruitment year 2012, 2013, 2014, 2015

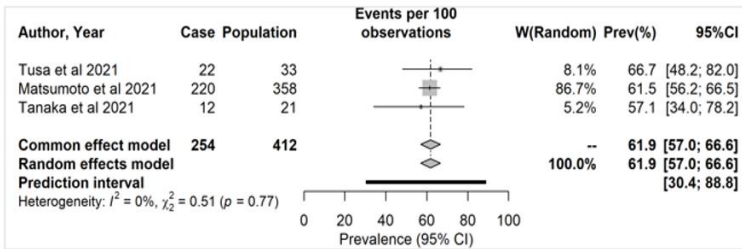
Male 2016



Male 2017

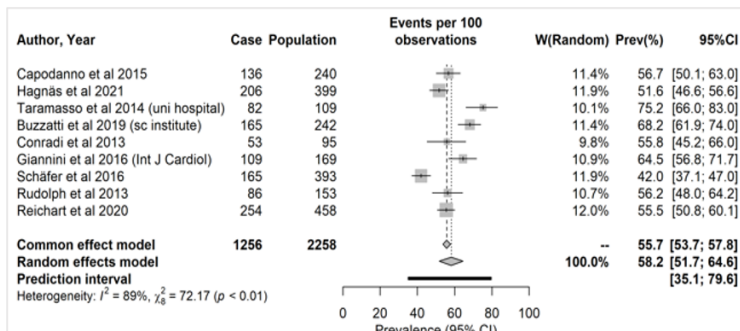


Male 2018

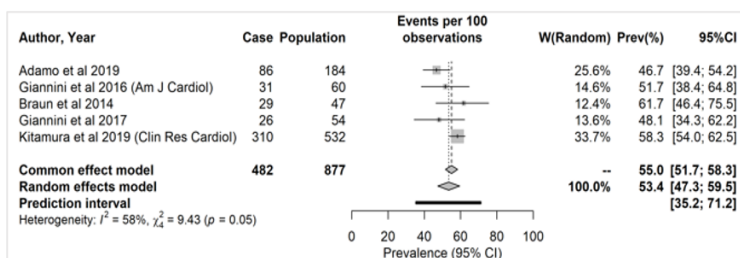


Supplementary Figure 27. Pooled male variable according to start of recruitment year 2016, 2017, 2018

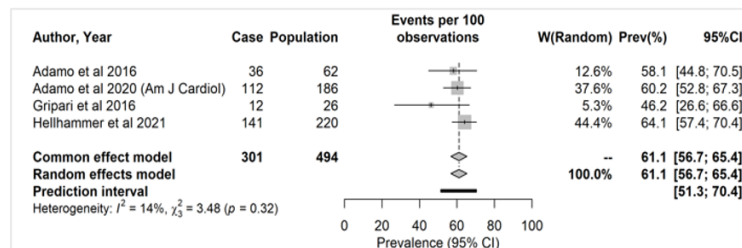
NICM 2008



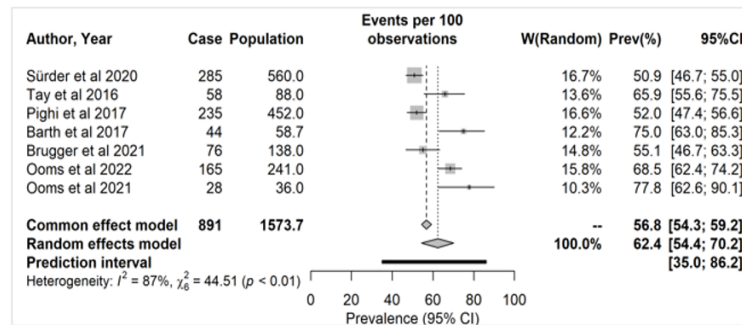
NICM 2009



NICM 2010

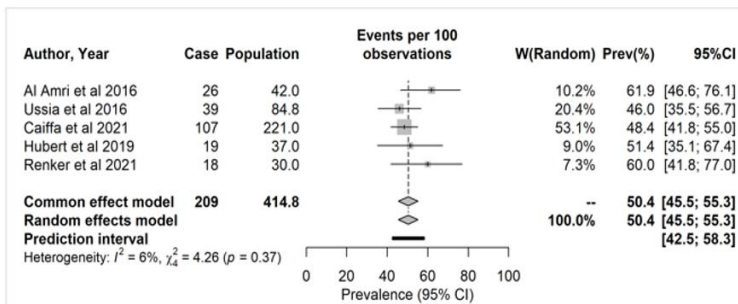


NICM 2011

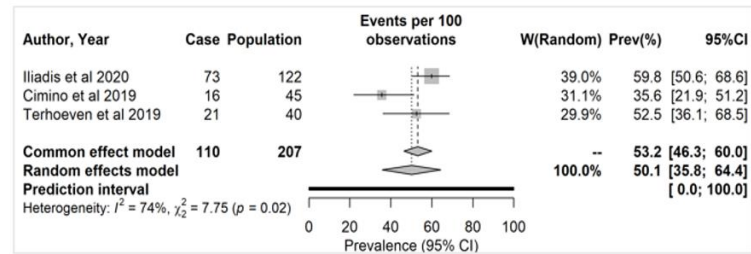


Supplementary Figure 28. Pooled NICM variable according to start of recruitment year 2008, 2009, 2010, 2011

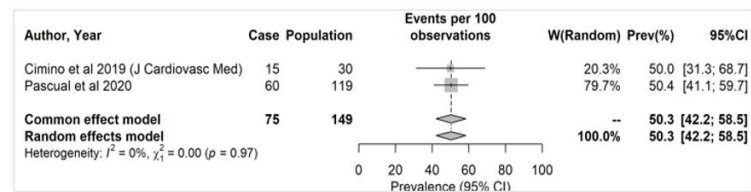
NICM2012



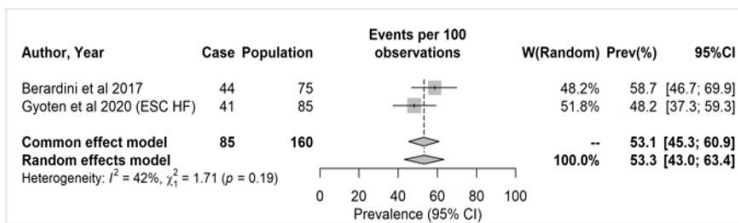
NICM 2014



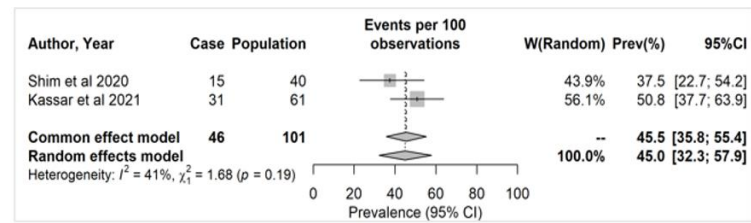
NICM 2015



NICM 2013



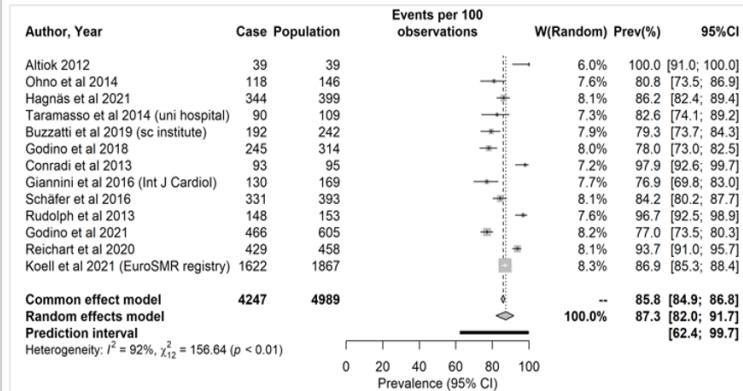
NICM 2017



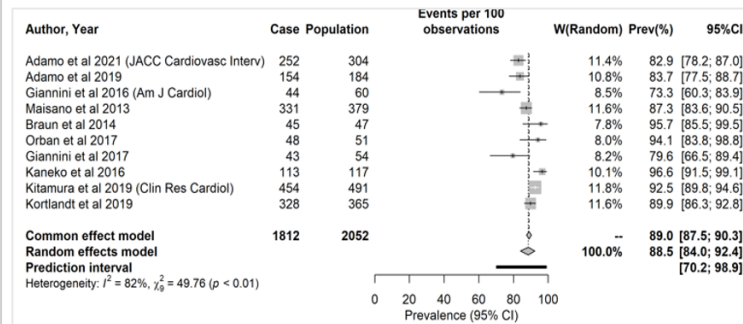
Supplementary Figure 29. Pooled NICM variable according to start of recruitment year 2012, 2013, 2014, 2015, 2017

NYHA III/IV at baseline

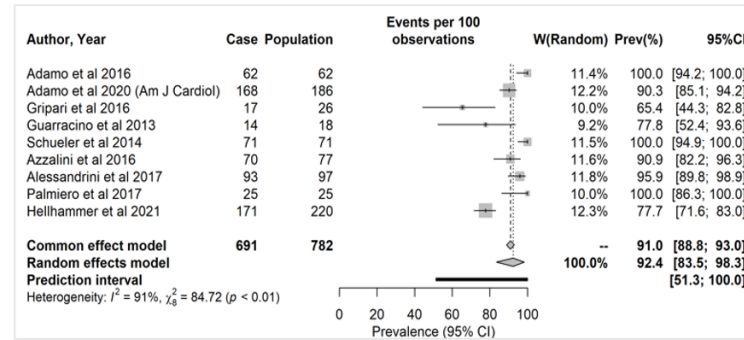
NYHA III/IV 2008



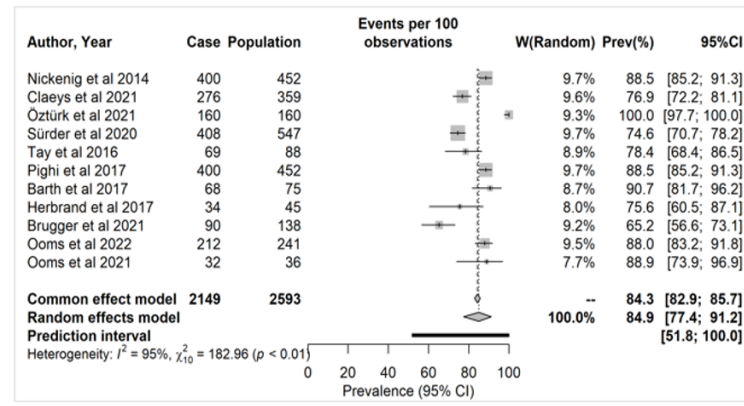
NYHA III/IV 2009



NYHA III/IV 2010

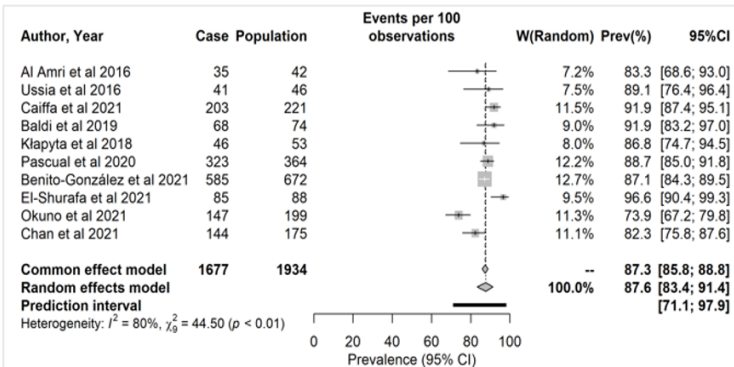


NYHA III/IV 2011

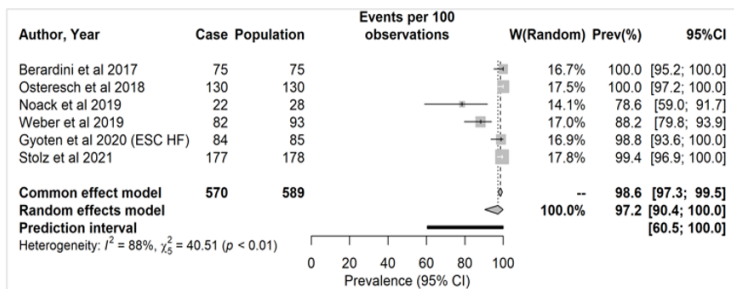


Supplementary Figure 30. Pooled NYHA class III/IV variable according to start of recruitment year 2008, 2009, 2010, 2011

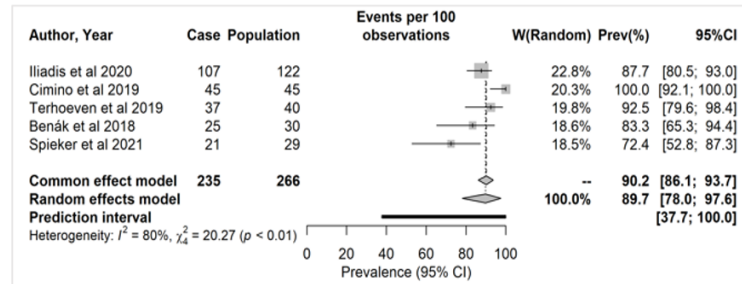
NYHA III/IV 2012



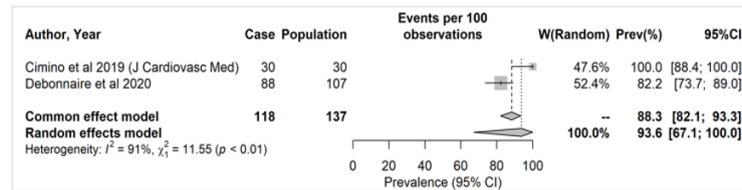
NYHA III/IV 2013



NYHA III/IV 2014

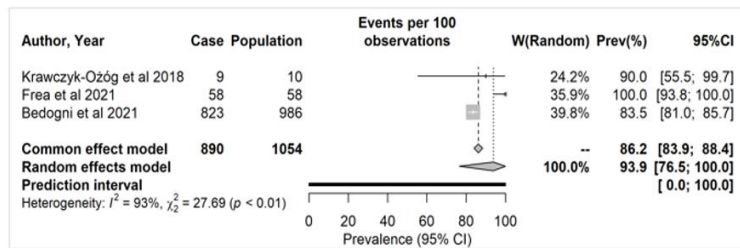


NYHA III/IV 2015



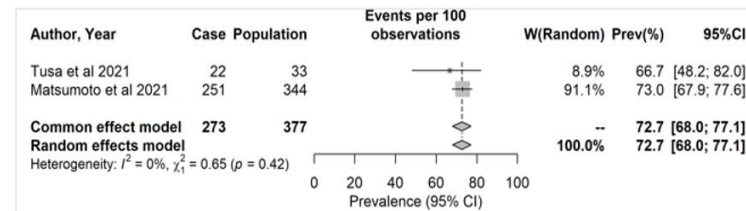
Supplementary Figure 31. Pooled NYHA class III/IV variable according to start of recruitment year 2012, 2013, 2014, 2015

NYHA III/IV 2016



NYHA III/IV 2017 – 1 study: 70.0%

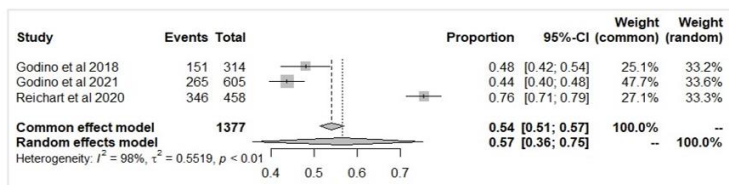
NYHA III/IV 2018



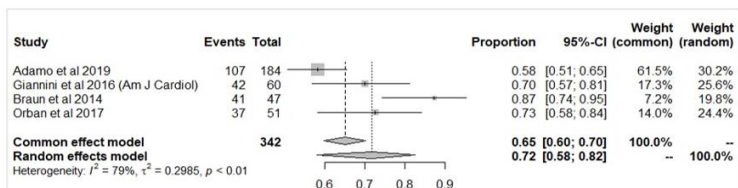
Supplementary Figure 32. Pooled NYHA class III/IV variable according to start of recruitment year 2016, 2017, 2018

ACEI/ARB

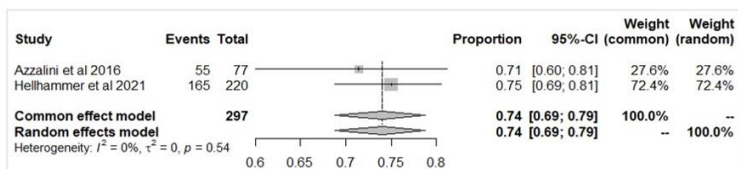
ACEI/ARB 2008



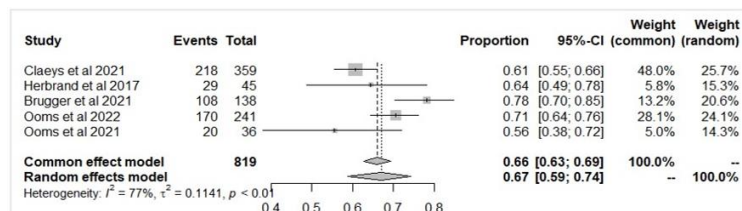
ACEI/ARB 2009



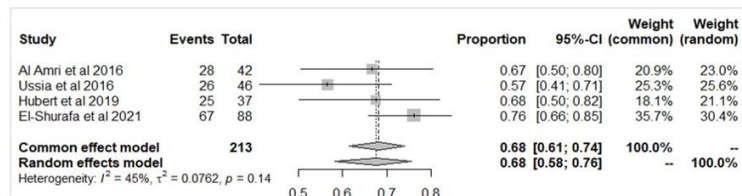
ACEI/ARB 2010



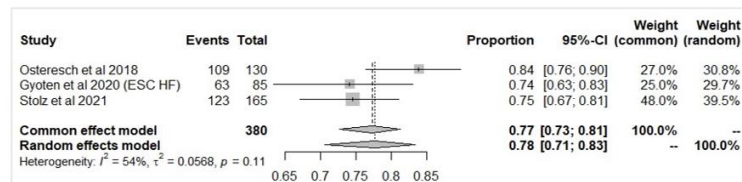
ACEI/ARB 2011



ACEI/ARB 2012

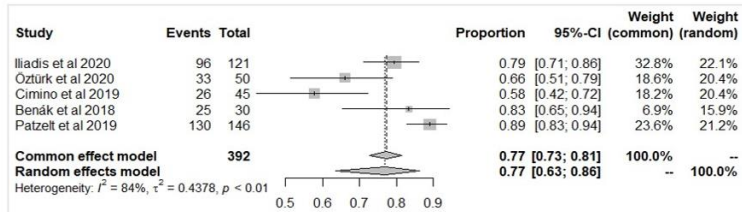


ACEI/ARB 2013



Supplementary Figure 33. Pooled ACEI/ARB variable according to start of recruitment year 2008, 2009, 2010, 2011, 2012, 2013

ACEI/ARB 2014

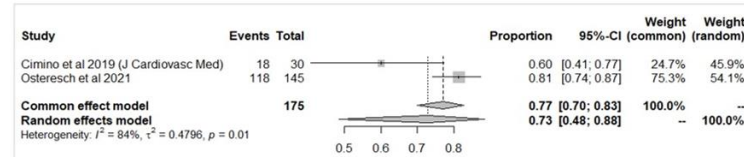


ACEI/ARB 2016 – not reported in the related studies

ACEI/ARB 2017 – not reported in the related studies

ACEI/ARB 2018 – 1 study: 80.9%

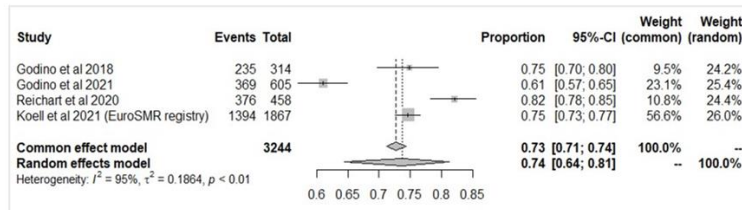
ACEI/ARB 2015



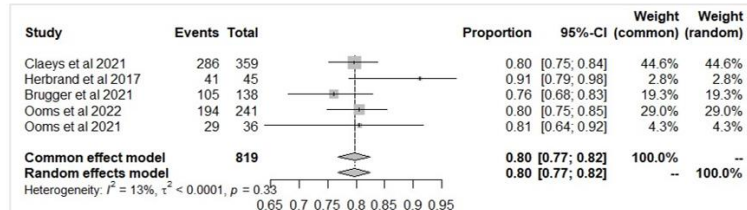
Supplementary Figure 34. Pooled ACEI/ARB variable according to start of recruitment year 2014, 2015, 2016, 2017, 2018

Beta-blockers

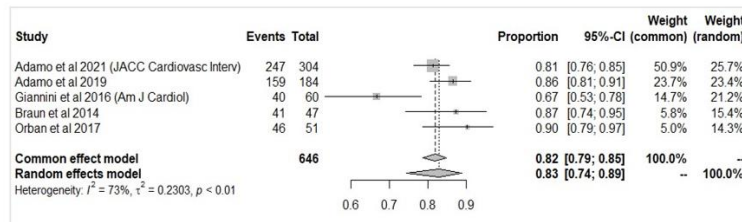
Beta-blockers 2008



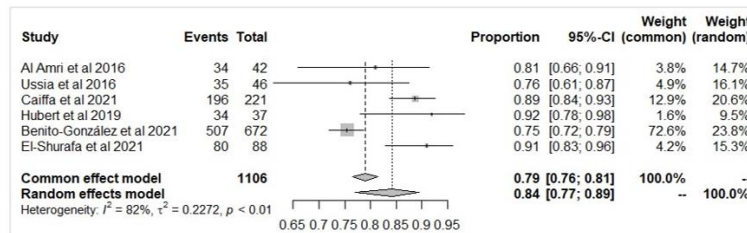
Beta-blockers 2011



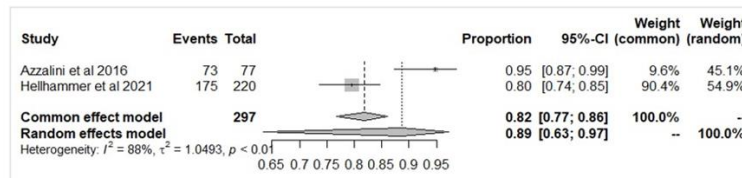
Beta-blockers 2009



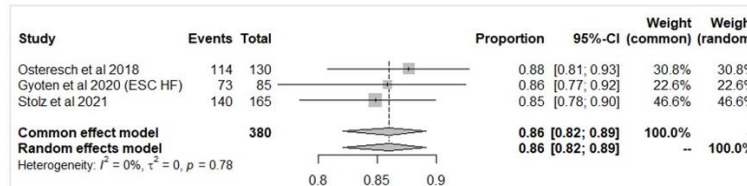
Beta-blockers 2012



Beta-blockers 2010

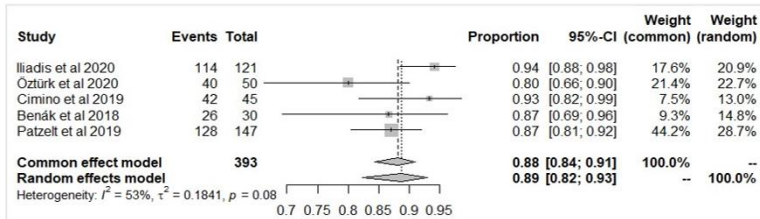


Beta-blockers 2013



Supplementary Figure 35. Pooled beta-blockers variable according to start of recruitment year 2008, 2009, 2010, 2011, 2012, 2013

Beta-blockers 2014

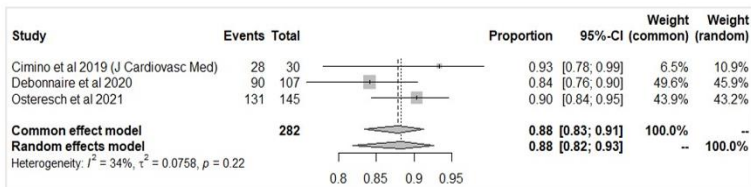


Beta-blockers 2016 – 1 study: 83.1%

Beta-blockers 2017 – not reported in the related studies

Beta-blockers 2018 – 1 study: 86.0%

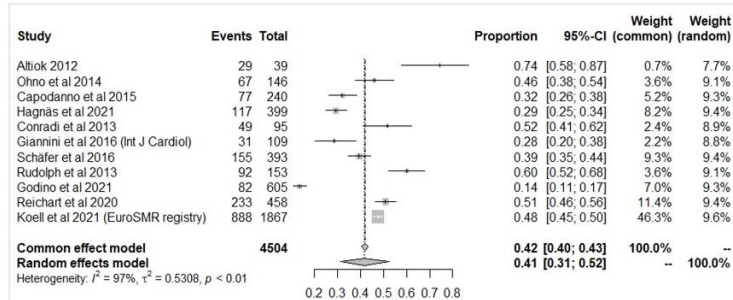
Beta-blockers 2015



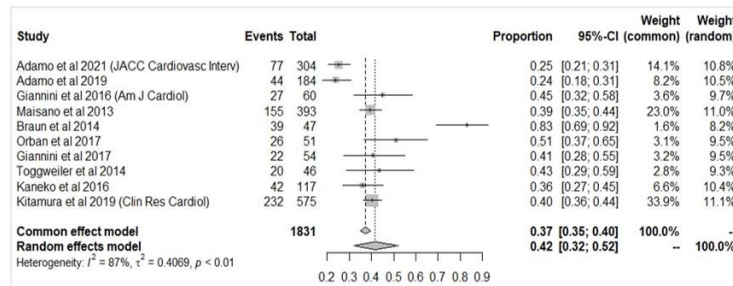
Supplementary Figure 36. Pooled beta-blockers variable according to start of recruitment year 2014, 2015, 2016, 2017, 2018

MR grade 3+ at baseline

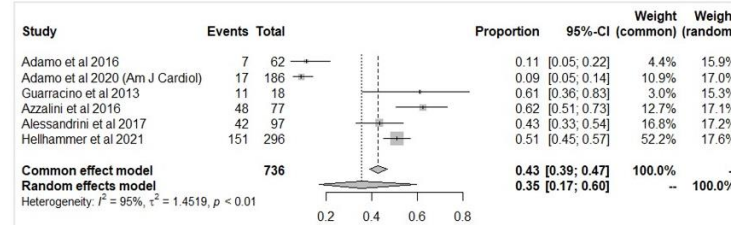
MR grade 3+ 2008



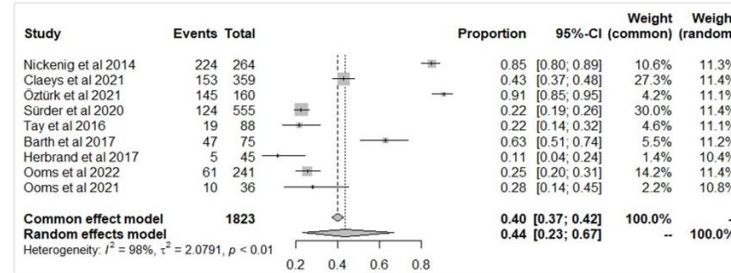
MR grade 3+ 2009



MR grade 3+ 2010

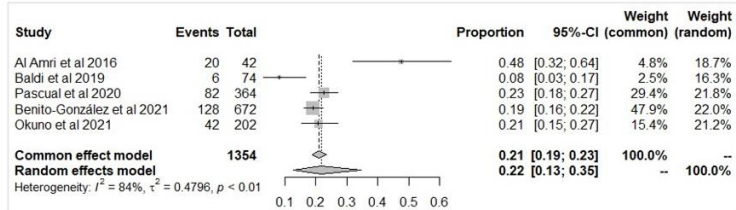


MR grade 3+ 2011

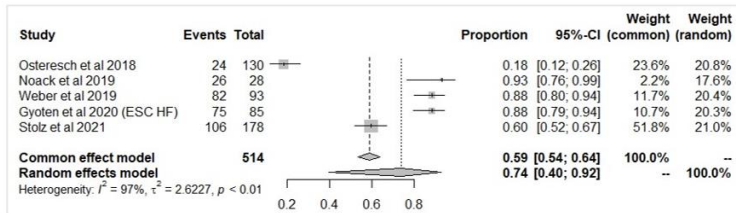


Supplementary Figure 37. Pooled MR grade 3+ at baseline according to start of recruitment year 2008, 2009, 2010, 2011

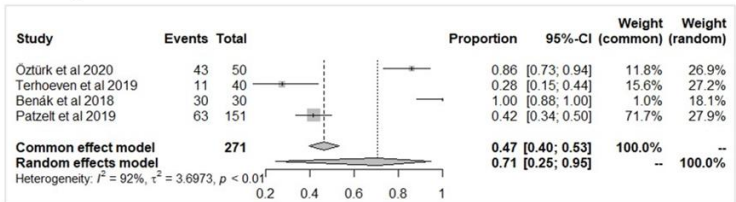
MR grade 3+ 2012



MR grade 3+ 2013



MR grade 3+ 2014

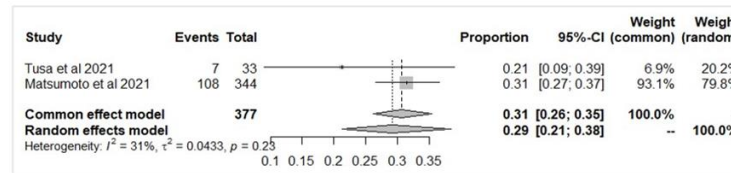


MR grade 3+ 2015 – not reported in the related studies

MR grade 3+ 2016 – 1 study: 23.3%

MR grade 3+ 2017 – 1 study: 34.4%

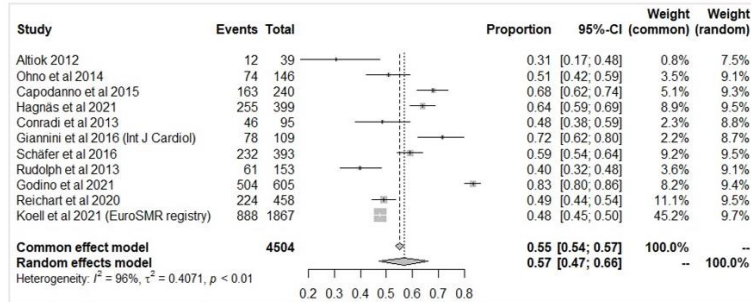
MR grade 3+ 2018



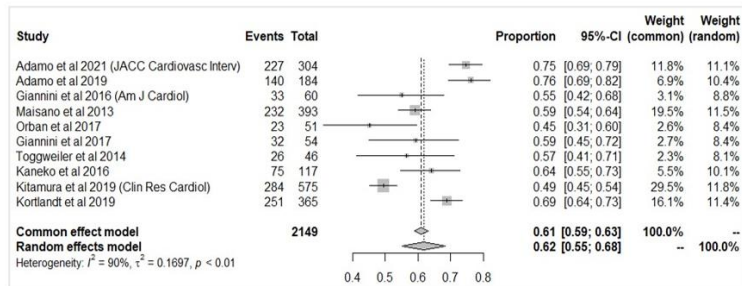
Supplementary Figure 38. Pooled MR grade 3+ at baseline according to start of recruitment year 2012, 2013, 2014, 2015, 2016, 2017, 2018

MR grade 4+ at baseline

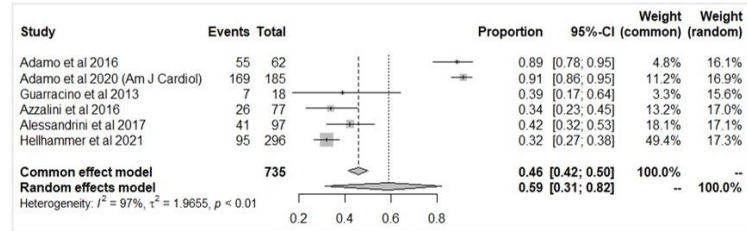
MR grade 4+ 2008



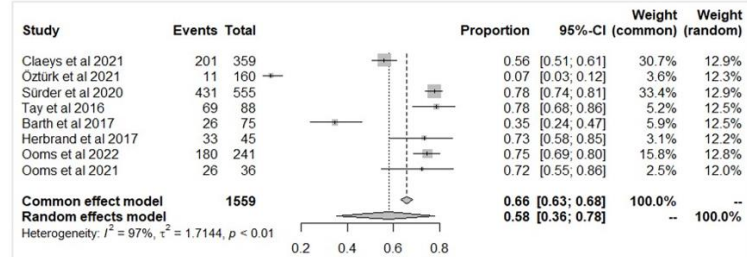
MR grade 4+ 2009



MR grade 4+ 2010

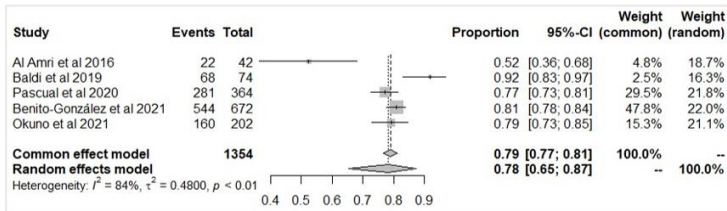


MR grade 4+ 2011

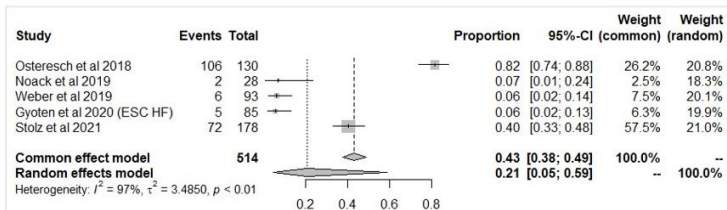


Supplementary Figure 39. Pooled MR grade 4+ at baseline according to start of recruitment year 2008, 2009, 2010, 2011

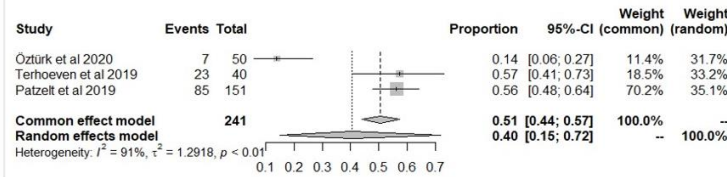
MR grade 4+ 2012



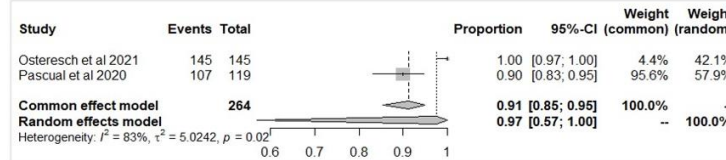
MR grade 4+ 2013



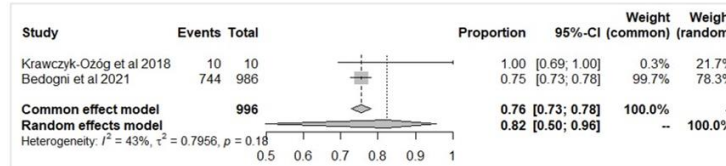
MR grade 4+ 2014



MR grade 4+ 2015

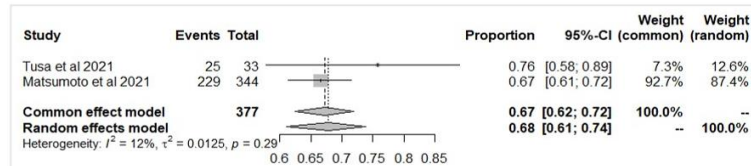


MR grade 4+ 2016



MR grade 4+ 2017 – 1 study: 59.0%

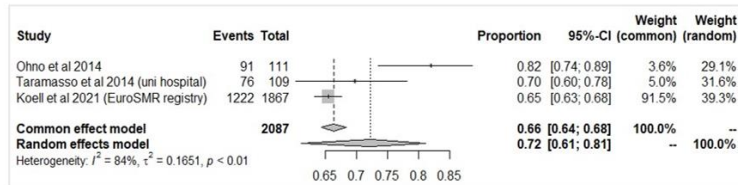
MR grade 4+ 2018



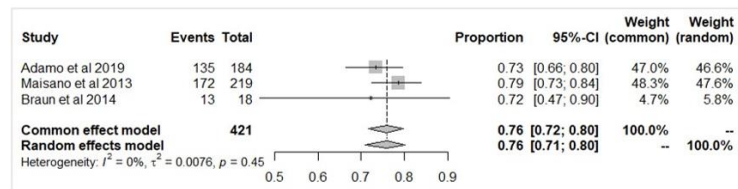
Supplementary Figure 40. Pooled MR grade 4+ at baseline according to start of recruitment year 2012, 2013, 2014, 2015, 2016, 2017, 2018

MR grade $\leq 2+$ at 12-month follow-up

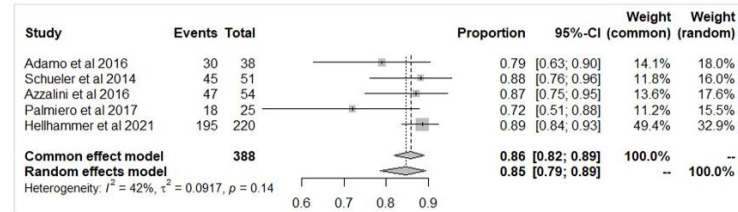
MR grade $\leq 2+$ at follow-up 2008



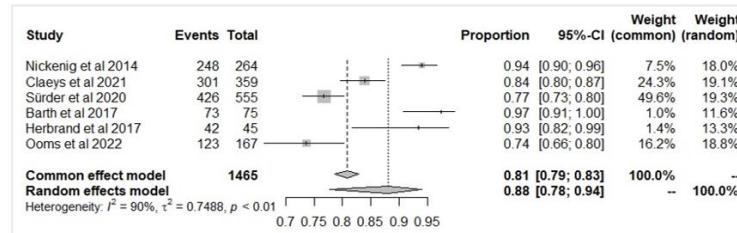
MR grade $\leq 2+$ at follow-up 2009



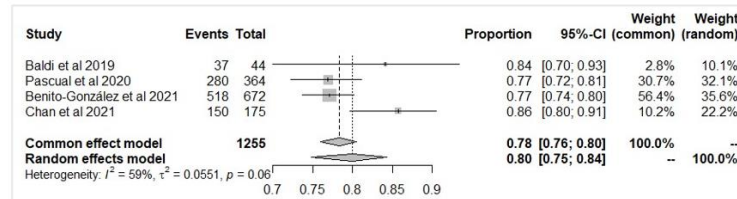
MR grade $\leq 2+$ at follow-up 2010



MR grade $\leq 2+$ at follow-up 2011



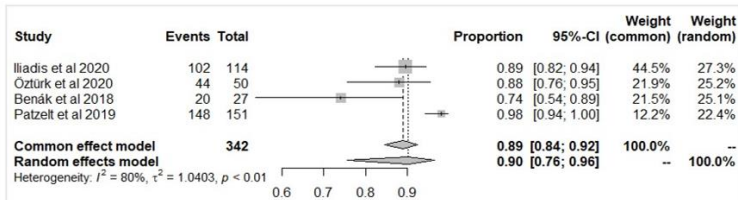
MR grade $\leq 2+$ at follow-up 2012



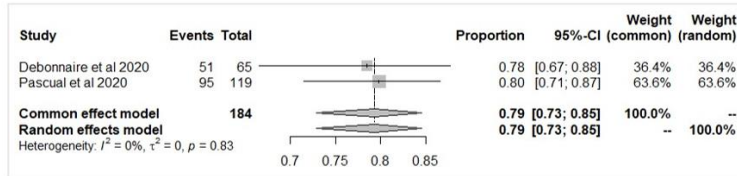
MR grade $\leq 2+$ at follow-up 2013 – 1 study: 87.5%

Supplementary Figure 41. Pooled MR grade $\leq 2+$ at 12-month follow-up according to start of recruitment year 2008, 2009, 2010, 2011, 2012, 2013

MR grade $\leq 2+$ at follow-up 2014



MR grade $\leq 2+$ at follow-up 2015



MR grade $\leq 2+$ at follow-up 2016 – not reported in the related studies

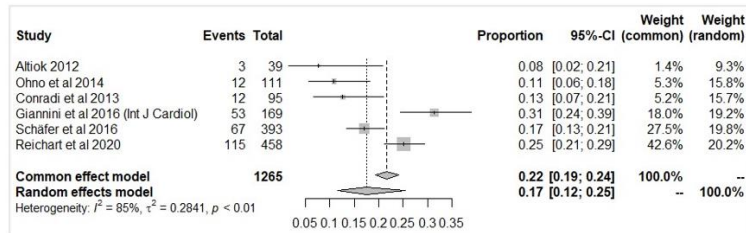
MR grade $\leq 2+$ at follow-up 2017 – not reported in the related studies

MR grade $\leq 2+$ at follow-up 2018 – 1 study: 90.1%

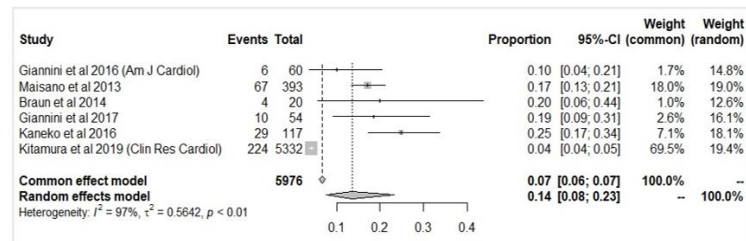
Supplementary Figure 42. Pooled MR grade $\leq 2+$ at 12-month follow-up according to start of recruitment year 2014, 2015, 2016, 2017, 2018

Death at 12-month follow-up

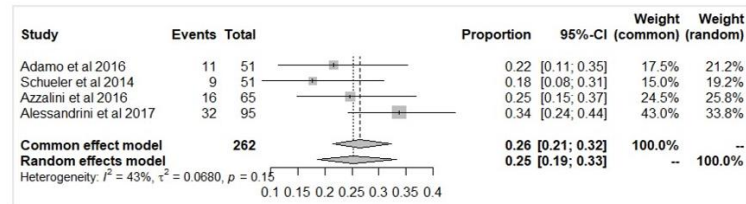
Death 2008



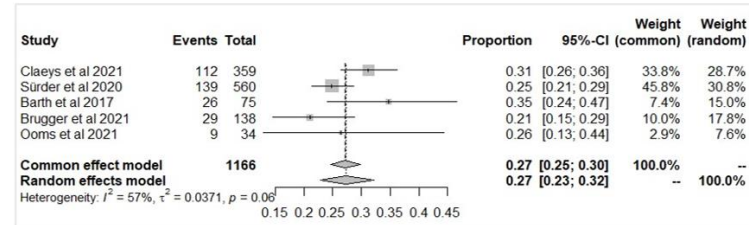
Death 2009



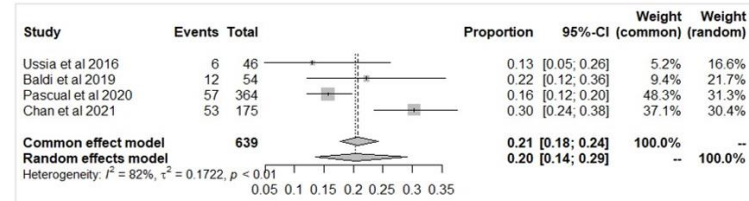
Death 2010



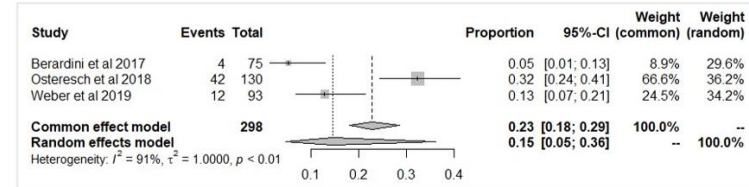
Death 2011



Death 2012

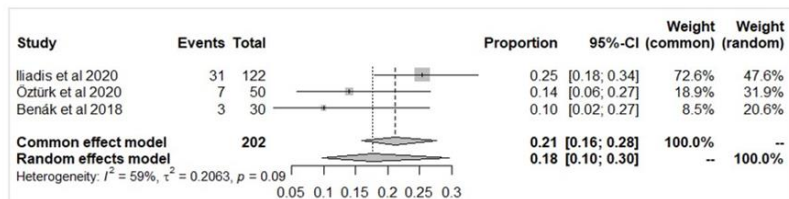


Death 2013



Supplementary Figure 43. Pooled all-cause death at 12-month follow-up according to start of recruitment year 2008, 2009, 2010, 2011, 2012, 2013

Death 2014



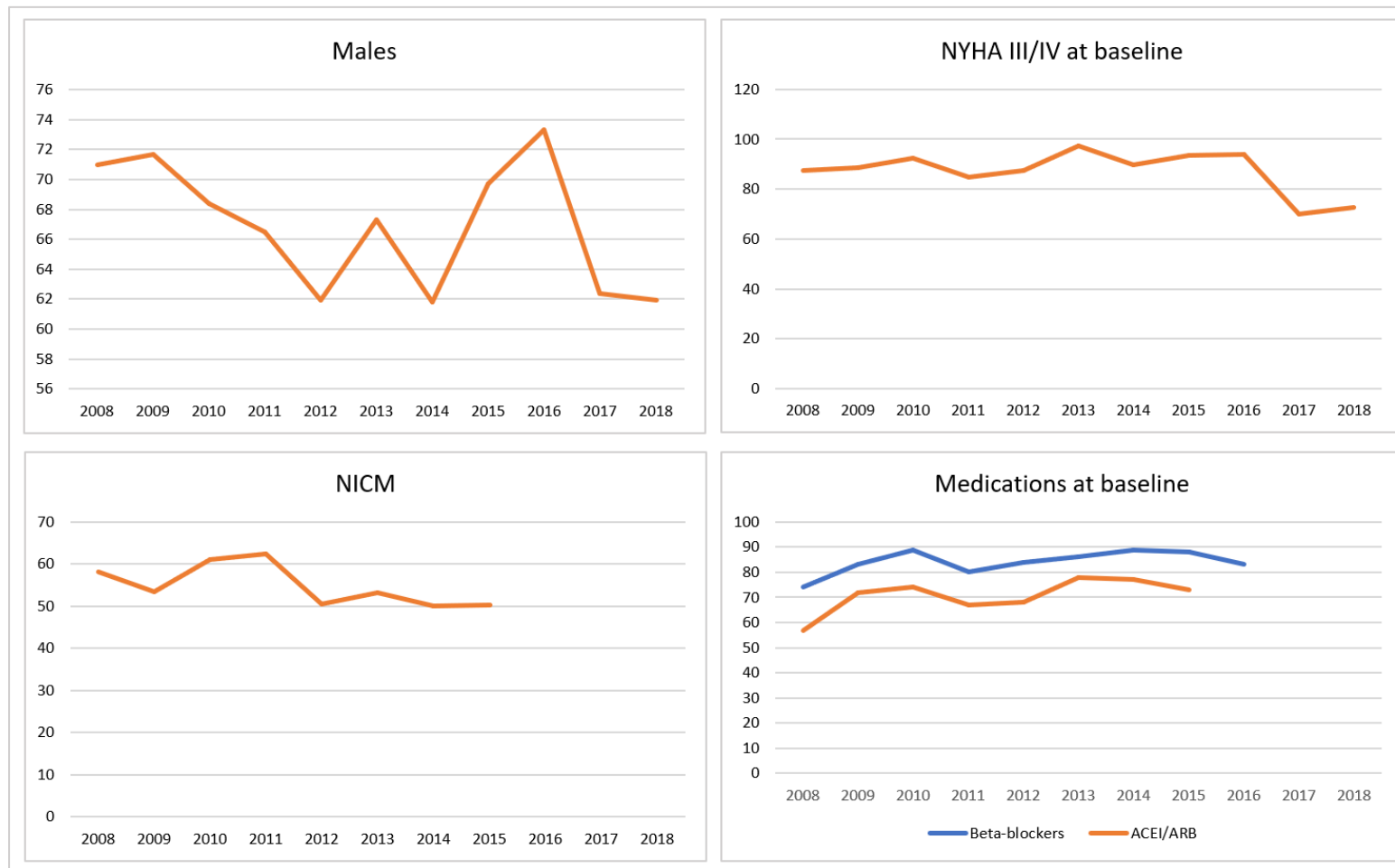
Death 2015 – 1 study: 32.4%

Death 2016 – not reported in the related studies

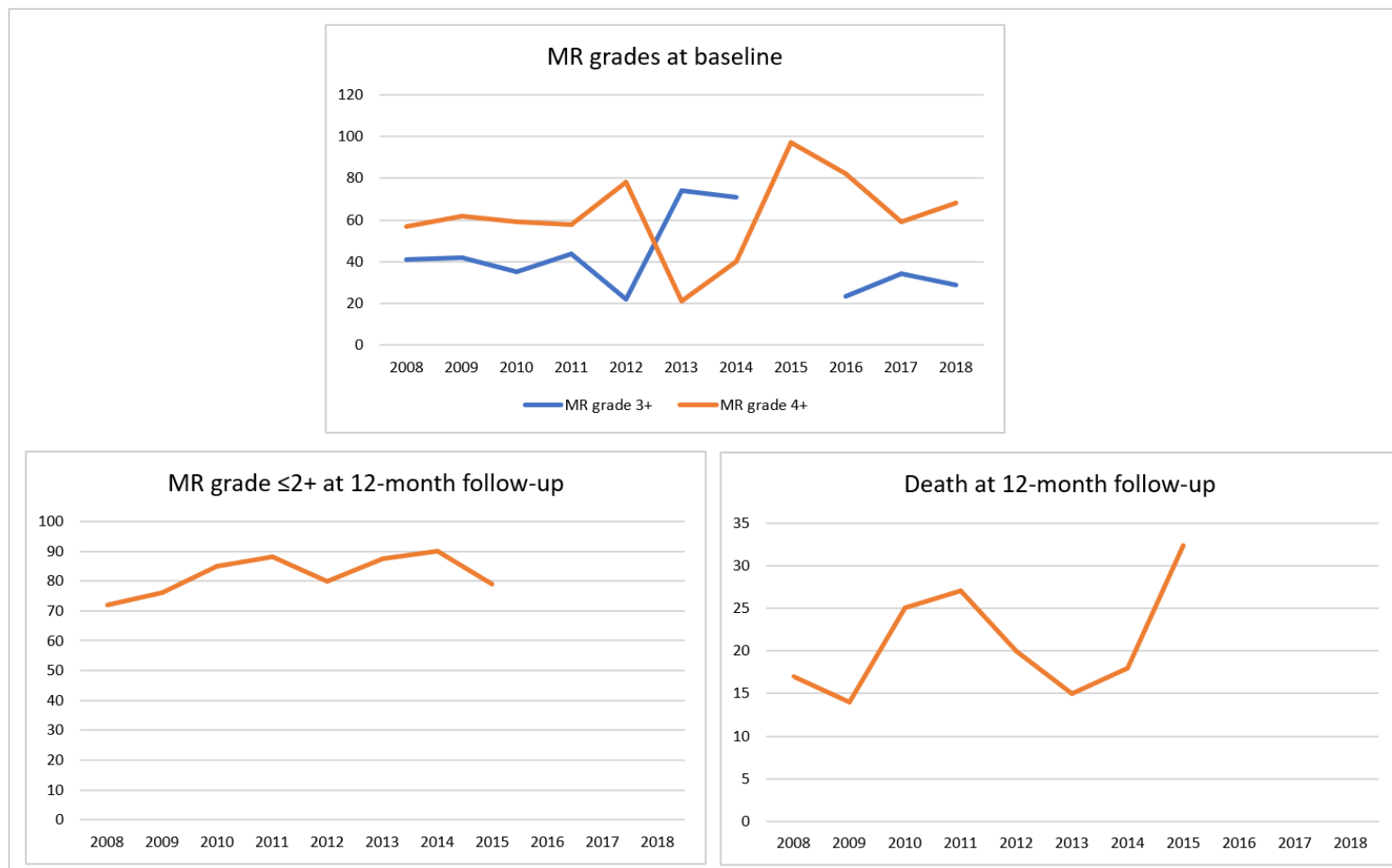
Death 2017– not reported in the related studies

Death 2018 2018 – 1 study: 15.8%

Supplementary Figure 44. Pooled all-cause death at 12-month follow-up according to start of recruitment year 2014, 2015, 2016, 2017, 2018



Supplementary Figure 45. Pooled male, NICM, NYHA III/IV, and medications at baseline according to start of recruitment year from 2008 to 2018



Supplementary Figure 46. Pooled MR grades 3+/4+ at baseline and outcomes according to start of recruitment year from 2008 to 2018