

SUPPLEMENTARY APPENDIX

Transcatheter closure of atrial septal defect in the elderly: a systematic review and meta-analysis

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Appendix 1. Quality assessment of the present meta-analysis according to PRISMA 2020 checklist for systematic reviews and Meta-Analyses (From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71)

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 6
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 6
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Pages 6-7
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 7, Appendix 3
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Appendix 3
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 8

Section and Topic	Item #	Checklist item	Location where item is reported
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 8
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g., for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Pages 8-9
	10b	List and define all other variables for which data were sought (e.g., participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Pages 8-9
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 8
Effect measures	12	Specify for each outcome the effect measure(s) (e.g., risk ratio, mean difference) used in the synthesis or presentation of results.	Page 9
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g., tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 9
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 9
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 9
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 9
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup	Page 9

Section and Topic	Item #	Checklist item	Location where item is reported
		analysis, meta-regression).	
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Page 8
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 8
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page 8
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 10, Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Page 10, Appendix 4
Study characteristics	17	Cite each included study and present its characteristics.	Pages 10-11, Tables 2-3
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Page 11, Appendix 5
Results of individual	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Pages 11-12

Section and Topic	Item #	Checklist item	Location where item is reported
studies			
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Pages 11-12
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Pages 11-12
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Pages 11-12
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Pages 11-12
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Page 11
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Page 13
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 13
	23b	Discuss any limitations of the evidence included in the review.	Pages 16-17
	23c	Discuss any limitations of the review processes used.	Pages 16-17
	23d	Discuss implications of the results for practice, policy, and future research.	Page 17
OTHER INFORMATION			

Section and Topic	Item #	Checklist item	Location where item is reported
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 7
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 7
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Page 7
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 18
Competing interests	26	Declare any competing interests of review authors.	Page 18
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Page 18

Appendix 2. Quality assessment of the present meta-analysis according to MOOSE checklist for observational studies (From: Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, Moher D, Becker BJ, Sipe TA, Thacker SB. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA. 2000; 283(15):2008-2012. doi: 10.1001/jama.283.15.2008.)

Item No	Recommendation	Reported on Page No
Reporting of background should include		
1	Problem definition	Page 6
2	Hypothesis statement	Page 6
3	Description of study outcome(s)	Page 6
4	Type of exposure or intervention used	Page 6
5	Type of study designs used	Page 6
6	Study population	Page 6
Reporting of search strategy should include		
7	Qualifications of searchers (eg, librarians and investigators)	Page 7
8	Search strategy, including time period included in the synthesis and key words	Page 7, Appendix 3
9	Effort to include all available studies, including contact with authors	Page 7
10	Databases and registries searched	Page 7, Figure 1, Appendix 3
11	Search software used, name and version, including special features used (eg, explosion)	Page 7, Appendix 3

12	Use of hand searching (eg, reference lists of obtained articles)	Page 7, Appendix 3
13	List of citations located and those excluded, including justification	Page 7, Appendix 4
14	Method of addressing articles published in languages other than English	Page 7, Appendix 3
15	Method of handling abstracts and unpublished studies	Page 7, Appendix 3
16	Description of any contact with authors	Page 7
Reporting of methods should include		
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	Pages 7-8
18	Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	Pages 7-8
19	Documentation of how data were classified and coded (eg, multiple raters, blinding and interrater reliability)	Pages 7-8
20	Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	Page 7
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	Page 8
22	Assessment of heterogeneity	Page 9
23	Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	Page 9

24	Provision of appropriate tables and graphics	Pages 10-12
Reporting of results should include		
25	Graphic summarizing individual study estimates and overall estimate	Figures 2-6
26	Table giving descriptive information for each study included	Tables 1,2
27	Results of sensitivity testing (e.g., subgroup analysis)	Appendix 6-7
28	Indication of statistical uncertainty of findings	Pages 16-17

Appendix 3. Search strategy

The search strategy was constructed for PubMed and amended accordingly for other electronic databases. No restrictions on language or publication date were applied. The reference lists of the retrieved reports were manually searched for other non-identified relevant reports. Additionally, grey literature sources were scanned, including abstracts from conferences organized by two major health societies (European Society of Cardiology and American Heart Association). We also searched for eligible reports in the International Journal of Cardiology Congenital Heart Disease, an online journal that includes articles exclusively about congenital heart disease and is not yet indexed in the above electronic databases. Furthermore, Clinicaltrials.gov was searched for ongoing or completed unpublished trials, according to the snowball effect. The search syntax and search string for each electronic database is presented below:

Search strategy in PubMed

1. Heart Septal Defects, Atrial [MeSH Terms]
2. Atrial Septal Defect, Secundum Type [Supplementary Concept]
3. Atrial septal defect [All Fields]
4. ASD [All Fields]
5. Atrial septal shunt [All Fields]
6. Atrium septal shunt [All Fields]
7. Atrium septal defect [All Fields]
8. Secundum defect [All Fields]
9. Secundum atrial septal defect [All Fields]
10. Ostium secundum [All Fields]
11. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10
12. Aged [MeSH Terms]
13. Elderly [All Fields]
14. Older [All Fields]
15. Senior [All Fields]
16. Geriatric [All Fields]
17. Aged [All Fields]
18. #12 OR #13 OR #14 OR #15 OR #16 OR #17

19. Septal Occluder Device [MeSH Terms]
20. Transcatheter closure [All Fields]
21. Catheter closure [All Fields]
22. Device closure [All Fields]
23. Percutaneous closure [All Fields]
24. Transcatheter occlusion [All Fields]
25. Percutaneous occlusion [All Fields]
26. #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25
27. #11 AND #18 AND #26

("heart septal defects, atrial"[MeSH Terms] OR "atrial septal defect secundum type"[Supplementary Concept] OR ("heart septal defects, atrial"[MeSH Terms] OR ("heart"[All Fields] AND "septal"[All Fields] AND "defects"[All Fields] AND "atrial"[All Fields]) OR "atrial heart septal defects"[All Fields] OR ("atrial"[All Fields] AND "septal"[All Fields] AND "defect"[All Fields]) OR "atrial septal defect"[All Fields]) OR ("arthropod struct dev"[Journal] OR "agron sustain dev"[Journal] OR "asd"[All Fields]) OR (("atrialisation"[All Fields] OR "atrialization"[All Fields] OR "atrialized"[All Fields] OR "atrially"[All Fields] OR "heart atria"[MeSH Terms] OR ("heart"[All Fields] AND "atria"[All Fields]) OR "heart atria"[All Fields] OR "atrial"[All Fields]) AND ("septal"[All Fields] OR "septally"[All Fields] OR "septals"[All Fields]) AND ("shunt"[All Fields] OR "shunt s"[All Fields] OR "shunted"[All Fields] OR "shunting"[All Fields] OR "shuntings"[All Fields] OR "shunts"[All Fields])) OR (("atriums"[All Fields] OR "heart atria"[MeSH Terms] OR ("heart"[All Fields] AND "atria"[All Fields]) OR "heart atria"[All Fields] OR "atrium"[All Fields]) AND ("septal"[All Fields] OR "septally"[All Fields] OR "septals"[All Fields]) AND ("shunt"[All Fields] OR "shunt s"[All Fields] OR "shunted"[All Fields] OR "shunting"[All Fields] OR "shuntings"[All Fields] OR "shunts"[All Fields])) OR (("atriums"[All Fields] OR "heart atria"[MeSH Terms] OR ("heart"[All Fields] AND "atria"[All Fields]) OR "heart atria"[All Fields] OR "atrium"[All Fields]) AND ("heart septal defects"[MeSH Terms] OR ("heart"[All Fields] AND "septal"[All Fields] AND "defects"[All Fields]) OR "heart septal defects"[All Fields] OR ("septal"[All Fields] AND "defect"[All Fields]) OR "septal defect"[All Fields])) OR ("Secundum"[All Fields] AND ("abnormalities"[MeSH

Subheading] OR "abnormalities"[All Fields] OR "defects"[All Fields] OR "defect"[All Fields] OR "defect s"[All Fields] OR "defected"[All Fields] OR "defective"[All Fields] OR "defectively"[All Fields] OR "defectives"[All Fields])) OR ("foramen ovale, patent"[MeSH Terms] OR ("foramen"[All Fields] AND "ovale"[All Fields] AND "patent"[All Fields]) OR "patent foramen ovale"[All Fields] OR ("Secundum"[All Fields] AND "atrial"[All Fields] AND "septal"[All Fields] AND "defect"[All Fields]) OR "secundum atrial septal defect"[All Fields]) OR (("ostium"[All Fields] OR "ostiums"[All Fields]) AND "Secundum"[All Fields])) AND ("aged"[MeSH Terms] OR ("aged"[MeSH Terms] OR "aged"[All Fields] OR "elderly"[All Fields] OR "elderlies"[All Fields] OR "elderly s"[All Fields] OR "elderlys"[All Fields]) OR ("older"[All Fields] OR "olders"[All Fields]) OR ("senior"[All Fields] OR "seniorities"[All Fields] OR "seniority"[All Fields] OR "seniors"[All Fields]) OR ("geriatric"[All Fields] OR "geriatrics"[MeSH Terms] OR "geriatrics"[All Fields]) OR ("aged"[MeSH Terms] OR "aged"[All Fields])) AND ("septal occluder device"[MeSH Terms] OR ("Transcatheter"[All Fields] AND ("closure"[All Fields] OR "closure s"[All Fields] OR "closures"[All Fields])) OR (("catheter s"[All Fields] OR "catheters"[MeSH Terms] OR "catheters"[All Fields] OR "catheter"[All Fields]) AND ("closure"[All Fields] OR "closure s"[All Fields] OR "closures"[All Fields])) OR (("device s"[All Fields] OR "equipment and supplies"[MeSH Terms] OR "equipment"[All Fields] AND "supplies"[All Fields]) OR "equipment and supplies"[All Fields] OR "device"[All Fields] OR "instrumentation"[MeSH Subheading] OR "instrumentation"[All Fields] OR "devices"[All Fields]) AND ("closure"[All Fields] OR "closure s"[All Fields] OR "closures"[All Fields])) OR (("percutaneous"[All Fields] OR "percutaneously"[All Fields] OR "percutaneous"[All Fields]) AND ("closure"[All Fields] OR "closure s"[All Fields] OR "closures"[All Fields])) OR ("Transcatheter"[All Fields] AND ("dental occlusion"[MeSH Terms] OR ("dental"[All Fields] AND "occlusion"[All Fields]) OR "dental occlusion"[All Fields] OR "occlusion"[All Fields] OR "occluded"[All Fields] OR "occlusions"[All Fields] OR "occlusive"[All Fields] OR "occlusives"[All Fields])) OR (("percutaneous"[All Fields] OR "percutaneously"[All Fields] OR "percutaneous"[All Fields]) AND ("dental occlusion"[MeSH Terms] OR ("dental"[All Fields] AND "occlusion"[All Fields]) OR "dental occlusion"[All Fields] OR "occlusion"[All Fields] OR "occluded"[All Fields] OR "occlusions"[All Fields] OR "occlusive"[All Fields] OR "occlusives"[All Fields]))))

Search strategy in CENTRAL

- #1 MeSH descriptor: [Heart Septal Defects, Atrial] explode all trees
- #2 (Atrial septal defect)
- #3 (ASD)
- #4 (Atrial septal shunt)
- #5 (Atrium septal shunt)
- #6 (Atrium septal defect)
- #7 (Secundum defect)
- #8 (Secundum atrial septal defect)
- #9 (Ostium secundum)
- #10 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9
- #11 MeSH descriptor: [Aged] explode all trees
- #12 (elderly)
- #13 (older)
- #14 (senior)
- #15 (geriatric)
- #16 (aged)
- #17 #11 or #12 or #13 or #14 or #15 or #16
- #18 MeSH descriptor: [Septal Occluder Device] explode all trees
- #19 (transcatheter closure)
- #20 (catheter closure)
- #21 (device closure)
- #22 (percutaneous closure)
- #23 (transcatheter occlusion)
- #24 (percutaneous occlusion)
- #25 #18 or #19 or #20 or #21 or #22 or #23 or #24
- #26 #10 and #17 and #25

Search strategy in Scopus

TITLE-ABS-KEY (((atrial AND septal AND defect) OR (asd) OR (atrial AND septal AND shunt) OR (atrium AND septal AND shunt) OR (atrium AND septal AND defect) OR (secundum AND atrial AND septal AND defect

) OR (secundum AND defect) OR (ostium AND secundum)) AND ((aged) OR (elderly) OR (older) OR (senior) OR (geriatric)) AND ((transcatheter AND closure) OR (catheter AND closure) OR (device AND closure) OR (percutaneous AND closure) OR (transcatheter AND occlusion) OR (percutaneous AND occlusion)))

Search strategy in Web of science

Query #1

(((((ALL=(Atrial septal defect)) OR ALL=(ASD)) OR ALL=(Atrial septal shunt)) OR ALL=(Atrium septal shunt)) OR ALL=(Atrium septal defect)) OR ALL=(Secundum atrial septal defect)) OR ALL=(Secundum defect)) OR ALL=(Ostium secundum)

Query #2

((((ALL=(Aged)) OR ALL=(Elderly)) OR ALL=(Older)) OR ALL=(Senior)) OR ALL=(Geriatric)

Query #3

(((((ALL=(transcatheter closure)) OR ALL=(catheter closure)) OR ALL=(Device closure)) OR ALL=(percutaneous closure)) OR ALL=(transcatheter occlusion)) OR ALL=(percutaneous occlusion)

#1 AND #2 AND #3

Appendix 4. Reasons for excluding records at the full-text level

Study	Reason for exclusion
1. Giardini A, Donti A, Specchia S, Formigari R, Oppido G, Picchio FM. Long-term impact of transcatheter atrial septal defect closure in adults on cardiac function and exercise capacity. <i>Int J Cardiol.</i> 2008 Feb;124(2):179–82.	Not reporting the population of interest
2. Yong G, Khairy P, De Guise P, Dore A, Marcotte F, Mercier L-A, et al. Pulmonary arterial hypertension in patients with transcatheter closure of secundum atrial septal defects: a longitudinal study. <i>Circ Cardiovasc Interv.</i> 2009 Oct;2(5):455–62.	Not reporting the population of interest
3. Demkow M, Ruzyllo W, Konka M, Kepka C, Wolski P, Banas S, et al. Ten-year experience with transcatheter closure of secundum atrial septal defects. <i>Postep W Kardiologii INTERWENCYJNEJ.</i> 2007;3(4):184–92.	Not reporting the population of interest
4. Luermans JGLM, Post MC, ten Berg JM, Plokker HWT, Suttorp MJ. Long-term outcome of percutaneous closure of secundum-type atrial septal defects in adults. <i>EuroIntervention J Eur Collab with Work Gr Interv Cardiol Eur Soc Cardiol.</i> 2010 Nov;6(5):604–10.	Unavailable full text
5. Eun LY, Park HK, Choi JY. Comparison of the Change in Diastolic Dysfunction after Transcatheter Atrial Septal Defect Closure between Asymptomatic Younger and Older Age Groups. <i>J Clin Med.</i> 2020 Nov;9(11).	Not reporting the outcome of interest
6. Lopez KN, Patel A, Cao QL, Sandhu SK, Hijazi ZM. Transcatheter closure of atrial septal defects in adults greater than forty years of age: Immediate and follow-up results. <i>Circulation.</i> 2005;112(78th Annual Scientific Session of the American-Heart-Association): U755–U755.	Not reporting the population of interest
7. Sievert H, Ensslen R, Spies H, Scherer D, Merle H, Schulze R, et al. [Non-surgical closure of atrial septal defect in adults. Experiences with the Rashkind and the Sideris occluder]. <i>Dtsch Med Wochenschr.</i> 1994 Oct;119(40):1341–5.	Not reporting the population of interest
8. Yu M-L, Wang J-F, Liu J, Qin Y-W, Wang K, Zhao X-X, et al. Transcatheter closure of secundum atrial septal defects in patients aged over 40: A follow-up of outcome. <i>Acad J Second Mil Med Univ [Internet].</i> 2009;30(1):61–4.	Unavailable full text
9. Hongxin L, Lijun S, Wang Z, Zi J, Zhang W, Zhang H, et al. Intraoperative device closure of large secundum atrial septal defects; a safe alternative to transcatheter closure. <i>Eur J cardio-thoracic Surg Off J Eur Assoc Cardio-thoracic Surg.</i> 2008 Jun;33(6):1055–60.	Not reporting the population of interest
10. Giardini A, Donti A, Sciarra F, Bronzetti G, Mariucci E, Picchio FM. Long-term incidence of atrial fibrillation and flutter after transcatheter atrial septal defect closure in adults. <i>Int J Cardiol.</i> 2009 May;134(1):47–51.	Not reporting the population of interest

11. Tashiro H, Suda K, Iemura M, Teramachi Y. Intergenerational differences in the effects of transcatheter closure of atrial septal defects on cardiac function. <i>J Cardiol</i> . 2017 Dec;70(6):620–6.	Not reporting the population of interest
12. Haas NA, Soetemann DB, Ates I, Baspinar O, Ditkivskyy I, Duke C, et al. Closure of Secundum Atrial Septal Defects by Using the Occlutech Occluder Devices in More Than 1300 Patients: The IRFACODE Project: A Retrospective Case Series. <i>Catheter Cardiovasc Interv Off J Soc Card Angiogr Interv</i> . 2016 Oct;88(4):571–81.	Not reporting the population of interest
13. Sun P, Wang Z-B, Xu C-J, Yang S-M, Jiang L. Echocardiographic and morphological evaluation of the right heart after closure of atrial septal defects. <i>Cardiol Young</i> . 2008 Dec;18(6):593–8.	Not reporting the population of interest
14. Bruch L, Winkelmann A, Sonntag S, Scherf F, Rux S, Grad MO, et al. Fenestrated occluders for treatment of ASD in elderly patients with pulmonary hypertension and/or right heart failure. <i>J Interv Cardiol</i> . 2008;21(1):44–9.	Not reporting the population of interest
15. Thilen M, Christersson C, Dellborg M, Mattsson E, Trzebiatowska-Krzynska A, Thilen U. Atrial septal defect device closure in the elderly, symptomatic benefits except for arrhythmia. <i>Eur Heart J</i> . 2015;36 MA-P(Congress of the European-Society-of-Cardiology (ESC)):624–5.	Unavailable full text
16. Boudiche S, Chatti S, Amroussia R, Mghaieth F, Ziadi J, Farhati A, et al. Atrial septal defect closure in adults: A ten-year experience. <i>Tunisie Medicale [Internet]</i> . 2019;97(12):1363–9.	Not reporting the population of interest
17. Behjati M, Rafiei M, Soltani MH, Emami M, Dehghani M. Transcatheter closure of atrial septal defect with amplatzer septal occluder in adults: Immediate, short, and intermediate-term results. <i>J Tehran Univ Hear Cent [Internet]</i> . 2011;6(2):79–84.	Not reporting the population of interest
18. Vijarnsorn C, Durongpisitkul K, Chanthong P, Chungsomprasong P, Soongswang J, Loahaprasitiporn D, et al. Beneficial effects of transcatheter closure of atrial septal defects not only in young adults. <i>J Interv Cardiol</i> . 2012 Aug;25(4):382–90.	Not reporting the population of interest
19. Duong P, Ferguson LP, Lord S, Murray S, Shepherd E, Bourke JP, et al. Atrial arrhythmia after transcatheter closure of secundum atrial septal defects in patients ≥ 40 years of age. <i>Eur Eur pacing, arrhythmias, Card Electrophysiol J Work groups Card pacing, arrhythmias, Card Cell Electrophysiol Eur Soc Cardiol</i> . 2017 Aug;19(8):1322–6.	Not reporting the population of interest
20. Wang S, Pan J, Xiao B, Tang Y, Lan J, Zheng X, et al. Immediate and short-term effects of transcatheter device closure of large atrial septal defect in senior people. <i>Congenit Heart Dis</i> . 2019 Nov;14(6):939–44.	Not reporting the population of interest

21. Ewert P, Berger F, Nagdyman N, Kretschmar O, Dittrich S, Abdul-Khaliq H, et al. Masked left ventricular restriction in elderly patients with atrial septal defects: a contraindication for closure? <i>Catheter Cardiovasc Interv Off J Soc Card Angiogr Interv.</i> 2001 Feb;52(2):177–80.	Not reporting the outcome of interest
22. Mates M, Popelova J, Vojacek J, Hrabos V, Rataj O. Transcatheter closure of atrial septal defects II with amplatzer device in older patients. <i>Am J Cardiol.</i> 2004;94(16th Annual Transcatheter Cardiovascular Therapeutics Symposium):178E-178E.	Incomplete data
23. Billinger K, Trepels T, Wilson N, Sievert H. Transcatheter closure of atrial septal defects in elderly patients with the amplatzer ASD occluder: Acute and follow-up results in 56 consecutive patients. Kimchi A, editor. <i>ADVANCES IN HEART FAILURE.</i> 2002. p. 177–81.	Incomplete data
24. Sandhu SK. Transcatheter closure of the atrial septal defect in the elderly. <i>J Invasive Cardiol.</i> 2007 Dec;19(12):513–4.	Commentary
25. Zhu P, Qiang H, Liu F, Xie P, Zheng S, Sun Y. Clinical evaluation of percutaneous and intra-operative device closure of atrial septal defects under transesophageal echocardiographic guidance: one center experience and mid-term follow-up. <i>J Cardiothorac Surg.</i> 2020 Jan;15(1):20.	Not reporting the population of interest
26. Johri AM, Witzke C, Solis J, Palacios IF, Inglessis I, Picard MH, et al. Real-time three-dimensional transesophageal echocardiography in patients with secundum atrial septal defects: outcomes following transcatheter closure. <i>J Am Soc Echocardiogr Off Publ Am Soc Echocardiogr.</i> 2011 Apr;24(4):431–7.	Not reporting the population of interest
27. Takaya Y, Akagi T, Kijima Y, Nakagawa K, Ito H. INFLUENCE OF PROCEDURE AGE ON CLINICAL OUTCOMES AFTER TRANSCATHETER CLOSURE OF ATRIAL SEPTAL DEFECT. <i>J Am Coll Cardiol.</i> 2014;63(12 MA-2101–306):A1750–A1750.	Incomplete data
28. Khan AA, Tan J-L, Li W, Dimopoulos K, Spence MS, Chow P, et al. The impact of transcatheter atrial septal defect closure in the older population: a prospective study. <i>JACC Cardiovasc Interv.</i> 2010 Mar;3(3):276–81.	Not reporting the population of interest
29. Khan MA, Korejo H, Sohail A, Shaikh AS, Patel N. Immediate and Short-Term Outcome of Percutaneous Atrial Septal Defects Closure in Adult Patients. <i>CUREUS.</i> 2020;12(10).	Not reporting the population of interest
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Appendix 5. Risk of bias assessment of the included studies according to the Newcastle-Ottawa Scale

Study	Selection Overall			Comparability	Outcome overall			Overall score	
	Representativeness	Selection of non-exposed	Exposure ascertainment		Outcome absent at baseline	Outcome assessment	Length of follow-up		Adequacy of follow-up
Swan et al. 2006	★	★	★	★	N/A	★	★	N/A	6
Elshershari et al. 2008	★	★	★	★	N/A	★	★	★	7
Jategaonkar et al. 2009	★	★	★	★	N/A	★	★	★	7
Spies et al. 2009	★	★	★	★	N/A	★	★	★	7
Taniguchi et al. 2009	★	★	★	★	N/A	★	★	★	7
Yalonetsky et al. 2009	★	★	★	★	N/A	★	★	★	7
Hanninen et al. 2011	★	★	★	★	N/A	★	★	N/A	6
Humenberger et al. 2011	★	★	★	★	N/A	★	★	★	7
Nakagawa et al. 2012	★	★	★	★	N/A	★	★	N/A	6
Woo et al. 2013	★	★	★	★	N/A	★	★	★	7
Stroker et al. 2013	★	★	★	★	N/A	★	★	N/A	6
Komar et al. 2014	★	★	★	★	N/A	★	★	★	7
Jampates et al. 2014	★	★	★	★	N/A	★	★	N/A	6
Takaya et al. 2015	★	★	★	★	N/A	★	★	★	7
Thilen et al. 2016	★	★	★	★	N/A	★	★	N/A	6
Chen et al. 2017	★	★	★	★	N/A	★	★	★	7
Giordano et al. 2020	★	★	★	★	N/A	★	★	★	7
Leong et al. 2020	★	★	★	★	N/A	★	★	★	7
Sun et al. 2022	★	★	★	★	N/A	★	★	★	7

NA, not applicable

The Newcastle-Ottawa scale uses a nine-star rating system to assess the study quality with regard to 3 domains: Selection of the study groups (including 4 items), Comparability of the groups (including 1 item), and Ascertainment of the outcome of interest (including 3 items). Each item within the Selection and Outcome domains can be rated with maximum one star, whereas Comparability can be rated with maximum two stars. Overall NOS scores range from 0 to 9, with 9 indicating the highest possible quality. Overall scores 7-9, 4-6, and <4 were regarded as low, intermediate and high risk, respectively. The systematic review included exclusively cohort studies assessing patients before and after the intervention; consequently, patients before the ASD transcatheter closure were considered to compose the non-exposed cohort, while patients after the ASD transcatheter closure composed the exposed cohort.

Appendix 6. Subgroup analyses

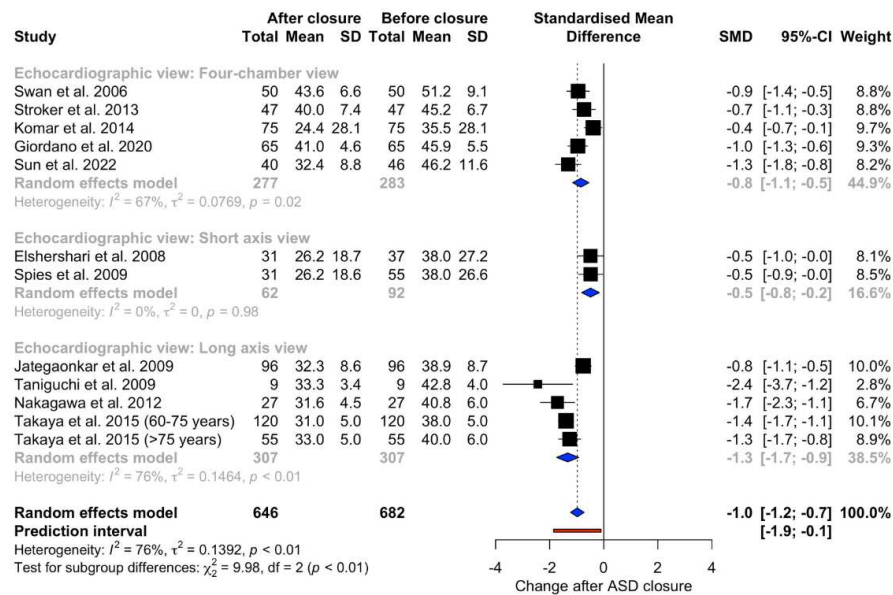


Figure S1. Subgroup analysis for RVEDD by the echocardiographic view of assessment.

ASD, atrial septal defect; CI, confidence interval; RVEDD, right ventricular end-diastolic diameter; SD, standard deviation; SMD, standardized mean difference; RVEDD, end-diastolic diameter of the right ventricle

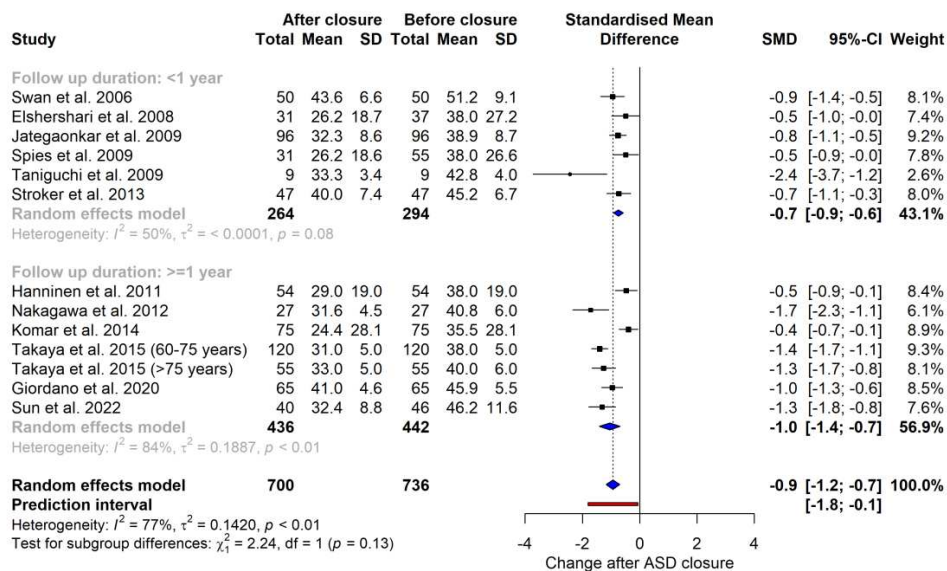


Figure S2. Subgroup analysis for RVEDD by follow-up duration.

ASD, atrial septal defect; CI, confidence interval; RVEDD, right ventricular end-diastolic diameter; SD, standard deviation; SMD, standardized mean difference

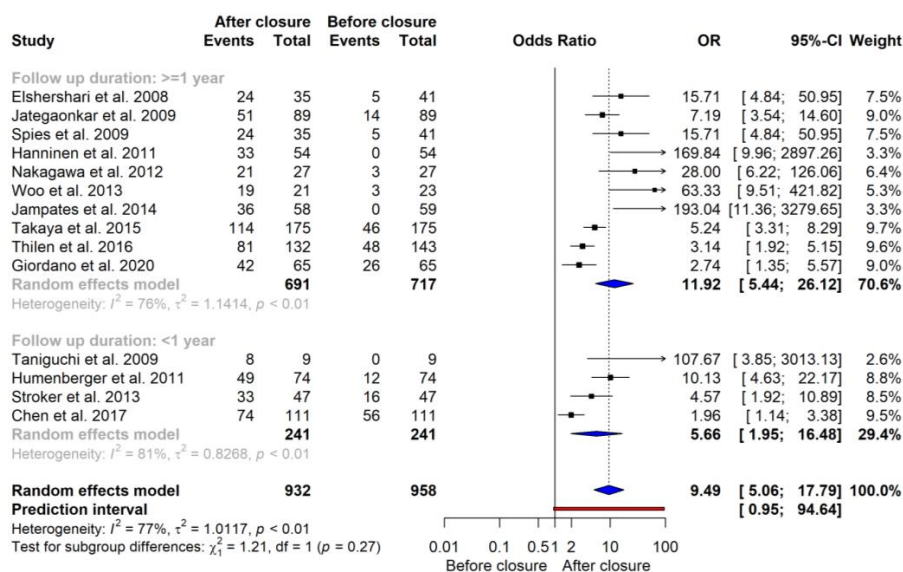


Figure S3. Subgroup analysis for NYHA I by follow-up duration.

ASD, atrial septal defect; CI, confidence interval; NYHA, New York Heart Association; OR, odds ratio

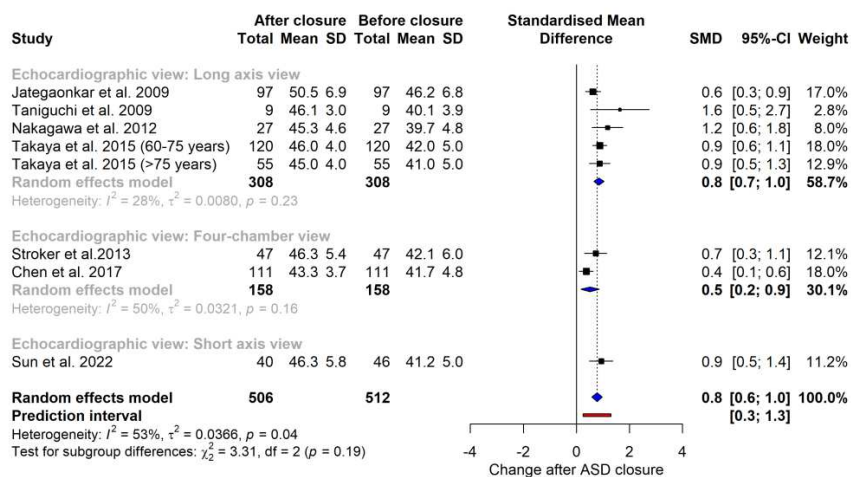


Figure S4. Subgroup analysis for LVEDD by the echocardiographic view of assessment.

ASD, atrial septal defect; CI, confidence interval; LVEDD, left ventricular end-diastolic diameter; SD, standard deviation; SMD, standardized mean difference

Appendix 7. Sensitivity analysis

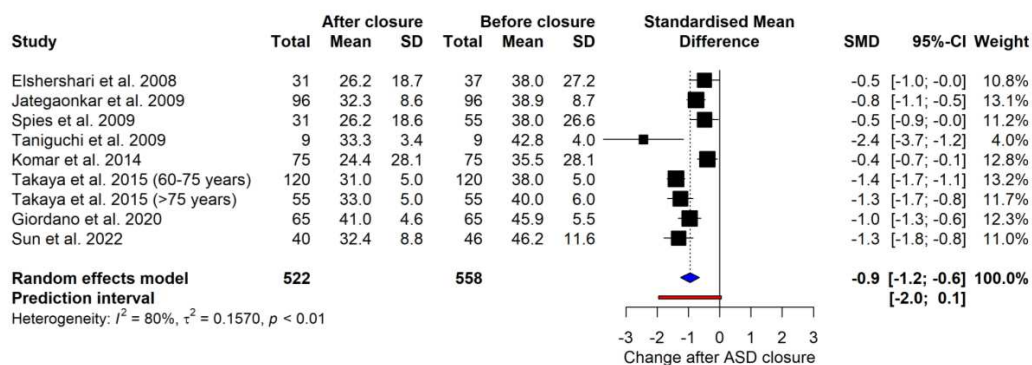


Figure S5. Sensitivity analysis for RVEDD including only studies with low risk of bias (Newcastle-Ottawa Scale score ≥ 7).

ASD, atrial septal defect; CI, confidence interval; RVEDD, right ventricular end-diastolic diameter; SD, standard deviation; SMD, standardized mean difference

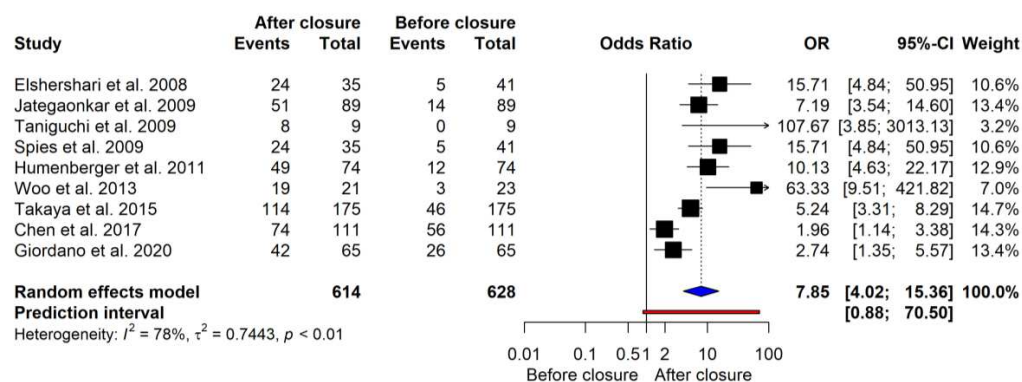


Figure S6. Sensitivity analysis for NYHA I including only studies with low risk of bias (Newcastle-Ottawa Scale score ≥ 7).

ASD, atrial septal defect; CI, confidence interval; NYHA, New York Heart Association; OR, odds ratio

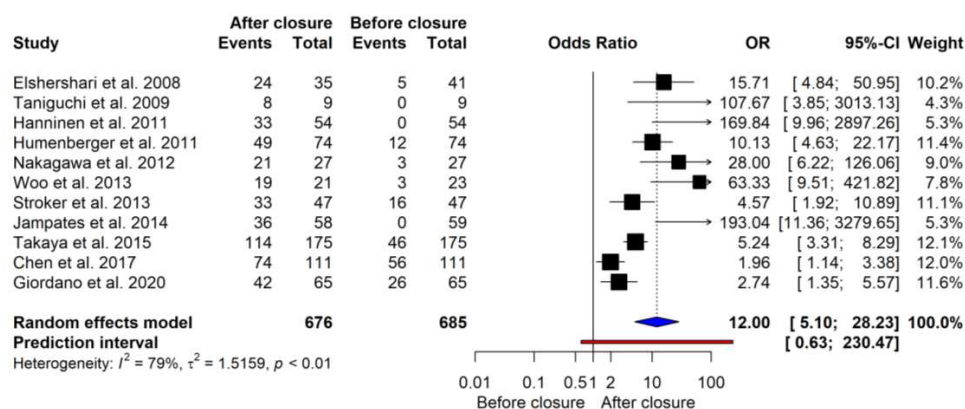


Figure S7. Sensitivity analysis for NYHA I excluding studies from which data were extracted using the WebPlotDigitizer tool.

ASD, atrial septal defect; CI, confidence interval; NYHA, New York Heart Association; OR, odds ratio

Appendix 8. Publication bias assessment

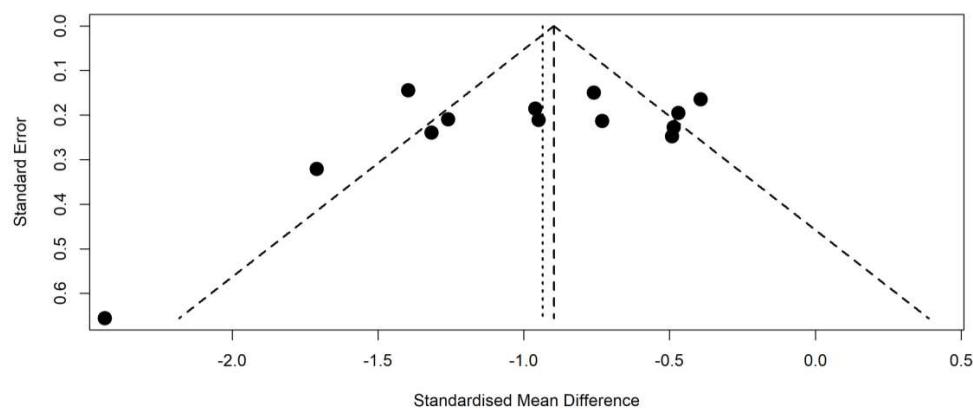


Figure S8. Publication bias assessment for the primary outcome of RVEDD.

RVEDD, end-diastolic diameter of the right ventricle

The funnel plot for the RVEDD did not reveal severe asymmetry. Consistent with this, the Egger's regression test demonstrated no significant evidence of publication bias ($t = -0.97$, p -value = 0.35).

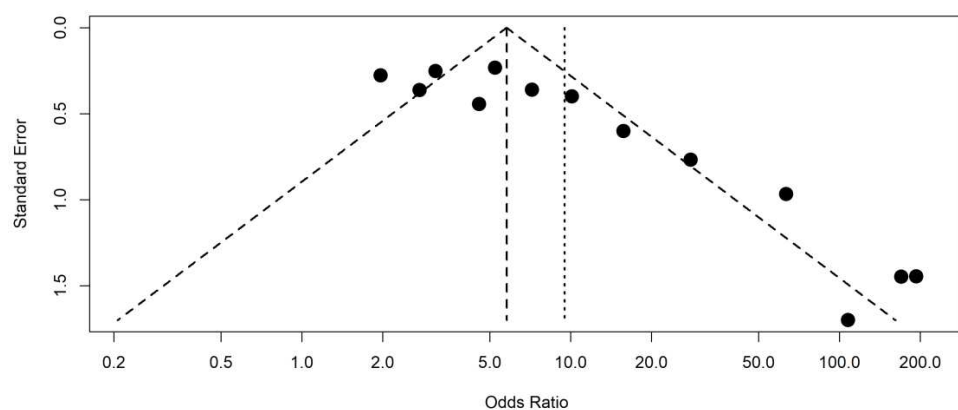


Figure S9. Publication bias assessment for the primary outcome of NYHA.

NYHA, New York Heart Association

The visual inspection of the funnel plot for the NYHA functional class displayed asymmetry of studies (Figure S2). Peter's regression test also confirmed the presence of potential publication bias ($t = 3.35$, p -value = 0.006).

Appendix 9. Grade assessment

Primary Outcomes	Number of patients (studies)	Effect measure	Quality of evidence (GRADE)
RVEDD	736 (12 studies)	SMD -0.9 (95% CI -1.2 to -0.7)	⊕○○○ Downgrade due to inconsistency ^a
NYHA	658 (14 studies)	OR 9.49 (95% CI 5.06 to 17.79)	⊕○○○ Downgrade due to inconsistency ^a , imprecision ^b , publication bias ^c
<p>⊕⊕⊕⊕High = This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different is low.</p> <p>⊕⊕⊕○Moderate = This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different is moderate.</p> <p>⊕⊕○○Low = This research provides some indication of the likely effect. However, the likelihood that it will be substantially different is high.</p> <p>⊕○○○Very low = This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different is very high.</p>			
<p><i>Starting from low quality for observational studies, we downgraded by one level in case of serious risk of bias, indirectness, inconsistency, imprecision or publication bias.</i></p>			
<p>^aSignificant unexplained heterogeneity</p> <p>^b95% CIs are wide</p>			
<p><i>CI, confidence interval; GRADE, Grading of Recommendations, Assessment, Development and Evaluation; NYHA, New York Heart Association; OR, odds ratio; RVEDD, end-diastolic diameter of the right ventricle; SMD, standardized mean difference</i></p>			