Supplementary file S1. Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) checklist

Section/Topic	Item #	Checklist Item	Reported on Page #
TITLE			
Title	1	Identify the report as a systematic review *incorporating a network meta-analysis (or related form of meta-analysis).*	***1***
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: **Background:** main objectives **Methods:** data sources; study eligibility criteria, participants, and interventions; study appraisal; and *synthesis methods, such as network meta-analysis.* **Results:** number of studies and participants identified; summary estimates with corresponding confidence/credible intervals; *treatment rankings may also be discussed. Authors may choose to summarize pairwise comparisons against a chosen treatment included in their analyses for brevity.* **Discussion/Conclusions:** limitations; conclusions and implications of findings. **Other:** primary source of funding; systematic review registration number with registry name.	3

INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known, *including mention of why a network meta-analysis has been conducted.*	***4***
Objectives	4	Provide an explicit statement of questions being addressed, with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists and if and where it can be accessed (e.g., Web address); and, if available, provide registration information, including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. *Clearly describe eligible treatments included in the treatment network, and note whether any have been clustered or merged into the same node (with justification).*	***5***
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	S3

Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5,6
Geometry of the network	**S1**	Describe methods used to explore the geometry of the treatment network under study and potential biases related to it. This should include how the evidence base has been graphically summarized for presentation, and what characteristics were compiled and used to describe the evidence base to readers.	***6***
Risk of bias within individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means). *Also describe the use of additional summary measures assessed, such as treatment rankings and surface under the cumulative ranking curve (SUCRA) values, as well as modified approaches used to present summary findings from meta-analyses.*	6
Planned methods of	14	Describe the methods of handling data and combining results of studies for each network meta-analysis. This should include, but not be limited to:	6,7

analysis		• *Handling of multi-arm trials;* • *Selection of variance structure;* • *Selection of prior distributions in Bayesian analyses; and* • *Assessment of model fit.*	
Assessment of Inconsistency	**S2**	Describe the statistical methods used to evaluate the agreement of direct and indirect evidence in the treatment network(s) studied. Describe efforts taken to address its presence when found.	7
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	**7**
Additional analyses	16	Describe methods of additional analyses if done, indicating which were pre-specified. This may include, but not be limited to, the following: • Sensitivity or subgroup analyses; • Meta-regression analyses; • *Alternative formulations of the treatment network; and* • *Use of alternative prior distributions for Bayesian analyses (if applicable).*	*7*

RESULTS†			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7
Presentation of network structure	**S3**	Provide a network graph of the included studies to enable visualization of the geometry of the treatment network.	***34***
Summary of network geometry	**S4**	Provide a brief overview of characteristics of the treatment network. This may include commentary on the abundance of trials and randomized patients for the different interventions and pairwise comparisons in the network, gaps of evidence in the treatment network, and potential biases reflected by the network structure.	***7***
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	22-30
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment.	S6
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: 1) simple summary data for each intervention group, and 2) effect estimates and confidence intervals. *Modified approaches may be needed to deal with information from larger networks.*	***8,9***
Synthesis of results	21	Present results of each meta-analysis done, including confidence/credible intervals. *In larger networks, authors may focus on comparisons versus a*	***8,9***

		particular comparator (e.g. placebo or standard care), with full findings presented in an appendix. League tables and forest plots may be considered to summarize pairwise comparisons. If additional summary measures were explored (such as treatment rankings), these should also be presented.	
Exploration for inconsistency	**S5**	Describe results from investigations of inconsistency. This may include such information as measures of model fit to compare consistency and inconsistency models, *P* values from statistical tests, or summary of inconsistency estimates from different parts of the treatment network.	***S8***
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies for the evidence base being studied.	S5
Results of additional analyses	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression analyses*, alternative network geometries studied, alternative choice of prior distributions for Bayesian analyses,* and so forth).	***S12***
DISCUSSION			
Summary of evidence	24	Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy-makers).	10,11
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias). *Comment on the validity of the assumptions, such as transitivity and consistency. Comment on any concerns regarding network geometry (e.g.,*	10-12

		avoidance of certain comparisons).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	14
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. This should also include information regarding whether funding has been received from manufacturers of treatments in the network and/or whether some of the authors are content experts with professional conflicts of interest that could affect use of treatments in the network.	***2***

Supplementary file S2. AMSTAR-2 (Assessing the methodological quality of systematic reviews-2) Guidelines checklist

AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both

1. Did the research questions and inclusion criteria for the review include the components of PICO?

For Yes:
- ☑ Population
- ☑ Intervention
- ☑ Comparator group
- ☑ Outcome

Optional (recommended)
- ☐ Timeframe for follow-up

☑ Yes
☐ No

2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?

For Partial Yes:
The authors state that they had a written protocol or guide that included ALL the following:
- ☑ review question(s)
- ☑ a search strategy
- ☑ inclusion/exclusion criteria
- ☑ a risk of bias assessment

For Yes:
As for partial yes, plus the protocol should be registered and should also have specified:
- ☐ a meta-analysis/synthesis plan, if appropriate, *and*
- ☐ a plan for investigating causes of heterogeneity
- ☐ justification for any deviations from the protocol

☐ Yes
☑ Partial Yes
☐ No

3. Did the review authors explain their selection of the study designs for inclusion in the review?

For Yes, the review should satisfy ONE of the following:
- ☑ *Explanation for* including only RCTs
- ☐ OR *Explanation for* including only NRSI
- ☐ OR *Explanation for* including both RCTs and NRSI

☑ Yes
☐ No

4. Did the review authors use a comprehensive literature search strategy?

For Partial Yes (all the following):
- ☑ searched at least 2 databases (relevant to research question)
- ☑ provided key word and/or search strategy
- ☑ justified publication restrictions (e.g. language)

For Yes, should also have (all the following):
- ☐ searched the reference lists / bibliographies of included studies
- ☐ searched trial/study registries
- ☐ included/consulted content experts in the field
- ☐ where relevant, searched for grey literature
- ☐ conducted search within 24 months of completion of the review

☐ Yes
☑ Partial Yes
☐ No

5. Did the review authors perform study selection in duplicate?

For Yes, either ONE of the following:
- ☑ at least two reviewers independently agreed on selection of eligible studies and achieved consensus on which studies to include
- ☐ OR two reviewers selected a sample of eligible studies and achieved good agreement (at least 80 percent), with the remainder selected by one reviewer.

☑ Yes
☐ No

AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both

6. Did the review authors perform data extraction in duplicate?

For Yes, either ONE of the following:

- ☒ at least two reviewers achieved consensus on which data to extract from included studies
- ☐ OR two reviewers extracted data from a sample of eligible studies and achieved good agreement (at least 80 percent), with the remainder extracted by one reviewer.

☒ Yes
☐ No

7. Did the review authors provide a list of excluded studies and justify the exclusions?

For Partial Yes:

- ☒ provided a list of all potentially relevant studies that were read in full-text form but excluded from the review

For Yes, must also have:

- ☐ Justified the exclusion from the review of each potentially relevant study

☐ Yes
☒ Partial Yes
☐ No

8. Did the review authors describe the included studies in adequate detail?

For Partial Yes (ALL the following):

- ☐ described populations
- ☐ described interventions
- ☐ described comparators
- ☐ described outcomes
- ☐ described research designs

For Yes, should also have ALL the following:

- ☒ described population in detail
- ☒ described intervention in detail (including doses where relevant)
- ☒ described comparator in detail (including doses where relevant)
- ☒ described study's setting
- ☒ timeframe for follow-up

☒ Yes
☐ Partial Yes
☐ No

9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?

RCTs

For Partial Yes, must have assessed RoB from

- ☐ unconcealed allocation, *and*
- ☐ lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all-cause mortality)

For Yes, must also have assessed RoB from:

- ☒ allocation sequence that was not truly random, *and*
- ☒ selection of the reported result from among multiple measurements or analyses of a specified outcome

☒ Yes
☐ Partial Yes
☐ No
☐ Includes only NRSI

NRSI

For Partial Yes, must have assessed RoB:

- ☐ from confounding, *and*
- ☐ from selection bias

For Yes, must also have assessed RoB:

- ☐ methods used to ascertain exposures and outcomes, *and*
- ☐ selection of the reported result from among multiple measurements or analyses of a specified outcome

☐ Yes
☐ Partial Yes
☐ No
☒ Includes only RCTs

10. Did the review authors report on the sources of funding for the studies included in the review?

For Yes

- ☐ Must have reported on the sources of funding for individual studies included in the review. Note: Reporting that the reviewers looked for this information but it was not reported by study authors also qualifies

☐ Yes
☒ No

AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both

11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?

RCTs
For Yes:

- ☑ The authors justified combining the data in a meta-analysis
  - ☑ AND they used an appropriate weighted technique to combine study results and adjusted for heterogeneity if present.
  - ☑ AND investigated the causes of any heterogeneity

☑ Yes
☐ No
☐ No meta-analysis conducted

For NRSI
For Yes:

- ☐ The authors justified combining the data in a meta-analysis
  - ☐ AND they used an appropriate weighted technique to combine study results, adjusting for heterogeneity if present
  - ☐ AND they statistically combined effect estimates from NRSI that were adjusted for confounding, rather than combining raw data, or justified combining raw data when adjusted effect estimates were not available
  - ☐ AND they reported separate summary estimates for RCTs and NRSI separately when both were included in the review

☐ Yes
☐ No
☐ No meta-analysis conducted

12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?

For Yes:

- ☐ included only low risk of bias RCTs
- ☑ OR, if the pooled estimate was based on RCTs and/or NRSI at variable RoB, the authors performed analyses to investigate possible impact of RoB on summary estimates of effect.

☑ Yes
☐ No
☐ No meta-analysis conducted

13. Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?

For Yes:

- ☐ included only low risk of bias RCTs
- ☑ OR, if RCTs with moderate or high RoB, or NRSI were included the review provided a discussion of the likely impact of RoB on the results

☑ Yes
☐ No

14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?

For Yes:

- ☐ There was no significant heterogeneity in the results
- ☑ OR if heterogeneity was present the authors performed an investigation of sources of any heterogeneity in the results and discussed the impact of this on the results of the review

☑ Yes
☐ No

15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?

For Yes:

- ☐ performed graphical or statistical tests for publication bias and discussed the likelihood and magnitude of impact of publication bias

☐ Yes
☑ No
☐ No meta-analysis conducted

AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both

16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?

For Yes:

- ☒ The authors reported no competing interests OR
- ☐ The authors described their funding sources and how they managed potential conflicts of interest

- ☒ Yes
- ☐ No

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Supplementary file S3. Research Question, PICO, MeSH, Keywords, and Search Strategy

Research question: What is the efficacy and safety of bivalirudin and heparin with or without Glycoprotein IIb/IIIa inhibitors in patients who underwent percutaneous coronary intervention?

PICO	
Population	Patients who underwent percutaneous coronary intervention
Intervention	Bivalirudin plus GP IIb/IIIa inhibitors, bivalirudin monotherapy, Heparin plus GP IIb/IIIa inhibitors
Comparison	Heparin monotherapy
Outcomes	**Primary Outcomes:** Bleeding risk, Major adverse cardiovascular events **Secondary Outcomes:** Cardiovascular death, all-cause mortality, re-infarction, stent thrombosis

Study Type: Relative risk to compare outcomes systematic review and network meta-analysis

MeSH Terms and Keywords:

MeSH Terms			
Population	**Intervention**	**Control**	**Outcomes**
"Non-ST Elevated Myocardial Infarction"[Mesh] OR "ST Elevation Myocardial Infarction"[Mesh] OR "Percutaneous Coronary Intervention"[Mesh]	"bivalirudin" [Supplementary Concept]	"Heparin"[Mesh]	-

Keywords			
Population	**Intervention**	**Comparison**	**Outcome**
Non ST Elevated Myocardial Infarction NSTEMI Non-ST-Elevation Myocardial Infarction Infarctions, Non-ST-Elevation Myocardial Non ST Elevation Myocardial Infarction Non-ST-Elevation Myocardial Infarctions OR ST Segment Elevation Myocardial Infarction ST Elevated Myocardial Infarction STEMI OR Percutaneous Coronary	Phe-Pro-Arg-Pro-(Gly)4-desulfohirudin-(53-64) Phe-Pro-Arg-Pro-(Gly)4-Asn-Gly-Asp-Phe-Glu-Glu-Ile-Pro-Glu-Glu-Tyr-Leu L-leucine, D-phenylalanyl-L-prolyl-L-arginyl-L-prolylglycylglycylglycylglycyl-L-asparaginylglycyl-L-alpha-aspartyl-L-phenylalanyl-L-alpha-glutamyl-L-alpha-glutamyl-L-isoleucyl-L-prolyl-L-alpha-glutamyl-L-alpha-glutamyl-L-tyrosyl- Phe-Pro-Arg-Pro-(Gly)4 desulfato-Tyr63'-hirugen Angiomax Angiomax RTU CTB-001 bivalirudin trifluoroacetate BG 8967 BG8967 BG-8967 Hirulog Hirulog-1	Unfractionated Heparin Heparinic Acid Liquaemin Sodium Heparin alpha-Heparin alpha Heparin	

Interventions Percutaneous Coronary Revascularization Percutaneous Coronary Revascularizations			

Data Bases	Search Strategy	Results
Pubmed	((((((((((("Non-ST Elevated Myocardial Infarction"[Mesh]) OR (Non ST Elevated Myocardial Infarction)) OR (NSTEMI)) OR (Non-ST-Elevation Myocardial Infarction)) OR (Infarctions, Non-ST-Elevation Myocardial)) OR (Non ST Elevation Myocardial Infarction)) OR (Non-ST-Elevation Myocardial Infarctions)) OR ((((("ST Elevation Myocardial Infarction"[Mesh]) OR (ST Segment Elevation Myocardial Infarction)) OR (ST Elevated Myocardial Infarction)) OR (STEMI))) OR ((((("Percutaneous Coronary Intervention"[Mesh]) OR (Percutaneous Coronary Interventions)) OR (Percutaneous Coronary Revascularization)) OR (Percutaneous Coronary Revascularizations))) AND (((((((("Heparin"[Mesh]) OR (Unfractionated Heparin)) OR (Heparinic Acid)) OR (Liquaemin)) OR (Sodium Heparin)) OR (alpha-Heparin)) OR (alpha Heparin))) AND ((((((((((("bivalirudin" [Supplementary Concept]) OR (Phe-Pro-Arg-Pro-(Gly)4-desulfohirudin-(53-64))) OR (Phe-Pro-Arg-Pro-(Gly)4-Asn-Gly-Asp-Phe-Glu-Glu-Ile-Pro-Glu-Glu-Tyr-Leu)) OR (L-leucine, D-phenylalanyl-L-prolyl-L-arginyl-L-prolylglycylglycylglycylglycyl-L-asparaginylglycyl-L-alpha-aspartyl-L-phenylalanyl-L-alpha-glutamyl-L-alpha-glutamyl-L-isoleucyl-L-prolyl-L-alpha-glutamyl-L-alpha-glutamyl-L-tyrosyl- Phe-Pro-Arg-Pro-(Gly)4 desulfato-Tyr63'-hirugen)) OR (Angiomax)) OR (Angiomax RTU)) OR (CTB-001)) OR (bivalirudin trifluoroacetate)) OR (BG 8967)) OR (BG8967)) OR (BG-8967)) OR (Hirulog)) OR (Hirulog-1)) Filters: Clinical Study, Clinical Trial, Clinical Trial, Phase I, Clinical Trial, Phase II, Clinical Trial, Phase III, Clinical Trial, Phase IV, Comparative Study, Controlled Clinical Trial, Meta-Analysis, Multicenter Study, Observational Study, Pragmatic Clinical Trial, Randomized Controlled Trial, Validation Study	405

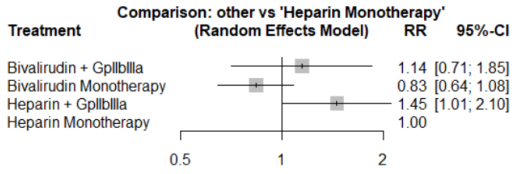
Embase	('percutaneous coronary intervention'/exp OR 'percutaneous coronary intervention' OR 'st segment elevation myocardial infarction'/exp OR 'st elevated mi' OR 'st elevated myocardial infarction' OR 'st elevation mi' OR 'st elevation myocardial infarction' OR 'st segment elevated myocardial infarction' OR 'st segment elevation mi' OR 'st segment elevation heart infarction' OR 'st segment elevation myocardial infarction' OR 'stemi' OR 'non st segment elevation myocardial infarction'/exp OR 'nstemi' OR 'non st elevated mi' OR 'non st elevated myocardial infarction' OR 'non st elevation mi' OR 'non st elevation myocardial infarction' OR 'non st segment elevated myocardial infarction' OR 'non st segment elevation mi' OR 'non st segment elevation heart infarction' OR 'non st segment elevation myocardial infarction' OR 'non stemi' OR 'non-st elevated myocardial infarction') AND ('bivalirudin'/exp OR 'angiomax' OR 'angiomax rtu' OR 'angiox' OR 'bg 8967' OR 'bg8967' OR 'bivalirudin' OR 'bivalirudin in sodium chloride 0.9%' OR 'bivalurudin trifluoroacetate' OR 'd phe pro arg pro (gly) 4 desulfohirudin [53-64]' OR 'd phe pro arg pro gly gly gly gly asn gly asp phe glu glu ile pro glu glu tyr leu' OR 'dextro phenylalanylprolylarginylprolylglycylglycylglycylglycylasparaginylglycyl alpha aspartylphenylalanyl alpha glutamyl alpha glutamylisoleucylprolyl alpha glutamyl alpha glutamyl alpha tyrosyleucine' OR 'dextro phenylalanylprolylarginylprolylglycylglycylglycylglycylasparaginylglycyl alpha aspartylphenylalanyl alpha glutamyl alpha glutamylisoleucylprolyl alpha glutamyl alpha glutamyl alpha tyrosyleucine bis (2, 2, 2 trifluoroacetate)' OR 'ep 6101' OR 'ep6101' OR 'hirulog' OR 'hirulog 1') AND ('heparin'/exp OR 'alpha heparin' OR 'ammonium heparinate' OR 'benzalkonium heparin' OR 'beparine' OR 'clarin' OR 'contusol' OR 'disebrin' OR 'eleparon' OR 'elheparin' OR 'elheparon' OR 'endogenous heparin' OR 'epiheparin' OR 'gag 98' OR 'helberina' OR 'hep flush kit' OR 'hep lock' OR 'hep-lock' OR 'hep-lock u/p' OR 'hep-pak cvc' OR 'hepaflex' OR 'hepalean' OR 'heparin' OR 'heparin injection b.p.' OR 'heparin leo' OR 'heparin lock flush' OR 'heparin lock flush plus sodium chloride' OR 'heparin lock flush preservative free' OR 'heparin monosulfate' OR 'heparin monosulphate' OR 'heparin novo' OR 'heparin ointment' OR 'heparin potassium' OR 'heparin sodium' OR 'heparin sodium 1, 000 units and sodium chloride 0.9%' OR 'heparin sodium 1, 000 units in dextrose 5%' OR 'heparin sodium 1, 000 units in sodium chloride 0.9%' OR 'heparin sodium 10, 000 units in dextrose 5%' OR 'heparin sodium 10, 000 units in sodium chloride 0.45%' OR 'heparin sodium 10, 000 units in sodium chloride 0.9%' OR 'heparin sodium 12, 500 units in dextrose 5%' OR 'heparin sodium 12, 500 units in sodium chloride 0.45%' OR 'heparin sodium 12, 500 units in sodium chloride 0.9%' OR 'heparin sodium 2, 000 units and sodium chloride 0.9%' OR 'heparin sodium 2, 000 units in dextrose 5%' OR 'heparin sodium 2, 000 units in sodium chloride 0.9%' OR 'heparin sodium 20, 000 units and dextrose 5%' OR 'heparin sodium 20, 000 units in dextrose 5%' OR 'heparin sodium 25, 000 units and dextrose 5%' OR 'heparin sodium 25, 000 units in dextrose 5%' OR 'heparin sodium 25, 000 units in sodium chloride 0.45%' OR 'heparin sodium 25, 000 units in sodium chloride 0.9%' OR 'heparin sodium 5, 000 units and	1546

	sodium chloride 0.9%' OR 'heparin sodium 5, 000 units in dextrose 5%' OR 'heparin sodium 5, 000 units in sodium chloride 0.45%' OR 'heparin sodium 5, 000 units in sodium chloride 0.9%' OR 'heparin sodium b braun' OR 'heparin sodium preservative free' OR 'heparin subcutaneous' OR 'heparin sulfate' OR 'heparin sulfuric acid' OR 'heparin sulphate' OR 'heparina' OR 'heparina leo' OR 'heparinate sodium' OR 'heparine' OR 'heparine choay' OR 'heparine novo' OR 'heparinic acid' OR 'heparitin monosulfate' OR 'heparitin monosulphate' OR 'hepcon' OR 'hepflush-10' OR 'hepsal' OR 'inhepar' OR 'inviclot' OR 'lipo hepin' OR 'lipo-hepin' OR 'lipohepin' OR 'liquaemin' OR 'liquaemin lock flush' OR 'liquaemin sodium' OR 'liquaemin sodium preservative free' OR 'liquemin' OR 'liquemine' OR 'menaven' OR 'monoparin' OR 'mucoitin polysulfate' OR 'mucoitin polysulfate ester' OR 'mucoitin polysulphate' OR 'mucoitin polysulphate ester' OR 'mucoitin sodium polysulfate' OR 'mucoitin sodium polysulphate' OR 'multiparin' OR 'nevparin' OR 'noparin' OR 'panheparin' OR 'panhepin' OR 'panheprin' OR 'parinix' OR 'phlebotroy qps' OR 'praecivenin' OR 'pularin' OR 'sodium heparin' OR 'thrombareduct' OR 'thrombo vetren' OR 'thromboliquin' OR 'thromboliquine' OR 'thrombophlogat' OR 'thrombophob' OR 'thrombophob gel' OR 'thromboreduct' OR 'thrombosamine' OR 'thrombosamine heparin' OR 'thrombosamine heparine' OR 'unfractionated heparin' OR 'uniparin' OR 'vetren' OR 'vister' OR 'vr 496' OR 'vr496') AND ('clinical study'/exp OR 'clinical data' OR 'clinical studies as topic' OR 'clinical study' OR 'medical trial' OR 'clinical trial'/exp OR 'clinical drug trial' OR 'clinical trial' OR 'major clinical trial' OR 'trial, clinical' OR 'phase 1 clinical trial'/exp OR 'clinical trial, phase 1' OR 'phase 1 clinical study' OR 'phase 1 clinical trial' OR 'phase 1 study' OR 'phase 1 trial' OR 'phase i clinical study' OR 'phase i clinical trial' OR 'phase i study' OR 'phase i trial' OR 'phase 2 clinical trial'/exp OR 'clinical trial, phase 2' OR 'phase 2 clinical study' OR 'phase 2 clinical trial' OR 'phase 2 study' OR 'phase 2 trial' OR 'phase ii clinical study' OR 'phase ii clinical trial' OR 'phase ii study' OR 'phase ii trial' OR 'phase 3 clinical trial'/exp OR 'clinical trial, phase 3' OR 'phase 3 clinical study' OR 'phase 3 clinical trial' OR 'phase 3 study' OR 'phase 3 trial' OR 'phase iii clinical study' OR 'phase iii clinical trial' OR 'phase iii study' OR 'phase iii trial' OR 'phase 4 clinical trial'/exp OR 'clinical trial, phase 4' OR 'phase 4 clinical study' OR 'phase 4 clinical trial' OR 'phase 4 study' OR 'phase 4 trial' OR 'phase iv clinical study' OR 'phase iv clinical trial' OR 'phase iv study' OR 'phase iv trial' OR 'comparative study'/exp OR 'comparative studies' OR 'comparative study' OR 'comparison' OR 'controlled study'/exp OR 'control group study' OR 'control group trial' OR 'controlled study' OR 'controlled trial' OR 'meta analysis'/exp OR 'analysis, meta' OR 'meta analysis' OR 'meta-analysis' OR 'metaanalysis' OR 'multicenter study'/exp OR 'multi-center study' OR 'multi-center trial' OR 'multi-centre study' OR 'multi-centre trial' OR 'multicenter study' OR 'multicenter trial' OR 'multicentre study' OR 'multicentre trial' OR 'study, multicenter' OR 'trial, multicenter' OR 'observational study'/exp OR 'non experimental studies' OR 'non experimental study' OR 'nonexperimental studies' OR 'nonexperimental study' OR 'observation studies' OR 'observation study' OR 'observational studies' OR 'observational studies as topic' OR 'observational study' OR 'observational study as topic' OR 'randomized controlled trial'/exp	

	OR 'controlled trial, randomized' OR 'randomised controlled study' OR 'randomised controlled trial' OR 'randomized controlled study' OR 'randomized controlled trial' OR 'trial, randomized controlled' OR 'validation study'/exp OR 'validation studies' OR 'validation studies as topic' OR 'validation study') NOT ('case report'/exp OR 'case report') NOT ('case study'/exp OR 'case series' OR 'case studies' OR 'case study' OR 'large case series') NOT ('review'/exp OR 'review')	

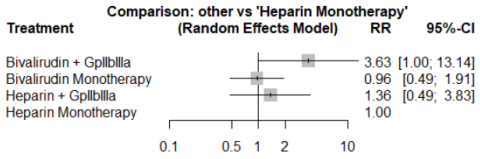
Supplementary file S4. Forest plots of outcomes

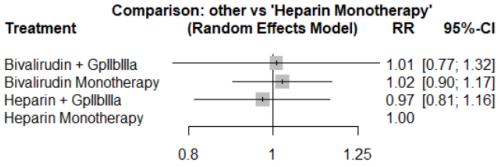
Figure S4: Forest plots using random effect values showing relative risk for the treatment groups



Bleeding

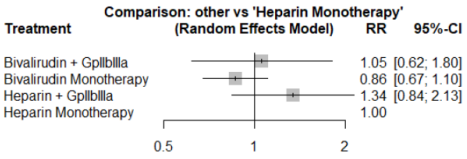
Stent Thrombosis

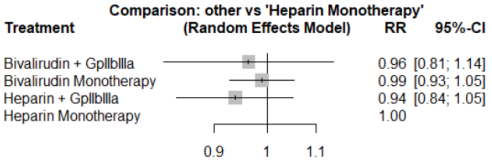




Reinfarction

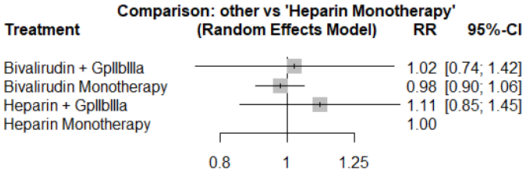
Cardiovascular Death





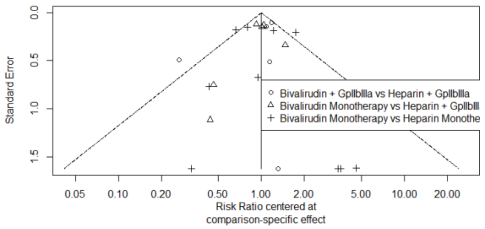
Major Adverse Cardiac Effects

All Cause Mortality

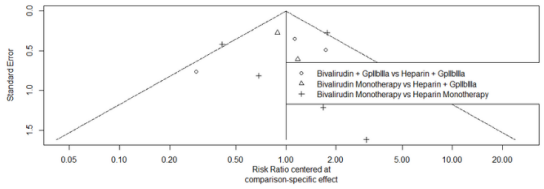


Supplementary file S5. Funnel Plots and Egger's p test values

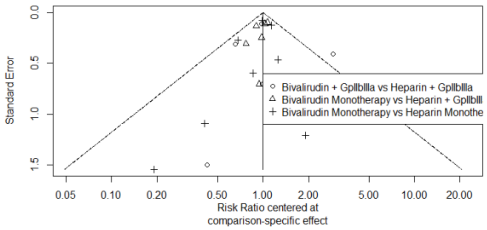
Funnel plot



Bleeding

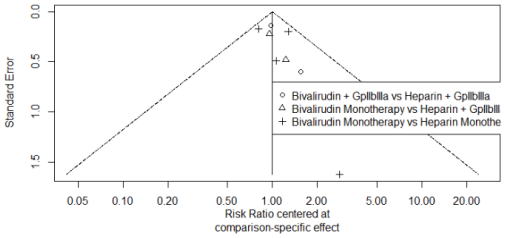


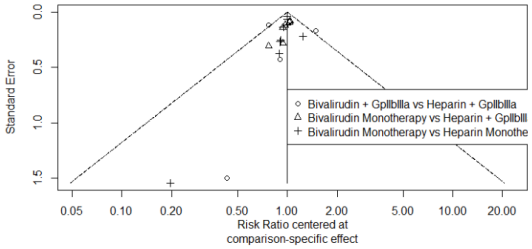
Stent Thrombosis



Reinfarction

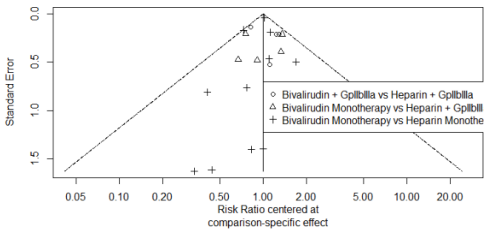
Cardiovascular Death





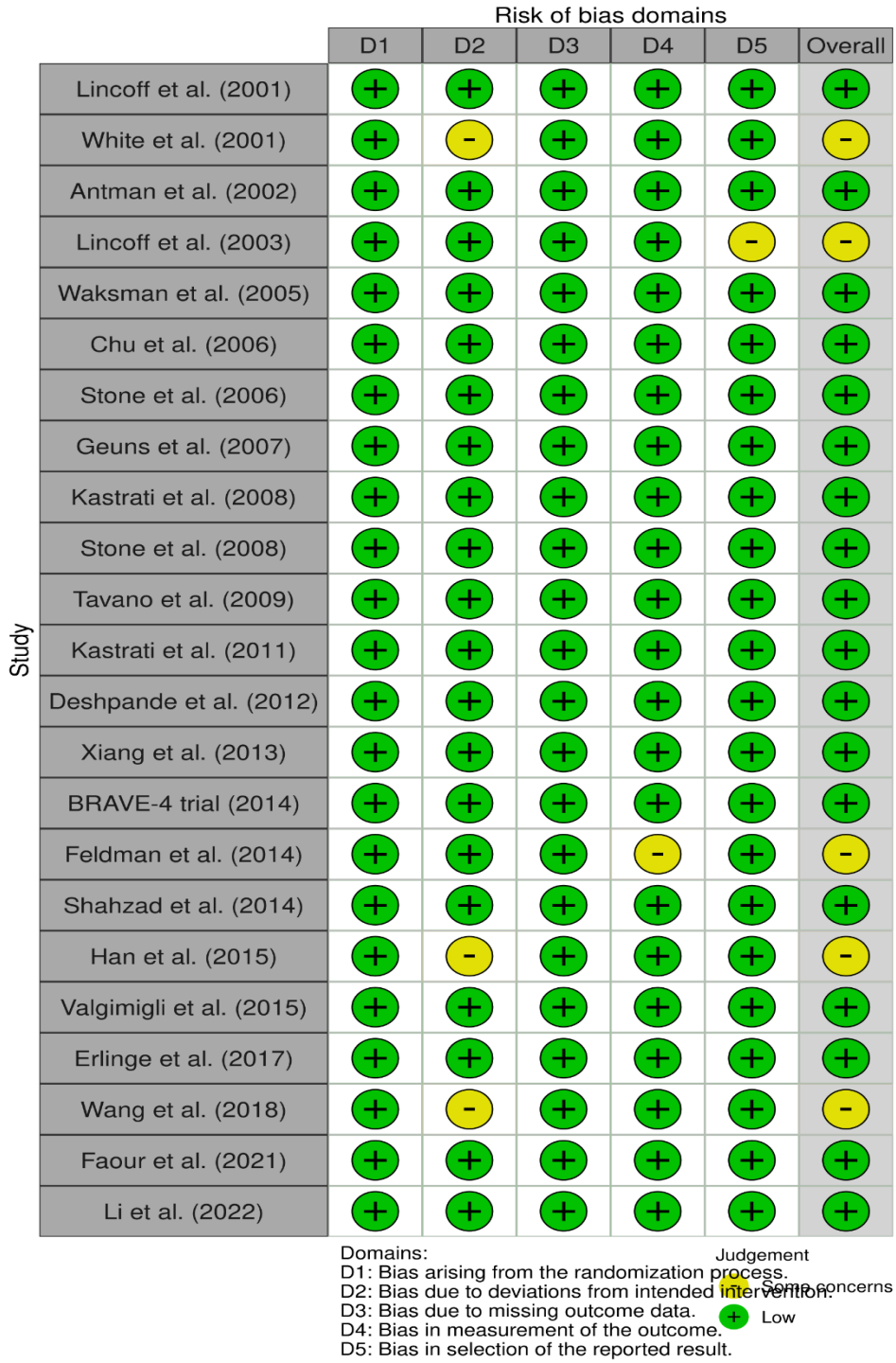
Major Adverse Cardiac Effects

All Cause Mortality



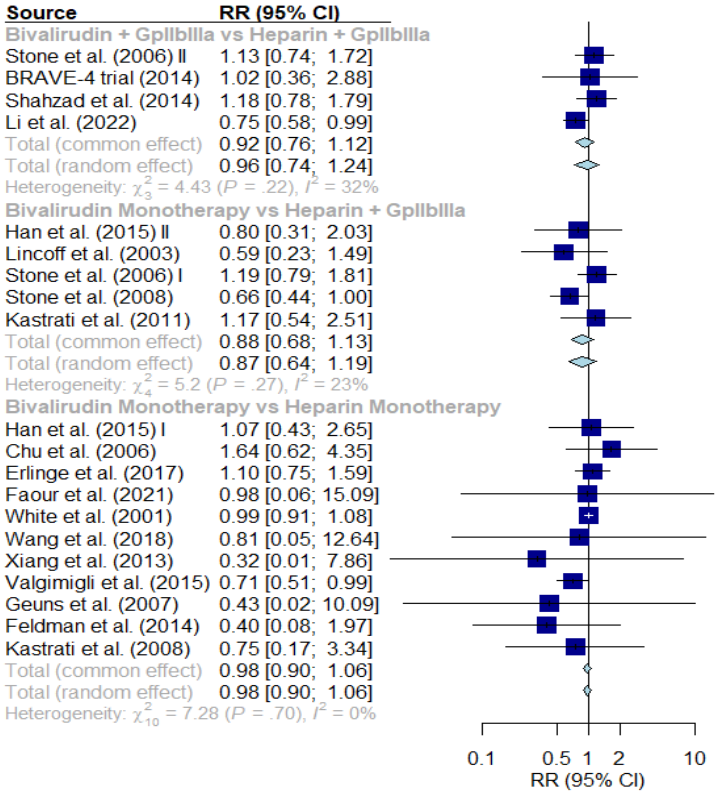
Outcome Measured	Egger's p-value
All cause mortality	0.5964
Cardiovascular death	0.1763
Bleeding	0.6402
Reinfarction	0.4485
Major adverse cardiovascular events	0.6396
Stent Thrombosis	0.7080

Supplementary file S6. Cochrane Risk of Bias (ROB) tool assessment for included randomized controlled trials (RCTs)

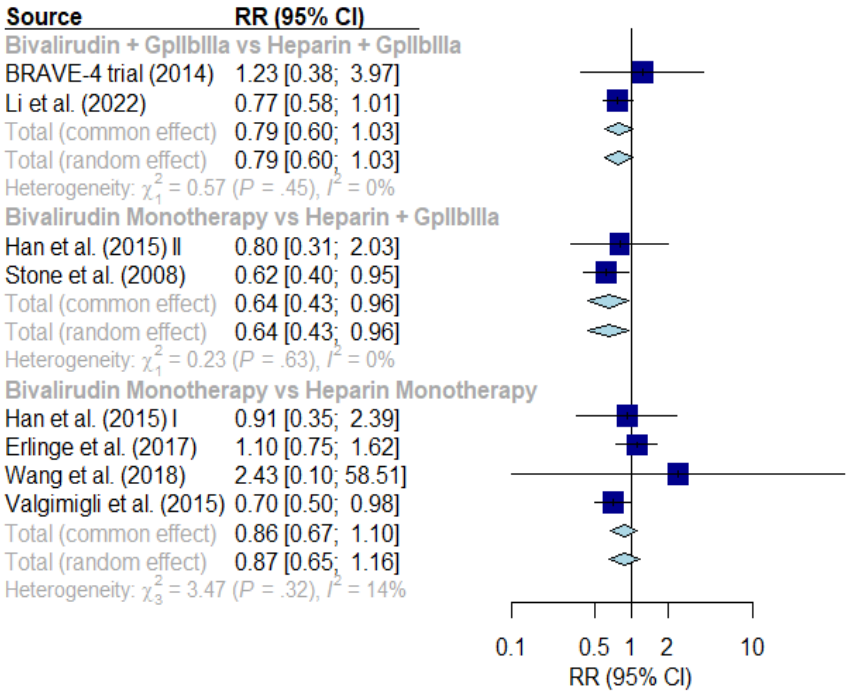

Risk of bias domains
D1
D2
D3
D4
D5
Overall
Study
Lincoff et al. (2001)
White et al. (2001)
Antman et al. (2002)
Lincoff et al. (2003)
Waksman et al. (2005)
Chu et al. (2006)
Stone et al. (2006)
Geuns et al. (2007)
Kastrati et al. (2008)
Stone et al. (2008)
Tavano et al. (2009)
Kastrati et al. (2011)
Deshpande et al. (2012)
Xiang et al. (2013)
BRAVE-4 trial (2014)
Feldman et al. (2014)
Shahzad et al. (2014)
Han et al. (2015)
Valgimigli et al. (2015)
Erlinge et al. (2017)
Wang et al. (2018)
Faour et al. (2021)
Li et al. (2022)
Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.
Judgement
Some concerns
Low

Supplementary file S7. Pairwise Comparisons of Intervention Groups

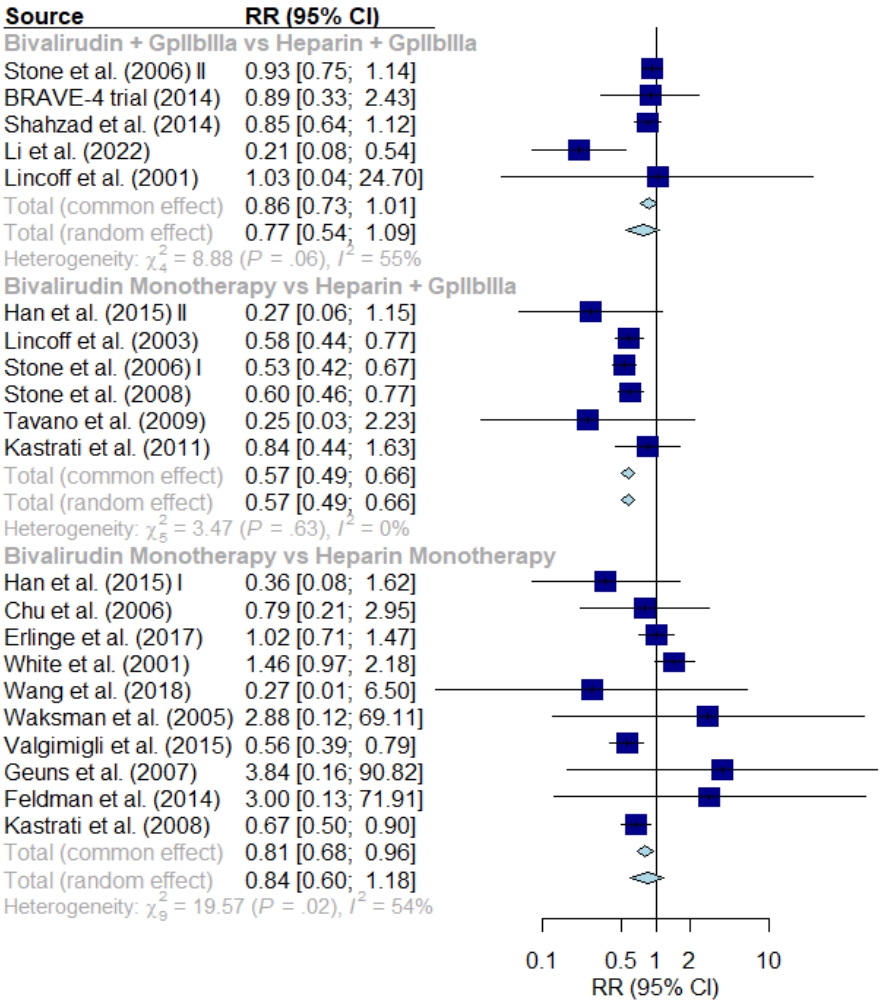
All-cause mortality



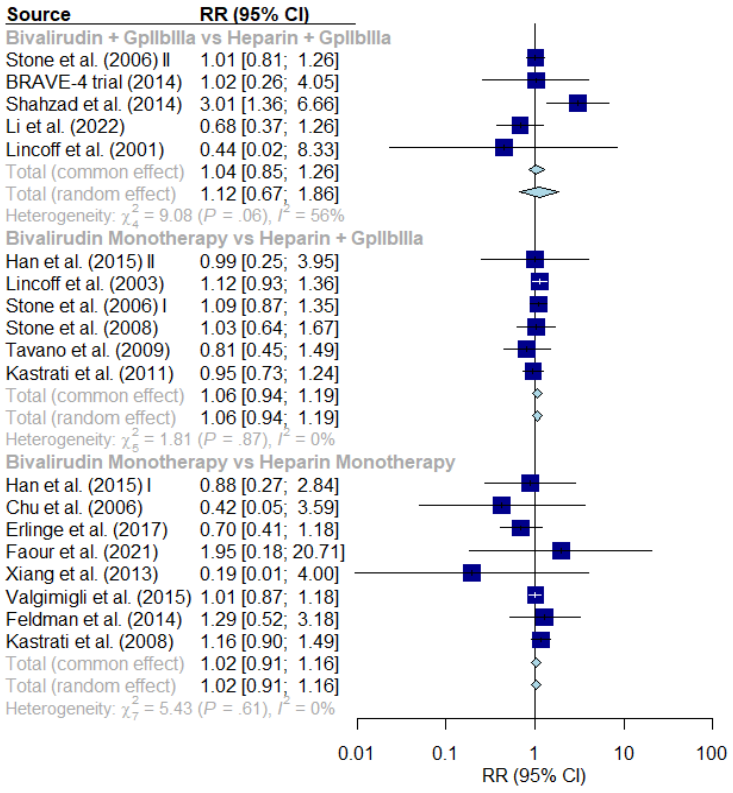
Cardiovascular Death



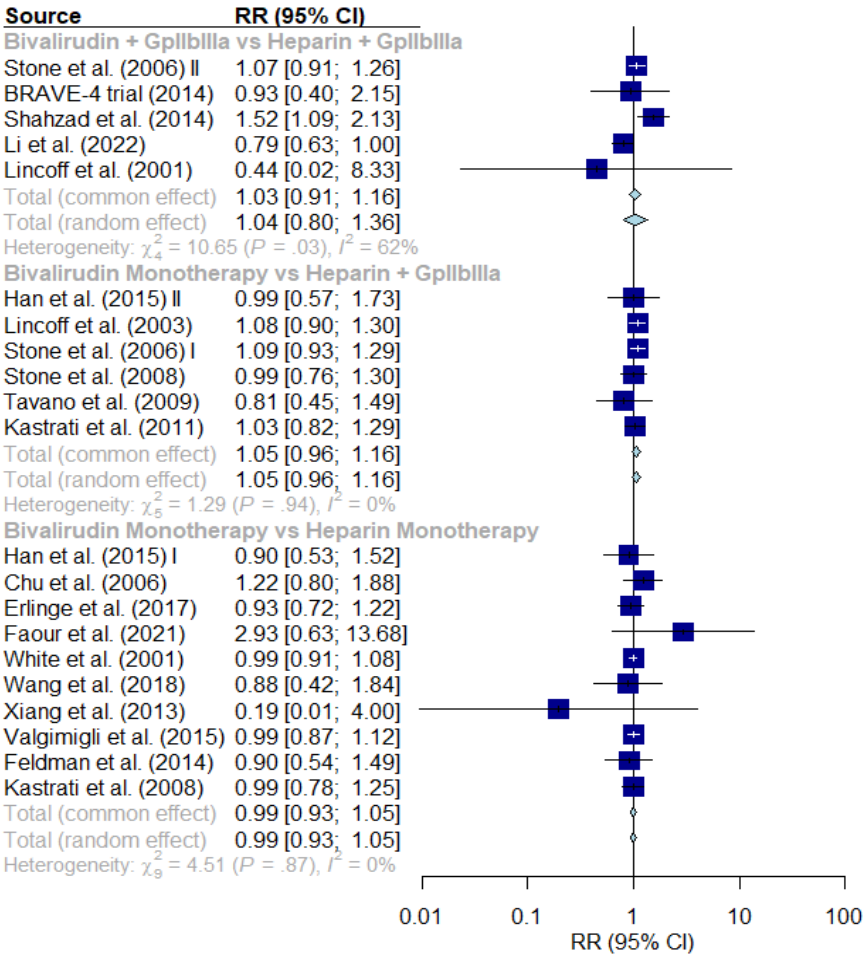
Bleeding


Source
RR (95% CI)
Bivalirudin + GpIIbIIIa vs Heparin + GpIIbIIIa
Stone et al. (2006) II 0.93 [0.75; 1.14]
BRAVE-4 trial (2014) 0.89 [0.33; 2.43]
Shahzad et al. (2014) 0.85 [0.64; 1.12]
Li et al. (2022) 0.21 [0.08; 0.54]
Lincoff et al. (2001) 1.03 [0.04; 24.70]
Total (common effect) 0.86 [0.73; 1.01]
Total (random effect) 0.77 [0.54; 1.09]
Heterogeneity: χ^2_4 = 8.88 (P = .06), I^2 = 55%
Bivalirudin Monotherapy vs Heparin + GpIIbIIIa
Han et al. (2015) II 0.27 [0.06; 1.15]
Lincoff et al. (2003) 0.58 [0.44; 0.77]
Stone et al. (2006) I 0.53 [0.42; 0.67]
Stone et al. (2008) 0.60 [0.46; 0.77]
Tavano et al. (2009) 0.25 [0.03; 2.23]
Kastrati et al. (2011) 0.84 [0.44; 1.63]
Total (common effect) 0.57 [0.49; 0.66]
Total (random effect) 0.57 [0.49; 0.66]
Heterogeneity: χ^2_5 = 3.47 (P = .63), I^2 = 0%
Bivalirudin Monotherapy vs Heparin Monotherapy
Han et al. (2015) I 0.36 [0.08; 1.62]
Chu et al. (2006) 0.79 [0.21; 2.95]
Erlinge et al. (2017) 1.02 [0.71; 1.47]
White et al. (2001) 1.46 [0.97; 2.18]
Wang et al. (2018) 0.27 [0.01; 6.50]
Waksman et al. (2005) 2.88 [0.12; 69.11]
Valgimigli et al. (2015) 0.56 [0.39; 0.79]
Geuns et al. (2007) 3.84 [0.16; 90.82]
Feldman et al. (2014) 3.00 [0.13; 71.91]
Kastrati et al. (2008) 0.67 [0.50; 0.90]
Total (common effect) 0.81 [0.68; 0.96]
Total (random effect) 0.84 [0.60; 1.18]
Heterogeneity: χ^2_9 = 19.57 (P = .02), I^2 = 54%
0.1
0.5
1
2
10
RR (95% CI)

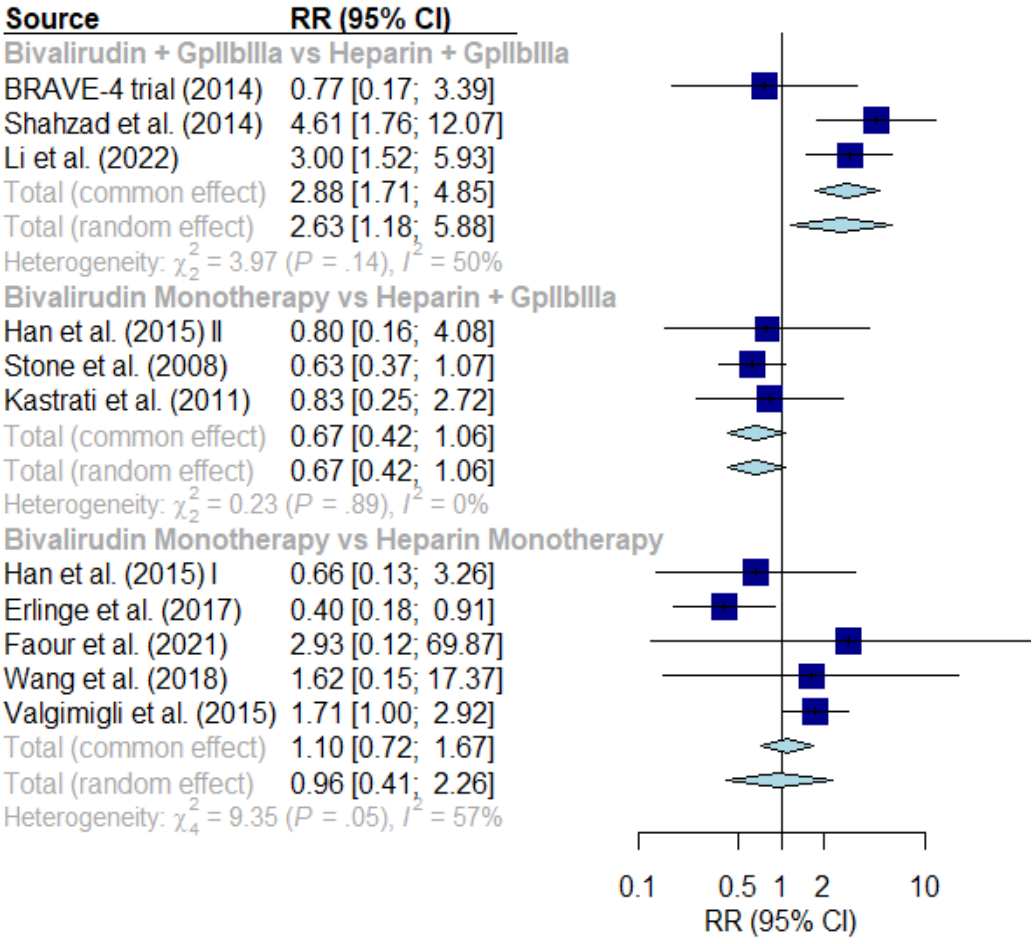
Reinfarction



Major Adverse Cardiovascular Events


Source
RR (95% CI)
Bivalirudin + GpIIbIIIa vs Heparin + GpIIbIIIa
Stone et al. (2006) II 1.07 [0.91; 1.26]
BRAVE-4 trial (2014) 0.93 [0.40; 2.15]
Shahzad et al. (2014) 1.52 [1.09; 2.13]
Li et al. (2022) 0.79 [0.63; 1.00]
Lincoff et al. (2001) 0.44 [0.02; 8.33]
Total (common effect) 1.03 [0.91; 1.16]
Total (random effect) 1.04 [0.80; 1.36]
Heterogeneity: χ^2_4 = 10.65 (P = .03), I^2 = 62%
Bivalirudin Monotherapy vs Heparin + GpIIbIIIa
Han et al. (2015) II 0.99 [0.57; 1.73]
Lincoff et al. (2003) 1.08 [0.90; 1.30]
Stone et al. (2006) I 1.09 [0.93; 1.29]
Stone et al. (2008) 0.99 [0.76; 1.30]
Tavano et al. (2009) 0.81 [0.45; 1.49]
Kastrati et al. (2011) 1.03 [0.82; 1.29]
Total (common effect) 1.05 [0.96; 1.16]
Total (random effect) 1.05 [0.96; 1.16]
Heterogeneity: χ^2_5 = 1.29 (P = .94), I^2 = 0%
Bivalirudin Monotherapy vs Heparin Monotherapy
Han et al. (2015) I 0.90 [0.53; 1.52]
Chu et al. (2006) 1.22 [0.80; 1.88]
Erlinge et al. (2017) 0.93 [0.72; 1.22]
Faour et al. (2021) 2.93 [0.63; 13.68]
White et al. (2001) 0.99 [0.91; 1.08]
Wang et al. (2018) 0.88 [0.42; 1.84]
Xiang et al. (2013) 0.19 [0.01; 4.00]
Valgimigli et al. (2015) 0.99 [0.87; 1.12]
Feldman et al. (2014) 0.90 [0.54; 1.49]
Kastrati et al. (2008) 0.99 [0.78; 1.25]
Total (common effect) 0.99 [0.93; 1.05]
Total (random effect) 0.99 [0.93; 1.05]
Heterogeneity: χ^2_9 = 4.51 (P = .87), I^2 = 0%
0.01
0.1
1
10
100
RR (95% CI)

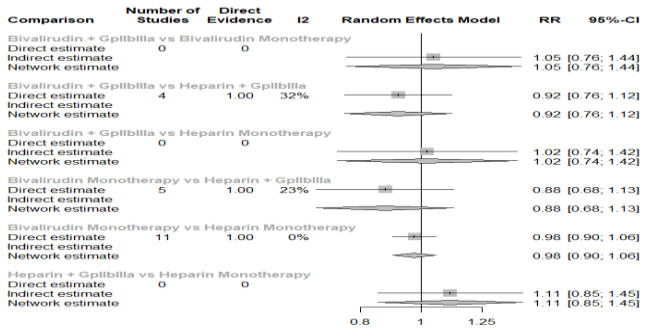
Stent Thrombosis:



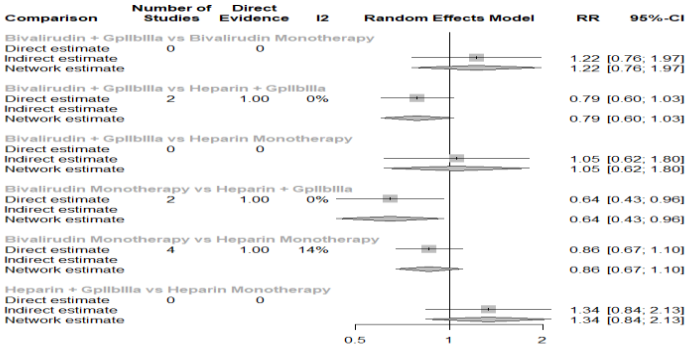
Supplementary file S8. Inconsistency

Direct, Indirect, and Network Estimate of Treatment Groups

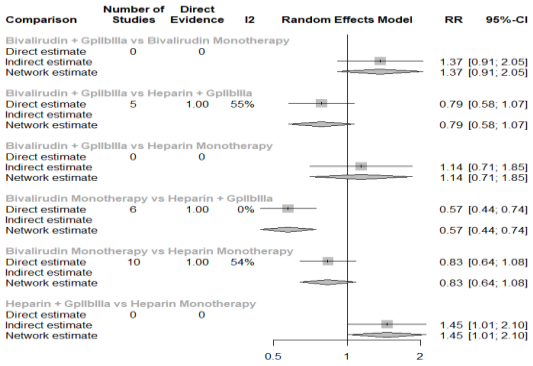
All-cause mortality



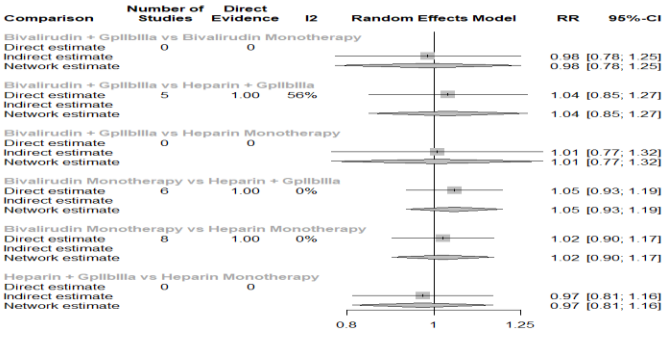
Cardiovascular Death



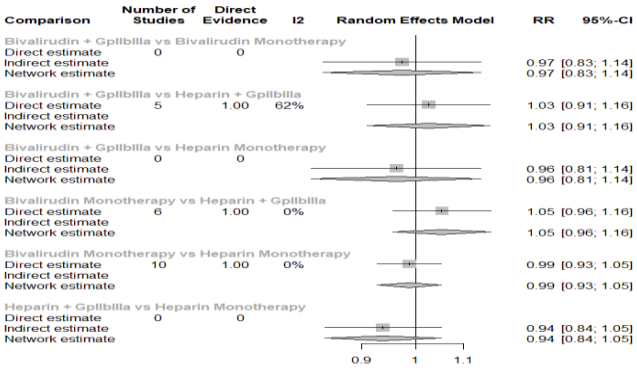
Bleeding



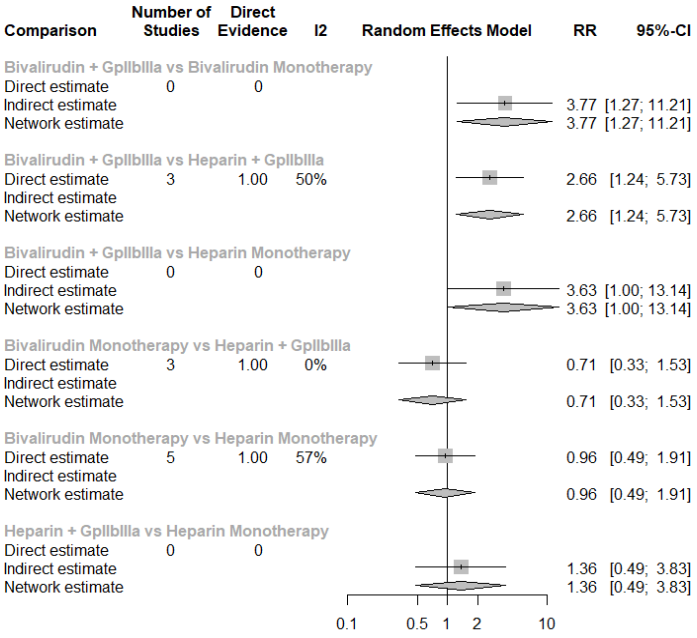
Reinfarction



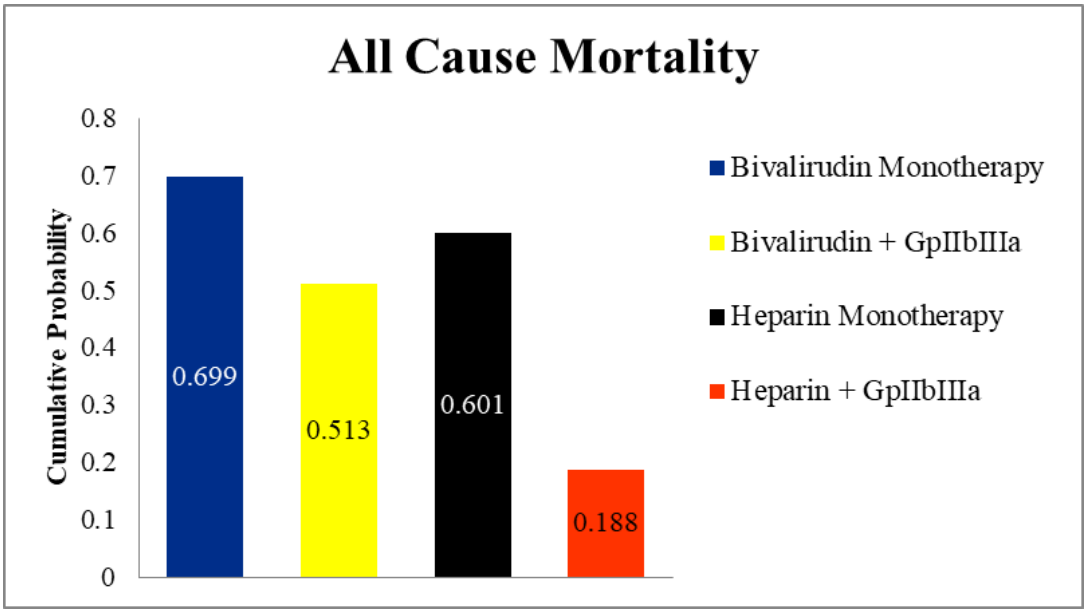
Major Adverse Cardiovascular Events

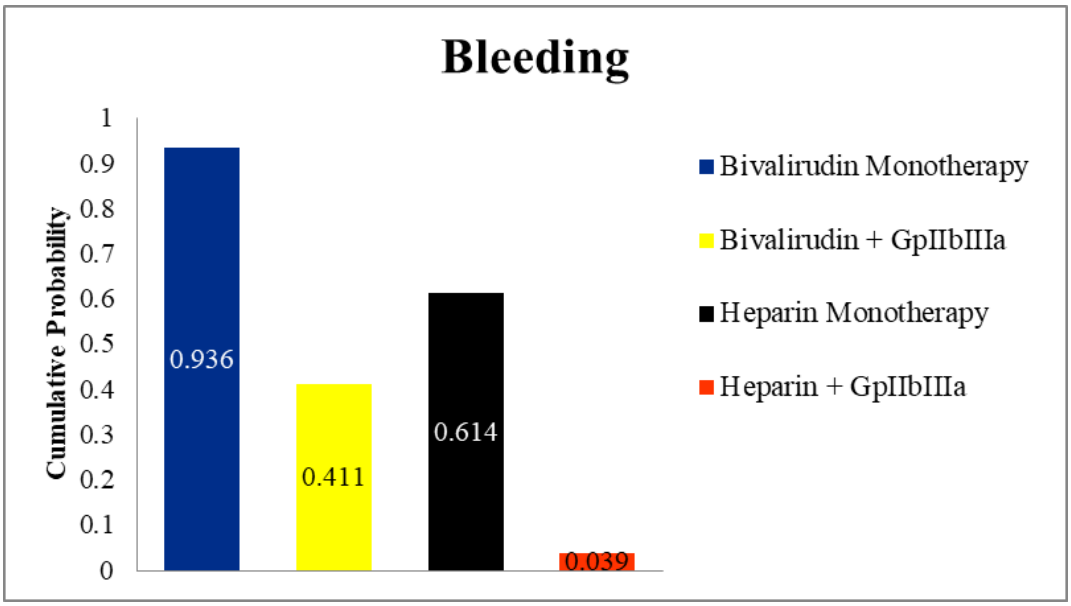


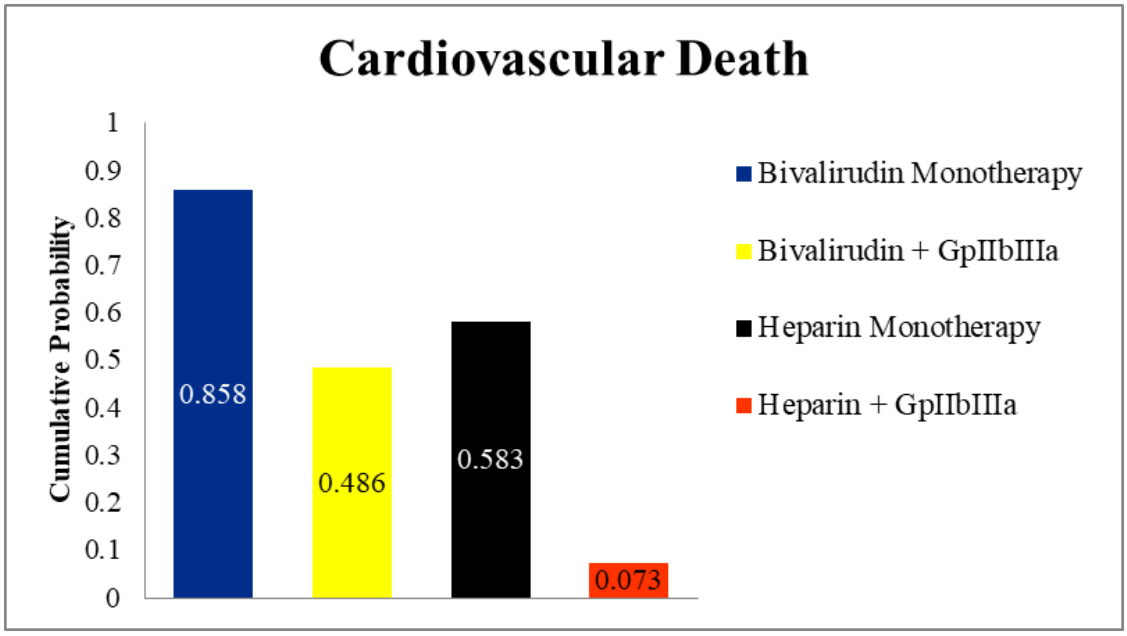
Stent Thrombosis:

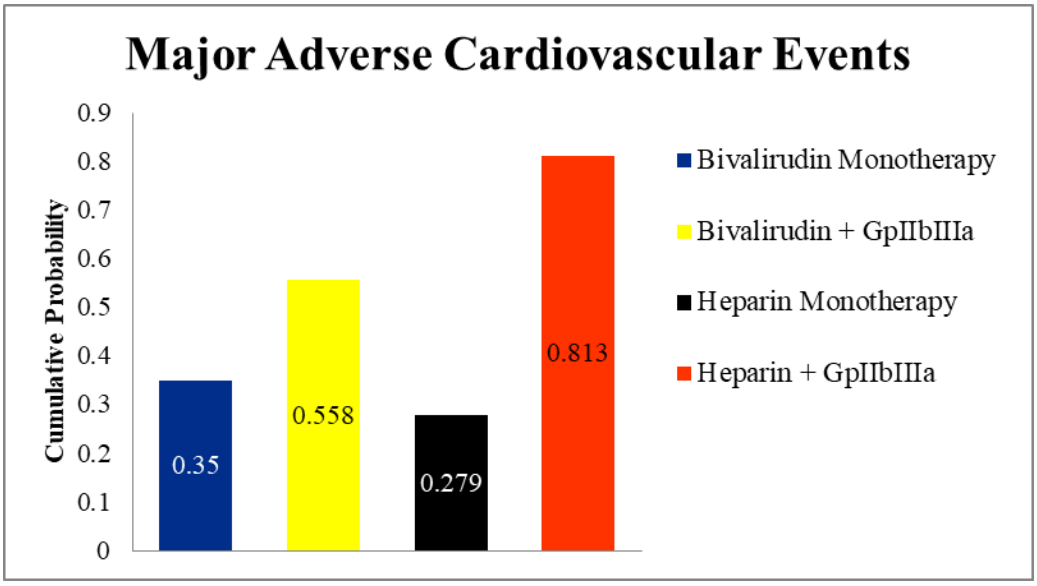

Comparison
Number of Studies
Direct Evidence
I2
Random Effects Model
RR
95%-CI
Bivalirudin + GpIIbIIIa vs Bivalirudin Monotherapy
Direct estimate 0 0
Indirect estimate 3.77 [1.27; 11.21]
Network estimate 3.77 [1.27; 11.21]
Bivalirudin + GpIIbIIIa vs Heparin + GpIIbIIIa
Direct estimate 3 1.00 50% 2.66 [1.24; 5.73]
Indirect estimate
Network estimate 2.66 [1.24; 5.73]
Bivalirudin + GpIIbIIIa vs Heparin Monotherapy
Direct estimate 0 0
Indirect estimate 3.63 [1.00; 13.14]
Network estimate 3.63 [1.00; 13.14]
Bivalirudin Monotherapy vs Heparin + GpIIbIIIa
Direct estimate 3 1.00 0% 0.71 [0.33; 1.53]
Indirect estimate
Network estimate 0.71 [0.33; 1.53]
Bivalirudin Monotherapy vs Heparin Monotherapy
Direct estimate 5 1.00 57% 0.96 [0.49; 1.91]
Indirect estimate
Network estimate 0.96 [0.49; 1.91]
Heparin + GpIIbIIIa vs Heparin Monotherapy
Direct estimate 0 0
Indirect estimate 1.36 [0.49; 3.83]
Network estimate 1.36 [0.49; 3.83]
0.1
0.5
1
2
10

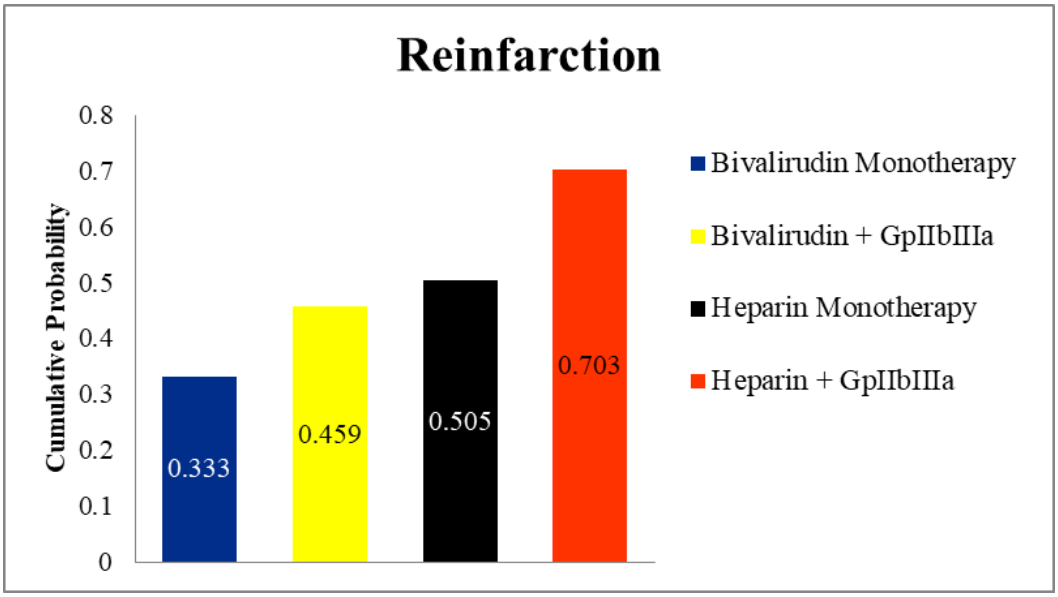
Supplementary file S9. Bar chart of cumulative probability of treatment groups in all assessed outcomes depicted by SUCRA model

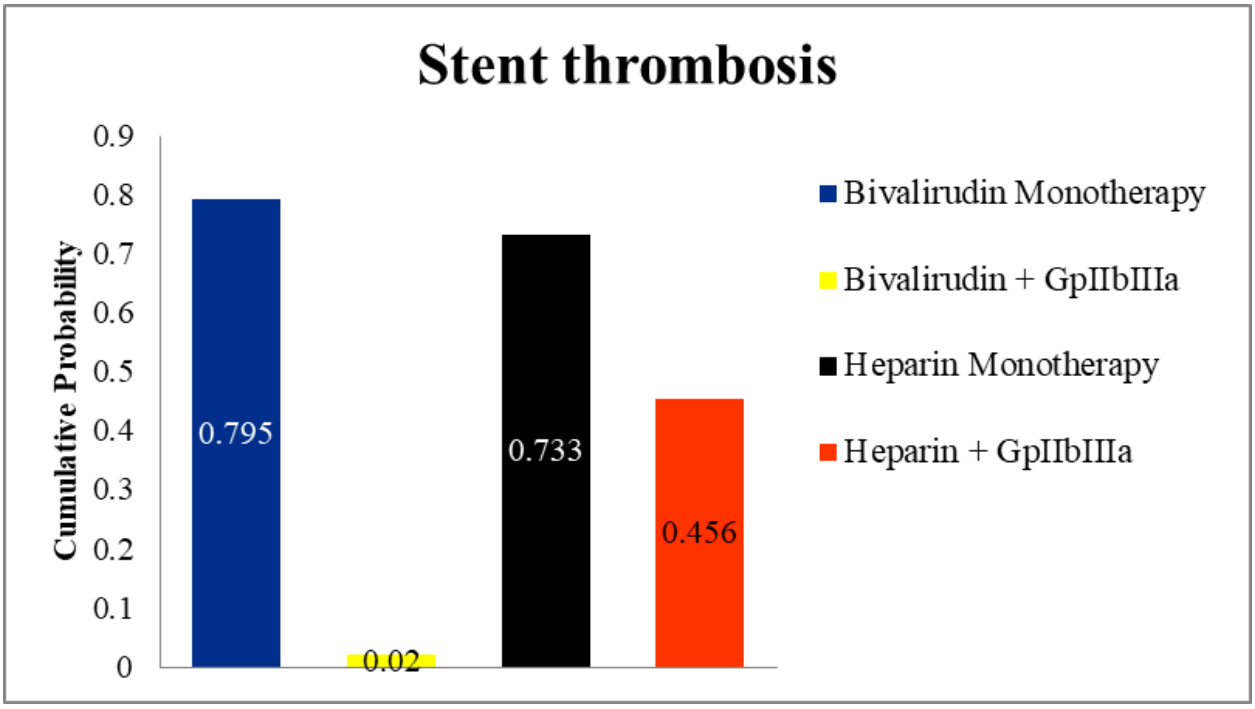





Cardiovascular Death
Cumulative Probability
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0.858
0.486
0.583
0.073
Bivalirudin Monotherapy
Bivalirudin + GpIIbIIIa
Heparin Monotherapy
Heparin + GpIIbIIIa


Major Adverse Cardiovascular Events
Cumulative Probability
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0.35
0.558
0.279
0.813
Bivalirudin Monotherapy
Bivalirudin + GpIIbIIIa
Heparin Monotherapy
Heparin + GpIIbIIIa


Reinfarction
Cumulative Probability
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0.333
0.459
0.505
0.703
Bivalirudin Monotherapy
Bivalirudin + GpIIbIIIa
Heparin Monotherapy
Heparin + GpIIbIIIa


Stent thrombosis
Cumulative Probability
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0.795
0.02
0.733
0.456
Bivalirudin Monotherapy
Bivalirudin + GpIIbIIIa
Heparin Monotherapy
Heparin + GpIIbIIIa

Supplementary file S10. Heterogeneity

Outcome	Higgin's I squared value
All-cause mortality	0%
CV Death	0%
Bleeding	43.6%
Reinfarction	2%
MACE	0%
Stent Thrombosis	40.9%

Supplementary file S11. Patient baseline Characteristics

First Author	Comparator Group	Sample Size	Age	Gender Men	BMI (kg/msq)	Hypertension n(%)	Diabetes (n/%)	Smoking (n/%)	Hyperlipidemia (n/%)	Previous MI (n/%)	Previous PCI (n/%)
Lincoff et al. (2001)	Bivalirudin + Gp IIb/IIIa inhibitor	30	58.6(11.8)	26(87)	-	-	-	-	-	-	-
	Heparin + Gp IIb/IIIa inhibitor	94	62.4(10.4)	73(77)	-	-	-	-	-	-	-
White et al. (2001)	Bivalirudin Monotherapy	8516	61.8	6012(70.60)	26.3	4410(51.8%)	1195(14.0%)	3728(43.8%)	2081(24.6%)	1287(15.1%)	99(1.2%)
	Heparin Monotherapy	8557	61.8	6218(72.7)	26.4	4416(51.6%)	1200(14.0%)	3780(44.2%)	2161(25.4%)	1299(15.2%)	106(1.2%)
Antman et al. (2002)	Heparin Monotherapy	65	68	45(69)	-	40(62)	22(34)	39(60)	24(37)	27(42)	-
	Bivalirudin Monotherapy	68	66	39(58)	-	45(67)	16(24)	36(54)	30(45)	26(39)	-
Lincoff et al. (2003)	Bivalirudin Monotherapy	2994	62.6(10.8)	2236(74.7)	-	1965(66)	840(28.1)	796(27.2)	-	248(8.4)	1029(34.5)
	Heparin + Gp IIb/IIIa inhibitor	3008	62.6(11.0)	2229(74.1)	-	2040(68)	784(26.1)	762(26)	-	248(8.4)	1059(35.3)
Waksman et al. (2005)	Bivalirudin Monotherapy	51	63.3(12.2)	37(72.5%)	27.3(4.2)	35(68.6%)	7(12.72)	41(80.4%)	33(64.7%)	-	7(13.7%)
	Heparin Monotherapy	49	62.3(13.4)	31(63.3%)	29.4(4.7)	37(75.5%)	10(20.41)	35(71.4%)	31(63.3%)	-	12(24.5%)
Chu et al. (2006)	Bivalirudin Monotherapy	216	66.4(12.5)	127(58.8%)	-	170(78.7%)	77(35.6%)	58(26.9%)	164(75.9%)	111(51.4%)	(review)
	Heparin Monotherapy	456	64.5(13.3)	286(62.7%)	-	333(73.0%)	155(34.0%)	129(28.3%)	366(80.3%)	220(48.2%)	(review)
Stone et al. (2006)	UFH + Gp IIb/IIIa inhibitor	4603	63	3249(70.6)	-	3058/4577 (66.8)	1298/4564 (28.4)	1308/4508 (29.0)	2580/4511 (57.2)	1419/4493 (31.6)	1780/4567 (39.0)
	Bivalirudin + Gp IIb/IIIa inhibitor	4604	63	3218(69.9)	-	3074/4577 (67.2)	1267/4568 (27.7)	1323/4522 (29.3)	2588/4508 (57.4)	1372/4491 (30.5)	1720/4554 (37.8)

	Bivalirudin Monotherapy	4612	63	3195(69.3)	-	3080/4593 (67.1)	1287/4577 (28.1)	1312/4527 (29.0)	2579/4521 (57.0)	1431/4499 (31.8)	1820/4562 (39.9)
Geuns et al. (2007)	Bivalirudin Monotherapy	28	62.9(10.6)	22(79)	-	9(32)	0	-	7(25)	0	(review)
	Heparin Monotherapy	36	62.8(12.8)	30(83)	-	15(42)	4(11)	-	13(36)	4(11)	(review)
Kastrati et al. (2008)	Bivalirudin Monotherapy	2289	66.9(10.0)	1744(76.2)	27.5(4.0)	2034(88.9)	618(27.0)	328(14.3)	1850(80.8)	734(32.1)	-
	Heparin Monotherapy	2281	67.0(10.0)	1751(76.8)	27.7(4.1)	2044(89.6)	636(27.9)	337(14.8)	1795(78.7)	689(30.2)	-
Stone et al. (2008)	Heparin + Gp IIb/IIIa inhibitor	1802	60.7	1372(76.1)	-	993/1800(55.2)	312/1800(17.3)	807/1792(45.0)	769/1800 (42.7)	205/1800(11.4)	198/1800(11.0)
	Bivalirudin Monotherapy	1800	59.8	1388(77.1)	-	931/1799(51.8)	281/1799(15.6)	845/1789(47.2)	781/1798 (43.4)	187/1799(10.4)	188/1799(10.5)
Tavano et al. (2009)	Heparin + Gp IIb/IIIa inhibitor	168	65.6(8.3)	108(64.3)	28.7(4.6)	131(78.0 %)	168(100)	35(20.8 %)	109(64.9 %)	75(44.6 %)	41(24.4 %)
	Bivalirudin Monotherapy	167	65.0(9.8)	110(65.9)	28.7(4.1)	125(74.9 %)	167(100)	34(20.4 %)	105(62.9 %)	75(44.9 %)	46(27.5 %)
Kastrati et al. (2011)	Heparin + Gp IIb/IIIa inhibitor	861	67.5(11.2)	661(76.8)	-	745(86.5)	257(29.8)	215(25.0)	600(69.7)	188 (21.8)	292 (33.9)
	Bivalirudin Monotherapy	860	67.5(10.8)	661(76.9)	-	727(84.5)	243(28.3)	195(22.7)	580(67.4)	163 (19.0)	267 (31.0)
Deshpande et al. (2012)	Heparin + Gp IIb/IIIa inhibitor	52	56.577 (10.044)	44(84.6)	24.14(2.62)	39(75)	22(42.3)	11(21.2)	3(5.8)	18 (34.6)	-
	Bivalirudin + Gp IIb/IIIa inhibitor	49	55.26(10.412)	44(89.8)	23.78(2.86)	38(77.6)	18(36.7)	8(16.3)	9(18.4)	12 (24.5)	-
Xiang et al. (2013)	Bivalirudin Monotherapy	109	57	92 (84.4)	-	-	-	-	-	(review)	(review)
	Heparin Monotherapy	108	59	89 (82.4)	-	-	-	-	-	(review)	(review)
BRAVE-4 trial (2014)	Bivalirudin + Gp IIb/IIIa inhibitor	271	61.4	205(76)	26.6	178 (66)	45 (17)	155 (57)	154 (57)	21 (8)	-
	Heparin + Gp IIb/IIIa	277	61.4	219(79)	26.3	177 (64)	41 (15)	186 (67)	142 (51)	30 (11)	-

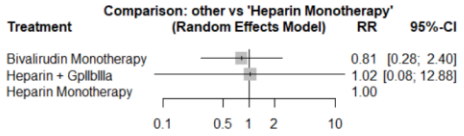
	inhibitor										
Feldman et al. (2014)	Heparin Monotherapy	50	64.9(13.4)	30 (60)	-	49 (98)	45 (90)	-	-	17 (34)	-
	Bivalirudin Monotherapy	50	68.3(10.9)	39 (78)	-	49 (98)	42 (84)	-	-	20 (40)	-
Shahzad et al. (2014)	Bivalirudin	905	62.9	647 (71)	-	362/902 (40)	114/902 (13)	371/888 (42)	327/893 (37)	122/903 (14)	76/903 (8)
	Heparin	907	63.6	663 (73)	-	388/903 (43)	136/899 (15)	379/888 (43)	342/899 (38)	93/906 (10)	54/904 (6)
Han et al. (2015)	Bivalirudin Monotherapy	735	57.3(11.6)	608(82.7)	25.6(3.5)	301(41)	168(22.9)	463(63)	266(36.5)	32(4.4)	37(5.0)
	Heparin Monotherapy	729	58.1 (11.7)	595 (81.6)	25.3 (3.5)	312 (42.8)	137 (18.8)	429 (58.8)	275 (38.0)	33 (4.5)	35 (4.8)
	Heparin + Gp IIb/IIIa inhibitor	730	58.2 (11.8)	599 (82.1)	25.2 (3.6)	311 (42.6)	160 (21.9)	449 (61.5)	267 (36.8)	33 (4.5)	37 (5.1)
Valgimigli et al. (2015)	Bivalirudin Monotherapy	3610	65.4(11.9)	2731 (75.7)	27.2(4.2)	2264 (62.7)	815 (22.6)	1307 (36.2)	1596 (44.2)	530 (14.7)	536 (14.8)
	Heparin Monotherapy	3603	65.4(11.9)	2764 (76.7)	27.0(4.1)	2222 (61.7)	786 (21.8)	1302 (36.1)	1558 (43.2)	500 (13.9)	504 (14.0)
Erlinge et al. (2017)	Bivalirudin Monotherapy	3004	68	2229 (74.2)	26.8	1557 (51.8)	491 (16.3)	716 (23.8)	953 (31.7)	490 (16.3)	456 (15.2)
	Heparin Monotherapy	3002	68	2177 (72.5)	26.9	1548 (51.6)	508 (16.9)	710 (23.7)	936 (31.2)	484 (16.1)	426 (14.2)
Wang et al. (2018)	Bivalirudin Monotherapy	68	69.4 (9.4)	36 (53.7)	23.8(3.5)	54 (79.4)	19 (27.9)	38 (55.9)	-	31 (45.6)	-
	Heparin Monotherapy	55	70.2 (8.9)	30 (54.5)	24.2(2.9)	49 (89.1)	18 (32.7)	40 (72.7)	-	28 (50.1)	-
Faour et al. (2021)	Bivalirudin Monotherapy	42	64	30 (71)	28	26 (62)	14 (33)	16 (38)	19 (45)	0	1 (2.4)
	Heparin Monotherapy	41	62	34 (83)	29	24 (59)	7 (17)	18 (44)	12 (29)	5 (12)	7 (17)
Li et al. (2022)	Heparin	3007	60.6 (12.2)	2372 (78.9)	25.0 (3.8)	1518 (50.5)	698 (23.2)	1392 (46.3)	-	197 (6.6)	186 (6.2)
	Bivalirudin	3009	60.5 (12.1)	2350 (78.1)	24.8 (3.6)	1564 (52.0)	667 (22.2)	1360 (45.2)	-	188 (6.2)	186 (6.2)
		72628									

Supplementary file S12. Subgroup Analysis

Table showing risk ratio of outcomes with their 95% Confidence Intervals and p-values

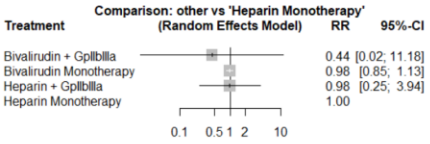
		Major Bleeding		Stent thrombosis		Major Adverse Cardiovascular Events		All-cause mortality		Reinfarction		Cardiovascular Death	
STEMI + NSTEMI	Bivalirudin Monotherapy	0.71 [0.45; 1.12]	p=0.14	0.81 [0.28; 2.40]	p=0.71	0.99 [0.89; 1.10]	p=0.87	0.95 [0.68; 1.32]	p=0.75	0.98 [0.85; 1.13]	p=0.76	0.87 [0.62; 1.21]	p=0.41
	Bivalirudin + GP IIb/IIIa inhibitors	2.77 [0.07;104.4]	p=0.58	NA	NA	0.44 [0.02; 8.75]	p=0.59	NA	NA	0.44 [0.02; 11.18]	p=0.62	NA	NA
	Heparin + GP IIb/IIIa inhibitors	2.68 [0.51; 13.99]	p=024	-1.02 [0.08; 12.88]	p=0.98	1.00 [0.57; 1.75]	p=0.99	1.19[0.41; 3.46]	p=075	0.98 [0.25; 3.94]	p=0.98	1.09 [0.38; 3.12]	p=0.87
STEMI	Bivalirudin Monotherapy	1.63 [0.53; 5.03]	p=0.4	2.93 [0.10; 81.00]	p=0.52	1.18 [0.59; 2.39]	p=0.64	0.99 [0.90; 1.08]	p=0.84	1.95 [0.12; 32.85]	p=0.64	NA	NA
	Bivalirudin + GP IIb/IIIa inhibitors	1.58 [0.26; 9.55]	p=0.62	12.29 [0.34; 446.27]	p=0.17	1.25 [0.38; 4.12]	p=0.70	1.30 [0.81; 2.09]	p=0.28	2.42 [0.08; 73.83]	p=0.61	NA	NA
	Heparin + GP IIb/IIIa inhibitors	2.71 [0.54; 13.71]	p=0.22	4.66 [0.14; 154.72]	p=0.39	1.20 [0.41; 3.49]	p=0.74	1.50 [0.99; 2.28]	p=0.06	1.89 [0.07; 48.99]	p=0.70	NA	NA
UA NSTEMI	Bivalirudin Monotherapy	3.00 [0.12; 73.86]	p=0.50	NA	NA	0.90 [0.54; 1.49]	p=0.68	0.40 [0.08; 1.97]	p=0.26	1.29 [0.52; 3.18]	p=0.59	NA	NA
	Bivalirudin + GP IIb/IIIa inhibitors	4.63 [0.18; 120.81]	p=0.36	NA	NA	0.90 [0.52; 1.55]	p=0.70	0.38 [0.07; 2.06]	p=0.26	1.27 [0.49; 3.26]	p=0.62	NA	NA
	Heparin + GP IIb/IIIa inhibitors	4.99 [0.20; 126.09]	p=0.33	NA	NA	0.84 [0.50; 1.41]	p=0.51	0.34 [0.07; 1.73]	p=0.19	1.25 [0.50; 3.14]	p=0.64	NA	NA

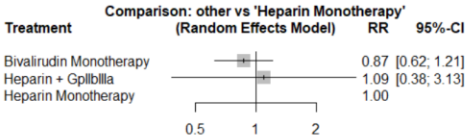
STEMI + NSTEMI:



Stent Thrombosis

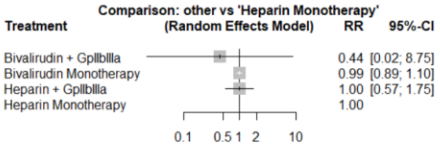
Reinfarction

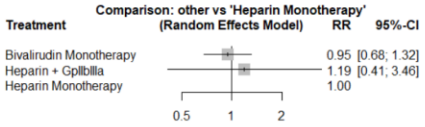




Cardiovascular Death

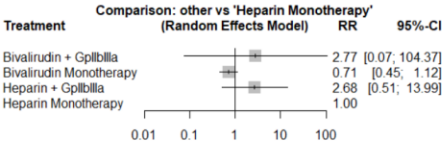
Major Adverse Cardiac Effects





All Cause Mortality

Bleeding



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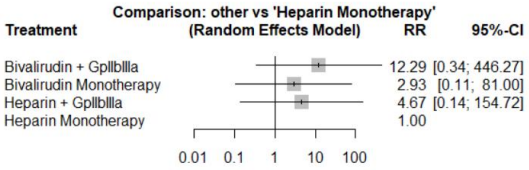
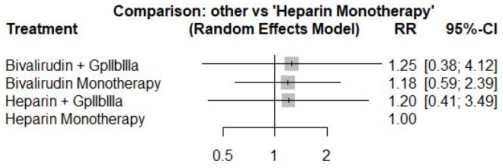
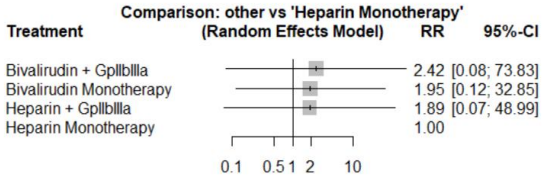


Stent Thrombosis

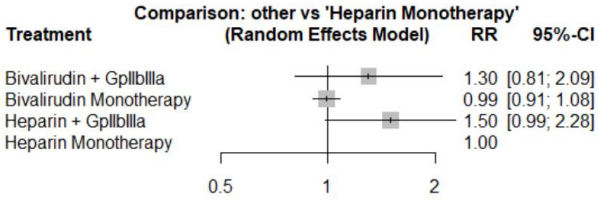
Major Adverse Cardiac Effects

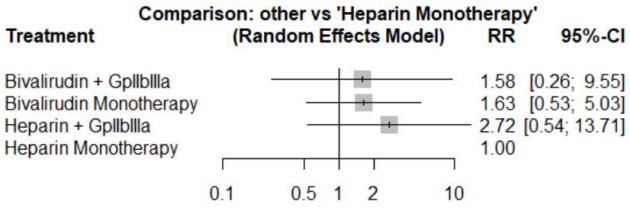




Reinfarction

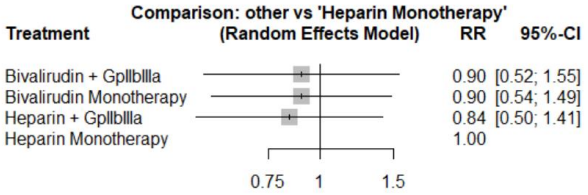
All Cause Mortality





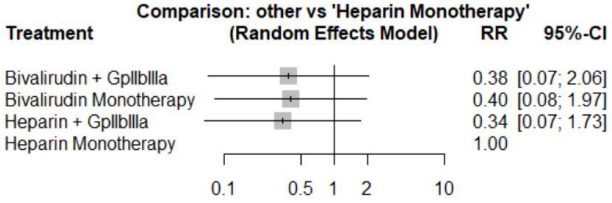
Bleeding

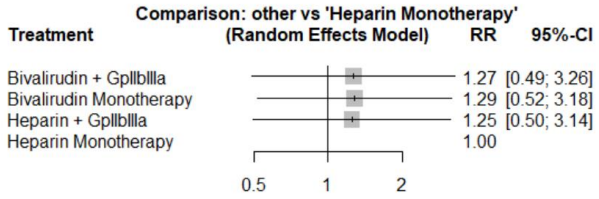
UA + NSTEMI:



Major Adverse Cardiac Effects

Reinfarction





All Cause Mortality

Bleeding