

SUPPLEMENTAL MATERIAL

Literature search string

Supplemental material – Figure I. PRISMA flow-chart.

Supplemental material – Table I. Excluded studies.

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Supplemental material – Table III. Meta-regression analysis for time of rescue and reperfusion depending on stroke network model.

Supplemental material – Figure II. Funnel plots for studies reporting incidence rate ratio (IRR) of stroke admissions (top), intravenous thrombolysis rate ratio (center) and endovascular treatment rate ratio (bottom) in the two timeframes.

Supplemental material – Figure III. Combinatorial meta-analysis showing homogeneous distribution and no cluster segregation for weekly stroke admissions incidence rate ratio (IRR, top), weekly intravenous thrombolysis rate ratio (center), and endovascular thrombectomy (bottom).

Supplemental material – Figure IV. Meta-analysis of intravenous thrombolysis incidence (IVT-IRR, top) and endovascular thrombectomy incidence rate ratio (EVT-IRR, bottom), comparing stroke admissions during COVID-period vs control-period, depending on stroke network model.

Supplemental material – Figure V. Variations in National Institutes of Health Stroke Scale (NIHSS) score between COVID-period and control-period, depending on stroke network model (top). Sensitivity analysis excluding studies with unknown stroke network model (centre), and restricting analysis to studies with prospective design only (bottom).

Supplemental material – Figure VI. Variations in the proportion of people with large vessel occlusion among those presenting with acute ischemic stroke during the timeframes considered (COVID-period vs control-period), depending on stroke network model.

Supplemental material – Figure VII. Sensitivity analysis for proportion of patients undergoing intravenous thrombolysis (IVT) among those admitted with acute ischemic stroke during the timeframes considered (COVID-period vs control-period), removing studies with unknown stroke network model (top), or including only prospective studies (bottom).

Supplemental material – Figure VIII. Sensitivity analysis for proportion of patients undergoing endovascular treatment (EVT) among those admitted with acute ischemic stroke during the timeframes considered (COVID-period vs control-period), removing studies with unknown stroke network model (top), or including only prospective studies (bottom).

Supplemental material – Figure IX. Sensitivity analysis for onset-to-door time across the timeframes considered, removing studies with unknown stroke network model (top), or including only prospective studies (bottom).

Supplemental material – Figure X. Variation in door-to-scan time depending on timeframes considered (COVID-19 period vs control period), with studies grouped for stroke network model used.

Supplemental material – Figure XI. Variation in door-to-needle time in patients receiving intravenous thrombolysis (IVT) for acute ischemic stroke during COVID-19 and control period, depending on stroke network model adopted.

Supplemental material – Figure XII. Variations in onset-to-needle time across the timeframes considered, depending on stroke network model organization.

Supplemental material – Figure XIII. Variations in door-to-groin time across the timeframes considered depending on stroke network model organization.

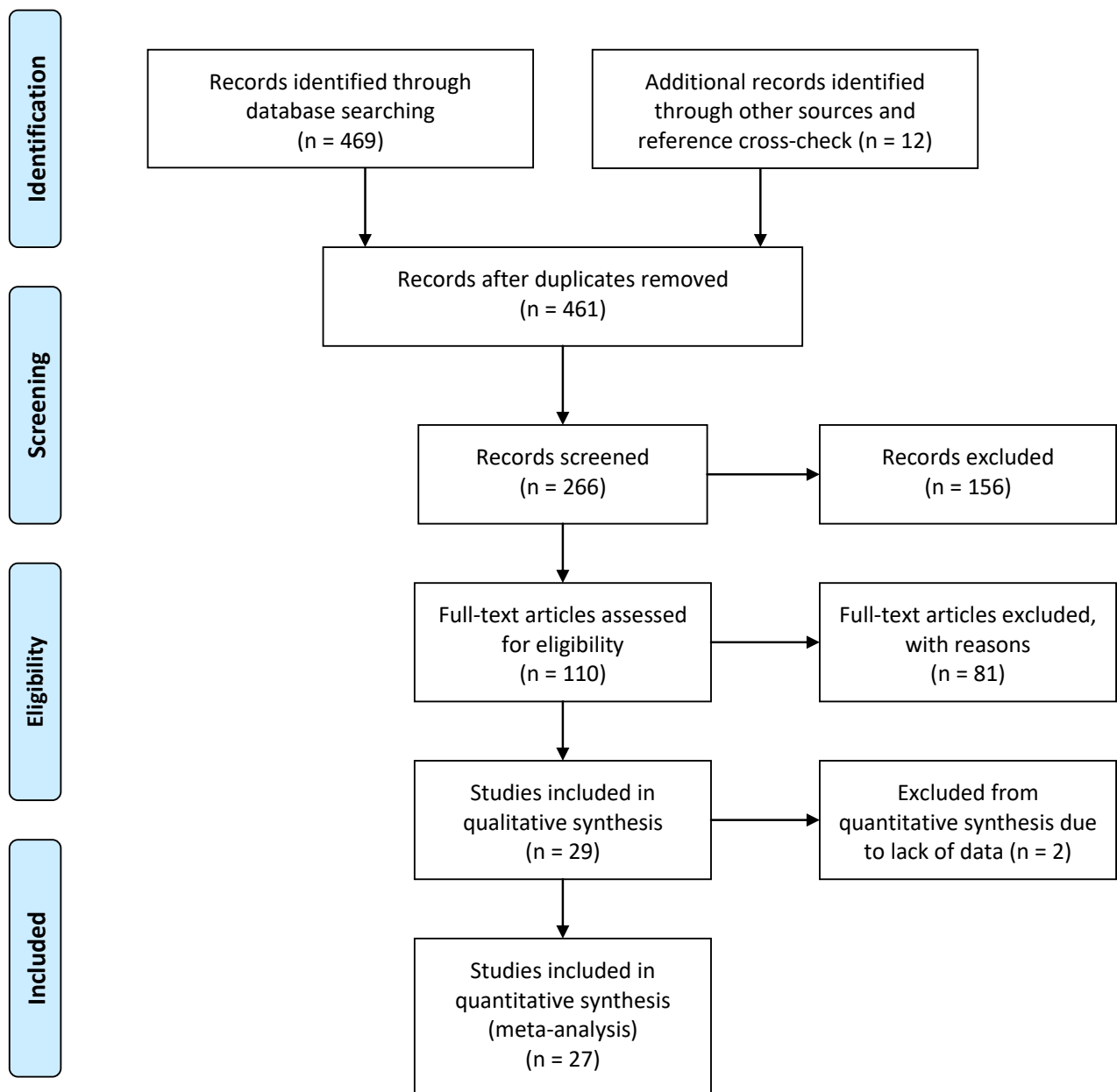
Supplemental material – Figure XIV. Sensitivity analysis for variations in door-to-groin time across the timeframes considered, removing studies with unknown stroke network model (top), or including only prospective studies (bottom).

Supplemental material – Figure XV. Variations in door-to-recanalization time across the timeframes considered depending on stroke network model organization.

Literature search string

("cerebrovascular disease" [All Fields] OR "stroke" [All Fields] OR cerebrovascular accident [All Fields]) AND ("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields] OR "COVID-19"[Supplemental Concept] OR "severe acute respiratory syndrome coronavirus 2"[Supplemental Concept] OR COVID[All Fields] OR "covid-19"[All Fields] OR "covid19"[All Fields] OR "novel coronavirus"[All Fields] OR nCoV[All Fields] OR "SARS-CoV2"[All Fields]); until 8/10/2020, only 2019 or 2020 published papers, English language only.

Supplemental material – Figure I. PRISMA flow-chart.



Supplemental material – Table I. Excluded studies

Author	Year	Reason for exclusion
Aggarwal[1]	2020	No data, association of stroke with/without COVID
Al Kasab[2]	2020	Letter to the editor, no data
Al-Ani[3]	2020	Review on thrombosis risk in COVID
Alqahtani[4]	2020	Description of code stroke protocol, no data
Azarpazhooh[5]	2020	No data on stroke admissions/incidence
Beghi[6]	2020	Review only, no data
Belani[7]	2020	No data, only COVID cohort
Bersano[8]	2020	Recommendation only, no data
Bhaskar[9]	2020	Guidelines, no data
Bress Bullrich[10]	2020	Unclear identification of stroke (ischemic/hemorrhagic)
Cantador[11]	2020	No data, only COVID cohort
Cavallieri[12]	2020	Case report
Chaturvedi[13]	2020	Recommendation only, no data
Cummings[14]	2020	Unclear identification of stroke
Dafer[15]	2020	No data on stroke incidence/treatment
D'Anna[16]	2020	No data, only COVID cohort
de Sousa[17]	2020	Editorial, no data
Derraz[18]	2020	Editorial, no data
Escalard[19]	2020	Case series, EVT in COVID+ patients
Frisullo[20]	2020	No data, letter
Frisullo[21]	2020	No data
Fuentes[22]	2020	Survey, no data
Gao[23]	2020	No data on stroke incidence/treatment
Goldberg[24]	2020	Case report
Goyal[25]	2020	No data
Gulko[26]	2020	Case report
Hajdu[27]	2020	Multiple timepoints, no raw data, EVT only
Hecht[28]	2020	No data on stroke incidence/treatment
Holt[29]	2020	Not pertinent (addressed new-onset atrial fibrillation)
Hoyer[30]	2020	No data (TIA/stroke admissions considered; data not provided)
Immovilli[31]	2020	No data, only COVID cohort
Jillela[32]	2020	No control group, case series
Jin[33]	2020	MERS, not SARS-CoV2
Kansagra[34]	2020	No data on stroke incidence/treatment
Katz[35]	2020	No data, only COVID cohort
Khosravani[36]	2020	Description of protected code stroke, no data
Lange[37]	2020	Unclear identification of stroke (ischemic/hemorrhagic)
Leira[38]	2020	Review, no original data
Leslie-Mazwi[39]	2020	Review, no original data
Li[40]	2020	No data on stroke incidence/treatment
Lima[41]	2020	Case report
Lumley-Holmes[42]	2020	Letter, no data
Majidi[43]	2020	No temporal trend comparison
Maldonad Sloopjes[44]	2020	Case report
Mansoor[45]	2020	case report
Markus[46]	2020	Editorial, no data
Masroor[47]	2020	Case report
Merkler[48]	2020	No data, only COVID cohort
Meyer[49]	2020	No data
Mishra[50]	2020	Letter to the editor, no data
Mohamud[51]	2020	Case series on COVID, no data
Morelli[52]	2020	Control period not defined
Morelli[53]	2020	Reply, no data
Nguyen[54]	2020	Recommendation only, no data
Ntaios[55]	2020	No temporal trend comparison
Ospel[56]	2020	Recommendation only, no data
Pasarikovski[57]	2020	No raw data
Paterson[58]	2020	No raw data
Pedicelli[59]	2020	No raw data
Qureshi [60]	2020	Recommendation only
Qureshi [61]	2020	Not pertinent
Qureshi[62]	2020	No data on stroke incidence/treatment

Reddy[63]	2020	Review only, no data
Rodriguez-Pardo [64]	2020	Recommendation only
Saggese[65]	2020	Case report
Salahuddin[66]	2020	Recommendation only
Sangalli[67]	2020	Case series
Shahjouei[68]	2020	No control group, hospitalized patients only
Sheth[69]	2020	No data
Sierra-Hidalgo[70]	2020	No data, only COVID cohort
Sweid[71]	2020	Case series, COVID cohort
Sylaja[72]	2020	Survey, no data
Tsivgoulis[73]	2020	Editorial
Valdes Valderrama[74]	2020	Case report
Varatharaj[75]	2020	Survey of acute neurological and psychiatric complications of COVID-19
Venketasubramanian[76]	2020	Editorial, no data
Wang[77]	2020	Commentary, no data
Yaeger[78]	2020	No data, only COVID cohort
Yaghi[79]	2020	Stroke patients with COVID vs without COVID vs historical cohort
Zhai[80]	2020	Case report
Zhao[81]	2020	Editorial, no data

Supplemental material – Table II. Bias assessment.

Author	Year	1) Representativeness of the exposed cohort	2) Selection of the non exposed cohort	3) Ascertainment of exposure	4) Demonstration that outcome of interest was not present at start of study	5) comparability of the cohorts included	6) Assessment of outcome	7) Length of follow-up	8) Adequacy of follow up of cohorts	Global score	Risk of bias
Agarwal[82]	2020	1	1	1	1	1	1	1	1	8	low
Baracchini[83]	2020	0	0	1	1	0	0	0	0	2	high
De Havenon[84]	2020	1	1	1	1	1	1	1	1	8	low
Diegoli[85]	2020	1	1	1	1	1	1	1	1	8	low
Esenwa[86]	2020	1	1	0	1	1	1	1	1	7	low
Hsiao[87]	2020	1	1	1	1	1	1	1	1	8	low
Huang[88]	2020	1	1	1	1	2	1	1	1	9	low
Jasne[89]	2020	1	1	1	1	1	1	1	1	8	low
Kerleroux[90]*	2020	1	1	1	1	1	1	0	1	7	low
Mehrpour[91]	2020	0	1	1	1	1	1	1	1	7	low
Montaner[92]	2020	1	1	1	1	0	1	0	0	5	moderate
Naccarato[93]	2020	1	1	1	1	1	1	1	1	8	low
Nguyen-Huynh[94]	2020	1	1	1	1	1	1	1	1	8	low
Onteddu[95]	2020	1	1	0	1	1	1	1	1	7	low
Paliwal[96]	2020	1	1	1	1	2	1	1	1	9	low
Pandey[97]	2020	1	1	1	1	1	1	1	1	8	low
Perry[98]	2020	1	1	0	0	2	0	0	0	4	moderate
Pop[99]	2020	1	1	1	1	1	1	0	1	7	low
Rudilosso[100]	2020	1	1	0	1	1	1	1	1	7	low
Saxhaug Kristoffersen[101]	2020	1	1	1	1	2	1	1	1	9	low
Schirmer[102]	2020	1	1	1	1	0	1	1	1	7	low
Siegler[103]	2020	1	1	1	1	1	1	1	1	8	low
Strasser[104]	2020	1	1	1	1	1	1	1	1	8	low
Tejada Meza[105]	2020	1	1	1	1	1	1	1	1	8	low
Tejada Meza[106]	2020	1	1	1	1	1	1	0	1	7	low
Teo[107]	2020	1	1	1	1	1	0	1	1	7	low
Yang[108]	2020	1	1	1	1	1	1	0	1	7	low
Zhao[109]*	2020	1	1	0	1	1	0	0	0	4	moderate
Zini[110]	2020	1	1	1	1	1	1	1	1	8	low

Supplemental material – Table III. Meta-regression analysis for time of rescue and reperfusion depending on stroke network model.

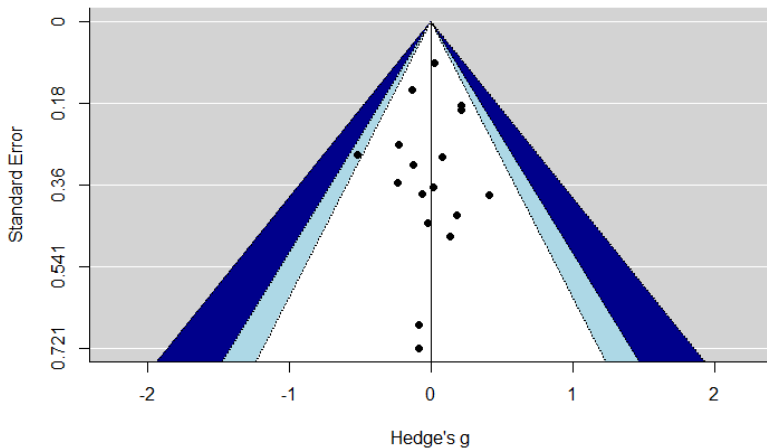
Legend. CI=confidence interval; NA=not available.

Time and model	Estimate (95%CI)(minutes)	p-value
Onset-to-door		
Drip&ship	reference	//
Mothership	-44.3 (-85.3 - -3.2)	0.03
Unknown	-17.8 (-115.3 - +79.6)	0.7
Door-to-groin		
Drip&ship	reference	//
Mothership	-14.4 (-10.5 - +39.23)	0.26
Unknown	10.2 (-23.4 - +43.7)	0.55
Onset-to-needle		
Drip&ship	reference	//
Mothership	-36.0 (-142.9 - +70.4)	0.50
Unknown	NA	NA

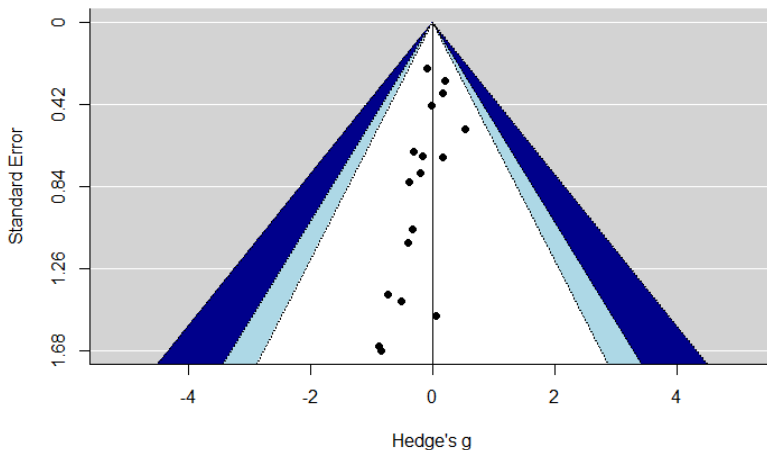
Supplemental material – Figure II. Funnel plots for studies reporting incidence rate ratio (IRR) of stroke admissions (top), intravenous thrombolysis rate ratio (center) and endovascular treatment rate ratio (bottom) in the two timeframes.

Legend. Light blue: $p < 0.05$; Dark blue: $p < 0.01$; Dots: studies.

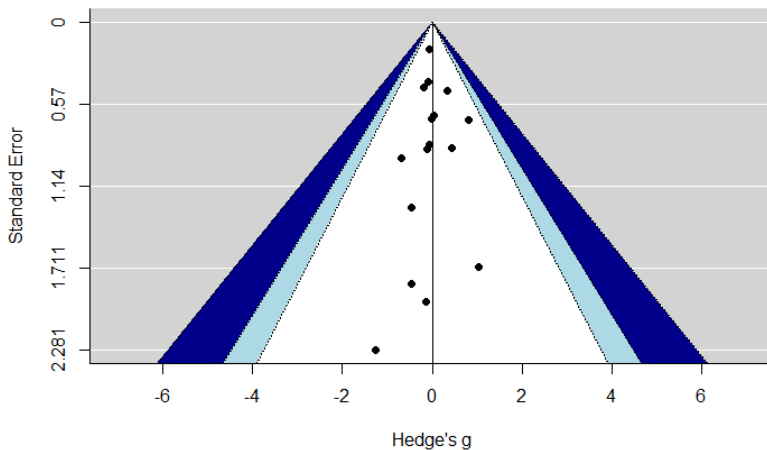
Stroke admissions IRR



Intravenous thrombolysis IRR

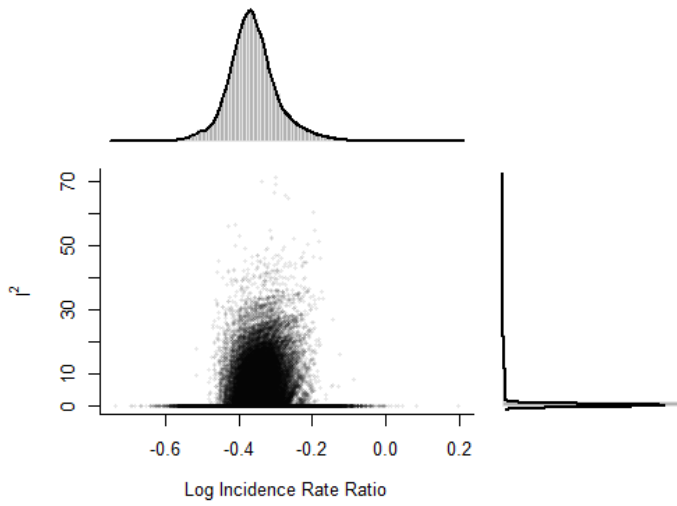


Endovascular thrombectomy IRR

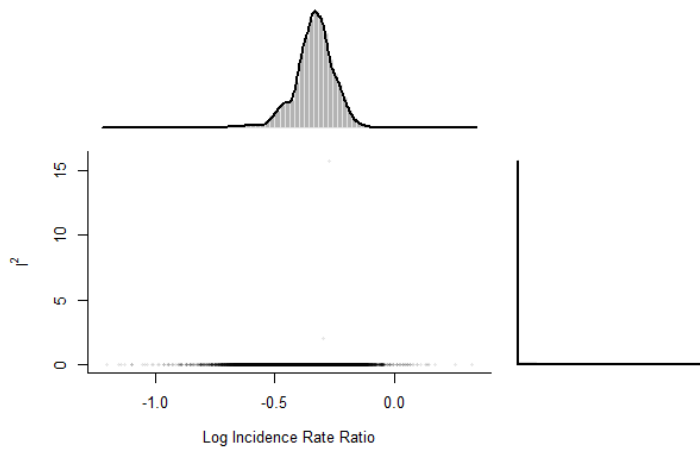


Supplemental material – Figure III. Combinatorial meta-analysis showing homogeneous distribution and no cluster segregation for weekly stroke admissions incidence rate ratio (IRR, top), weekly intravenous thrombolysis rate ratio (center), and endovascular thrombectomy (bottom).

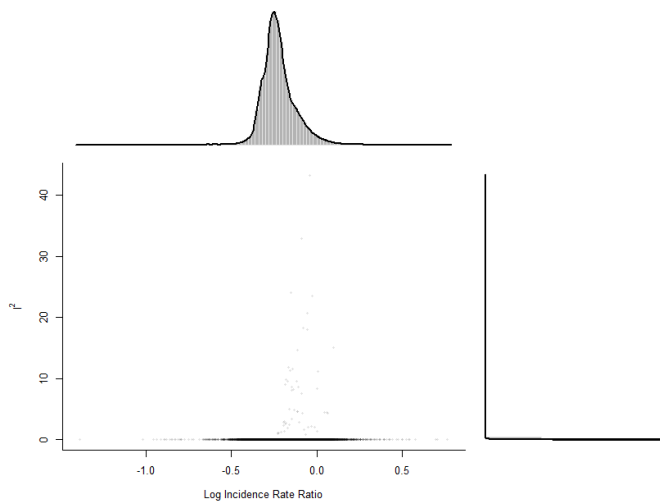
Stroke admissions IRR



Intravenous thrombolysis-IRR



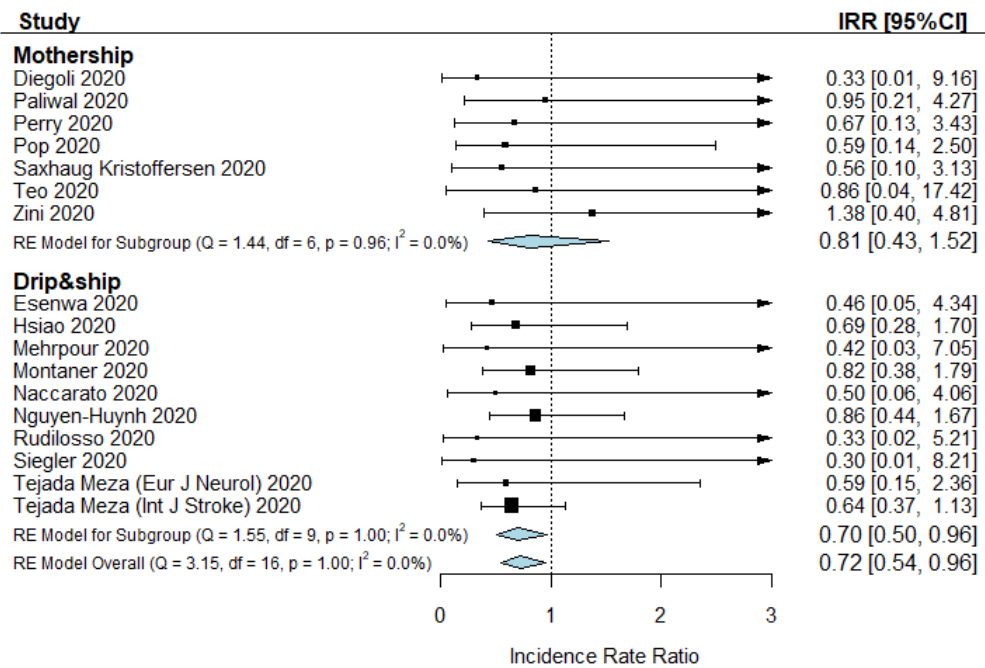
Endovascular thrombectomy-IRR



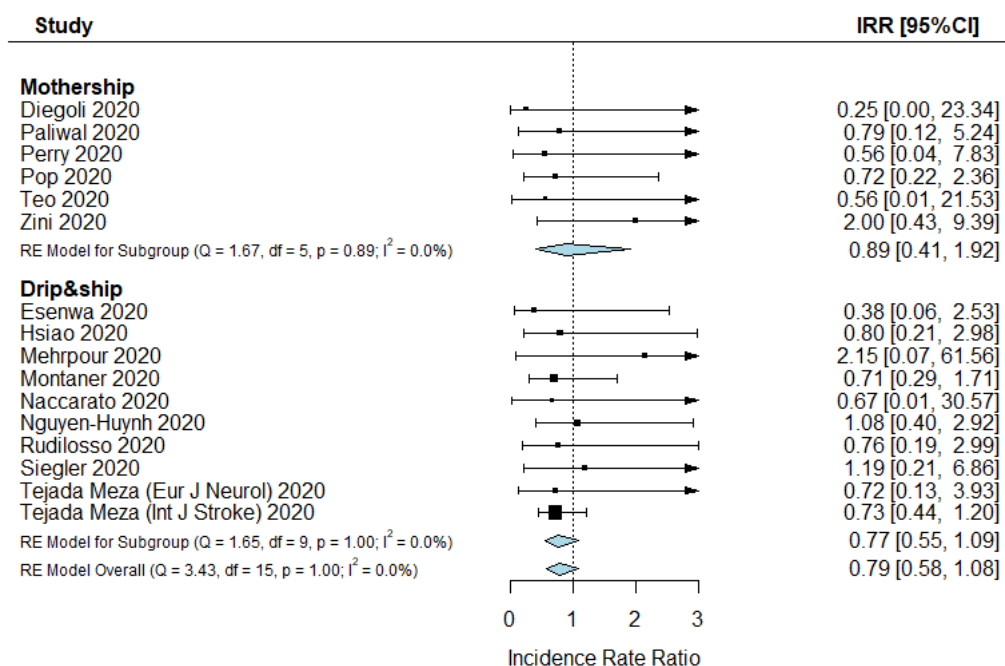
Supplemental material – Figure IV. Meta-analysis of intravenous thrombolysis incidence (IVT-IRR, top) and endovascular thrombectomy incidence rate ratio (EVT-IRR, bottom), comparing stroke admissions during COVID-period vs control-period, depending on stroke network model.

Legend. CI: confidence interval; EVT: endovascular thrombectomy; IRR: incidence rate ratio (equals treatment rate during COVID-19 period/treatment rate during control period); IVT: intravenous thrombolysis; RE: random effect.

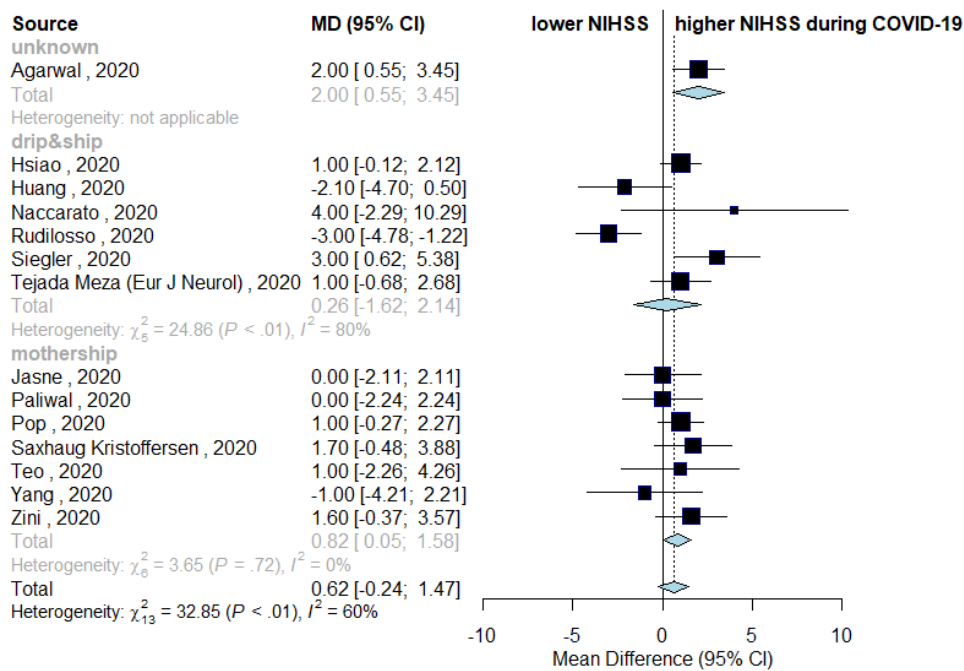
IVT-IRR



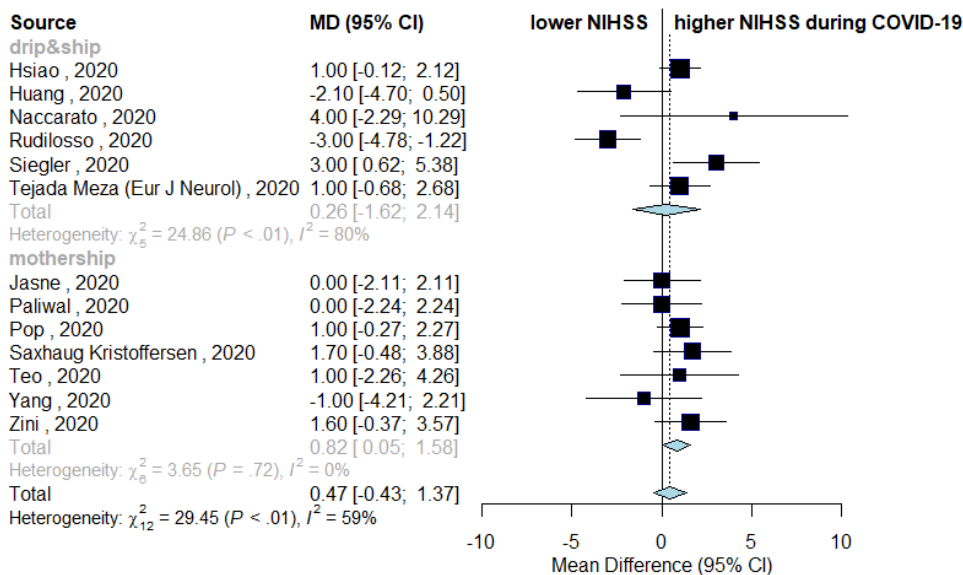
EVT-IRR



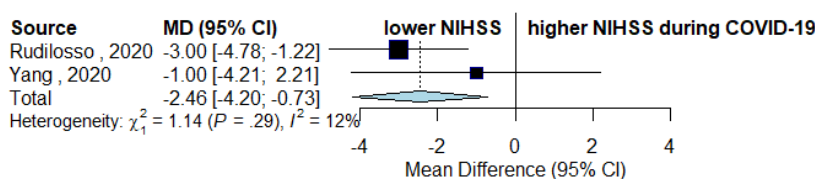
Supplemental material – Figure V. Variations in National Institutes of Health Stroke Scale (NIHSS) score between COVID-period and control-period, depending on stroke network model (top). Sensitivity analysis excluding studies with unknown stroke network model (centre), and restricting analysis to studies with prospective design only (bottom).



Sensitivity analysis excluding studies with unknown stroke network model

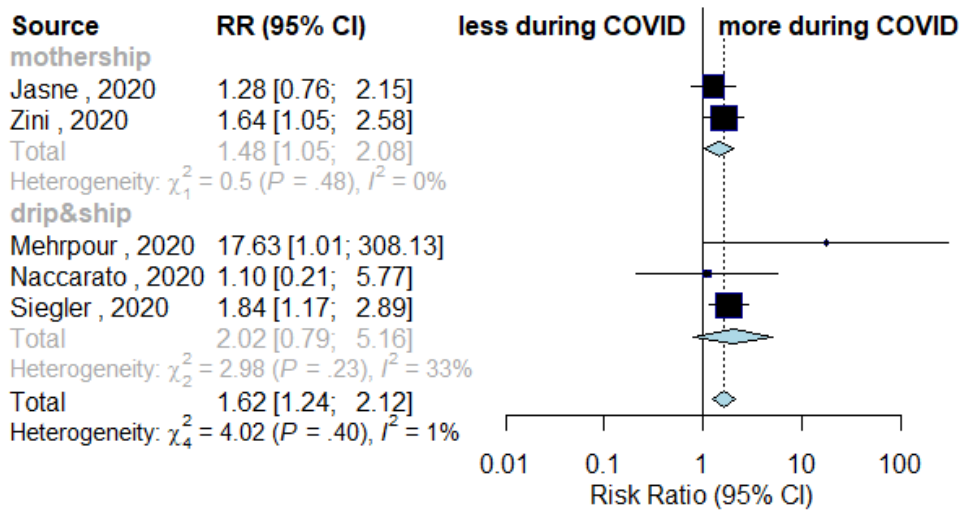


Sensitivity analysis with prospective design-only studies



Supplemental material – Figure VI. Variations in the proportion of people with large vessel occlusion among those presenting with acute ischemic stroke during the timeframes considered (COVID-period vs control-period), depending on stroke network model.

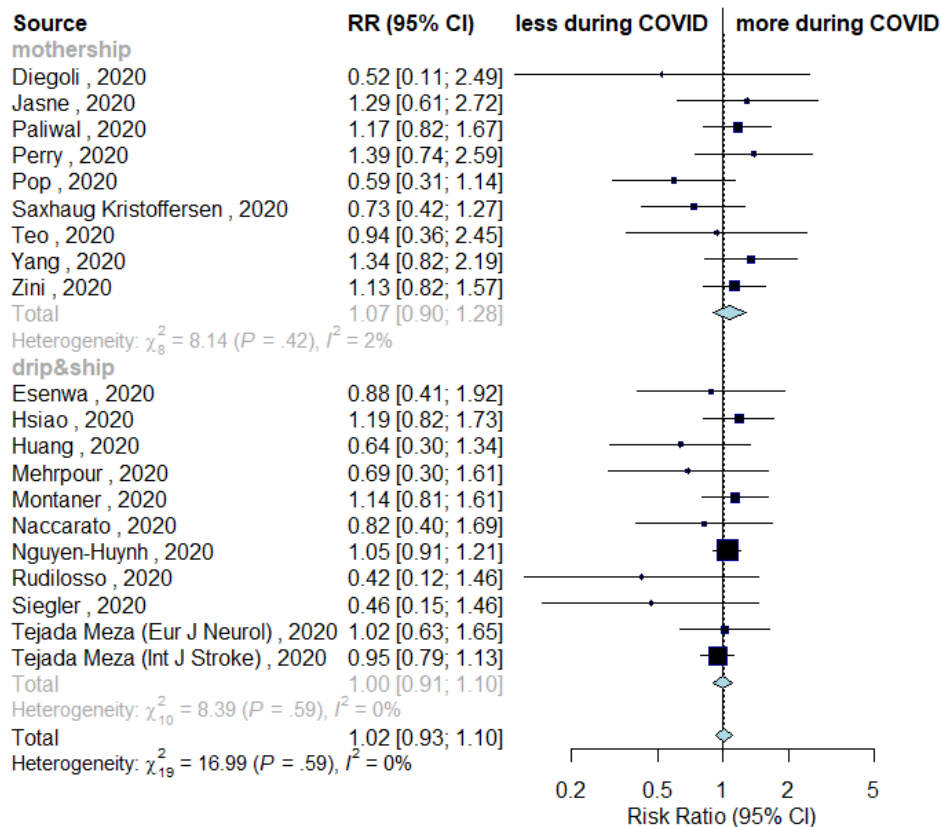
Legend. CI=confidence interval; COVID=period of SARS-CoV-2 pandemic (coronavirus pandemic); RR=relative risk.



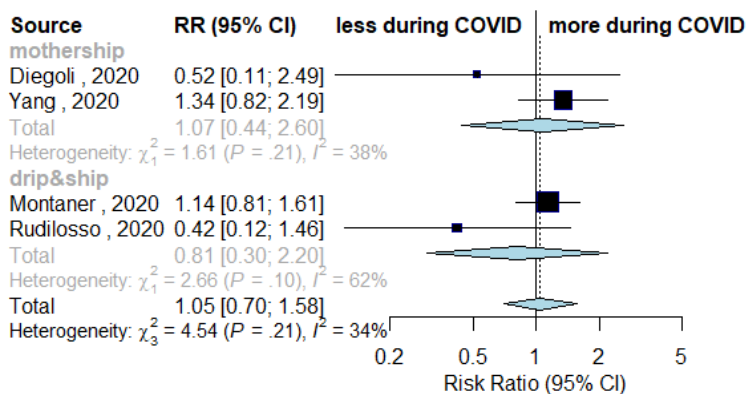
Supplemental material – Figure VII. Sensitivity analysis for proportion of patients undergoing intravenous thrombolysis (IVT) among those admitted with acute ischemic stroke during the timeframes considered (COVID-period vs control-period), removing studies with unknown stroke network model (top), or including only prospective studies (bottom).

Legend. CI=confidence interval; COVID=period of SARS-CoV-2 pandemic (coronavirus pandemic); RR=relative risk.

Sensitivity analysis excluding studies with unknown stroke network model



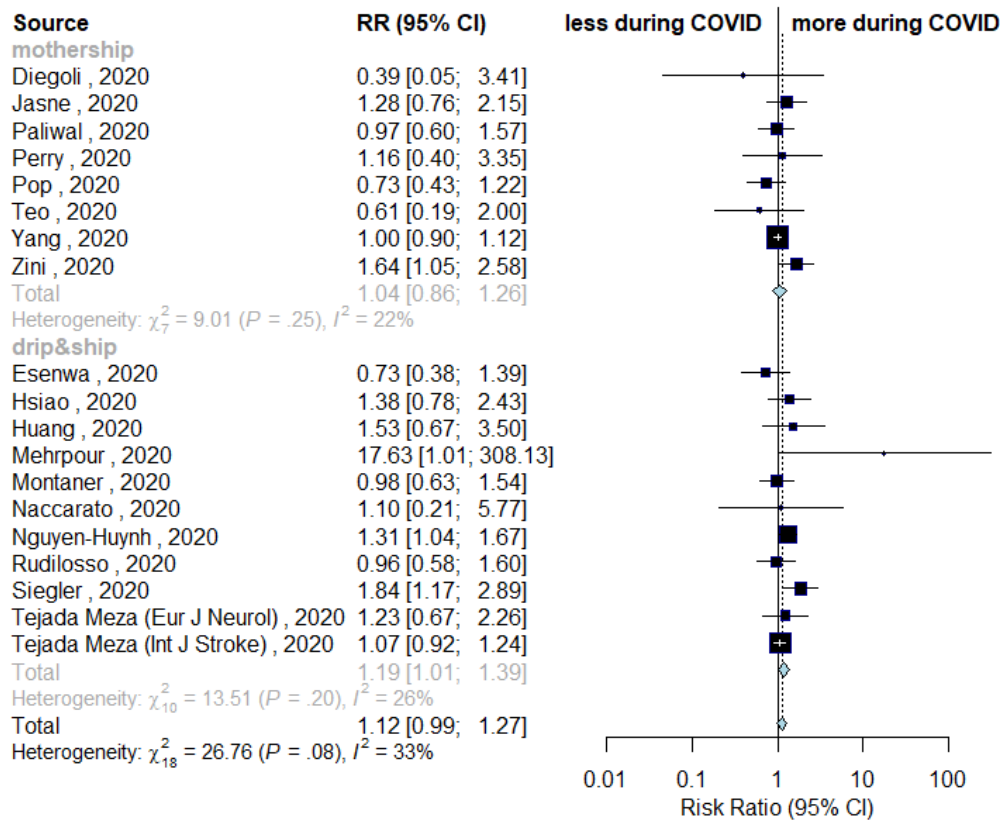
Sensitivity analysis with prospective studies-only



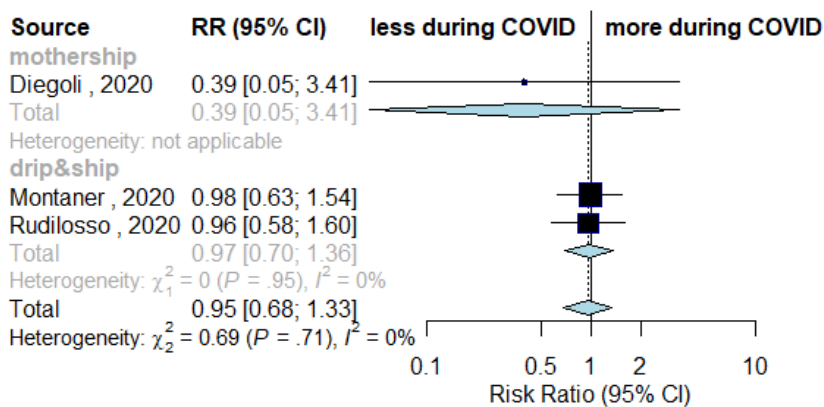
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Sensitivity analysis excluding studies with unknown stroke network model



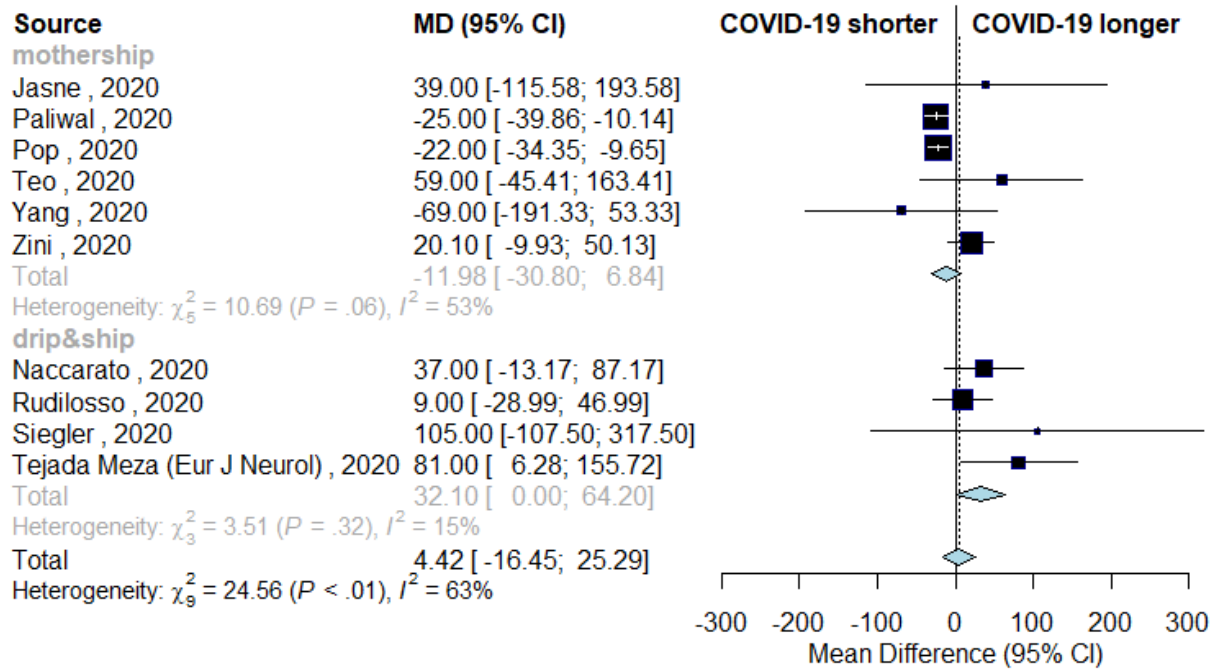
Sensitivity analysis with prospective studies-only



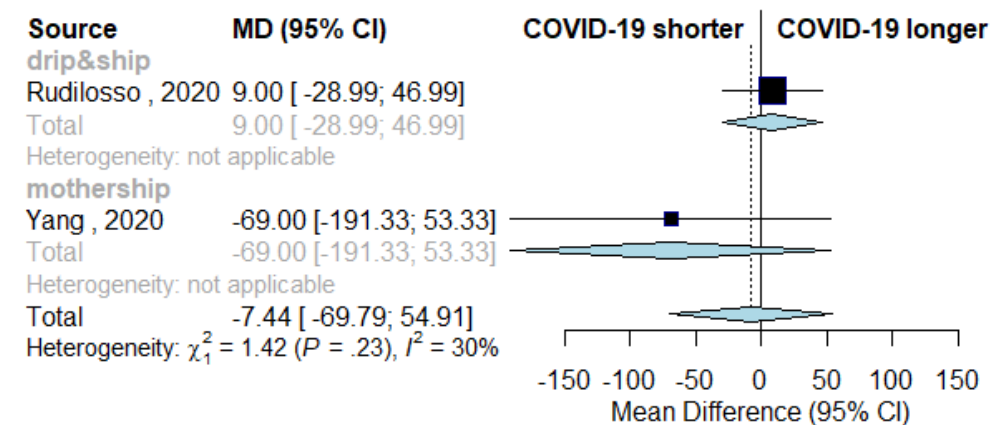
Supplemental material – Figure IX. Sensitivity analysis for onset-to-door time across the timeframes considered, removing studies with unknown stroke network model (top), or including only prospective studies (bottom).

Legend. CI=confidence interval; COVID-19=period of SARS-CoV-2 pandemic (coronavirus pandemic); MD=mean difference.

Sensitivity analysis excluding studies with unknown stroke network model

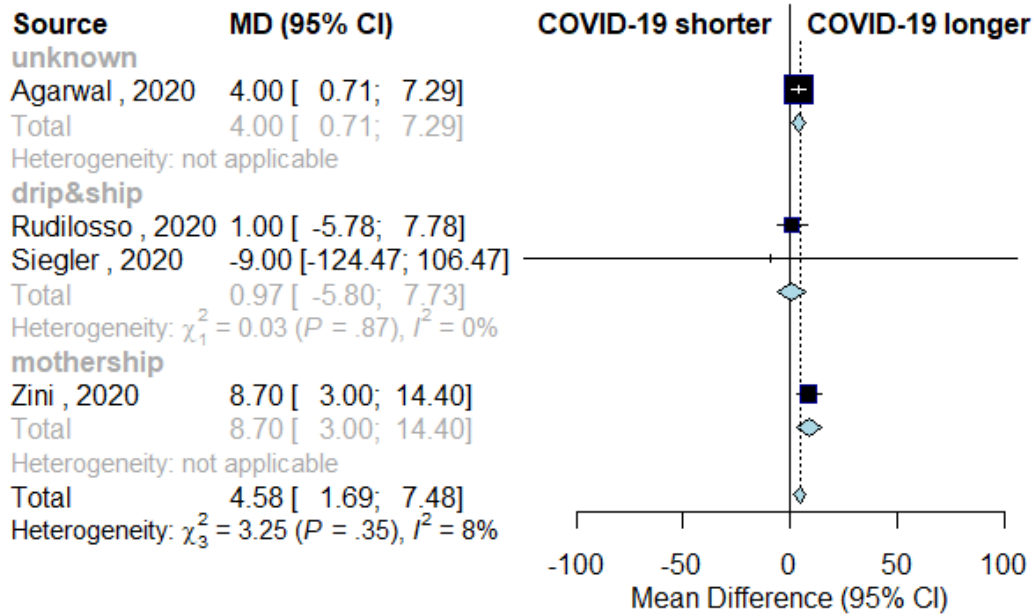


Sensitivity analysis with prospective studies-only



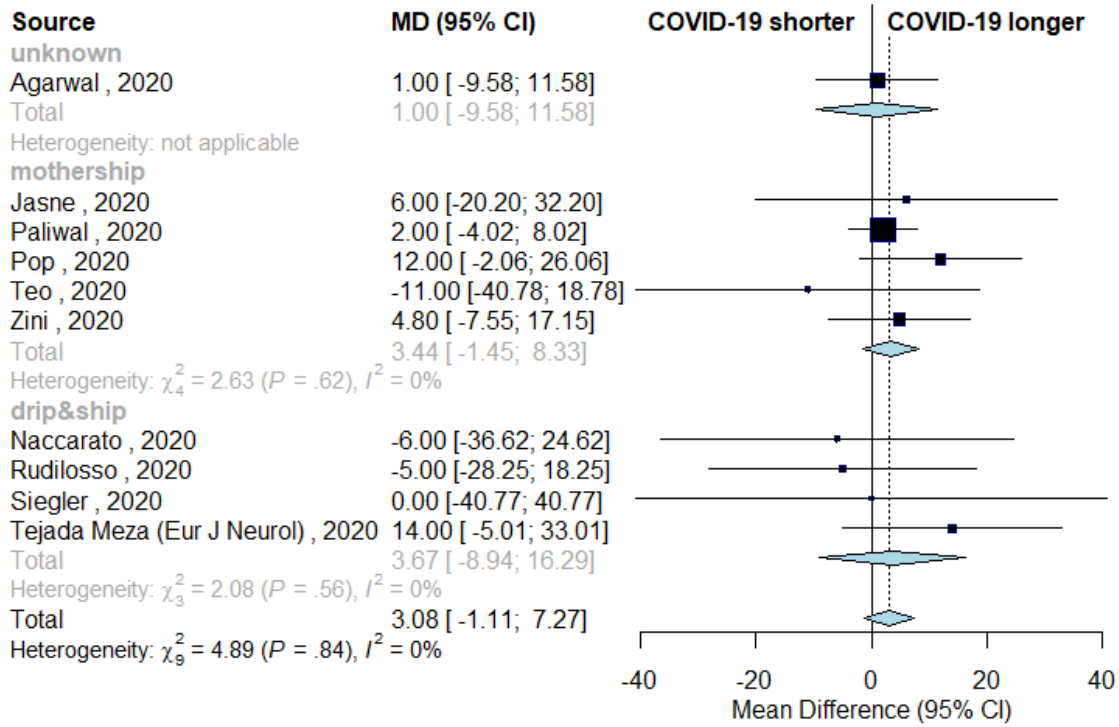
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Legend. CI=confidence interval; COVID-19=period of SARS-CoV-2 pandemic (coronavirus pandemic); MD=mean difference.



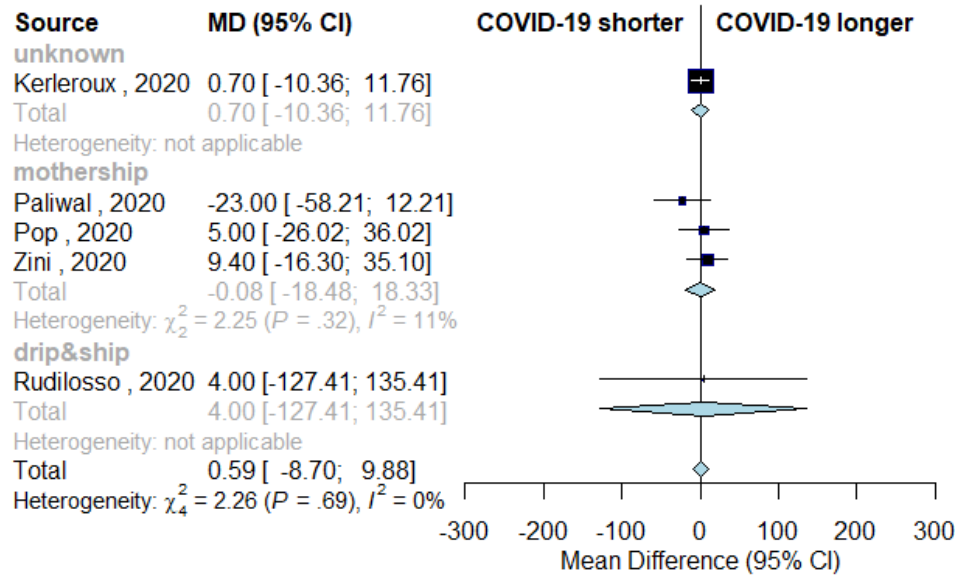
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Legend. CI=confidence interval; COVID-19=period of SARS-CoV-2 pandemic (coronavirus pandemic); MD=mean difference.



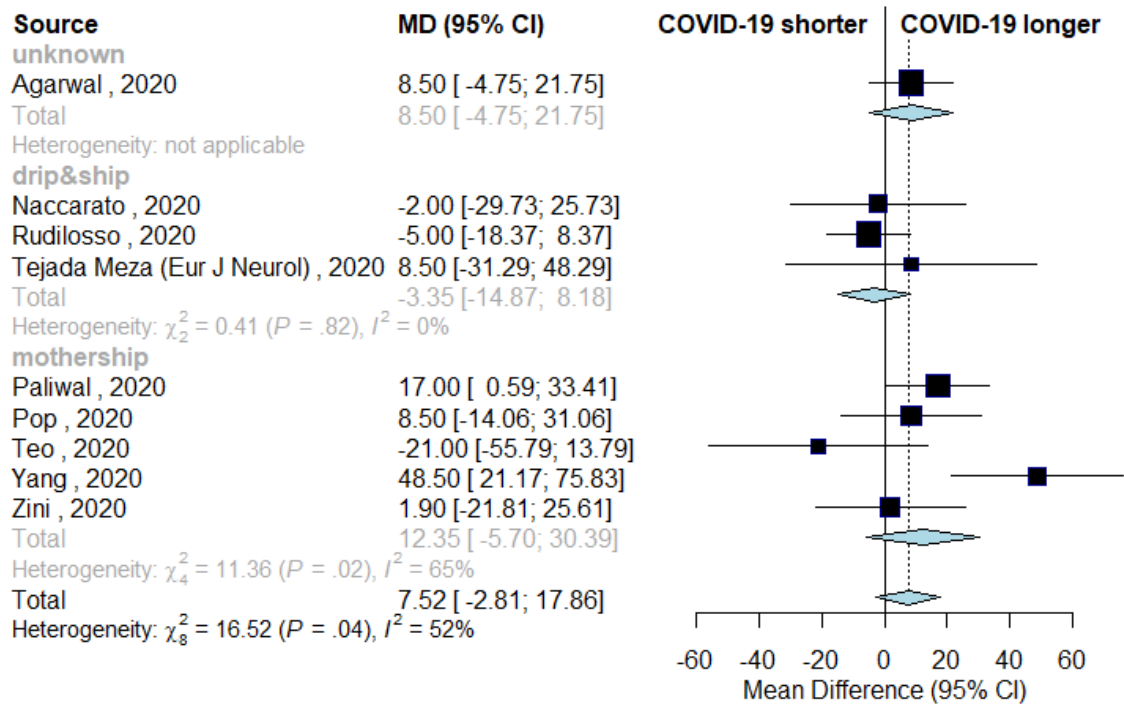
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Legend. CI=confidence interval; COVID-19=period of SARS-CoV-2 pandemic (coronavirus pandemic); MD=mean difference.



Supplemental material – Figure XIII. Variations in door-to-groin time across the timeframes considered depending on stroke network model organization.

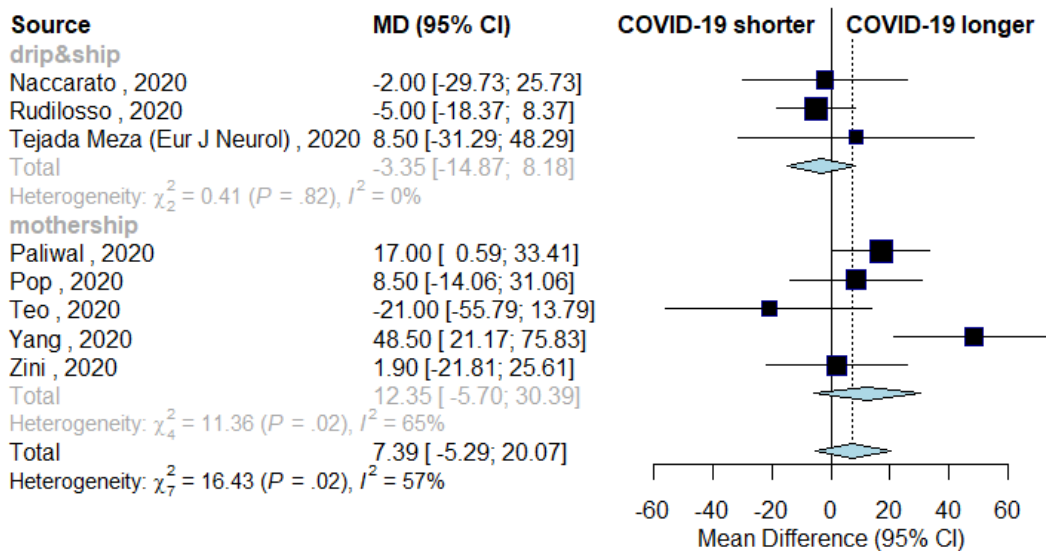
Legend. CI=confidence interval; COVID-19=period of SARS-CoV-2 pandemic (coronavirus pandemic); MD=mean difference.



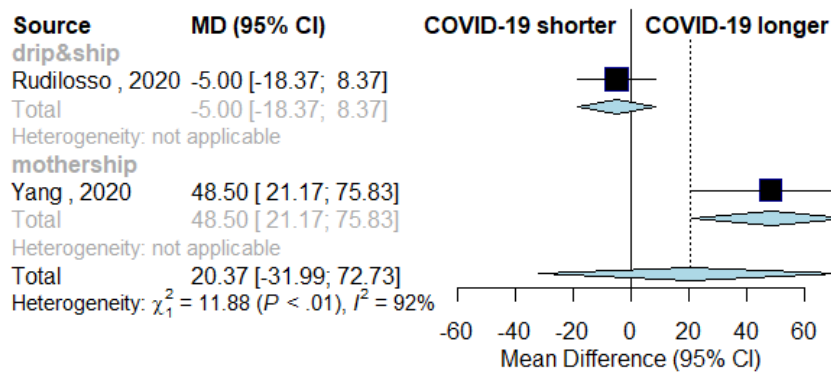
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Legend. CI=confidence interval; COVID-19=period of SARS-CoV-2 pandemic (coronavirus pandemic); MD=mean difference

Sensitivity analysis excluding studies with unknown network organization

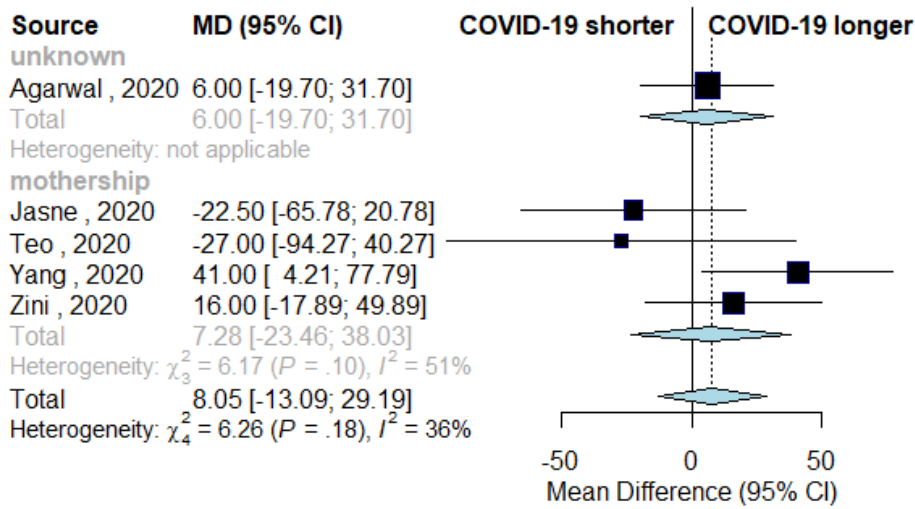


Sensitivity analysis with prospective studies-only



Supplemental material – Figure XV. Variations in door-to-recanalization time across the timeframes considered depending on stroke network model organization.

Legend. CI=confidence interval; COVID-19=period of SARS-CoV-2 pandemic (coronavirus pandemic); MD=mean difference.



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