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Original Article

Trends in Stroke Presentations before and during the COVID-19 Pandemic: A Meta-Analysis

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Background and Purpose There are reports of decline in the rates of acute emergency presentations during coronavirus disease 2019 (COVID-19) pandemic including stroke. We performed a meta-analysis of the impact of COVID-19 pandemic on rates of stroke presentations and on rates of reperfusion therapy.

Methods Following the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines, we systematically searched the literature for studies reporting changes in stroke presentations and treatment rates before and during the COVID-19 pandemic. Aggregated data were pooled using meta-analysis with random-effect models.

Results We identified 37 observational studies (n=375,657). Pooled analysis showed decline in rates of all strokes (26.0%; 95% confidence interval [CI], 22.4 to 29.7) and its subtypes; ischemic (25.3%; 95% CI, 21.0 to 30.0), hemorrhagic (27.6%; 95% CI, 20.4 to 35.5), transient ischemic attacks (41.9%; 95% CI, 34.8 to 49.3), and stroke mimics (45.6%; 95% CI, 33.5 to 58.0) during months of pandemic compared with the pre-pandemic period. The decline was most evident for mild symptoms (40% mild vs. 25%–29% moderate/severe). Although rates of intravenous thrombolytic (IVT) and endovascular thrombectomy (EVT) decreased during pandemic, the likelihood of being treated with IVT and EVT did not differ between the two periods, both in primary and in comprehensive stroke centers (odds ratio [OR], 1.08; 95% CI, 0.94 to 1.24 and OR, 0.95; 95% CI, 0.83 to 1.09, respectively).

Conclusions Rates of all strokes types decreased significantly during pandemic. It is of paramount importance that general population should be educated to seek medical care immediately for stroke-like symptoms during COVID-19 pandemic. Whether delay in initiation of secondary prevention would affect eventual stroke outcomes in the long run needs further study.

Keywords Stroke; COVID-19; Hospitalization; Fibrinolysis; Thrombectomy; Meta-analysis

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Introduction

Coronavirus disease 2019 (COVID-19) infection was initially reported from Wuhan, China in December 2019.[1] It was declared a pandemic by World Health Organization in March 2020.[2] There was a significant decrease in the hospital presentations and admissions, reported for most medical emergencies, including trauma, surgical emergencies, stroke, and acute coronary syndromes (ACSs) in regions with high numbers of COVID-19 cases.[3-6] A decrease in stroke admissions during the first peak of the pandemic was reported from Asia, Europe, North and South America.[7-14] While the decrease was predominantly recorded for those with milder symptoms, presentation for all stroke subtypes decreased substantially. This was suggested by decrease in the utilization of the computed tomography perfusion based rapid processing of perfusion and diffusion (RAPID, iSchemaView, Redwood City, CA, USA) software for acute stroke imaging in a report from USA.[8,13,15-17]

The decrease in stroke admissions reported during the COVID-19 pandemic; however, has not been uniform, with conflicting reports from across the globe.[18] In addition, late presentation as reported by few has raised concerns that the pandemic may result in fewer patients receiving thrombolysis or endovascular thrombectomy (EVT).[19] Several factors may have contributed to the recorded decrease in rates of stroke admissions and should be reviewed with caution.[20-24] Studies that provide information based on prospective registries or databases are more likely to offer accurate analysis of the changes developing during the pandemic. Reports comparing the change noticed during the pandemic to retrospectively collected pre-pandemic data tend to be less accurate and should be reviewed with caution. In view of above, a meta-analysis of the published reports may help establish the link between the impact of the COVID-19, rates of stroke admissions, rates of treatment with reperfusion therapy and likelihood of being treated with reperfusion therapy. We performed a systematic review and meta-analysis of observational studies during the COVID-19 pandemic between January 2020 and July 2021. We analyzed the data to answer following questions: (1) Was there a decrease in the rates of stroke hospitalization? (2) If a decrease in stroke rates was evident, was this specific to any particular stroke type (ischemic, hemorrhagic, transient ischemic attack [TIA]) and/or any National Institutes of Health Stroke Scale (NIHSS)-based severity (mild, moderate, severe)? (3) What was the effect of the pandemic on rates of thrombolysis and EVT?

Methods

Data sources and study selection

The data supporting the findings of study are available from the corresponding author upon reasonable request. The PubMed and Embase databases were systematically searched from January 1st, 2020, until July 24th, 2021, for studies published in English. We used a combination of the following terms for the database search: "Stroke," "Cerebrovascular accidents," "COVID-19," "Coronavirus Disease 2019." Details of the search strategy can be found in Supplementary Table 1. The current meta-analysis is compliant with the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) statement.[25]

Two authors (N.I. and A.J.B., both neurologists) independently screened the study titles and abstracts after removal of duplicates. Articles identified as potentially fulfilling our inclusion criteria underwent full-text evaluation by four authors (N.I., A.J.B., C.V., and R.N., all neurologists). We included studies only if they were original reports or observational studies with information on the rates of stroke cases and hospitalization before and during the COVID-19 pandemic. We excluded studies that did not provide information on the pre-COVID-19 stroke rates or were reviews without original data.

Data extractions and quality assessment

Publication quality was assessed using the Newcastle-Ottawa Quality assessment scale for cohort studies.[26] This scale is used to assess the Participant Selection, Comparability, and Outcome. A 'good quality' publication was defined as having 3 or 4 stars in selection domain and 1 or 2 stars in comparability domain and 2 or 3 stars in outcome domain. 'Fair quality' was defined as having 2 stars in selection domain and 1 or 2 stars in compatibility domain and 2 or 3 stars in outcome domain. 'Poor quality' was defined as having 0 or 1 star in selection domain or 0 stars in comparability domain or 0 or 1 stars in outcome domain. We only included studies that were of 'good or fair quality.'

N.I., A.J.B., C.V., and R.N. extracted relevant data using a standardized data extraction form. Any disagreements were resolved by discussion. Extracted data included name of first author, year of publication, geographical location of the study, rate of total strokes, rate of ischemic strokes, hemorrhagic strokes, TIAs, stroke mimics, onset to door times (mean±standard deviation [SD]), classification of stroke center (primary or comprehensive stroke center), rates of reperfusion therapies, and severity of stroke based on NIHSS scores (mean±SD at presentation and number of mild [NIHSS <5], moderate [NIHSS of

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5–15], and severe [NIHSS >15] strokes) before and during the pandemic. Wherever the mean±SD of NIHSS or onset-to-door time were not reported, they were estimated from the median and interquartile range.[27] Reperfusion therapy was defined as intravenous thrombolysis or EVT.

Statistical analysis

We used meta-analysis with random effects models to pool the percent change in the number of various stroke presentations (ischemic, hemorrhagic, TIA, stroke mimic, mild, moderate, severe) and the likelihood of receiving treatment with intravenous thrombolysis or thrombectomy across studies. For studies reporting the onset-to-door time, we pooled the standardized mean difference between the pre-pandemic and the pandemic period. Publication bias was assessed by inspecting funnels plots and performing the Egger test. Heterogeneity between studies and subgroups was assessed using the chi-square test on the Cochran Q statistic and quantified by the I^2 index. All analyses were performed with STATA version 17.0 (StataCorp., College Station, TX, USA). All tests were 2-tailed and unpaired with a significance threshold of $P \leq 0.05$.

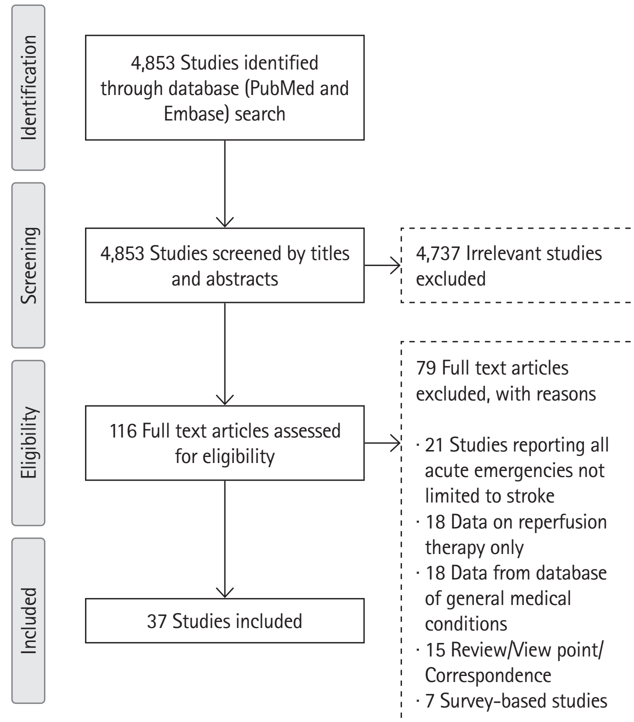

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow diagram of the observational studies selection process.

Results

The systematic database search retrieved 4,853 records, which were screened, and 116 studies underwent full-text evaluation. After excluding 79 studies for reasons outlined in Figure 1, 37 studies with 375,657 patients, meeting 'fair or good' quality criteria were selected for further analysis.[8,28-63] Twenty-four studies met criteria for 'good' quality and 13 met criteria for 'fair' quality (Supplemetary Tables 2-4). Most studies compared the pandemic period (ranging from January to June 2020) to a similar period in the preceding year (range January to June 2019)[28-31,33,35,39,41-43,45,46,48-50,52,54-58,60] or the months preceding the pandemic (range September 2019 to December 2019).[8,32,34,36-38,40,44,47,51,53,59,61-63]

Rates of stroke admissions and severity of symptoms

There was decline in rates of stroke admissions during the pandemic. The rate of all types of stroke presentations during pandemic was 26.0% lower than during pre-pandemic period (95% confidence interval [CI], 22.4 to 29.7) as shown in Table 1 and Figure 2. There was a publication bias with smaller studies reporting larger percent changes (Egger intercept=3.8; P=0.02) (Table 1 and Supplementary Figure 1). Analysis by stroke types showed that both ischemic and hemorrhagic stroke presentation rates decreased during the pandemic (Table 1). Specifically, the rate of ischemic stroke presentations during pandemic was 25.3% lower than during the pre-pandemic period (95% CI, 21.0 to 30.0) (Figure 3) while the rate of hemorrhagic stroke presentations during the pandemic was 27.6% lower (95% CI, 20.4 to 35.5) (Figure 4). Additionally, rates of TIAs and stroke mimics declined by 41.9% (95% CI, 34.8 to 49.3) (Supplementary Figure 2) and 45.6% (95% CI, 33.5 to 58.0) (Supplementary Figure 3), respectively.

Subgroup analysis revealed that there was a decrease in stroke rates during the pandemic for all severity categories with mild strokes (percent change, 40.2; 95% CI, 21.7 to 60.2) (Supplementary Figure 4) being the most affected (Table 1) as compared with moderate (percent change, 25.6; 95% CI, 11.0 to 43.8) (Supplementary Figure 5) and severe strokes (percent change, 29.1; 95% CI, 17.4 to 42.4) (Supplementary Figure 6). Regarding the distribution of mild, moderate, and severe strokes, there was an overall decrease in the share of mild strokes and a corresponding increase in the share of moderate and severe strokes (Supplementary Figures 7-9). During the pandemic, the odds for admitting a mild stroke versus a moderate or severe stroke was 0.78 (95% CI, 0.67 to 0.90; I^2=73.5%) (Supplementary Figure 7).

Table 1. Percent decrease in the number of strokes by type, region, and severity

Region	Studies	Percent change (95% CI)	Heterogeneity assessment		Egger test for publication bias	
			I^2	*P*	Intercept	*P*
All strokes						
Overall	37	26.0 (22.4–29.7)	99.6	<0.001	3.8	0.02
Asia	7	39.9 (32.7–47.4)	96.9	<0.001	–3.4	0.262
Europe	19	20.5 (17.9–23.3)	97.3	<0.001	0.5	0.47
Northern America	10	29.2 (16.7–43.5)	99.8	<0.001	6.4	0.13
Global	1	11.5 (11.3–11.7)	NA	NA	NA	NA
Ischemic strokes						
Overall	34	25.3 (21.0–30.0)	99.4	<0.001	2.7	0.02
Asia	7	40.8 (33.3–48.5)	95.8	<0.001	–1.3	0.58
Europe	18	17.8 (15.4–20.4)	96.2	<0.001	0.27	0.65
Northern America	9	29.9 (16.8–44.9)	99.7	<0.001	6.9	0.10
Hemorrhagic strokes						
Overall	24	27.6 (20.4–35.5)	98.1	<0.001	1.9	0.25
Asia	6	31.0 (11.2–55.2)	98.0	<0.001	–1.8	0.60
Europe	12	25.6 (18.8–33.0)	93.7	<0.001	1.1	0.06
Northern America	6	25.8 (10.9–44.1)	98.1	<0.001	3.6	0.13
Transient ischemic attacks						
Overall	22	41.9 (34.8–49.3)	96.4	<0.001	1.8	0.001
Asia	3	51.5 (47.1–56.0)	NA	NA	–0.3	0.77
Europe	15	38.3 (30.9–45.9)	93.3	<0.001	1.3	0.005
Northern America	3	49.9 (17.5–82.3)	98.5	<0.001	3.2	0.40
Stroke mimics						
Overall	8	45.6 (33.5–58.0)	95.9	<0.001	2.5	0.40
Asia	2	52.8 (47.5–58.1)	NA	NA	NA	NA
Europe	5	39.7 (29.2–50.7)	92.7	<0.001	2.7	0.40
Northern America	1	78.1 (68.9–85.2)	NA	NA	NA	NA
Stroke with NIHSS <5						
Overall	9	40.2 (21.7–60.2)	99.7	<0.001	6.8	0.21
Asia	5	54.4 (46.6–62.1)	93.2	<0.001	0.8	0.82
Europe	2	6.9 (6.0–7.8)	NA	NA	NA	NA
Northern America	2	50.4 (48.3–52.6)	NA	NA	NA	NA
Stroke with NIHSS 5–15						
Overall	8	25.6 (11.0–43.8)	98.9	<0.001	2.4	0.32
Asia	5	32.9 (20.6–46.5)	93.9	<0.001	–1.8	0.3
Europe	2	–6.6 (5.5–7.7)*	NA	NA	NA	NA
Northern America	1	33.8 (27.8–40.4)	NA	NA	NA	NA
Stroke with NIHSS >15						
Overall	9	29.1 (17.4–42.4)	97.1	<0.001	2.0	0.26
Asia	5	33.8 (18.7–50.8)	NA	NA	–0.8	0.70
Europe	2	12.4 (10.4–14.5)	NA	NA	NA	NA
Northern America	2	30.1 (26.4–33.9)	NA	NA	NA	NA

CI, confidence interval; NA, not available, the statistic cannot be computed due to the small number of studies (n ≤3); NIHSS, National Institutes of Health Stroke Scale.

*There was an increase in the number of moderate strokes in Europe which explains the minus sign.

Author	Year	All strokes pre–pandemic	All strokes pandemic	Absolute change	ES (95% CI)	% Weight
Asia						
Akhtar et al.	2021	420	314	−106	25.2 (21.3, 29.6)	2.71
Hasan et al.	2021	534	401	−133	24.9 (21.4, 28.7)	2.73
Kim et al.	2020	820	393	−427	52.1 (48.7, 55.5)	2.76
Librouder et al.	2021	1469	791	−678	46.2 (43.6, 48.7)	2.79
Tavanaei et al.	2021	210	106	−104	49.5 (42.8, 56.2)	2.62
Wu et al.	2020	2274	1222	−1052	46.3 (44.2, 48.3)	2.80
Zhang et al.	2020	407	257	−150	36.9 (32.3, 41.6)	2.71
Subtotal (I^2=96.9%, *P*=0.0)					39.9 (32.7, 47.4)	19.12
Europe						
Balestrino et al.	2020	165	123	−42	25.5 (19.4, 32.6)	2.57
Brunetti et al.	2021	156	142	−14	9.0 (5.4, 14.5)	2.56
Douiri et al.	2021	7902	6923	−979	12.4 (11.7, 13.1)	2.81
Dębiec et al.	2021	233	184	−49	21.0 (16.3, 26.7)	2.64
D'Anna et al.	2021	380	294	−86	22.6 (18.7, 27.1)	2.70
Gdovinová et al.	2020	1954	1521	−433	22.2 (20.4, 24.1)	2.79
Jansen et al.	2021	70	63	−7	10.0 (4.9, 19.2)	2.30
Kristoffersen et al.	2021	218	105	−113	51.8 (45.2, 58.4)	2.62
Kwan et al.	2020	196	168	−28	14.3 (10.1, 19.9)	2.60
Mariet et al.	2021	2362	2049	−313	13.3 (11.9, 14.7)	2.80
Melaika et al.	2021	304	168	−136	44.7 (39.2, 50.4)	2.68
Ramírez–Moreno et al.	2021	205	162	−43	21.0 (16.0, 27.1)	2.61
Raymaekers et al.	2021	1023	860	−163	15.9 (13.8, 18.3)	2.77
Richter et al.	2020	59149	47983	−11166	18.9 (18.6, 19.2)	2.82
Rinnkel et al.	2020	290	232	−58	20.0 (15.8, 25.0)	2.67
Sacco et al.	2020	3121	2328	−793	25.4 (23.9, 27.0)	2.80
Slowik et al.	2020	1126	993	−133	11.8 (10.1, 13.8)	2.78
Uidhir et al.	2020	881	703	−178	20.2 (17.7, 23.0)	2.77
Uphaus et al.	2020	194	146	−48	24.7 (19.2, 31.3)	2.60
Subtotal (I^2=97.3%, *P*=0.0)					20.5 (17.9, 23.3)	50.88
Northern America						
Aboul Nour et al.	2021	167	100	−67	40.1 (33.0, 47.7)	2.57
Balucani et al.	2021	7786	6330	−1456	18.7 (17.8, 19.6)	2.81
Desai et al.	2020	176	102	−74	42.0 (35.0, 49.4)	2.58
Esenwa et al.	2020	312	177	−135	43.3 (37.9, 48.8)	2.68
Havenon et al.	2020	11383	10830	−553	4.9 (4.5, 5.3)	2.81
Ortega–Gutierrez et al.	2020	1319	933	−386	29.3 (26.9, 31.8)	2.78
Pandey et al.	2020	722	573	−149	20.6 (17.8, 23.7)	2.76
Sharma et al.	2020	410	281	−129	31.5 (27.2, 36.1)	2.71
Wallace et al.	2021	2692	1225	−1467	54.5 (52.6, 56.4)	2.80
Wang et al.	2020	320	255	−65	20.3 (16.3, 25.1)	2.68
Subtotal (I^2=99.8%, *P*=0.0)					29.2 (16.7, 43.5)	27.18
Global						
Nogueira et al.	2021	91373	80894	−10479	11.5 (11.3, 11.7)	2.82
Heterogeneity between groups: *P*=0.000						
Overall (I^2=99.6%, *P*=0.0);					26.0 (22.4, 29.7)	100.00

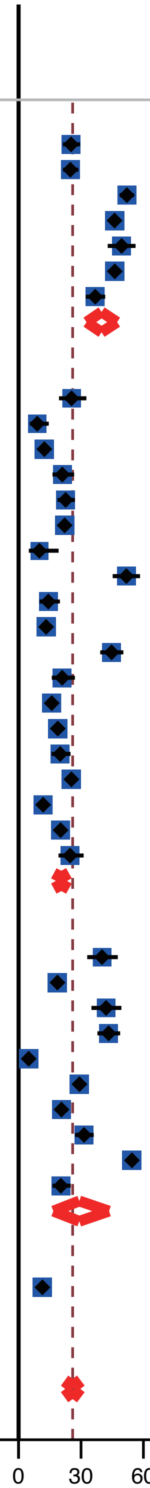

Figure 2. Percent change in all strokes by geographic region. ES, effect size; CI, confidence interval.

Regional difference

Included studies reported on rates of stroke presentations from Asia, Europe, and North America. The highest decrease in presentations for all types of strokes combined as well as ischemic strokes, hemorrhagic strokes, and TIAs during the pandemic was reported from Asia, 39.9% (95% CI, 32.7 to 47.4), 40.8% (95% CI, 33.3 to 48.5), 31.0% (95% CI, 11.2 to 55.2), and 51.5% (95% CI, 47.1 to 56.0), respectively (Table 1 and Figure 2). Whereas Europe had the smallest decrease in rates of presentations for all types of strokes combined, ischemic strokes,

Author	Year	Ischemic stroke pre–pandemic	Ischemic stroke pandemic	Absolute change	ES (95% CI)	% Weight
Asia						
Akhtar et al.	2021	286	225	–61	21.3 (17.0, 26.4)	2.95
Hasan et al.	2021	153	116	–37	24.2 (18.1, 31.5)	2.85
Kim et al.	2020	710	315	–395	55.6 (52.0, 59.2)	3.01
Librudier et al.	2021	948	550	–398	42.0 (38.9, 45.2)	3.02
Tavanaei et al.	2021	190	95	–95	50.0 (43.0, 57.0)	2.89
Wu et al.	2020	1984	1132	–852	42.9 (40.8, 45.1)	3.04
Zhang et al.	2020	337	167	–170	50.4 (45.1, 55.7)	2.96
Subtotal (I^2=95.8%, P=0.0)					40.8 (33.3, 48.5)	20.73
Europe						
Balestrino et al.	2020	99	79	–20	20.2 (13.5, 29.2)	2.75
Brunetti et al.	2021	148	135	–13	8.8 (5.2, 14.4)	2.85
Douiri et al.	2021	6864	5975	–889	13.0 (12.2, 13.8)	3.05
Dębiec et al.	2021	170	153	–17	10.0 (6.3, 15.4)	2.87
D'Anna et al.	2021	283	235	–48	17.0 (13.0, 21.8)	2.94
Gdovinová et al.	2020	1683	1332	–351	20.9 (19.0, 22.9)	3.04
Jansen et al.	2021	53	47	–6	11.3 (5.3, 22.6)	2.54
Kristoffersen et al.	2021	143	76	–67	46.9 (38.9, 55.0)	2.84
Kwan et al.	2020	177	142	–35	19.8 (14.6, 26.3)	2.88
Mariet et al	2021	1451	1308	–143	9.9 (8.4, 11.5)	3.04
Melaika et al.	2021	246	151	–95	38.6 (32.8, 44.8)	2.93
Ramírez–Moreno et al.	2021	155	124	–31	20.0 (14.5, 27.0)	2.86
Richter et al.	2020	37748	31165	–6583	17.4 (17.1, 17.8)	3.06
Rinnkel et al.	2020	194	180	–14	7.2 (4.3, 11.7)	2.89
Sacco et al.	2020	2399	1810	–589	24.6 (22.9, 26.3)	3.04
Slowik et al.	2020	1126	993	–133	11.8 (10.1, 13.8)	3.03
Uidhir et al.	2020	822	662	–160	19.5 (16.9, 22.3)	3.02
Uphaus et al.	2020	138	110	–28	20.3 (14.4, 27.8)	2.83
Subtotal (I^2=96.2%, P=0.0)					17.8 (15.4, 20.4)	52.46
Northern America						
Aboul Nour et al.	2021	144	83	–61	42.4 (34.6, 50.5)	2.84
Balucani et al.	2021	6144	4921	–1223	19.9 (18.9, 20.9)	3.05
Desai et al.	2020	161	96	–65	40.4 (33.1, 48.1)	2.86
Esenwa et al.	2020	270	153	–117	43.3 (37.6, 49.3)	2.94
Havenon et al.	2020	9662	9194	–468	4.8 (4.4, 5.3)	3.06
Ortega–Gutierrez et al.	2020	1319	933	–386	29.3 (26.9, 31.8)	3.03
Pandey et al.	2020	632	518	–114	18.0 (15.2, 21.2)	3.01
Sharma et al.	2020	391	274	–117	29.9 (25.6, 34.6)	2.97
Wallace et al.	2021	1912	877	–1035	54.1 (51.9, 56.4)	3.04
Subtotal (I^2=99.7%, P=0.0)					29.9 (16.8, 44.9)	26.81
Heterogeneity between groups: P=0.000						
Overall (I^2=99.4%, P=0.0);					25.3 (21.0, 30.0)	100.00

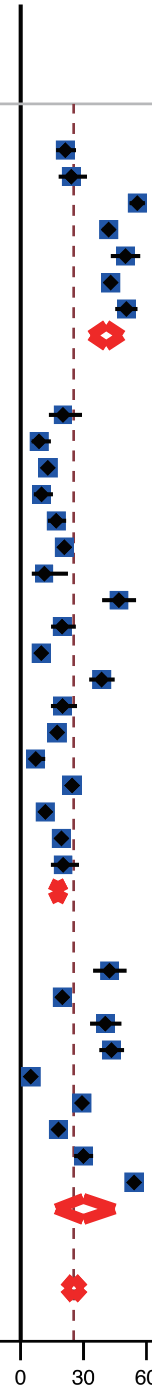

Figure 3. Percent change in the number of ischemic strokes. ES, effect size; CI, confidence interval.

hemorrhagic strokes, and TIAs, 20.5% (95% CI, 17.9 to 23.3), 17.8% (95% CI, 15.4 to 20.4), 25.6% (95% CI, 18.8 to 33.0), and 38.3% (95% CI, 30.9 to 45.9) (Table 1 and Figure 2). Rates of presentations for all strokes combined, ischemic strokes, hemorrhagic strokes, and TIA decreased in North America by 29.2% (95% CI, 16.7 to 43.5), 29.9% (95% CI, 16.8 to 44.9), 25.8% (95% CI, 10.9 to 44.1), and 49.9% (95% CI, 17.5 to 82.3) (Table 1 and Figure 2). Highest decrease in rates of stroke mimics was reported from North America 78.1% (95% CI, 68.9 to 85.2) in comparison to 52.8% (95% CI, 47.5 to 58.1) in Asia and 39.7% (95% CI, 29.2 to 50.7) in Europe (Table 1 and Figure 2).

The admission rates of all strokes were reported to have dropped maximally during the pandemic in regions of the world that were most severely affected by the pandemic like certain states of the USA (California, Texas, New York, Illinois,

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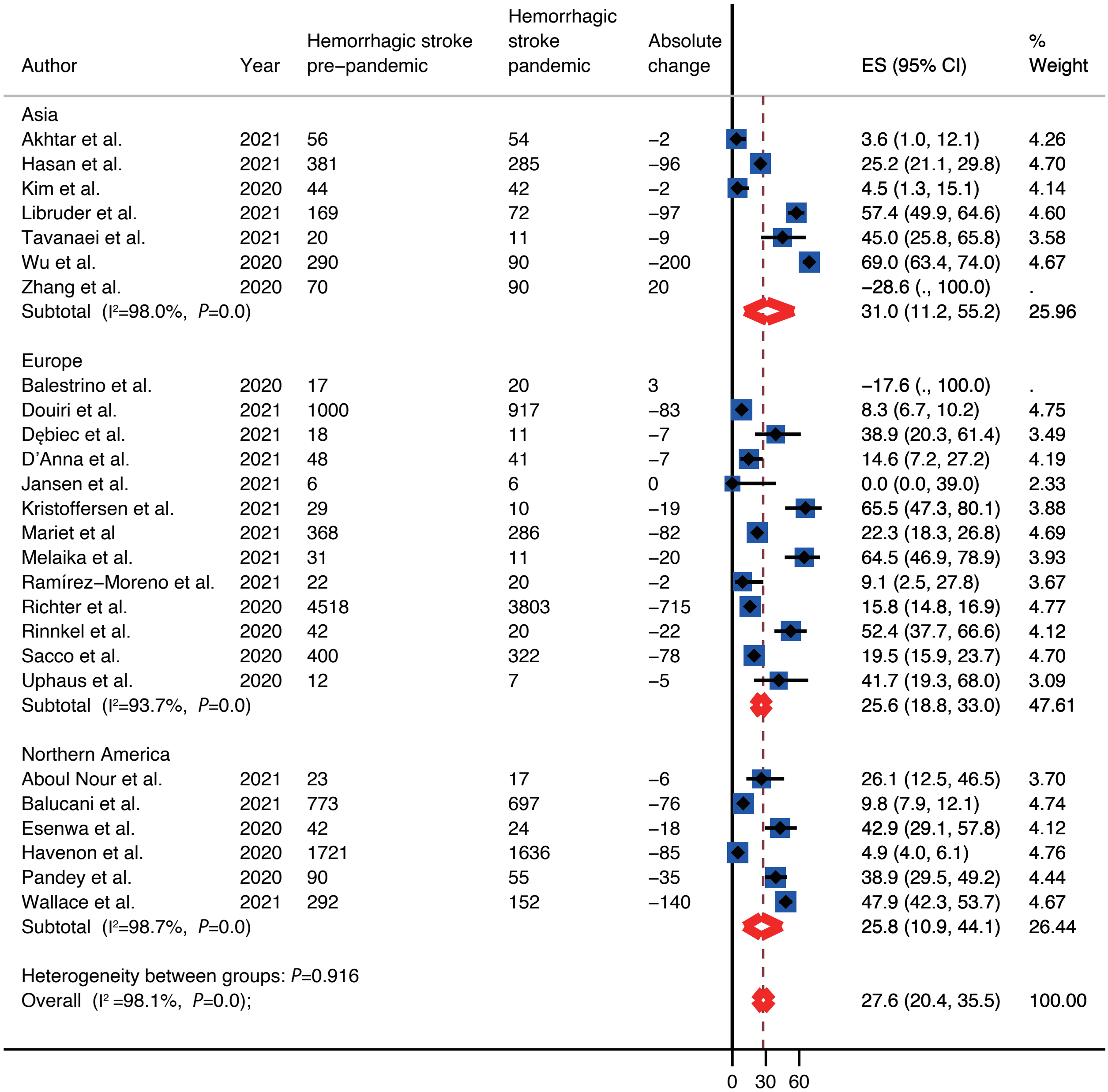


Figure 4. Percent change in the number of hemorrhagic strokes. ES, effect size; CI, confidence interval.

Georgia, Ohio, Pennsylvania, New Jersey),[31,32,41,46] Italy,[28,45] Iran,[48] and Germany.[50]

Time from onset to admission

As stroke treatment is time-sensitive, we next analyzed the time (in minutes) from onset/last seen well to hospital arrival. The onset-to-door time was reported in 14/37 studies.[29,30,44,46,48,49,52,54,55,57-59,61,63] There was no difference in mean onset-to-door time during pandemic when compared to pre-pandemic period (standardized mean difference=–0.2; 95% CI, –0.8 to 0.3).

Thrombolysis and endovascular treatment

The effect of the pandemic on the rates of thrombolysis was reported in 28/37 studies and 25/37 studies reported on the rates of EVT before and during the pandemic. The rate of intravenous thrombolytic (IVT) therapy for acute ischemic strokes dropped by 27.2% during the pandemic (95% CI, 22.7 to 32.0) (Supplementary Figure 10). This drop in rates of IVT was highest in Asia (40.3%; 95% CI, 27.8 to 53.3) followed by North America (26.9%; 95% CI, 12.7 to 43.9) and Europe (25.7%; 95% CI, 19.7 to 32.1) (Supplementary Figure 10). The likelihood of receiving IVT therapy did not differ between pre-pandemic and pandemic periods in primary stroke centers odds ratio (OR)

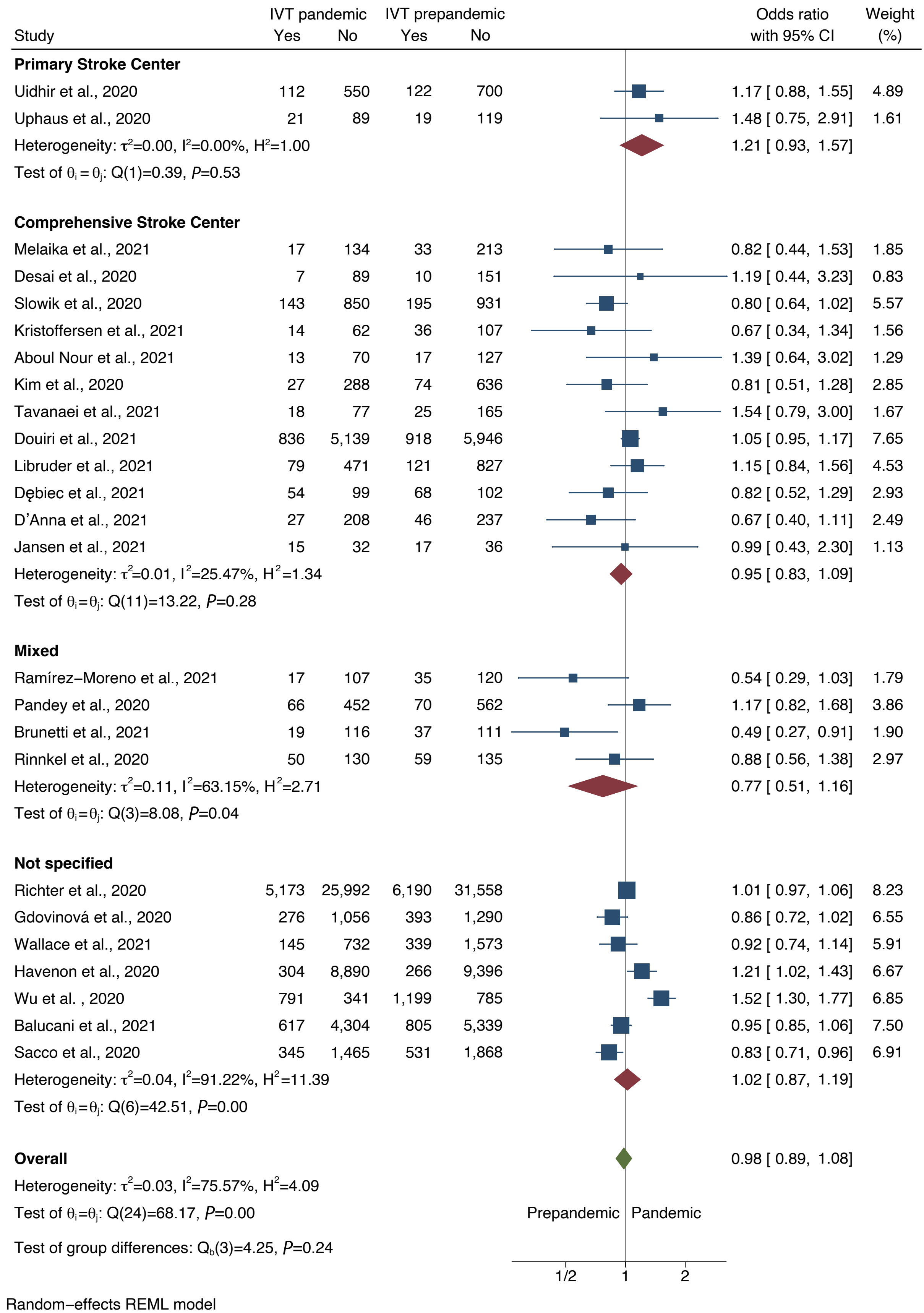
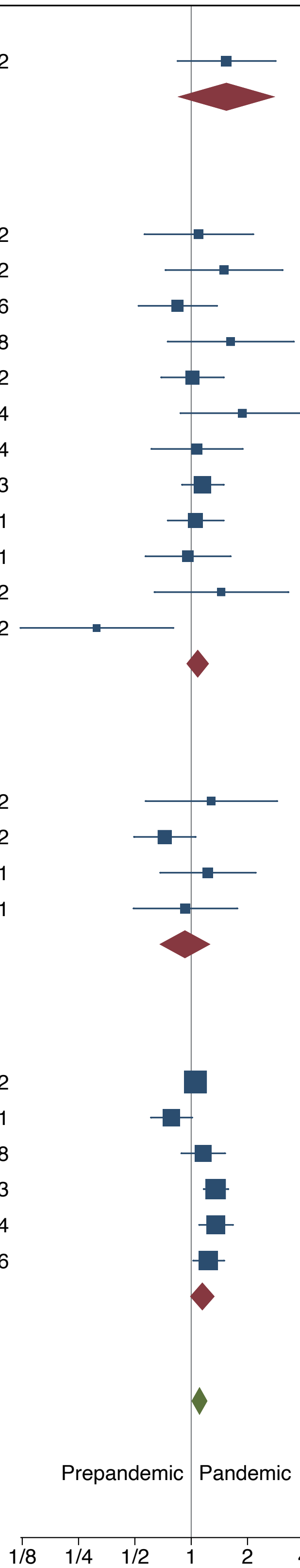


Figure 5. Probability of receiving intravenous thrombolytic (IVT) based on type of stroke center. CI, confidence interval; REML, restricted maximum likelihood.

Study	EVT Pandemic Yes	EVT Pandemic No	EVT Prepandemic Yes	EVT Prepandemic No	Odds ratio with 95% CI	Weight (%)
Primary Stroke Center						
Uphaus et al., 2020	29	81	26	112	1.54 [0.85, 2.81]	2.19
Heterogeneity: τ^2=0.00, I^2=NA, H^2=NA					1.54 [0.85, 2.81]	
Test of $\theta_i=\theta_j$: Q(0)=0.00, *P*=NA						
Comprehensive Stroke Center						
Melaika et al., 2021	16	135	24	222	1.10 [0.56, 2.14]	1.84
Desai et al., 2020	16	80	19	142	1.49 [0.73, 3.07]	1.61
Slowik et al., 2020	30	963	40	1,086	0.85 [0.52, 1.37]	3.14
Aboul Nour et al., 2021	14	69	16	128	1.62 [0.75, 3.52]	1.41
Kim et al., 2020	44	271	98	612	1.01 [0.69, 1.49]	4.37
Tavanaei et al., 2021	14	81	16	174	1.88 [0.88, 4.04]	1.45
Kwan et al., 2020	28	114	33	144	1.07 [0.61, 1.88]	2.47
Douiri et al., 2021	121	5,854	121	6,743	1.15 [0.89, 1.49]	7.02
Libruder et al., 2021	59	491	97	851	1.05 [0.75, 1.48]	5.06
Dębiec et al., 2021	34	119	39	131	0.96 [0.57, 1.62]	2.76
D’Anna et al., 2021	13	222	11	272	1.45 [0.64, 3.30]	1.27
Jansen et al., 2021	8	39	21	32	0.31 [0.12, 0.80]	1.00
Heterogeneity: τ^2=0.00, I^2=0.00%, H^2=1.00					1.08 [0.94, 1.24]	
Test of $\theta_i=\theta_j$: Q(11)=12.61, *P*=0.32						
Mixed						
Ramírez–Moreno et al., 2021	13	111	13	142	1.28 [0.57, 2.87]	1.31
Pandey et al., 2020	49	469	80	552	0.72 [0.49, 1.05]	4.48
Brunetti et al., 2021	29	106	27	121	1.23 [0.68, 2.20]	2.30
Rinnkel et al., 2020	20	160	23	171	0.93 [0.49, 1.76]	1.99
Heterogeneity: τ^2=0.02, I^2=20.53%, H^2=1.26					0.93 [0.68, 1.27]	
Test of $\theta_i=\theta_j$: Q(3)=3.14, *P*=0.37						
Not specified						
Richter et al., 2020	2,524	28,641	2,906	34,842	1.06 [1.00, 1.12]	12.92
Gdovinová et al., 2020	109	1,223	172	1,511	0.78 [0.61, 1.01]	7.10
Wallace et al., 2021	91	786	174	1,738	1.16 [0.89, 1.51]	6.69
Havenon et al., 2020	406	8,788	319	9,343	1.35 [1.17, 1.57]	10.23
Wu et al. , 2020	185	947	250	1,734	1.35 [1.10, 1.66]	8.41
Balucani et al., 2021	224	4,697	228	5,916	1.24 [1.03, 1.49]	8.96
Heterogeneity: τ^2=0.03, I^2=80.88%, H^2=5.23					1.15 [0.99, 1.33]	
Test of $\theta_i=\theta_j$: Q(5)=21.98, *P*=0.00						
Overall					1.11 [1.00, 1.22]	
Heterogeneity: τ^2=0.02, I^2=49.68%, H^2=1.99						
Test of $\theta_i=\theta_j$: Q(22)=41.17, *P*=0.01						
Test of group differences: Q_b(3)=2.71, *P*=0.44						



Random–effects REML model

Figure 6. Probability of being treated with endovascular thrombectomy (EVT) based on type of stroke center. CI, confidence interval; NA, not appplicable; REML, restricted maximum likelihood.

1.21 (95% CI, 0.93 to 1.57) as well as in comprehensive stroke centers OR 0.95 (95% CI, 0.83 to 1.09) (Figure 5). Although rates of EVT decreased during the pandemic by 20% (95% CI, 13.7 to 27.0) (Supplementary Figure 11), the likelihood of receiving EVT increased during the pandemic OR 1.11 (95% CI, 1.00 to 1.22) (Figure 6). Largest decrease in rates of EVT was in Asia 34.2% (95% CI, 19.4 to 50.7) followed by North America 20.7% (95% CI, 6.8 to 39.2) and Europe 15.6% (95% CI, 9.0 to 23.5). The likelihood of receiving EVT did not differ between two periods in comprehensive stroke center (OR, 1.08; 95% CI, 0.94 to 1.24) as well as in primary stroke center (OR, 1.54; 95% CI, 0.85 to 2.81) (Supplementary Figure 11).

Discussion

In this systematic review and meta-analysis of 37 fair-to-good quality studies reporting the rates of stroke presentations in relation to the COVID-19 pandemic, we found that there was an overall significant decrease ranging between 25% and 50% in all stroke types including ischemic, hemorrhagic, TIAs, and stroke mimics during the months of the COVID-19 pandemic when compared with the pre-pandemic period. Stroke presentations declined nearly by approximately 40% for patients with mild symptoms. Although the absolute rates of IVT and EVT decreased during the pandemic, the likelihood of being treated with reperfusion therapy did not change during the pandemic either in primary or in comprehensive stroke centers. This systematic review and meta-analysis included some observational studies with publication bias but it is because of observational nature of studies and unique period of pandemic that might have affected data collection.

Among stroke categories, patients presenting with TIA had the highest decline during pandemic, with a decrease of 40%. Due to transient nature of neurological symptoms, patients may have chosen not to seek medical care as it might increase the risk of contracting COVID-19 infection. This trend is worrisome as it may lead to delay in diagnosis and initiation of prevention therapies. Patients with TIA are at higher risk of stroke in early period after TIA.[14,21] There is considerable evidence that the risk of stroke is reduced significantly with appropriate assessment and early treatment.[21] Whether delay in delivery of appropriate treatment will affect stroke outcomes subsequently is therefore a big concern. Population-based awareness campaigns to highlight the need to seek early medical attention should be conducted in the community, especially for those with TIAs and milder symptoms.

The rates of stroke mimics were significantly reduced by a percentage ranging from 33.5% to 58%. In the study from Qatar, a striking decrease to nearly one-thirds in rates of stroke mimic admissions was the major reason for the fall in stroke admissions during the pandemic months compared with the preceding months.[8] Patients with stroke mimics may avoid hospitalization due to fear of contracting COVID-19 infection.[13,15,16,28]

Similar to TIAs, mild strokes decreased by 40% during the pandemic. In comparison, moderate strokes decreased by 25% and severe strokes decreased by 29%. Whereas, two recent systematic reviews and meta-analysis on stroke in patients with COVID-19 infections revealed that stroke is an uncommon complication of the illness and develops in less than 1.5% of patients.[64,65] Interestingly, initial reports also suggested that strokes of increased severity were seen more frequently in patients with severe COVID-19 infections admitted to hospitals.[7] These cases may be secondary to the direct prothrombotic effects of the COVID-19 illness. There are reports of the formation of recurrent thrombi during the treatment of acute stroke.[7] The COVID-19 virus may directly damage the cerebral vascular endothelium, making it more prothrombotic and this may explain the higher incidence of severe strokes.[8,9,66-69]

While different trends were observed for thrombolysis delivery in various studies across the globe, our composite analysis shows that the rates of both IVT and EVT dropped by slightly more than one-fourth and one-fifth during the pandemic. This may be related to possible delayed hospital arrival and an overall decrease in the absolute number of patients with mild and moderate stroke seeking medical care.[21,29,30,46,54,55,59,60,62,70] However, the likelihood of being treated with IVT did not differ between two periods in comprehensive stroke centers and that of being treated with EVT increased during the pandemic, which might be due to adequate changes made in workflow of acute stroke care in comprehensive stroke centers.[71] Higher likelihood of being treated with EVT might also have been caused by higher likelihood of large vessel occlusions due to prothrombotic state driven by COVID-19 virus, as reported by multiple studies.[7-9,66-69]

There was a decrease in the rates for all types of stroke from all geographical regions of the world. These findings are similar to the decrease in admission rates of several other illnesses.[4-6] A decrease in admission rates for ACS has been reported from all geographic regions of the world and appears to parallel the severity of the lockdowns.[72] A decrease for most acute and chronic illnesses has also been reported from New York recently, where the effect was most apparent for infections and septicemia.[73] In Qatar, a decline in admissions to the emergency department varying from 9% to 75% was observed for acute surgical emergencies, ACS, bone fractures, and cancer whereas

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admissions for respiratory conditions increased.[5] In Finland, there was a reduction in the rates of several acute medical illnesses seen in the emergency department, including infections (28%), back or limb pain (31%), and psychiatric illness (19%). Interestingly and in contrast, there was no decrease in the number of stroke or ACS admissions during the period of observation.[21] This may be driven by selection bias due to severity of stroke symptoms or reporting of acutely managed cases.

The most prevalent hypothesis for decline in rates of presentation of acute illnesses to the hospital relates to the fear of contracting COVID-19 when coming to the hospital. It may stand especially true for patients with transient or milder symptoms.[20,21,40] This in turn may be magnified from 'stay-at-home' orders, leading to deferring urgent care as suggested in a recent survey from the United Kingdom.[74] In Germany, the initial early decline in stroke-related consultations in the pandemic and later increase for telemedicine services, paralleled the population activities during lockdowns.[22] Another study from France also reported that there appeared to be a relationship between the decrease in stroke admissions and the severity of the COVID-19 pandemic.[60] The alternative hypothesis is that of decreased incidence of cardiovascular events related to lifestyle changes.[40,75] Similarly, in Greece the significant decrease in ACS admissions in three municipalities appeared to be directly related to lifestyle changes including reduced passive smoking, working hours, alcohol and junk food consumption, and increased sleeping hours related to lockdown.[76] Although appealing, the study mainly addressed people with low burden of cardiovascular risk factors and thus the results should be interpreted carefully.

Other factors proposed to explain the decrease in emergency visits for acute illnesses include reduced social contact resulting in lowered "third-party" detection of unappreciated acute stroke symptoms.[40] Another speculation is that of beneficial reduction in air pollution related to decreased carbon dioxide emissions and lower temperatures in relation to lockdowns during the peak of the pandemic.[21,22,77] A decrease in physical activity during lockdown may also have potential protective effects. An increase in physical activity is known to increase blood pressure, potentially increasing the risk of stroke and ACS.[20,78]

Our study has certain strengths and limitations. First, it is a composite analysis of studies comparing pre-pandemic to pandemic period and thus addresses the skepticism around the commonly raised concerns regarding stroke care. Second, we not only compared stroke presentations, but also analyzed the effect of stroke severity on relative differences in presentations. Third, the results are based on studies from multiple continents and diverse regions which is reflective of the global impact of the pandemic. The main limitation of this analysis is that this was based on observational studies. Also, although the likelihood of thrombolysis and thrombectomy seems unchanged, the effects the pandemic might have on stroke outcomes in terms of secondary prevention warrants further study. Comprehensive prospective registries recording the above stated parameter may help address these concerns as the pandemic evolves.

Conclusions

We meta-analyzed 37 studies that reported the rates of stroke presentation before and during the COVID-19 pandemic from various geographic regions. Rates of all stroke types declined significantly during the pandemic, but most profoundly for transient and milder symptoms, and stroke mimics. This resulted in lower rates of treatments with IVT as well as EVT. Whether delay in delivery of secondary prevention for those with mild symptoms would affect eventual stroke outcomes in the long run needs further study.

Supplementary materials

Supplementary materials related to this article can be found online at https://doi.org/10.5853/jos.2021.01571.

Disclosure

The authors have no financial conflicts of interest.

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Supplementary Table 1. Search strategy

Search number	Search description	No. of results
Full literature search on PubMed for COVID-19 and stroke		
1	Stroke OR cerebrovascular accident	378,999
2	COVID-19 OR Coronavirus Diseases 2019	160,172
3	Covid-19 OR Coronavirus Disease 2019 AND Stroke OR Cerebrovascular accident	2,179
Full literature search on EMBASE for COVID-19 and stroke		
1	Stroke.mp	543,619
2	Limit 1 to yr="2020 - 2021"	57,592
3	Covid-19.mp.	157,189
4	Limit 3 to (human and English language and yr="2020 - 2021")	143,572
5	2 and 4	2,674

COVID-19, coronavirus disease 2019.

Supplementary Table 2. Characteristics of the included studies

Author	Year	Location	Period* PreP	Period P	Male PreP	Male P	RoB NOS	IS PreP	IS P	HS PreP	HS P	TIA PreP	TIA P	SM PreP	SM P
Akhtar et al.[8]	2021	Qatar	Sep 2019–Feb 2020	Mar–May 2020	73.4%	73.3%	G	286	225	56	54	78	35	262	102
Balestrino et al.[28]	2020	Italy	Mar 8–May 2, 2019	Mar 8–May 2, 2020	NA	NA	G	99	79	17	20	49	24	NA	NA
Balucani et al.[29]	2021	USA	Mar 1–Sep 30, 2019	Mar 1–Sep 30, 2020	NA	NA	G	6,144	4,921	773	697	869	712	NA	NA
Brunetti et al.[30]	2021	Italy	Mar 11–May 4, 2019	Mar 11–May 4, 2020	47.4%	51.4%	G	148	135	NA	NA	8	7	NA	NA
Desai et al.[31]	2020	USA	Mar 2017/2018/2019	Mar 2020	NA	NA	G	161	96			15	6	NA	NA
Esenwa et al.[32]	2020	USA	Jan 1–Feb 25, 2020	Feb 26–Apr 18, 2020	48%	53%	F	270	153	42	24	NA	NA	NA	NA
Gdovinová et al.[33]	2020	Slovakia	Jan and Feb, 2020	Mar–Apr, 2020	NA	NA	G	1,683	1,332	NA	NA	271	189	NA	NA
Hasan et al.[34]	2021	Bangladesh	Jan 1–Mar 25, 2020	Mar 26–Jun 30, 2020	NA	NA	F	153	116	381	285	NA	NA	NA	NA
de Havenon et al.[35]	2020	USA	Feb–Mar 2018 and 2019	Feb–Mar 2020	NA	NA	F	9,662	9,194	1,721	1,636	NA	NA	NA	NA
Kim et al.[36]	2020	South Korea	Sep 2019– Feb 17, 2020	Feb 2020–May 2020	59.3%	60.8%	F	710	315	44	42	65	36	NA	NA
Kristoffersen et al.[37]	2021	Norway	Jan 3–Mar 12, 2020	Mar 13–Apr 30, 2020	55%	51%	F	143	76	29	10	46	19	NA	NA
Kwan et al.[38]	2020	UK	Jan 1–Mar 2, 2020	Mar 3–Apr 30, 2020	58%	64%	F	177	142	NA	NA	NA	NA	NA	NA
Nogueira et al.[40]	2021	Global	Nov, 2019–Feb, 2020	Mar–June 2020	NA	NA	G	NA	NA	NA	NA	NA	NA	NA	NA
Ortega-Gutierrez et al.[41]	2020	USA	Mar 1–May 31, 2019	Mar 1–May 31, 2020	53.5%	53%	G	1,319	933	NA	NA	NA	NA	NA	NA
Pandey et al.[42]	2020	USA	Mar 2019	Mar 2020	NA	NA	F	632	518	90	55	NA	NA	NA	NA
Ramírez-Moreno et al.[39]	2021	Spain	Mar 15–May 10, 2019	Mar 15–May 10, 2020	45%	52%	G	155	124	22	20	28	18	NA	NA
Richter et al.[43]	2020	Germany	Jan 16–Mar 15, 2020	Mar 16–May 15, 2020	51.7%	51.8%	F	37,748	31,165	4,518	3,803	16,883	1,3015	NA	NA
Rinkel et al.[44]	2020	Netherlands	Oct 21–Dec 8, 2019	Mar 16–May 3, 2020	47%	59%	F	194	180	42	20	54	32	115	77
Sacco et al.[45]	2020	Italy	Mar 2019	Mar 2020	53.4%	53%	G	2,399	1,810	400	322	322	196	531	345
Sharma et al.[46]	2020	USA	Dec 31, 2018–Apr 19, 2019	Dec 31, 2019–Apr 19, 2020	NA	NA	G	391	274	NA	NA	19	7	NA	NA
Słowik et al.[47]	2020	Poland	Jan 1–Mar 4, 2020	Mar 4–May 31, 2020	NA	NA	F	1,126	993	NA	NA	NA	NA	NA	NA
Tavanaei et al.[48]	2021	Iran	Mar 1 2019–Jun 1 2019	Mar 1 2020–Jun 1 2020	58.4%	52.6%	G	190	95	20	11	NA	NA	NA	NA
Mag Uidhir et al.[49]	2020	United Kingdom	Jan–Jun 2019	Jan–Jun 2020	NA	NA	G	822	662	NA	NA	59	41	275	206
Uphaus et al.[50]	2020	Germany	Jan 1 2019–Feb 2020	Mar–Apr 2020	54.3%	46.6%	G	138	110	12	7	44	29	NA	NA
Wang et al.[51]	2020	USA	Dec 1. 2019–Mar 11, 2020	Mar 12, 2020–Jun 30, 2020	51.9%	53.3%	F	NA	NA	NA	NA	NA	NA	NA	NA
Wu et al.[52]	2020	China	Jan 24–Apr 29, 2019	Jan 24–Apr 29, 2020	67.2%	66.7%	G	1,984	1,132	290	90	NA	NA	80	59
Zhang et al.[53]	2020	China	Nov 2019–Mar 2020	Apr 2020–Jul 2020	NA	NA	F	337	167	70	90	NA	NA	NA	NA
Aboul Nour et al.[54]	2021	USA	Mar 20–May 20, 2019	Mar 20–May 20, 2020	51%	55%	G	144	83	23	17	NA	NA	96	21
D'Anna et al.[55]	2021	United Kingdom	Mar 23–June 30, 2019	Mar 23–June 30, 2020	48.8%	56%	F	283	235	48	41	49	18	132	55
Dębiec et al.[56]	2021	Poland	Mar 1–Apr 30, 2019	Mar 1–Apr 30, 2020	46%	53%	F	170	153	18	11	45	20	NA	NA
Douiri et al.[57]	2021	United Kingdom	Mar 23–Apr 30, 2019	Mar 23–Apr 30, 2020	51.6%	52%	G	6,864	5,975	1,000	917	NA	NA	NA	NA
Jansen et al.[58]	2021	Germany	Mar 16–Apr 12 2019	Mar 16–Apr 12 2020	45.7%	47.6%	F	53	47	6	6	11	10	NA	NA
Libruder et al.[59]	2021	Israel	Jan 1–Mar 7, 2020	Mar 8–Apr 30, 2020	54.9%	56.2%	G	948	550	169	72	352	169	NA	NA
Mariet et al.[60]	2021	France	Apr, 2019	Apr, 2020	NA	NA	G	1,451	1,308	368	286	543	455	NA	NA
Melaika et al.[61]	2021	Lithuania	Dec 1, 2019–Mar 15, 2020	Mar 16–June 16, 2020	40.1%	39.8%	F	246	151	31	11	27	6	164	83
Raymaekers et al.[62]	2021	Belgium	Dec, 2019 till Feb, 2020	Mar–May 2020	NA	NA	F	NA	NA	NA	NA	NA	NA	NA	NA
Wallace et al.[63]	2021	USA	Jan 1–Feb 29, 2020	Mar 20–Apr 25, 2020	48.9%	48%	G	1,912	877	292	152	239	85	NA	NA

PreP, pre-pandemic; P, pandemic; RoB, risk of bias; NOS, Newcastle-Ottawa Quality Assessment Scale; IS, ischemic stroke; HS, hemorrhagic stroke; TIA, transient ischemic attack; SM, stroke mimics; G, good; NA, not available; F, fair.
*Months are provided in their 3-letter abbreviated form.

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Supplementary Table 3. Characteristics of included studies based on stroke severity, IVT, and EVT

Author	Year	All strokes PreP	All strokes P	NIHSS <5 PreP	NIHSS <5 P	NIHSS 5–15 PreP	NIHSS 5–15 P	NIHSS >15 PreP	NIHSS >15 P	IVT PreP	IVT P	EVT PreP	EVT P	NIHSS PreP (mean±SD or median [IQR])	NIHSS P (mean±SD or median [IQR])
Akhtar et al.[8]	2021	682	416	531	273	75	71	75	71	NA	NA	NA	NA	NA	NA
Balestrino et al.[28]	2020	165	123	NA	NA	NA	NA	NA	NA	195	143	NA	NA	NA	NA
Balucani et al.[29]	2021	7,786	6,330	NA	NA	NA	NA	NA	NA	805	617	228	224	NA	NA
Brunetti et al.[30]	2021	156	142	NA	NA	NA	NA	NA	NA	NA	NA	5,191	4,533	NA	NA
Desai et al.[31]	2020	176	102	636	412	210	139	275	233	NA	NA	NA	NA	NA	NA
Esenwa et al.[32]	2020	312	177	98	24	77	49	14	20	25	18	16	14	NA	NA
Gdovinová et al.[33]	2020	1,954	1,521	NA	NA	NA	NA	NA	NA	393	276	172	109	14.5±9	16.9±13.9
Hasan et al.[34]	2021	534	401	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
de Havenon et al.[35]	2020	11,383	10,830	NA	NA	NA	NA	NA	NA	266	304	319	406	NA	NA
Kim et al.[36]	2020	820	393	570	256	112	59	138	78	NA	NA	NA	NA	6.1±6.2	6.6±6
Kristoffersen et al.[37]	2021	218	105	NA	NA	NA	NA	NA	NA	35	17	13	13	4.2±6.1	5.9±8.6
Kwan et al.[38]	2020	196	168	NA	NA	NA	NA	NA	NA			19	16	NA	NA
Nogueira et al.[40]	2021	91,373	80,894	NA	NA	NA	NA	NA	NA	13,334	11,570	NA	NA	NA	NA
Ortega-Gutierrez et al.[41]	2020	1,319	933	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	10.4±12.5	11.3±12.2
Pandey et al.[42]	2020	722	573	NA	NA	NA	NA	NA	NA	70	66	80	49	NA	NA
Ramírez-Moreno et al.[39]	2021	205	162	NA	NA	NA	NA	NA	NA	19	21	26	29	6.4±1.4	7.1±1.6
Richter et al.[43]	2020	59,149	47,983	NA	NA	NA	NA	NA	NA	6,186	5,170	2,888	2,514	NA	NA
Rinkel et al.[44]	2020	405	309	NA	NA	NA	NA	NA	NA	59	50	23	20	NA	NA
Sacco et al.[45]	2020	3,652	2,673	NA	NA	NA	NA	NA	NA	531	345	NA	NA	NA	NA
Sharma et al.[46]	2020	410	281	NA	NA	NA	NA	NA	NA	20	30	43	49	8.2±2.5	9.7±1
Słowik et al.[47]	2020	1,126	993	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Tavanaei et al.[48]	2021	210	106	NA	NA	NA	NA	NA	NA	NA	NA	33	28	5.1±4.3	9.1±4.8
Mag Uidhir et al.[49]	2020	1,156	909	NA	NA	NA	NA	NA	NA	122	112	NA	NA	NA	NA
Uphaus et al.[50]	2020	194	146	89	85	25	27	33	24	37	19	27	29	NA	NA
Wang et al.[51]	2020	320	255	NA	NA	NA	NA	NA	NA	36	14	NA	NA	8.1±10.3	6.3±5.4
Wu et al.[52]	2020	2,354	1,281	1,075	468	886	501	324	192	1,199	791	250	185	8.4±7.8	9.4±7.7
Zhang et al.[53]	2020	407	257	NA	NA	NA	NA	NA	NA	36	17	NA	NA	NA	NA
Aboul Nour et al.[54]	2021	263	121	NA	NA	NA	NA	NA	NA	17	13	16	14	2 (1–6)	5 (1–9)
D'Anna et al.[55]	2021	512	349	NA	NA	NA	NA	NA	NA	46	27	11	13	4 (0–29)	7 (0–30)
Dębiec et al.[56]	2021	233	184	NA	NA	NA	NA	NA	NA	68	54	39	34	11.9±8	10.2±7
Douiri et al.[57]	2021	7,902	6,923	3,157	2,930	2,230	2,394	1,028	1,158	918	836	121	121	5 (2–10)	5 (2–12)
Jansen et al.[58]	2021	70	63	NA	NA	NA	NA	NA	NA	17	15	21	8	4 (1–11)	4 (1.8–10)
Libruder et al.[59]	2021	1,469	791	389	234	160	99	80	42	121	79	97	59	4.0 (2–9)	4.0 (2–8)
Mariet et al.[60]	2021	2,362	2,049	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Melaika et al.[61]	2021	468	251	NA	NA	NA	NA	NA	NA	33	17	24	16	8 (4–16)	7 (4–14)
Raymaekers et al.[62]	2021	1,023	860	NA	NA	NA	NA	NA	NA	207	177	166	145	NA	NA
Wallace et al.[63]	2021	2,692	1,225	1,473	632	NA	NA	308	168	339	145	174	91	3 (1–9)	4 (1–10)

PreP, pre-pandemic; P, pandemic; NIHSS, National Institutes of Health Stroke Scale; IVT, intravenous thrombolysis; EVT, endovascular thrombectomy; SD, standard deviation; IQR, interquartile range; NA, not available.

Supplementary Table 4. MOOSE statement: reporting checklist for authors, editors, and reviewers of meta-analyses of observational studies

Reporting criteria	Reported	Reported on page
Reporting of background		
Problem definition	Yes	5
Hypothesis statement	Yes	6
Description of study outcome(s)	Yes	6
Type of exposure or intervention used	Yes	6
Type of study design used	Yes	6
Study population	Yes	6
Reporting of search strategy		
Qualifications of searchers (e.g., librarians and investigators)	Yes	6
Search strategy, including time period included in the synthesis and keywords	Yes	6
Effort to include all available studies, including contact with authors	No	
Databases and registries searched	Yes	6
Search software used, name and version, including special features used (e.g., explosion)	No	
Use of hand searching (e.g., reference lists of obtained articles)	No	
List of citations located and those excluded, including justification	Yes	6
Method for addressing articles published in languages other than English	No	
Method of handling abstracts and unpublished studies	No	
Description of any contact with authors	No	
Reporting of methods		
Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	Yes	7
Rationale for the selection and coding of data (e.g., sound clinical principles or convenience)	Yes	6-7
Documentation of how data were classified and coded (e.g., multiple raters, blinding, and interrater reliability)	Yes	7
Assessment of confounding (e.g., comparability of cases and controls in studies where appropriate)	Yes	7
Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results YES 5	Yes	7
Assessment of heterogeneity	Yes	8
Description of statistical methods (e.g., 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	Yes	8
Provision of appropriate tables and graphics	Yes	
Reporting of results		
Table giving descriptive information for each study included	Yes	Supplementary Table 2
Results of sensitivity testing (e.g., subgroup analysis)	Yes	Supplementary Figures 2-11
Indication of statistical uncertainty of findings	Yes	8
Reporting of discussion		
Quantitative assessment of bias (e.g., publication bias)	Yes	11
Justification for exclusion (e.g., exclusion of non–English-language citations)	No	
Assessment of quality of included studies	Yes	11
Reporting of conclusions		
Consideration of alternative explanations for observed results	No	
Generalization of the conclusions (i.e., appropriate for the data presented and within the domain of the literature review)	Yes	15
Guidelines for future research	No	
Disclosure of funding source	Yes	15

MOOSE, Meta-analysis Of Observational Studies in Epidemiology.

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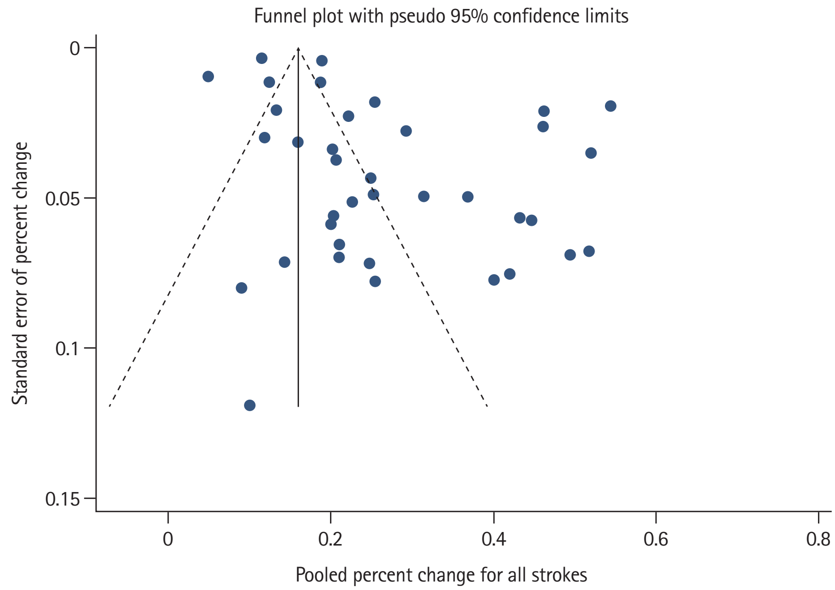
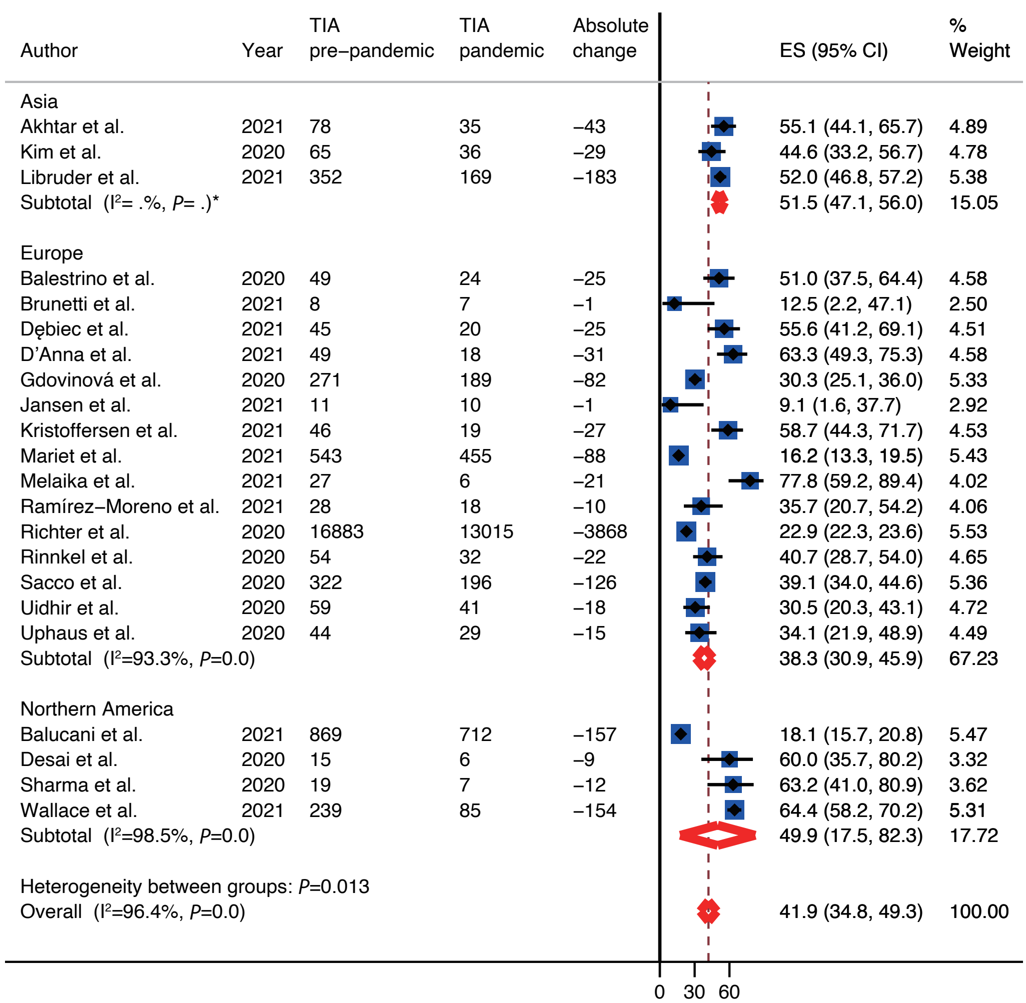
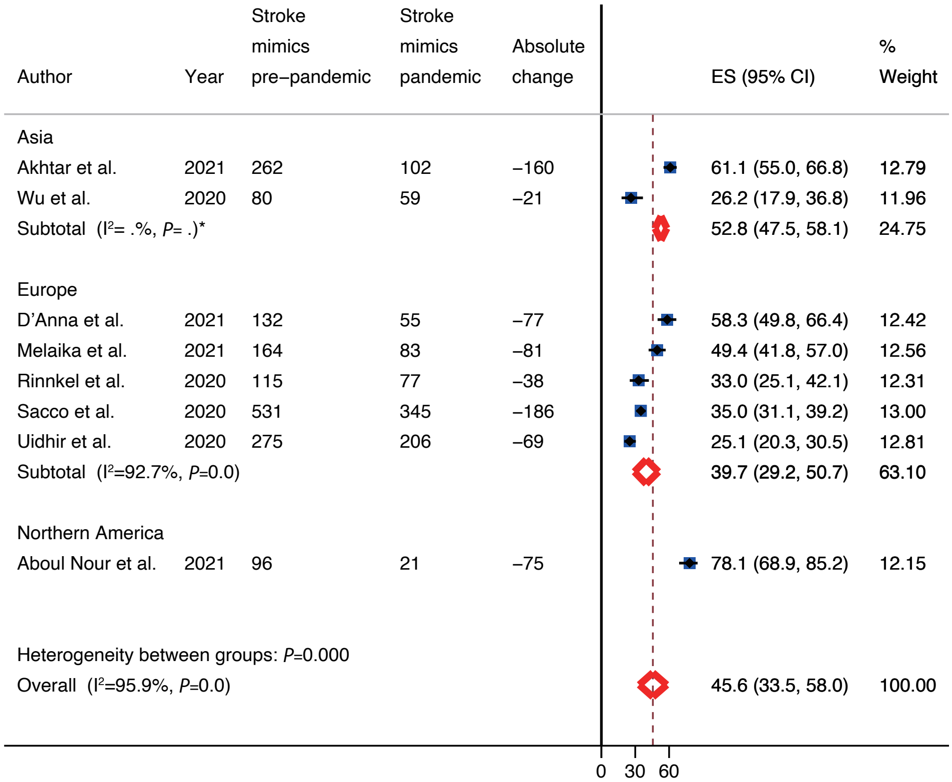


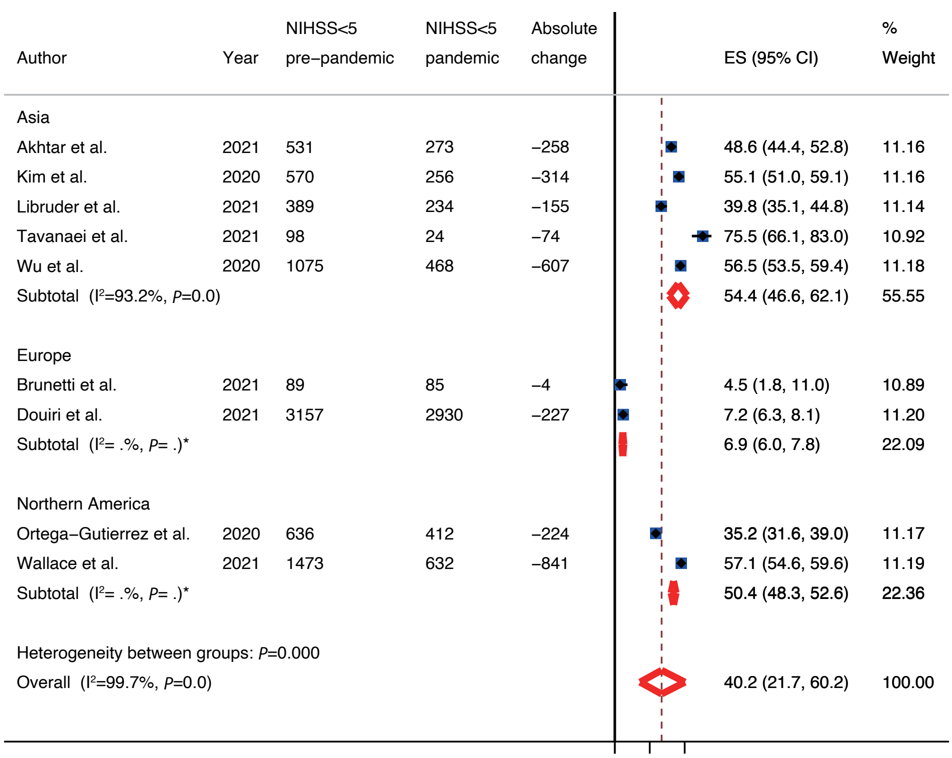
Supplementary Figure 1. Funnel plot for the meta-analysis of the percent changes in the number of all-type strokes.



Supplementary Figure 2. Percent change in the number of transient ischemic attacks. TIA, transient ischemic attack; ES, effect size; CI, confidence interval.
*This statistics could not be computed due to small number of studies (n≤3).



Supplementary Figure 3. Percent change in the number of stroke mimics. ES, effect size; CI, confidence interval. *This statistics could not be computed due to small number of studies (n≤3).



Supplementary Figure 4. Percent change in the number of mild strokes (National Institutes of Health Stroke Scale [NIHSS] <5). ES, effect size; CI, confidence interval. *This statistics could not be computed due to small number of studies (n≤3).

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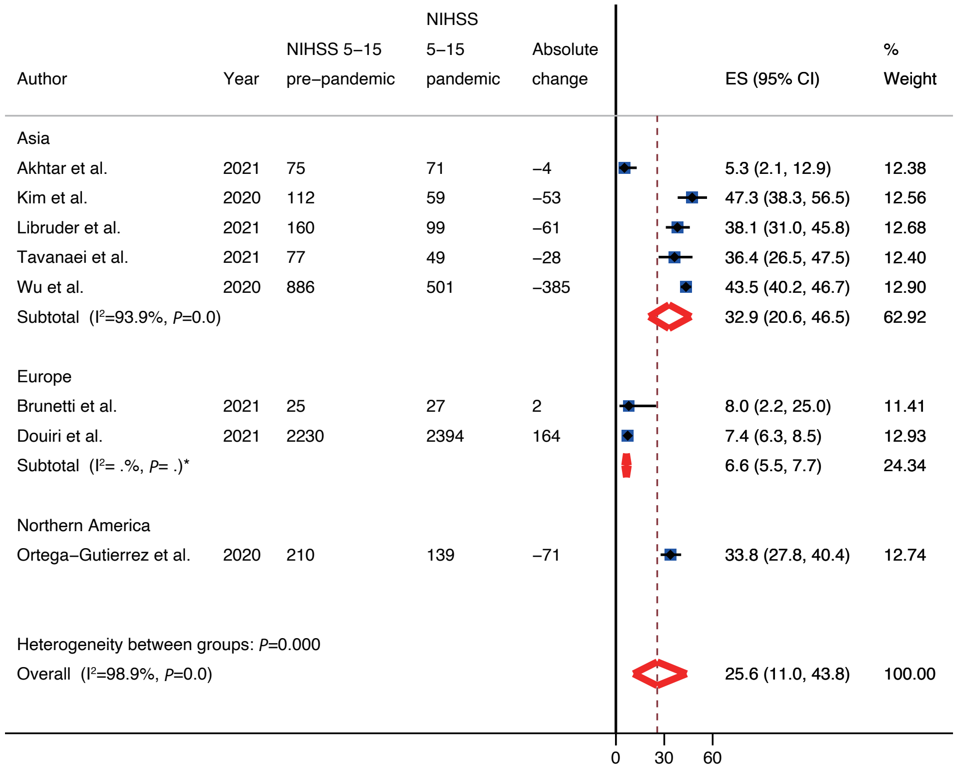
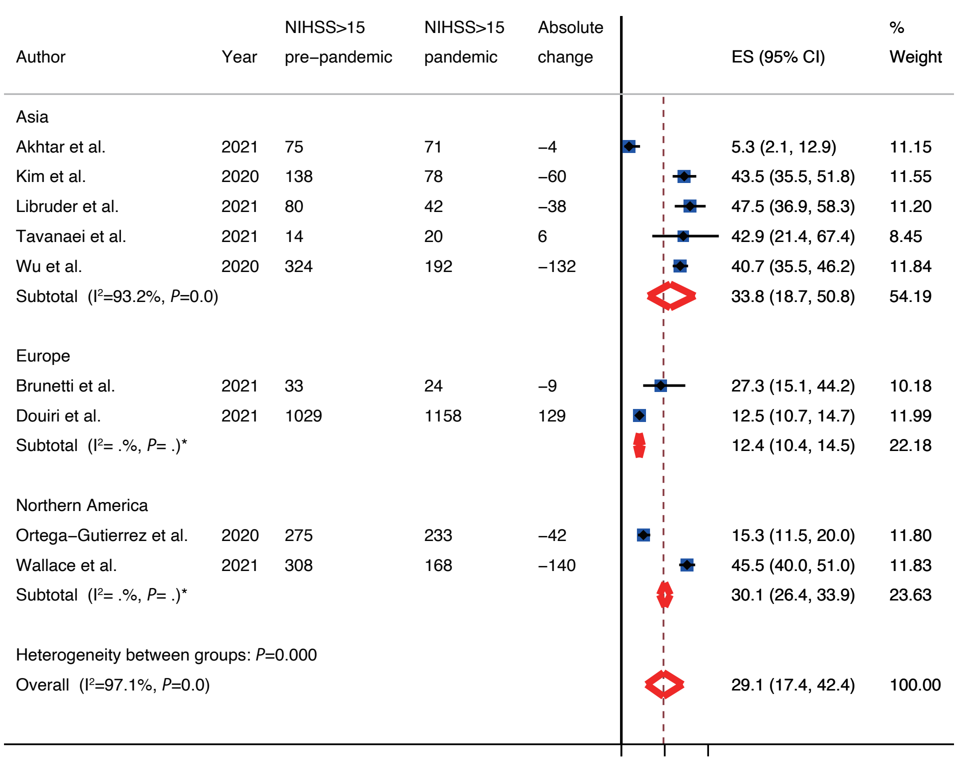
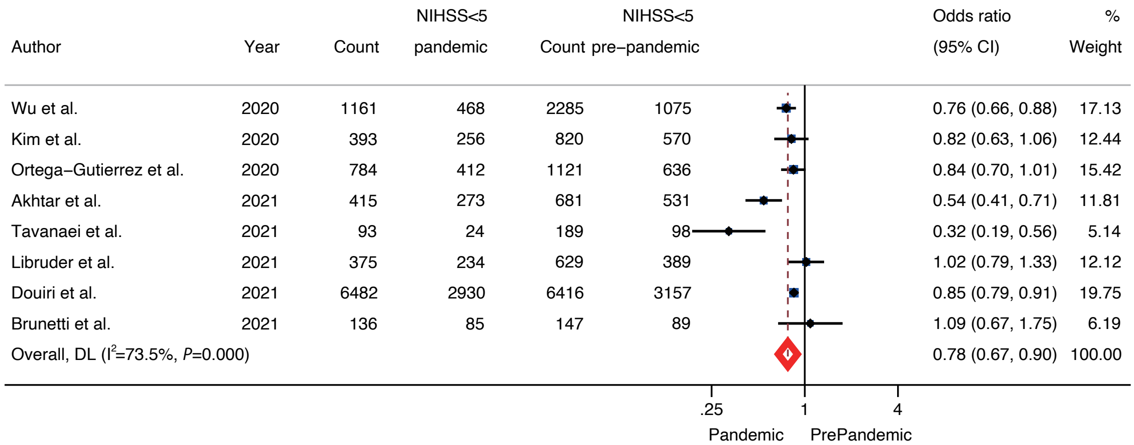


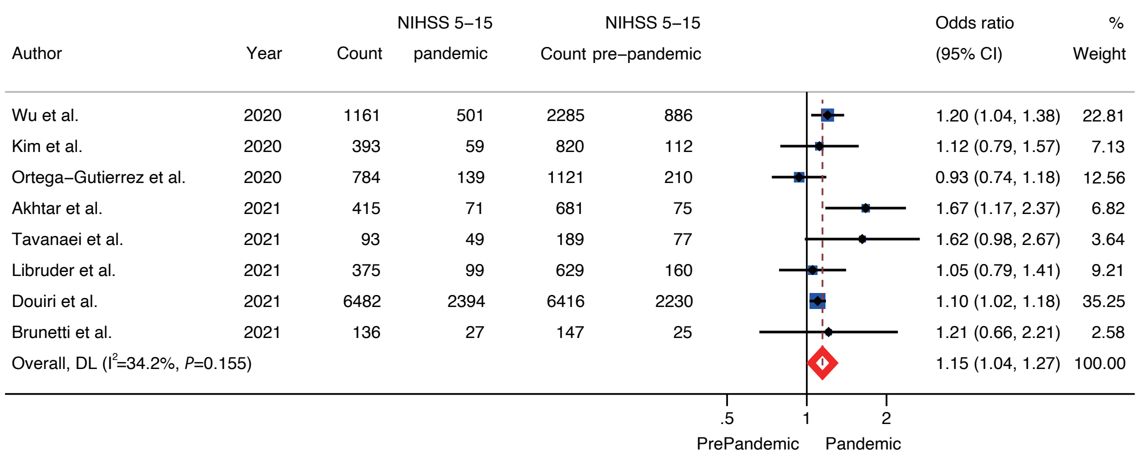
Supplementary Figure 5. Percent change in the number of moderate strokes (National Institutes of Health Stroke Scale [NIHSS] 5–15). ES, effect size; CI, confidence interval. *This statistics could not be computed due to small number of studies (n≤3).



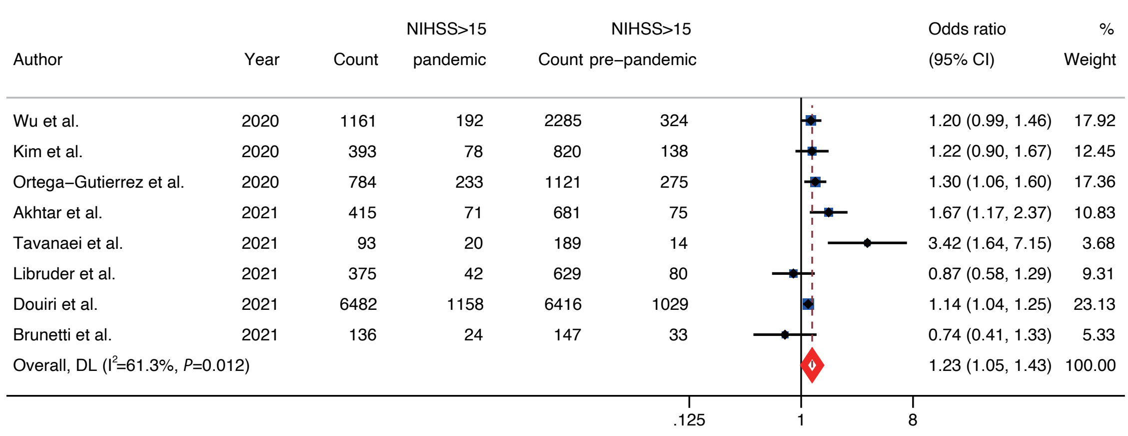
Supplementary Figure 6. Percent change in the number of severe strokes (National Institutes of Health Stroke Scale [NIHSS] >15). ES, effect size; CI, confidence interval. *This statistics could not be computed due to small number of studies (n≤3).



Supplementary Figure 7. Probability of having a mild stroke (National Institutes of Health Stroke Scale [NIHSS] <5). CI, confidence interval.



Supplementary Figure 8. Probability of having a moderate stroke (National Institutes of Health Stroke Scale [NIHSS] 5–15). CI, confidence interval.



Supplementary Figure 9. Probability of having a severe stroke (National Institutes of Health Stroke Scale [NIHSS] >15). CI, confidence interval.

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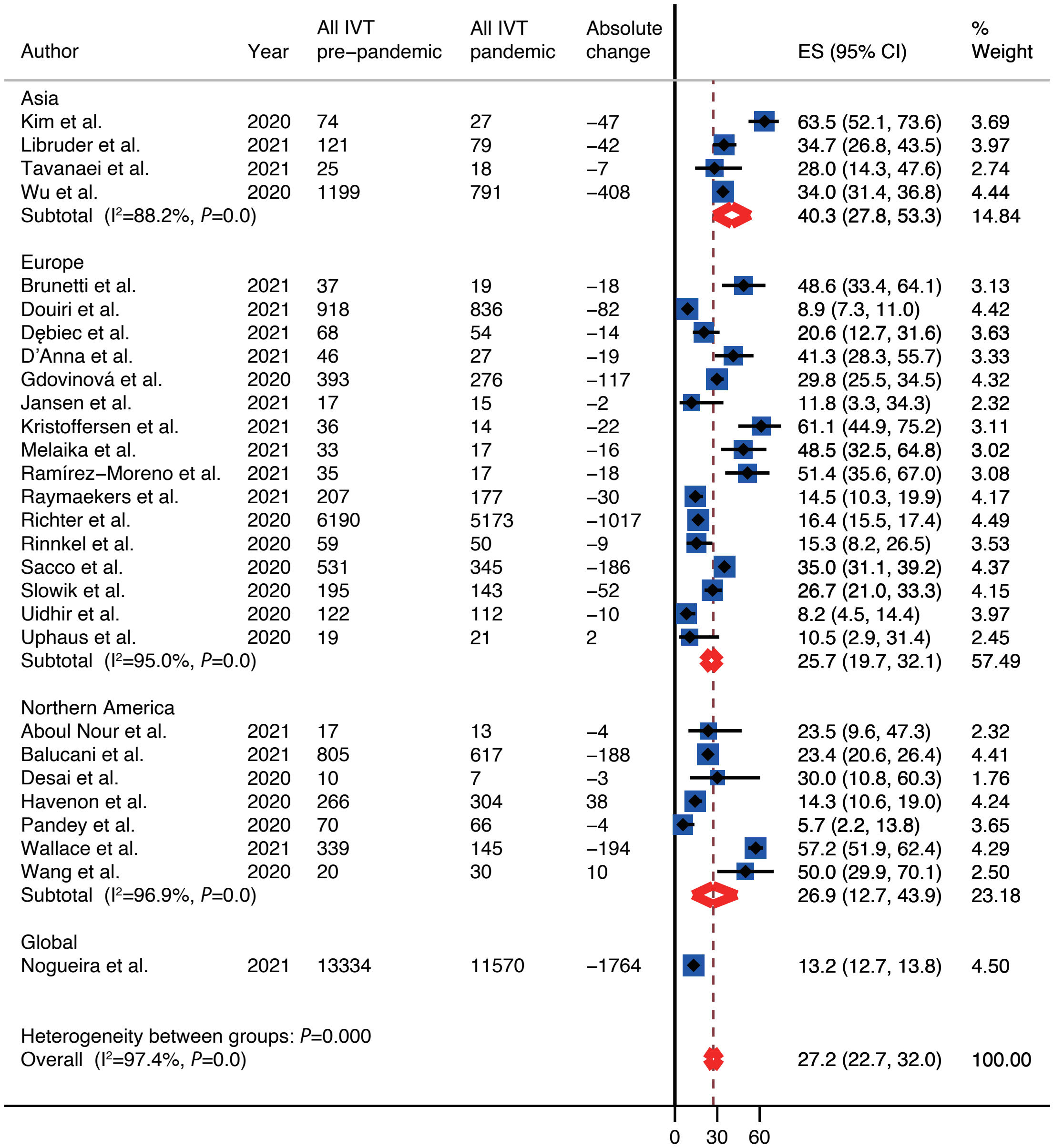
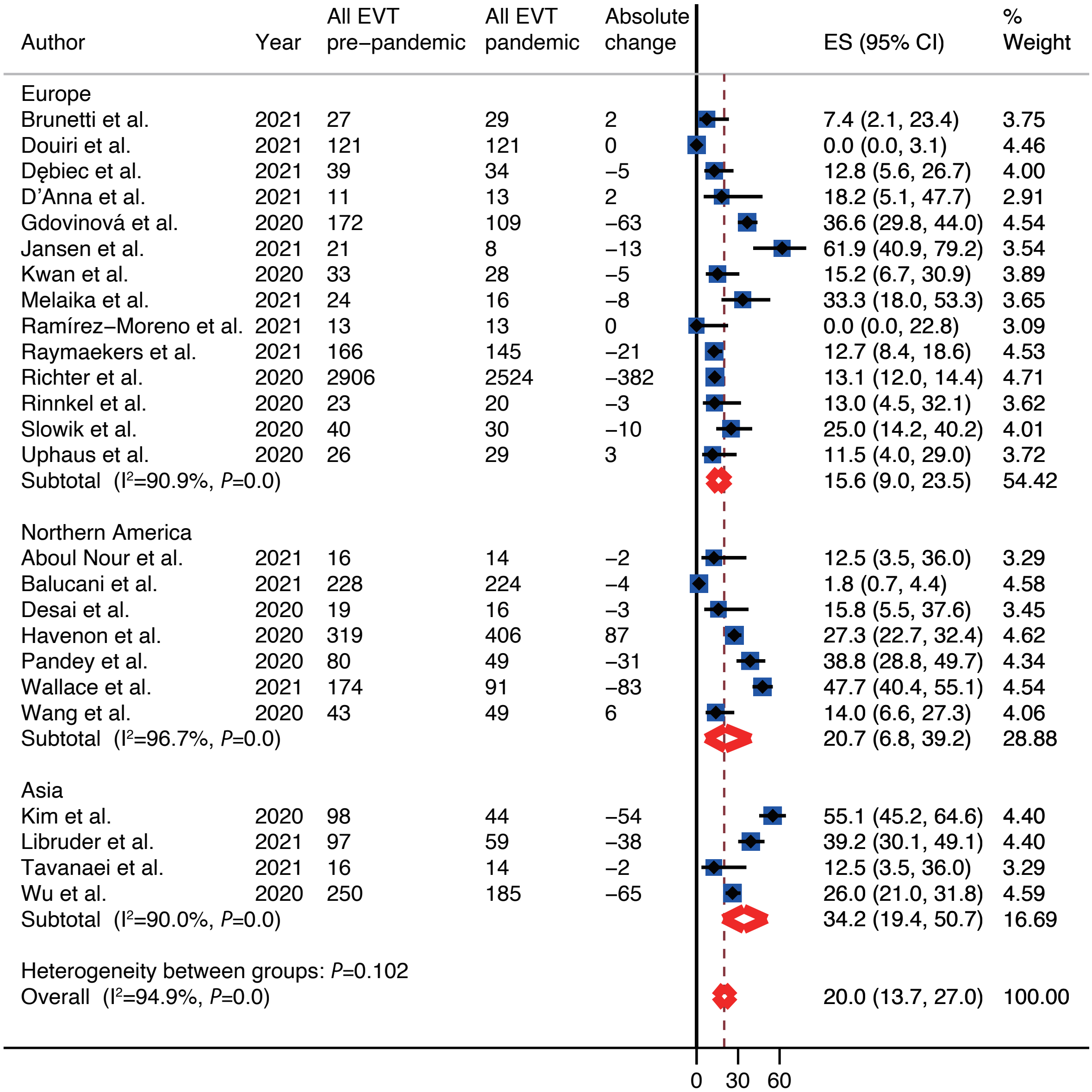


Supplementary Figure 10. Percent change in the total number of intravenous thrombolysis (IVT) performed. ES, effect size; CI, confidence interval.



Supplementary Figure 11. Percent change in the total number of endovascular thrombectomies (EVTs) performed. ES, effect size; CI, confidence interval.

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