2023 Edition

Ref	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN
ID						checklist score) and comment
16	Q. Hao et al. (2018). Clopidogrel plus aspirin versus aspirin alone for acute minor ischaemic stroke or high risk transient ischaemic attack: systematic review and meta-analysis. <i>BMJ</i> , 363: k5108	SR, international, included 3 RCTS included pateints with minor stroke (NIHSS≤3) or high risk TIA((ABCD2≥4) within 24 hours from symptoms onset, 1 north American, 1 Chinese, 1international, n=10447.	DAPT (Aspirin +Clopidogrel) n=5217 vs Aspirin, n=5230.	Non-fatal recurrent stroke, all cause mortality, non-fatal SICH, major/moderate non-fatal extracranial haemorrhage.	DAPT reduce the risk of non- fatal recurrent stroke (relative risk 0.7,95%Cl 0.61- 0.8,absolute risk reduction1.9%); all cause mortality: no significant difference (1.27,95%Cl 0.73- 2.23); Mayjor/moderate non- fatal extracranial haemorrhage: DAPT likely to increase the risk of haemorrhage (1.71, 95%Cl 0.92-3.2, absolute risk increase 0.2%); SICH (non- fatal) rate: no significant difference (1.27 95%Cl 0.55- 2.89).	++ Clear inclusion and exclusion criteria for studies selected, and clear statistic plan. All 3 RCTS compared DAPT (the loading strategies and duration are different) with Aspirin (dosage different in each study) no study compared DAPT against Clopidogrel, which is now the commonly used antiplatelet for secondary stroke prevention. Study population heterogeneous, subgroup stroke population such as large vessel atherosclerotic, small vessel

NB Any discrepancies between reviewers in evidence quality and comment were discussed at the corresponding evidence review meeting TIA = Transient Ischaemic Attack, DAPT = Dual antiplatelet therapy, SICH = Symptomatic Intracranial Haemorrhage, ICH = Intracerebral haemorrhage, HTPR = high ontreatment platelet reactivity, GI = gastrointestinal, MACE = major adverse cardiovascular event, HCPR = high on-clopidogrel platelet reactivity, SR = systematic review, MA =

meta-analysis, RCT = randomised controlled trial, IPDMA = individual patient data meta-analysis, MDT = multidisciplinary team, PICO = patient/population, intervention, comparison and outcomes, OR = odds ratio, CI = confidence interval, QoL = quality of life, ADL = activities of daily living, OR = odds ratio, RR = relative risk, aOR = adjusted

odds ratio, cOR = crude odds ratio, CI = confidence interval, RoB = risk of bias, I2 = heterogeneity statistic.

Question 13 evidence tables

Question 13: What is the best short term antiplatelet regimen for vascular prevention after TIA or Minor Stroke?

NATIONAL CLINICAL **GUIDELINE FOR STROKE**

for the United Kingdom and Ireland

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
16	Q. Hao et al. (2018). Clopidogrel plus aspirin versus aspirin alone for acute minor ischaemic stroke or high risk transient ischaemic attack: systematic review and meta-analysis. <i>BMJ</i> , 363: k5108	Systematic review and meta- analysis. Three trials included (FASTER 2007, CHANCE 2013, POINT 2018), with a total of 10 301 patients.	Dual antiplatelet therapy (DAPT) with Aspirin and Clopidogrel compared with Aspirin alone in patients with acute (<24hours) non- cardioembolic minor ischaemic stroke (NIH<=3) or TIA. DAPT continued for 90 days in FASTER and POINT, and 21 days in CHANCE.	Non-fatal recurrent stroke; all cause mortality; major or moderate non- fatal extracranial haemorrhage. Also functional outcome; quality of life; recurrent TIA; minor bleeding; Myocardial Infarction; recurrent stroke (fatal and non-fatal).	Relative risk of non-fatal recurrent stroke: 0.70 (95%CI: 0.61 - 0.80); absolute risk reduction of 1.9%. Relative risk of major or moderate haemorrhage: 1.71 (95%CI: 0.92 - 3.20); absolute risk increase of 0.2%. No difference in mortality. Most benefit occurred within 10 days, and no important reduction in recurrent stroke after 21 days.	++ High quality evidence regarding risk reduction in non-fatal recurrent stroke. Moderate quality evidence regarding increase risk of haemorrhage due to wide confidence intervals, and POINT was stopped early due to an increased risk of major haemorrhage which may result in an overestimation of this risk.
17	N. A. Hilkens et al. (2018). Early time course of major bleeding on antiplatelet therapy after TIA or ischemic stroke. <i>Neurology,</i> 90(8): e683-e689	Post hoc MA of 6 international RCT (1989-2006). On treatment analysis only. n=45,195. Median duration from symptom onset to randomisation varied from 15 - 126 days between trials. Ischaemic stroke population; 11% TIA. Possible cardioembolism excluded. Mean age 65.5years, 63% male.	Single or dual antiplatelet therapy (DAPT).	Incidence rate of major haemorrhage (per trial definitions) stratified by time.	Risk of major bleeding highest in first 30 days for all treatment regimens. Dual antiplatelet (aspirin + clopidogrel) was associated with more than 2-fold increased risk of major bleeding (specifically GI bleeding) in first 30 days in comparison to either aspirin or clopidogrel monotherapy. Risk of ICH is stable over time.	++ High quality evidence of early bleeding risk after antiplatelet initiation after stroke / TIA
17	N. A. Hilkens et al. (2018). Early time course of major bleeding on antiplatelet therapy after TIA or ischemic stroke. <i>Neurology,</i> 90(8): e683-e689	post hoc from 6 randomised trials. 45,195 patients, with TIA or non-cardioembolic "stroke".	SAP and DAP in various combinations e.g. C vs A in CAPRIE; A+D v C in Profess etc. etc. CAPRIE was only SAP only study.	Bleeding incidence stratified by time from randomisation.	DAPT increases risk of major and GI bleeding, but not incidence of ICH.	+

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
18	S. C. Johnston et al. (2016). Ticagrelor versus Aspirin in Acute Stroke or Transient Ischemic Attack. <i>New</i> <i>England Journal of</i> <i>Medicine,</i> 375:1 35-43	Multi-centre Rand. DB double- dummy parallel-group trial, sponsored by Pahrma (AZ). Subjects >=40 years with non- severe (NIHSS=<5) or high-risk TIA (ABCD2 >=4) or symptomatic intra/extra-cranial stenosis. Randomised within 24 hours, existing CT or MRI. N= 13,199 randomised	Ticagrelor 180mg loading followed by 90 mg/BD plus loading and daily aspirin placebo (N=6589) or Aspirin (loading Aspirin 300, daily 100mg) and Ticagrelor loading and twice daily placebo (N=6610) for duration of 90 days (and 30 days f/u)	Primary outcome: time to first occurrence of either stroke (ischemic or bleed), or MI or death within 90 days. Secondary outcome: time to ischemic stroke (if primary outcome significant)	Primary endpoint event in 6.7% of Ticagrelor and 7.5% of Aspirin group (HR: 0.89, 95%Cl 0.78 - 1.01; P=0.07). On the basis of hierarchical testing plan, all analysis of secondary end points were considered exploratory and were not used to make conclusions. Main secondary end point was ischemic stroke that occurred in 5.8% of Ticagrelor group and 6.7% of the Aspirin group	++ Internal validity: 1.9; overall assessment: high quality.
19	C. S. Kwok et al. (2015). Efficacy of Antiplatelet Therapy in Secondary Prevention Following Lacunar Stroke: Pooled Analysis of Randomized Trials. <i>Stroke,</i> 46(4): 1014- 1023	Meta analysis. Lacunar strokes. 17 Randomised Trials N 42,234 Follow up 4 weeks to 3.5 years looked at Ticlopidine, Cilostazol, Dipyridamole vs Aspirin. Looked at minor stroke and TIA.	Observational Metanalysis of Trials of Single vs DAPT.	Any single antiplatelets is adequate. No basis for long term DAPT.	No evidence for DAPT as 2nd prevention in lacunar strokes.	++ Methodology seems fine.
19	C. S. Kwok et al. (2015). Efficacy of Antiplatelet Therapy in Secondary Prevention Following Lacunar Stroke: Pooled Analysis of Randomized Trials. <i>Stroke,</i> 46(4): 1014- 1023	Systematic review & meta- analysis of randomised control trials (17 randomised control trials of which 14 were double- blind) N=42,200; f/u ranged 4 weeks to 3.5 years.	Meta-analysis of the available data.	Primary outcome: stroke recurrence (ischaemic or haemorrhagic). Secondary outcome: 1)recurrent ischaemic stroke 2) any stroke, MI and death.	Compared with placebo, single anti-platelet reduced risk of any recurrent stroke (risk ratio 0.77), and ischaemic stroke (RR 0.48), but not stroke, MI, death (RR 0.89). Dual antiplatelet, did not consistently confer clear benefit over monotherapy (any stroke RR 0.83, ischaemic stroke RR 0.80, composite outcome RR 0.90.	++ Internal validity: 1.11; overall assessment: high quality.

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
20	M. Lee et al. (2017). Antiplatelet Regimen for Patients with Breakthrough Strokes while on Aspirin: A Systematic Review and Meta-Analysis. <i>Stroke,</i> 48(9): 2610-2613	Systematic review and meta- analysis. 8723 patients included from five studies: 2 multicentre/national registries, and 3 RCTs.	Continuation of Aspirin vs switch to another antiplatelet (solely/mostly Clopidogrel in two studies and ticagrelor in one RCT) or addition of another antiplatelet (Clopidogrel in two RCTs).	Primary outcome: MACE (Major Adverse Cardiovasulcar Event). Secondary outcome: recurrent ischaemic or haemorrhagic stroke.	MACE (5 studies): HR of 0.68 (95% CI 0.54 -0.85) for addition of or switch to another antiplatelet. Recurrent stroke (4 studies): HR of 0.70 (95% CI 0.54 - 0.92) for addition of or switch to another antiplatelet.	- Limited electronic search. Heterogenous studies of mixed quality.
20	M. Lee et al. (2017). Antiplatelet Regimen for Patients with Breakthrough Strokes while on Aspirin: A Systematic Review and Meta-Analysis. <i>Stroke</i> , 48(9): 2610-2613	Systematic review and meta- analysis. 8723 patients included from five studies: 2 multicentre/national registries, and 3 RCTs.	Continuation of Aspirin vs switch to another antiplatelet (solely/mostly Clopidogrel in two studies and ticagrelor in one RCT) or addition of another antiplatelet (Clopidogrel in two RCTs).	Primary outcome: MACE (Major Adverse Cardiovascular Event). Secondary outcome: recurrent ischaemic or haemorrhagic stroke.	MACE (5 studies): HR of 0.68 (95% CI 0.54 -0.85) for addition of or switch to another antiplatelet. Recurrent stroke (4 studies): HR of 0.70 (95% CI 0.54 - 0.92) for addition of or switch to another antiplatelet.	- Limited electronic search. Heterogenous studies of mixed quality.
21	S. T. Lim et al. (2020). Platelet function/reactivity testing and prediction of risk of recurrent vascular events and outcomes after TIA or ischaemic stroke: systematic review and meta-analysis. <i>Journal</i> <i>of Neurology</i> , 267(10): 3021-3037	SR and MA, international, SR 34 studies, MA 20 studies(n=4989) in acute ischaemic stroke patients who are on antiplatelet treatment (single/dual with any combination) and had platelet function/reactivity test.	None.	Recurrent vascular events/neurological outcomes following index ischaemic stroke/TIA.	SR: Antiplatelet–HTPR prevalence was 3–65% with aspirin, 8–56% with clopidogrel, 1.8–35% with aspirin–clopidogrel therapy; MA: increased risk of the composite primary outcome of recurrent stroke/TIA, myocardial infarction/ vascular death in patients with vs. those without antiplatelet– HTPR on any antiplatelet regimen (OR = 2.93, 95% CI 1.90–4.51 with high heterogeneity between	(+) clear inclusion and exclusion criteria, and statistic plan. A significant proportion of studies included are cross- sectional or case control studies. Patients' demographics including ethnicity, the methods and timing for platelet function/reactivity test, definitions of HTPR are not clear. High heterogeneity in studies. Small numbers.

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
					studies (I2 = 80.7%, p < 0.001); and recurrent ischaemic stroke/ TIA (OR 2.43, 95% CI 1.51–3.91). The risk ≥ 2 fold in the group with antiplatelet- HTPR.	
21	S. T. Lim et al. (2020). Platelet function/reactivity testing and prediction of risk of recurrent vascular events and outcomes after TIA or ischaemic stroke: systematic review and meta-analysis. <i>Journal</i> of Neurology, 267(10): 3021-3037	Systematic review up to May 2019.	TIA/"Stroke" patients>18years who had platelet function/reactivity testing and then follow up	Primary outcome (composite of recurrent stroke/TIA, MI or vascular death). Secondary was recurrent stroke/TIA, severe stroke (NIHSS>16) or mRs3 or greater.	Alarming, and confusing. Antiplatelet HTPR was 3-65% on A, 8-56% on C, but 1.8-35% on A+C. Higher risk of composite primary outcome (OR 2.93 (1.9-4.51) and recurrent ischaemic stroke/TIA (2.43 (1.51-3.91) in those with anti-platelet-HTPR etc.	Strong enough for this to become a more routine part of clinical practice and for a big trial.
22	C. H. Tan et al. (2021). Cilostazol for secondary stroke prevention: Systematic review and meta- analysis. <i>Stroke and Vascular Neurology,</i> 6(3): 410-423	Systemic review. Meta analysis 18 RCTs N 11,429 East Asia most. Cilostazol vs Aspirin/Clopi/Dipyridamole	18 Studies. 11,429 pts Excluded cardoembolic strokes. Studies with C Vs Antiplatelets. C was given for 4 weeks to several years	Cilostazol.	Cilostazol has less haemorrhage. Reduced Stroke/ICH/MI Vasc deaths. P < 0.0001 However Mortality neutral. Functional neutral. No comparison with single agent Clopidogrel which was the key test.	++ Methodology seems fine.
22	C. H. Tan et al. (2021). Cilostazol for secondary stroke prevention: Systematic review and meta- analysis. <i>Stroke and Vascular Neurology,</i> 6(3): 410-423	SR&MA. 18 RCT, n=11,429 (2000- 2018). All Asia apart from one study in UK (only 83 participants, randomised up to 4 years from event). Patients primarily had ischaemic stroke, unclear what proportion were non-disabling. Majority of trials compared long term (No Suggestions) treatment.	Cilostazol as either antiplatelet monotherapy or combination antiplatelet with either aspirin or clopidogrel.	Primary outcome - ischaemic stroke recurrence. Safety outcome - ICH and major haemorrhage.	Cilostazol as monotherapy was superior to aspirin for the primary outcome. Cilostazol monotherapy has not been compared with clopidogrel. Insufficeint data on cilostazol as combination therapy. Analysis of short term Cilostazol treatment was underpowered.	+ Limited evidence for short term duration of treatment or follow-up.

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
23	Y. Wang et al. (2019). Ticagrelor plus aspirin versus clopidogrel plus aspirin for platelet reactivity in patients with minor stroke or transient ischaemic attack: open label, blinded endpoint, randomised controlled phase II trial. <i>Bmj</i> , 365: 12211	RCT, Chinese study, n=675, Chinese age 40-80, minor AIS NIHSS≤3), or TIA (ABCD2≥4, or ≥50% stenosis of cervical or intracranial vessels that could account for the presentation within 24 hours of the index event.	Ticagreor+Aspirin(n=3 36) vs Clopidogrel +Aspirin(n=339).	The proportion of patients with high platelet reactivity at 90 days, and major bleeding.	High platelet reactivity found in 35 /280 (12.5%) in the ticagrelor/aspirin group, and in 86 /290 (29.7%) in the clopidogrel/aspirin group at 90 days (risk ratio 0.40; 95% CI 0.28 to 0.56; P<0.001). No significant difference in the occurrence of major bleeding (1.5% vs1.2%, hazard ratio 1.27; 95% CI0.34 to 4.72). No significant difference in the rates of recurrent strokes in 1 year (6.3%vs8.8%, hazard ratio 0.70; 95% CI 0.40 to 1.22; P=0.20).	+ Phase 2 study, open label, terminated early because of the interim analysis felt achieving a prespecified threshold for efficacy (P<0.005). Not all recruited patients completed follow-up.
23	Y. Wang et al. (2019). Ticagrelor plus aspirin versus clopidogrel plus aspirin for platelet reactivity in patients with minor stroke or transient ischaemic attack: open label, blinded endpoint, randomised controlled phase II trial. <i>Bmj</i> , 365: 12211	Randomised, controlled trial	Ticagrelor (180 mg loading dose, 90 mg twice daily thereafter) or clopidogrel (300 mg loading dose, 75 mg daily thereafter) on a background of aspirin (100 mg daily for the first 21 days) within 24 hours of symptom onset.	Primary outcome was the proportion of patients with high platelet reactivity at 90 days.	At 90 days, high platelet reactivity occurred in 35 (12.5%) of 280 patients in the ticagrelor/aspirin group and 86 (29.7%) of 290 patients in the clopidogrel/aspirin group (risk ratio 0.40; 95% confidence interval 0.28 to 0.56; P<0.001. There was no significant effect on stroke in general. Patients with large artery atherosclerosis in the ticagrelor/aspirin group had a lower stroke recurrence at 90 days than those in the clopidogrel/aspirin group (6.0% v 13.1%; hazard ratio 0.45, 95% confidence interval 0.20 to 0.98; P=0.04).	This was a high quality study tackling the important issue of copidogrel resistance. It provides good evidence to suggest that CYP2C19 loss-of- function allele may be an important contributor to the efficacy of secondary prevention and that the use of ticagrelor may circumvent this problem.

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
24	S. C. Johnston et al. (2020). Ticagrelor and Aspirin or Aspirin Alone in Acute Ischemic Stroke or TIA. <i>New England Journal</i> of Medicine, 383:3 207-217	RCT NIHSS 5 or less or TIA. No thrombolysis or thrombectomy. N 5523	30 days of T+A or P+A (T Ticagrelor P Placebo) in those not thrombolysed or thrombectomy. Non cardioemboic ischameic stroke	PRIMARY Stroke/Death < 30 days SECONDARY First Subsequent AIS, Disability at D30	AIS Acute ischaemic stroke T+A AIS 276 A+P AIS 345 P 0.004 Severe Bleeding 28 (T+A) and 7 (P+A) Diability neutral. Composite stroke or death lower with T+A	Useful study. Methodology sound.
24	S. C. Johnston et al. (2020). Ticagrelor and Aspirin or Aspirin Alone in Acute Ischemic Stroke or TIA. <i>New England Journal</i> <i>of Medicine,</i> 383:3 207-217	Multi-centre Rand. Double-blind placebo-controlled parallel-group trial, sponsored by Pharma (AZ). Subjects >=40 years with mild- moderate (NIHSS=<5) or high-risk TIA (ABCD2 >=6) or symptomatic intra/extra-cranial stenosis (>=50%). Randomised within 24 hours (included wake-up stroke or within 24 hours from last seen normal), CT or MRI excluded bleed. N= 11,016 randomised	Either loading Ticagrelor 180mg or placebo ASAP after randomisation; followed by Ticagrelor 90mg or placebo BD. In addition they received loading Aspirin 300 to 325mg followed by Aspirin 75 to 100mg daily for duration of 30 days. N=5523 to ticagrelor & as	Primary outcome: first occurrence of stroke (ischemic or bleed or undetermined type), or death in a time-to-first- event analysis within 30 days. Secondary outcome: first subsequent ischemic stroke (expressed as hazard ratio) and the disability (measured on	Primary outcome event in 5.5% of Ticagrelor-aspirin (n=303) and 6.6% of Aspirin group (HR: 0.83, 95%Cl 0.71 - 0.96; P=0.02). The first secondary outcome, subsequent ischemic stroke, occurred in 276 (5.0%) in Ticagrelor-aspirin group and 345 (6.3%) in the Aspirin group (HR 0.79, 95%Cl 0.68% to 0.93%; p=0.004). The other secondary outcome of overall disability did not differ significantly between two groups.	++ Internal validity: 1.9; overall assessment: high quality.
25	S. C. Johnston et al. (2018). Clopidogrel and Aspirin in Acute Ischemic Stroke and High-Risk TIA. <i>New</i> <i>England Journal of</i> <i>Medicine</i> , 379:3 215- 225	RCT, parallel group, double blind, placebo-controlled trial (open label aspirin). 2010-2017. n=4881. 269 sites, 10 countries (83% USA). Minor ischaemic stroke or high-risk TIA, randomised within 12 hours from symptom onset. Non consensus TIA, suspected cardioembolism and patients for acute revascularization therapies excluded.	Clopidogrel 600mg loading day 1 -75 mg day 2-90 + open label aspirin vs Placebo (same appearance and taste) +open label aspirin	Primary efficacy outcome: major ischaemic event at 90 days (ischaemic stroke, MI, death from ischaemic vascular causes). Primary safety outcome: major haemorrhage. Multiple secondary efficacy and safety outcomes.	Reduction in primary outcome at 90 days in intervention group versus control (5% vs 6.5%; HR0.75(0.59-0.95)); driven entirely by reduction in ischaemic stroke. Increased risk major bleeding at 90 days 0.9% vs 0.4%; HR 2.32 (1.10- 4.87). No difference in rates of ICH, difference in bleeding events driven by non-fatal extracranial haemorrhage.	++ Well conducted RCT, predominantly white ethnicity. Trial halted early due to rate of bleeding events in intervention group but efficacy endpoint had been met.

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
	V. Alakbarzade et al (2020). High on- clopidogrel platelet reactivity in ischaemic stroke or transient ischaemic attack: Systematic review and meta-analysis.	Systematic review and meta- analysis.	Clopidogrel in IS/TIA.	Prevalence of HCPR in IS/TIA, and correlation with clinical outcomes and genetics.	In 21 studies prevalence of HCPR was 28% (24-32, 0.001). IClopidogrel non-responders did worse, and IS/TIA carriers of CYP2C19*2 or *3 loss-of- function alleles had higher risk of HCPR compared to wild type.	++
26	V. Alakbarzade et al. (2020). High on- clopidogrel platelet reactivity in ischaemic stroke or transient ischaemic attack: Systematic review and meta-analysis. <i>J Stroke</i> <i>Cerebrovasc Dis</i> , 29:7 104877	Systematic review and meta- analysis. 21 studies included with 4312 patients.	Observational study, looking at 'high on- clopidogrel platelet reactivity' (HCPR) in patients with Ischaemic Stroke or TIA (IS/TIA).	Primary endpoint: HCPR pooled proportion, and outcome, in clopidogrel- treated IS/TIA. Secondary endpoint: association between CYP2C19 loss of function allele carrier status and HCPR in IS/TIA.	Pooled prevalence of HCPR was 28% (95%CI: 24-32%). Patients with HCPR had a poorer outcome compared to Clopidogrel responders (RR = 2.09, 1.61-2.70). IS/TIA carriers of CYP2C19 loss of function alleles had a higher risk of HCPR (RR=1.69, 95% CI: 1.47-1.95).	++ High quality meta-analysis, but the quality of studies themselves is variable and there is highly significant heterogeneity, including the laboratory tests used and the definitions of HCPR as well as clinical and demographic factors.
26	V. Alakbarzade et al. (2020). High on- clopidogrel platelet reactivity in ischaemic stroke or transient ischaemic attack: Systematic review and meta-analysis. <i>J Stroke</i> <i>Cerebrovasc Dis</i> , 29:7 104877	RCT Looked at 11,000 screened 6412 enrolled Chinese pts CYP2C19 loss of function carriers with AIS . CYP2C19 produces active Clop. Median ag 64 1/3rd female. metabolite of clopidogrel	Half assigned Ticagrelor or Clopi gp. Apirin 21 days	Risk of stroke at 90 days events Each group N 3200 . At 90 days AIS 191 Ticagrelor and 243 Clopi P=0.008 Bleeding T 170 vsC 80	Sign reduction in AIS but sig increase in bleeds.	+ Very specific treatment group. Otherwise methodology seems sound.
27	Y. Wang et al. (2021). Ticagrelor versus Clopidogrel in CYP2C19 Loss-of-Function Carriers with Stroke or TIA. <i>New England</i> <i>Journal of Medicine</i> , :	RCT, parallel group, double blind, placebo controlled trial. N=6412. Minor stroke(80%) / high risk TIA (20%) patients within 24 hours of symptom onset who are carriers of CYP2C19 loss-of function allele	Ticagrelor (+placebo Clopidogrel) vs Clopidogrel (+placebo Ticagrelor) x 90 days. All patients also given Aspirin x 21 days.	Primary efficacy outcome: New stroke at 90 days (ischaemic or haemorrhagic). Primary Safety Outcome: Severe / Moderate Bleeding (GUSTO criteria) at 90	Modest reduction in recurrent stroke in Ticagrelor group vs Clopidogrel group(6% vs 7.6%; HR 0.77; 0.64-0.94). No significant difference in mod/severe bleeding but	+ Poor method of randomisation. 11% drop out intervention arm, 8% control. All patients completed FU and included in ITT analysis. 98% Han Chinese

Ref	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN
ID						checklist score) and comment
		on POC testing. 202 sites, all in China. 2019-2021		days. Multiple secondary efficacy and safety outcomes.	more overall bleeding events in Clopidogrel group.	population limits generalisability. Also dependent on proof of concept analysis of CYP2C19 allele status - testing unlikely to be widely available and carrier status less prevalent in other ethnicities. 9 month follow up is ongoing.