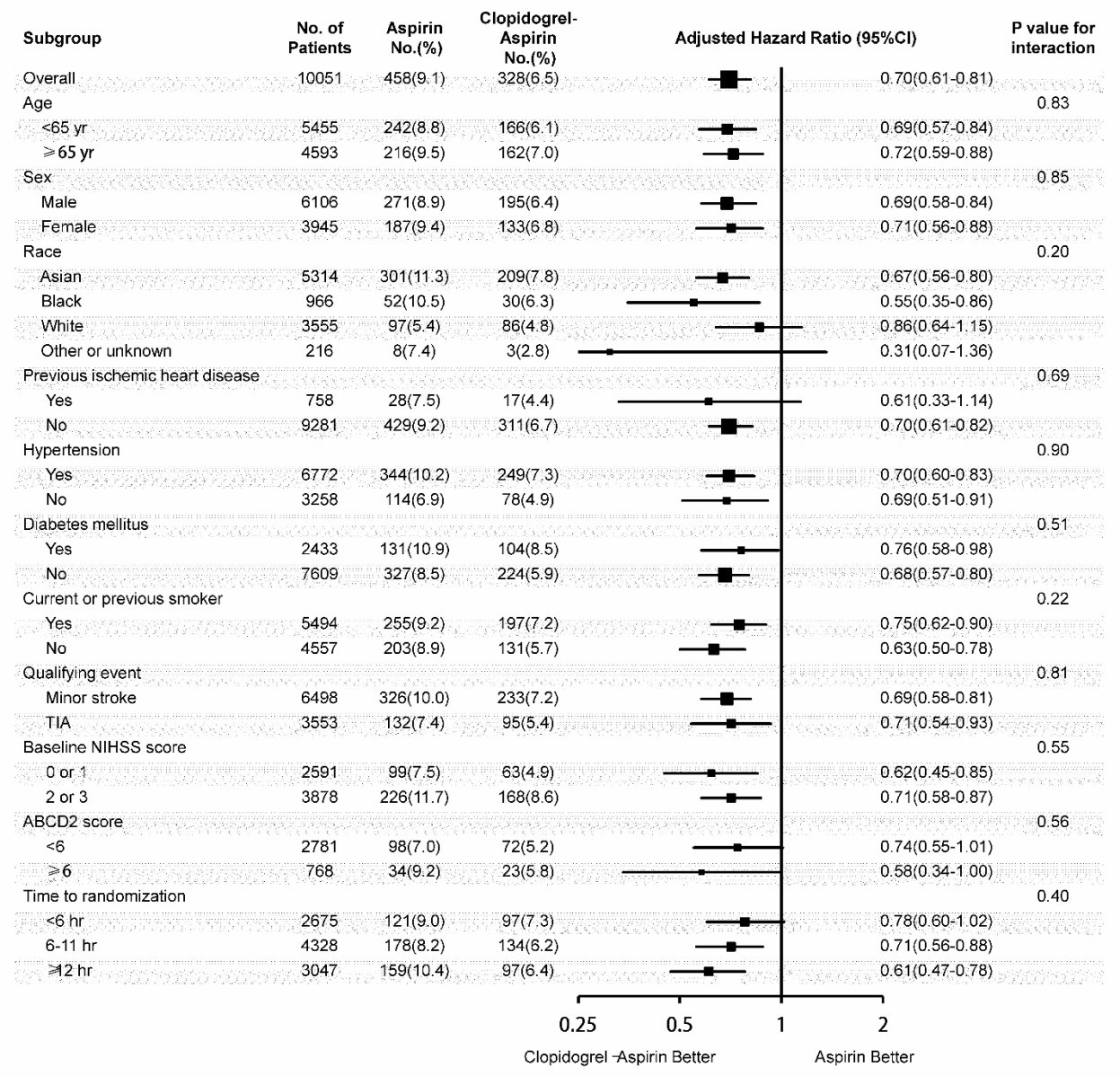
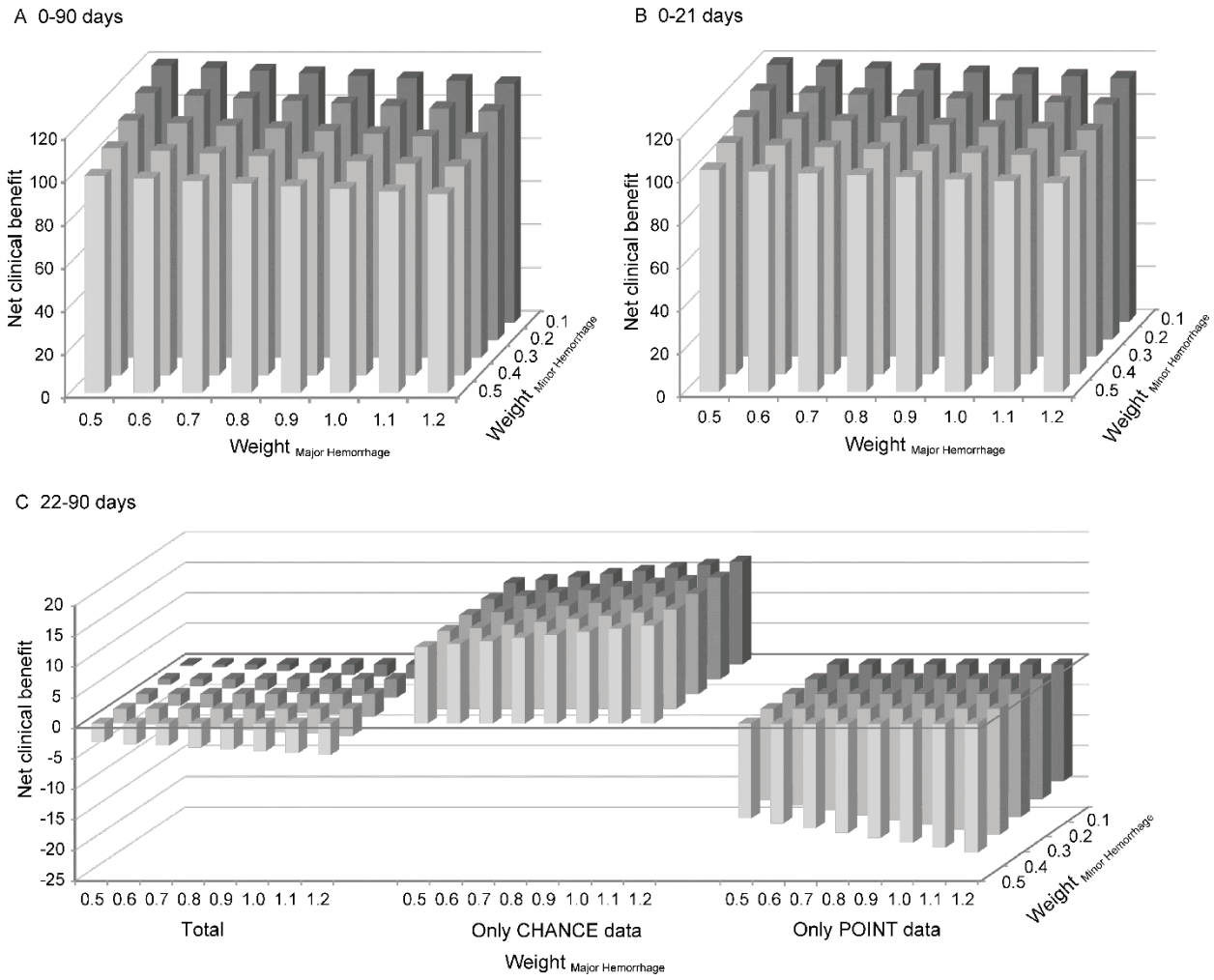
Supplementary Online Content

Pan Y, Elm JJ, Li H, et al. Outcomes associated with clopidogrel-aspirin use in minor stroke or transient ischemic attack: a pooled analysis of the Clopidogrel in High-Risk Patients With Acute Non-Disabling Cerebrovascular Events (CHANCE) and Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke (POINT) Trials. *JAMA Neurol*. Published online August 19, 2019. doi:10.1001/jamaneurol.2019.2531

This supplementary material has been provided by the authors to give readers additional information about their work.



eFigure 1. Hazard ratios for the primary efficacy outcome in prespecified subgroups. All the models were adjusted for the same covariates as the second model in primary analyses. n (%) referred to the number of subjects with a primary efficacy outcome event and the percent of the corresponding subgroup. Abbreviations: $ABCD^2$, Age, Blood pressure, Clinical features, Duration of symptoms, and presence of Diabetes; NIHSS, NIH Stroke Scale.



eFigure 2. Sensitivity analysis of net clinical benefit considering minor hemorrhage. Net clinical benefit was calculated as: Net Benefit=(Major Ischemic Event $_{\text{Aspirin Group}}$- Major Ischemic Event $_{\text{Clopidogrel-Aspirin Group}}$)-Weight $_{\text{Major Hemorrhage}}$×(Major Hemorrhage $_{\text{Clopidogrel-Aspirin Group}}$ - Major Hemorrhage $_{\text{Aspirin Group}}$) -Weight $_{\text{Minor Hemorrhage}}$×(Minor Hemorrhage $_{\text{Clopidogrel-Aspirin Group}}$ - Minor Hemorrhage $_{\text{Aspirin Group}}$). The weights account for the effects of a major (Weight $_{\text{Major Hemorrhage}}$) or minor (Weight $_{\text{Minor Hemorrhage}}$) hemorrhage compared with a major ischemic event. Major ischemic event included ischemic stroke, myocardial infarction, or death from ischemic vascular causes.

eTable 1. Characteristics of the CHANCE and POINT trials

Trial:	**CHANCE**	**POINT**
Published year:	2013	2018
Study design:	Randomized, double-blind, placebo-controlled trial	Randomized, double-blind, placebo-controlled trial
Time of enrollment:	From October 2009 to July 2012	From May 2010 to December 2017
Region of study cites:	114 sites in China	269 sites in 10 countries in North America, Europe, Australia, and New Zealand
Sample size:	5170	4881
Study Population:		
Ethnicity:	100% Asian	3.0% Asian; 75.0% White; 20.4% Black; 1.5% Other
Patients:	TIA ($ABCD^2$≥4): 27.9%; Minor stroke (NIHSS≤3): 72.1%	TIA ($ABCD^2$≥4): 43.2%; Minor stroke (NIHSS≤3): 56.8%
Time from onset to randomization:	≤24 h	≤12 h
Intervention group:	CLP: d1: 300 mg; d2-d90: 75 mg/d; ASA: d1: 75-300 mg; d2-d21: 75 mg/d	CLP: d1: 600 mg; d2-d90: 75 mg/d; ASA: d1-d90: 50-325 mg/d
Control group:	ASA: d1: 75-300 mg; d2-d21: 75 mg/d	ASA: d1-d90: 50-325 mg/d
Time of outcome:	Day 90	Day 90
Primary efficacy outcome:	Stroke: 8.2% vs. 11.7%; HR: 0.68(0.57-0.81), p<0.001	Stroke+MI+Cardiovascular death: 5.0% vs. 6.5%; HR: 0.75(0.59-0.95), p=0.02
Secondary efficacy outcome:	Stroke+MI+Cardiovascular death: 8.4% vs. 11.9%; HR: 0.69(0.58-0.82), p<0.001	Stroke: 4.8% vs. 6.4%; HR: 0.74(0.58-0.94), p=0.01
Primary safety outcome:	Moderate-to-Severe bleeding：0.4% vs. 0.3% HR: 0.84(0.30-2.31), p=0.73	Major hemorrhage：0.9% vs. 0.4% HR: 2.32(1.10-4.87), p=0.02

Abbreviations: $ABCD^2$, Age, Blood pressure, Clinical features, Duration of symptoms, and presence of Diabetes; NIHSS, NIH Stroke Scale; CLP, clopidogrel; ASA, aspirin; MI, myocardial infarction; HR, hazard ratio; TIA, transient ischemic attack; d1, Day 1; d2-d90, Day 2- Day 90.

eTable 2. Baseline characteristics of the patients

Characteristic	Total (n=10051)	Aspirin (n=5035)	Clopidogrel-aspirin (n=5016)	p value
Age (yr), median (IQR)	63.2(55.0-72.9)	63.0(55.0-72.7)	63.6(55.0-73.0)	0.16
Female, No. (%)	3945(39.2)	1996(39.6)	1949(38.9)	0.42
Race, No. (%)				0.94
Asian	5314(52.9)	2653(52.7)	2661(53.1)	
Black	966(9.6)	493(9.8)	473(9.4)	
White	3555(35.4)	1781(35.4)	1774(35.4)	
Other or unknown	216(2.1)	108(2.1)	108(2.2)	
Medical history, No. (%)				
Congestive heart failure	206/10044(2.1)	100/5032(2.0)	106/5012(2.1)	0.65
Known atrial fibrillation or flutter	145/10037(1.4)	66/5029(1.3)	79/5008(1.6)	0.27
Ischemic heart disease	758/10039(7.6)	373/5029(7.4)	385/5010(7.7)	0.61
Hypertension	6772/10030(67.5)	3363/5023(67.0)	3409/5007(68.1)	0.23
Diabetes mellitus	2433/10042(24.2)	1205/5033(23.9)	1228/5009(24.5)	0.50
Current or previous smoker, No. (%)	5494(54.7)	2765(54.9)	2729(54.4)	0.61
Qualifying event, No. (%)				1.00
Minor stroke	6498(64.7)	3255(64.6)	3243(64.7)	
TIA	3553(35.3)	1780(35.4)	1773(35.3)	
Median qualifying neurologic score (IQR)				
NIHSS for ischemic stroke	2(1-3)	2(1-3)	2(1-3)	0.30
$ABCD^2$ for TIA	5(4-5)	5(4-5)	5(4-5)	0.45
Time to randomization, No. (%)				0.95
<6 hr	2675/10050(26.6)	1346/5035(26.7)	1329/5015(26.5)	
6-11 hr	4328/10050(43.1)	2161/5035(42.9)	2167/5015(43.2)	
≥12 hr	3047/10050(30.3)	1528/5035(30.4)	1519/5015(30.3)	
Concomitant medication, No.(%)				
Anti-hypertensive agents [a]	3506/7683(45.6)	1735/3862 (44.9)	1771/3821 (46.3)	0.21
Lipid-lowing agents	5927/9878(60.0)	2961/4957(59.7)	2966/4921(60.3)	0.58

Abbreviations: IQR, interquartile range; NIHSS, NIH Stroke Scale; $ABCD^2$, Age, Blood pressure, Clinical features, Duration of symptoms, and presence of Diabetes; TIA, transient ischemic attack.

[a] Antihypertensive treatment was not collected in POINT before 2014.

eTable 3. Time course distribution of major ischemic events and major hemorrhages by treatment assignment

					No. of events			
Outcome	Treatment assignment	Total	1st week	2nd week	3rd week	4th week	5th week	6th week-day 90
Major ischemic events	ASA (n=5035)	458	330	36	21	10	5	56
	CLP+ASA(n=5016)	328	217	30	14	10	9	48
	Difference	130	113	6	7	0	-4	8
Major Hemorrhage	ASA (n=5035)	18	4	2	1	1	1	9
	CLP+ASA(n=5016)	30	10	4	2	1	3	10
	Difference	-12	-6	-2	-1	0	-2	-1

Abbreviations: ASA, aspirin; CLP, clopidogrel.