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PeriOperative ISchemic Evaluation-2 Trial

Aspirin in patients undergoing noncardiac surgery

PJ Devereaux, Population Health Research Institute, Hamilton, Canada
on behalf of POISE-2 Investigators

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Background

- Worldwide 200 million adults undergo noncardiac surgery annually
  - 10 million suffer major vascular complication
    - MI is most common
- Surgery – associated with platelet activation
  - thrombosis may be mechanism of periop MI

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Background

- Strong evidence aspirin prevents periop VTE
  - but physicians more commonly use anticoagulants
- Substantial variability in periop usage of aspirin
  - aspirin-naive patients and
  - patients taking aspirin chronically

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Methods

- Design – blinded 2 X 2 factorial RCT
  - aspirin vs placebo
  - clonidine vs placebo
- Eligibility criteria – undergoing noncardiac surgery, ≥45 yrs, at risk of vascular complication
- Excluded patients
  - BMS <6 weeks before surgery
  - DES <1 year before surgery
  - took aspirin within 72 hrs before surgery

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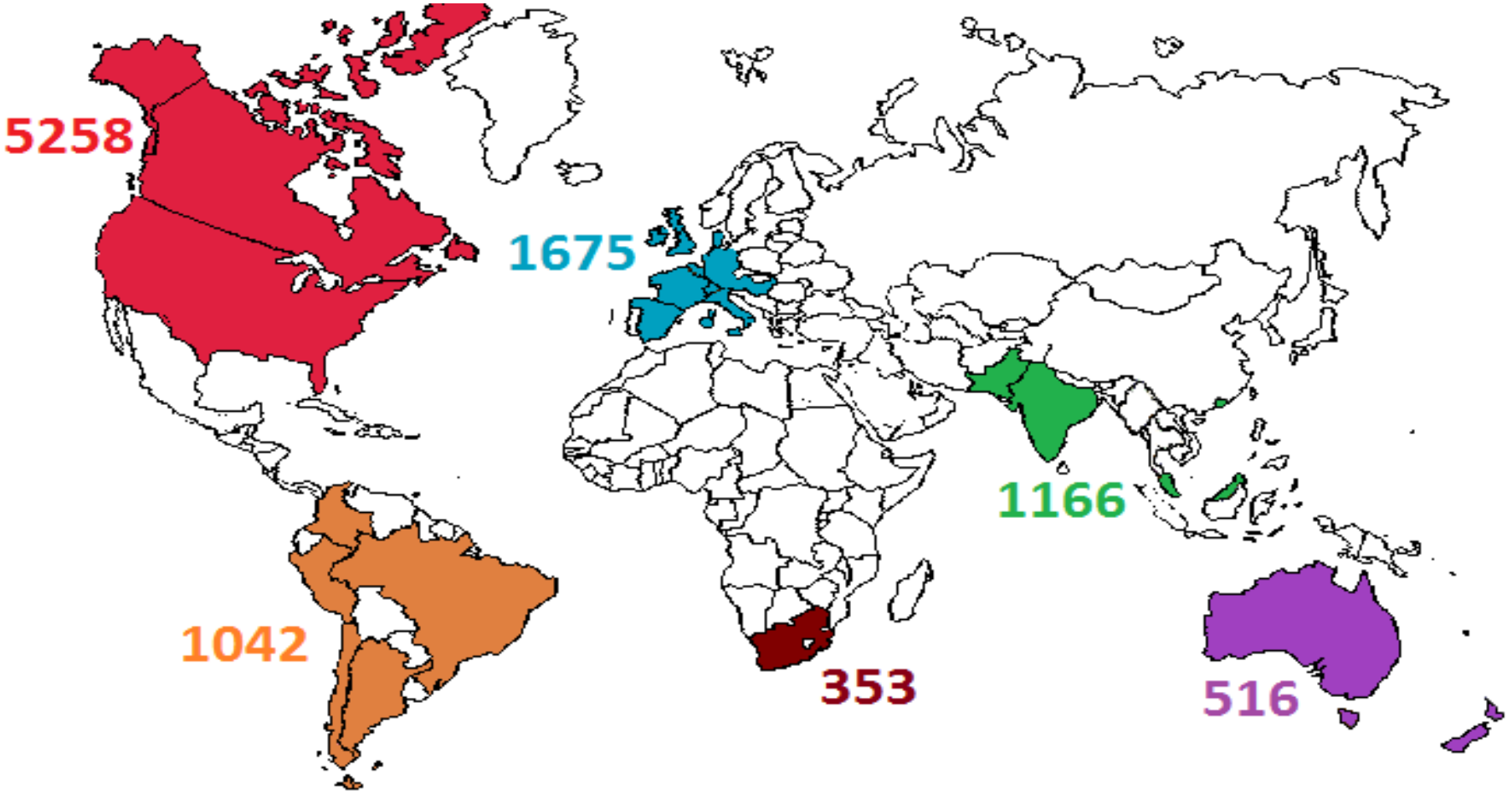
Methods

- 2 aspirin strata
  - Initiation Stratum (n=5628)
  - Continuation Stratum (n=4382)
- Intervention
  - aspirin/placebo (200 mg) just before surgery;
  - continued daily (100 mg) 30 days in Initiation Stratum and 7 days in Continuation Stratum
- Primary outcome
  - death or nonfatal MI at 30 days

Outcome definitions

- MI – universal definition of MI
- Life threatening bleed – bleeding event
  - emergent surgery, intracranial hemorrhage,
  - hypotension required inotrope or vasopressor, or
  - fatal outcome
- Major bleed – bleeding event
  - Hb ≤70 g/L and ≥2 units RBCs;
  - Hb drop ≥50 g/L and ≥2 units of RBCs;
  - ≥4 units of RBCs within 24 hr period;
  - intervention (e.g., embolization); or
  - retroperitoneal, intraspinal, or intraocular bleed

Recruitment by region



Follow-up complete on 99.9% of patients

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Preoperative characteristics

Characteristics	Aspirin (N=4998)	Placebo (N=5012)
Age – (mean yrs)	68.6	68.6
Male (%)	52.0	53.6
Known vascular disease	32.7	32.6
History of PCI	4.7	4.7

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Type of surgery and periop anticoagulant prophylaxis

Surgery	**Aspirin** (N=**4998**)	**Placebo** (**N=5012**)
Orthopedic	38.2	39.2
General	26.8	26.8
Urologic or gynecologic	16.7	16.8
Vascular	6.2	5.9
Other	12.1	11.3

65% of patients received prophylactic anticoagulant

1^{O} and 2^{O} outcome results

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Outcome	Aspirin (4998)	Placebo (5012)	HR (95% CI)	P
1^{O} outcome: death or nonfatal MI	351 (7.0)	355 (7.1)	0.99 (0.86-1.15)	0.92
2^{O} outcomes: death, MI, or stroke	362 (7.2)	370 (7.4)	0.98 (0.85-1.13)	0.80
death, MI, revasc, PE, DVT	402 (8.0)	407 (8.1)	0.99 (0.86-1.14)	0.90

No interaction with clonidine study drug

Tertiary outcome results

Outcome	Aspirin (4998)	Placebo (5012)	HR (95% CI)	P
Mortality	65 (1.3)	62 (1.2)	1.05 (0.74-1.49)	0.78
MI	309 (6.2)	315 (6.3)	0.98 (0.84-1.15)	0.85
Periph arterial thrombosis	13 (0.3)	15 (0.3)	0.87 (0.41-1.83)	0.71

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PE	33 (0.7)	31 (0.6)	1.07 (0.65-1.74)	0.79
DVT	25 (0.5)	35 (0.7)	0.72 (0.43-1.20)	0.20
acute kidney injury, dialysis	33 (0.7)	19 (0.4)	1.75 (1.00-3.09)	0.05

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Safety outcome results

Outcome	Aspirin (4998)	Placebo (5012)	HR (95% CI)	P
Major bleed	230 (4.6)	188 (3.8)	1.23 (1.01-1.49)	0.04
Life-threat bleed	87 (1.7)	73 (1.5)	1.19 (0.88-1.63)	0.26
Stroke	16 (0.3)	19 (0.4)	0.84 (0.43-1.64)	0.62

Strata and bleeding results

- Primary and 2nd outcome results similar in both aspirin strata
- Multivariable regression – life-threatening or major bleed independent predictor of periop MI
  - HR, 1.82; (95% CI, 1.40-2.36); P<0.001

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Conclusions

- Periop aspirin did not prevent death or MI
  - but increased risk of major bleeding
    - findings apply to both patients naive to aspirin and patients taking aspirin chronically
- Life-threatening and major bleeding
  - independent predictor of MI
    - may explain difference b/w non-operative & periop aspirin results

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P.J. Devereaux, M. Mrkobrada, D.I. Sessler, K. Leslie, P. Alonso-Coello, A. Kurz, J.C. Villar, A. Sigamani, B.M. Biccard, C.S. Meyhoff, J.L. Parlow, G. Guyatt, A. Robinson, A.X. Garg, R.N. Rodseth, F. Botto, G. Lurati Buse, D. Xavier, M.T.V. Chan, M. Tiboni, D. Cook, P.A. Kumar, P. Forget, G. Malaga, E. Fleischmann, M. Amir, J. Eikelboom, R. Mizera, D. Torres, C.Y. Wang, T. VanHelder, P. Paniagua, O. Berwanger, S. Srinathan, M. Graham, L. Pasin, Y. Le Manach, P. Gao, J. Pogue, R. Whitlock, A. Lamy, C. Kearon, C. Baigent, C. Chow, S. Pettit, S. Chrolavicius, and S. Yusuf, for the POISE-2 Investigators*