MONASH University

MONASH
Faculty of
Medicine,
Nursing and
Health Sciences

BARIATRIC SURGERY REGISTRY

IN-REGISTRY RANDOMIZED CONTROLLED TRIALS AND SURGICAL RESEARCH

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theAlfred

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PLATINUM BARIATRIC SURGERY REGISTRY SPONSOR

GORE Creative Technologies Worldwide

ETHICON PART OF THE Johnson&Johnson FAMILY OF COMPANIES Shaping the future of surgery

GOLD BARIATRIC SURGERY REGISTRY SPONSOR

Medtronic

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BARIATRIC SURGERY REGISTRY

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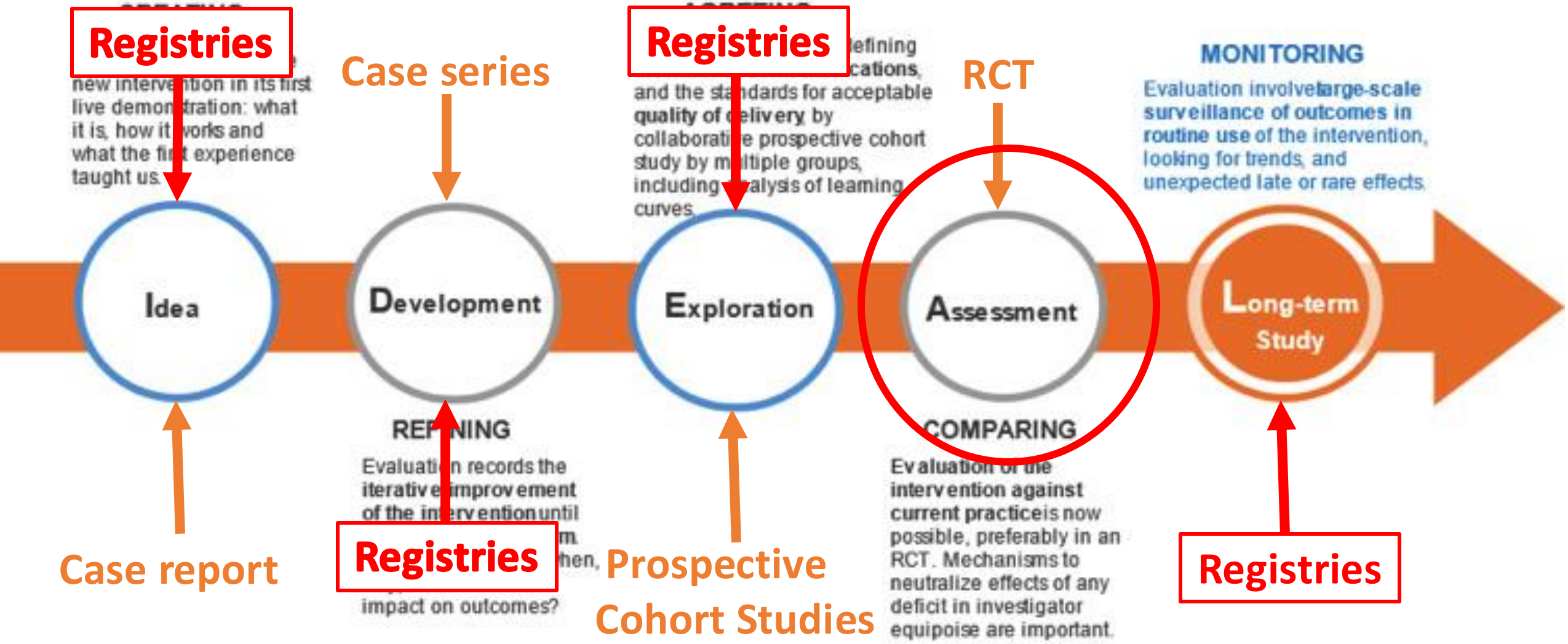
REGISTRIES

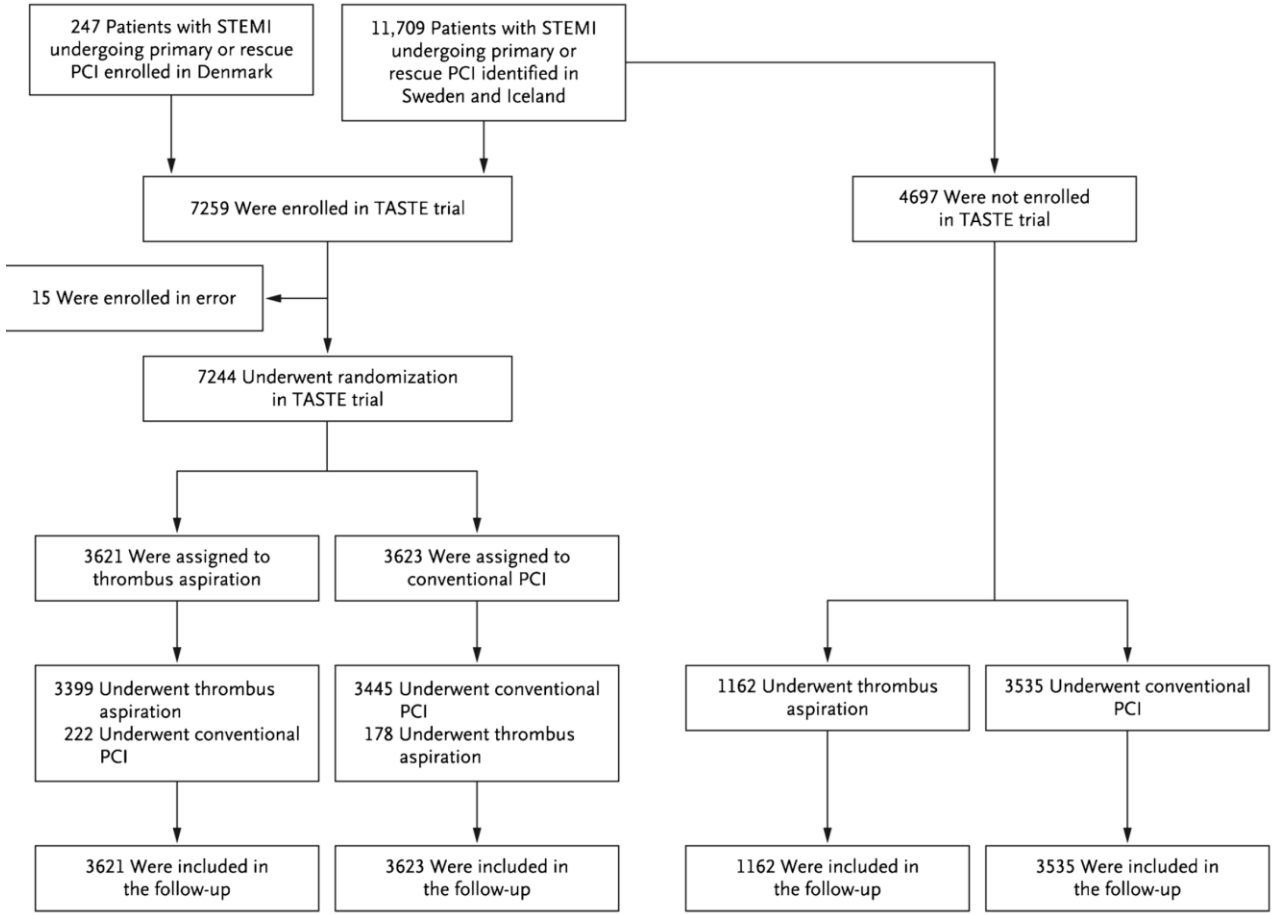
- Registries prospectively collate purposeful data
  - Heath Service
  - Clinical Quality
  - Disease or treatment
  - Product or device
- Whole population
  - Often rely on opt-out process
- Complete follow-up
  - Cross-linkages
  - PROMS/PREMS

The IDEAL evaluation pathway

defines the types of evaluation which are appropriate at successive stages in the life cycle of complex interventions



TASTE trial

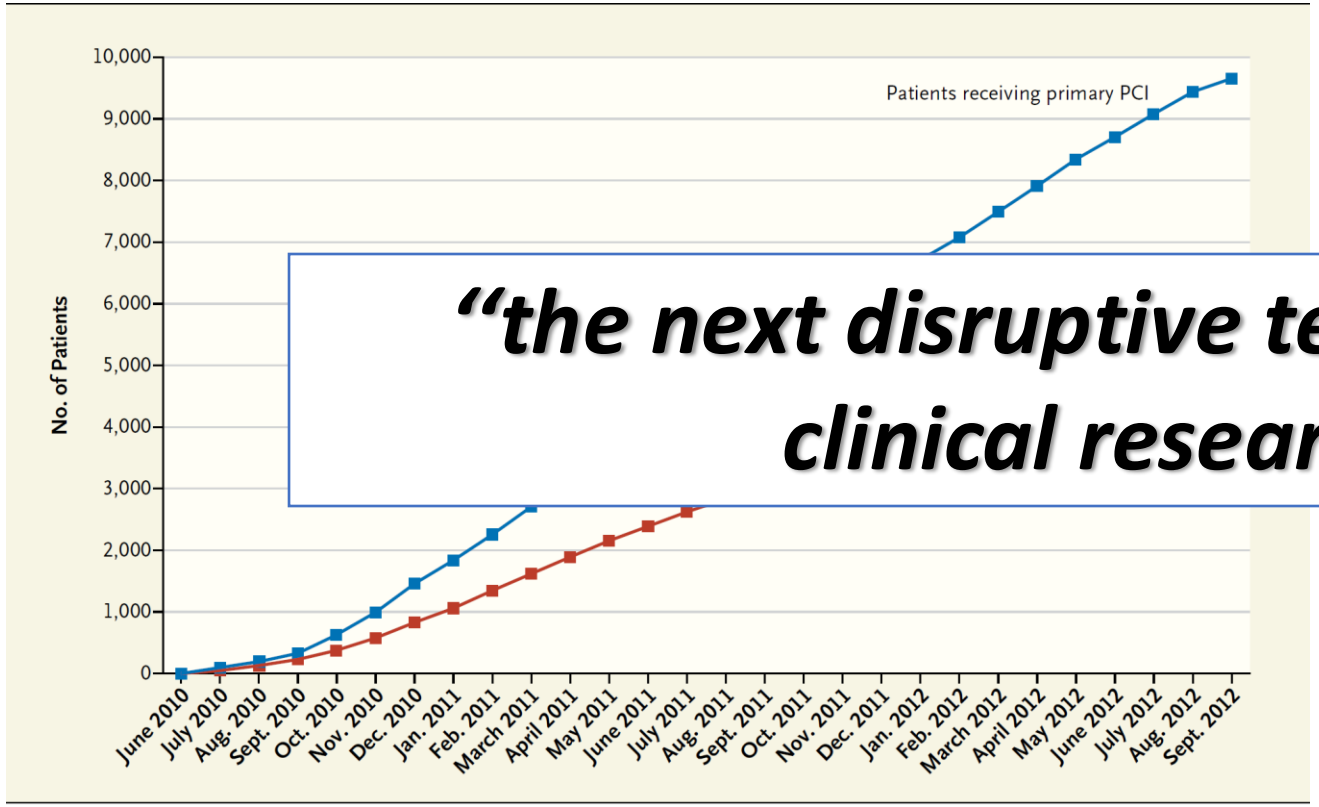


- Swedish Coronary Angiography and Angioplasty Registry
- Evaluated the effectiveness of intracoronary thrombus aspiration plus PCI compared with PCI alone
- Primary outcome measure 30-day mortality from death registry
- Secondary outcomes from registry data

N Engl J Med 2013;369:1587-97.
DOI: 10.1056/NEJMoa1308789

Curr Cardiol Rep (2016) 18: 11
DOI 10.1007/s11886-015-0677-6

TASTE trial



"the next disruptive technology in clinical research"

- Rapid accrual
- No patient was lost to follow-up
- ~US $50 per patient ($300,000 for trial)
- all cause
  ays (2.8% vs
  HR 0.94, 95 %
  CI 0.72–1.22; p = 0.63)).
- No difference all cause mortality 1-year (5.3% vs 5.6% PCI-only (HR 0.94, 95 % CI 0.78–1.15; p=0.57

N Engl J Med 2013;369:1587-97.
DOI: 10.1056/NEIMoa1308789
N ENGL J MED 369;17 NEJM.ORG OCTOBER 24, 2013

CRISTAL trial

JAMA

QUESTION Is aspirin monotherapy noninferior to enoxaparin in preventing symptomatic venous thromboembolism (VTE) within 90 days following primary total hip or knee arthroplasty performed for osteoarthritis?

CONCLUSION In patients undergoing hip or knee arthroplasty for osteoarthritis, aspirin compared with enoxaparin resulted in a significantly higher rate of symptomatic VTE, defined as below- or above-knee deep venous thrombosis or pulmonary embolism.

POPULATION

5511 Women
4200 Men

Adults undergoing hip or knee arthroplasty who had no contraindications to either study drug

Median age: **68** years

LOCATIONS

31 Hospitals in Australia

INTERVENTION

9711 Patients randomized
9203 Patients analyzed

5416
Aspirin
Aspirin, 100 mg/d, orally for 35 days after hip arthroplasty and for 14 days after knee arthroplasty

3787
Enoxaparin
Enoxaparin, 40 mg/d, subcutaneously for 35 days after hip arthroplasty and for 14 days after knee arthroplasty

PRIMARY OUTCOMES

Occurrence of symptomatic VTE, including pulmonary embolism and deep venous thrombosis, within 90 days

FINDINGS

Patients with symptomatic VTE within 90 days

Aspirin	Enoxaparin
3.45%	1.82%
187 of 5416 patients	69 of 3787 patients

The difference failed to meet the noninferiority margin criterion for aspirin of 1% and was significantly superior for enoxaparin:

Estimated between-group difference, 1.97%
(95% CI, 0.54% to 3.41%); *P* = .007

CRISTAL Study Group. Effect of aspirin vs enoxaparin on symptomatic venous thromboembolism in patients undergoing hip or knee arthroplasty: the CRISTAL randomized trial. *JAMA*. Published August 23, 2022. doi:10.1001/jama.2022.13416

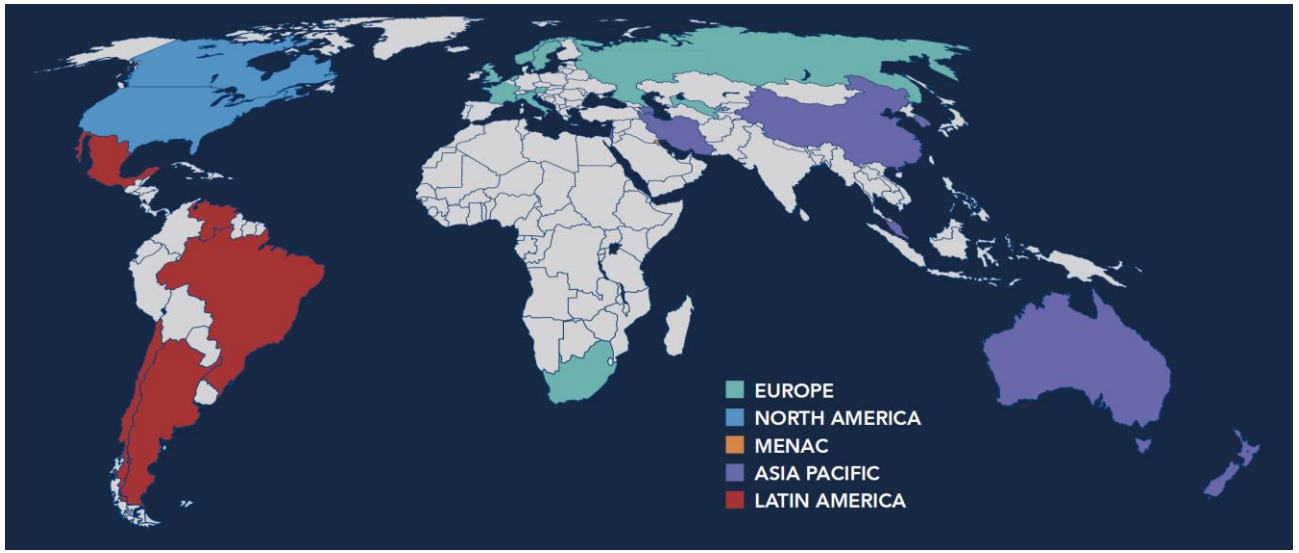
Benefits of IR-RCT

- Pragmatic RCT
  - Translates to a real-world setting
- Quick accrual
- Complete follow-up
- Reduced per-person cost

Challenges of IR-RCT

- Registry data quality
- Ethical issues including consent
- Data and participant privacy
- Participant withdrawal
- Data and Safety Monitoring Board in the trial vs registry SC.
- Require bespoke infrastructure
- Research questions, study designs, and types of outcomes limited by quality and features of registry

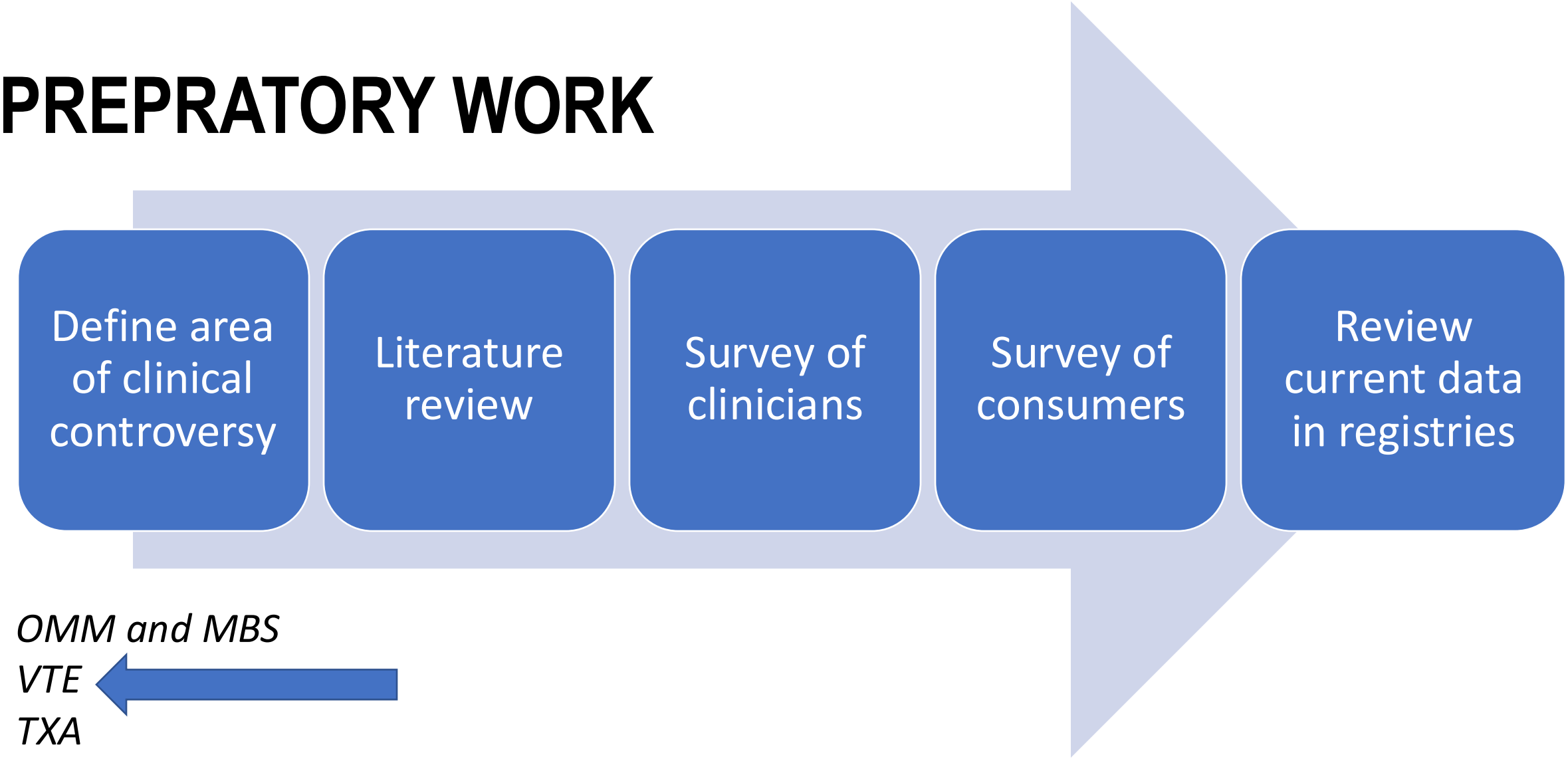
Why consider in Metabolic Bariatric Surgery?



IFSO

- Practice that lack evidence
- Traditional RCT difficult
  - Expense
  - Equipoise
  - Numbers needed to recruit
  - Ability to deliver internationally
- International network of mature registries with platforms with interest in developing trial activity

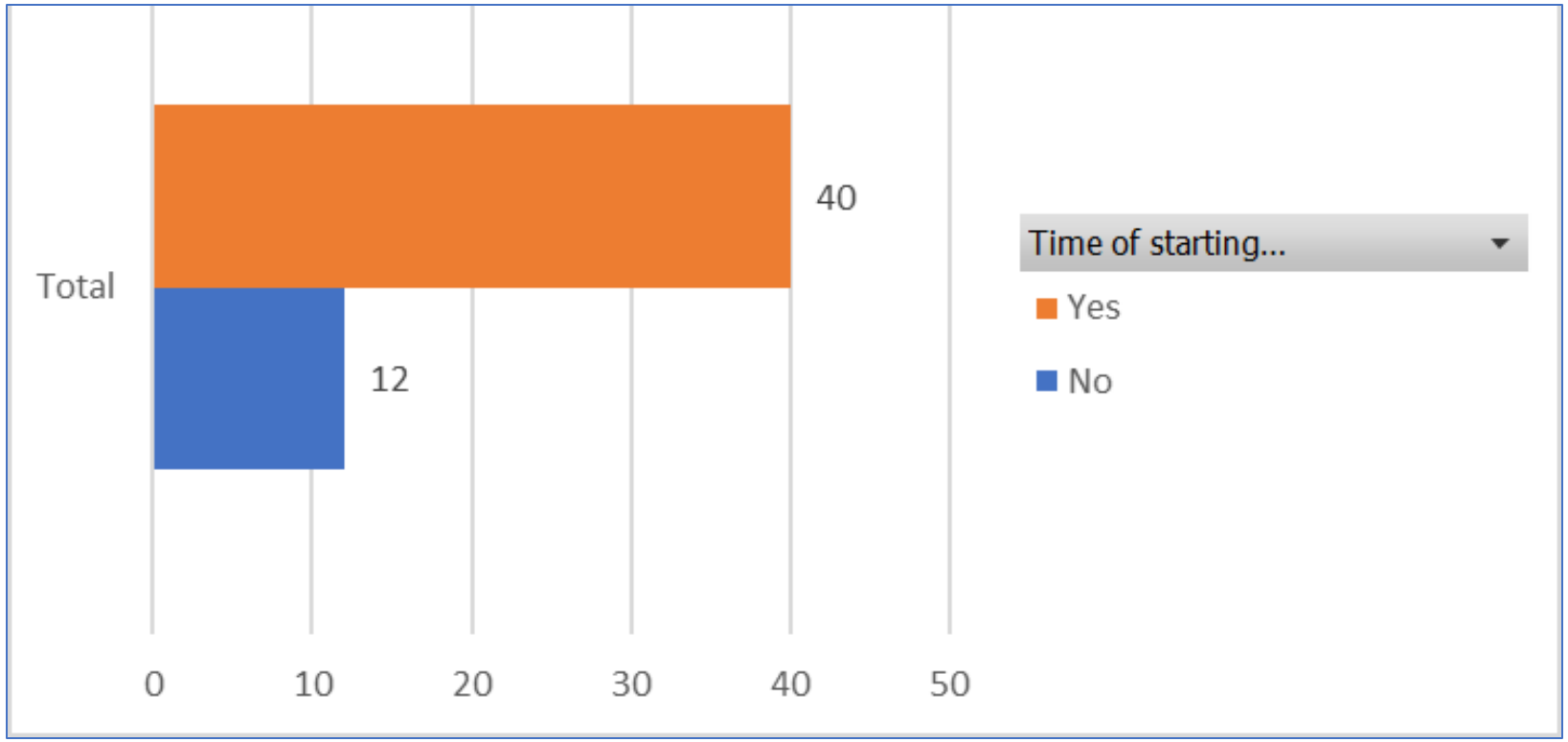
PREPRATORY WORK



OMM and MBS
VTE
TXA

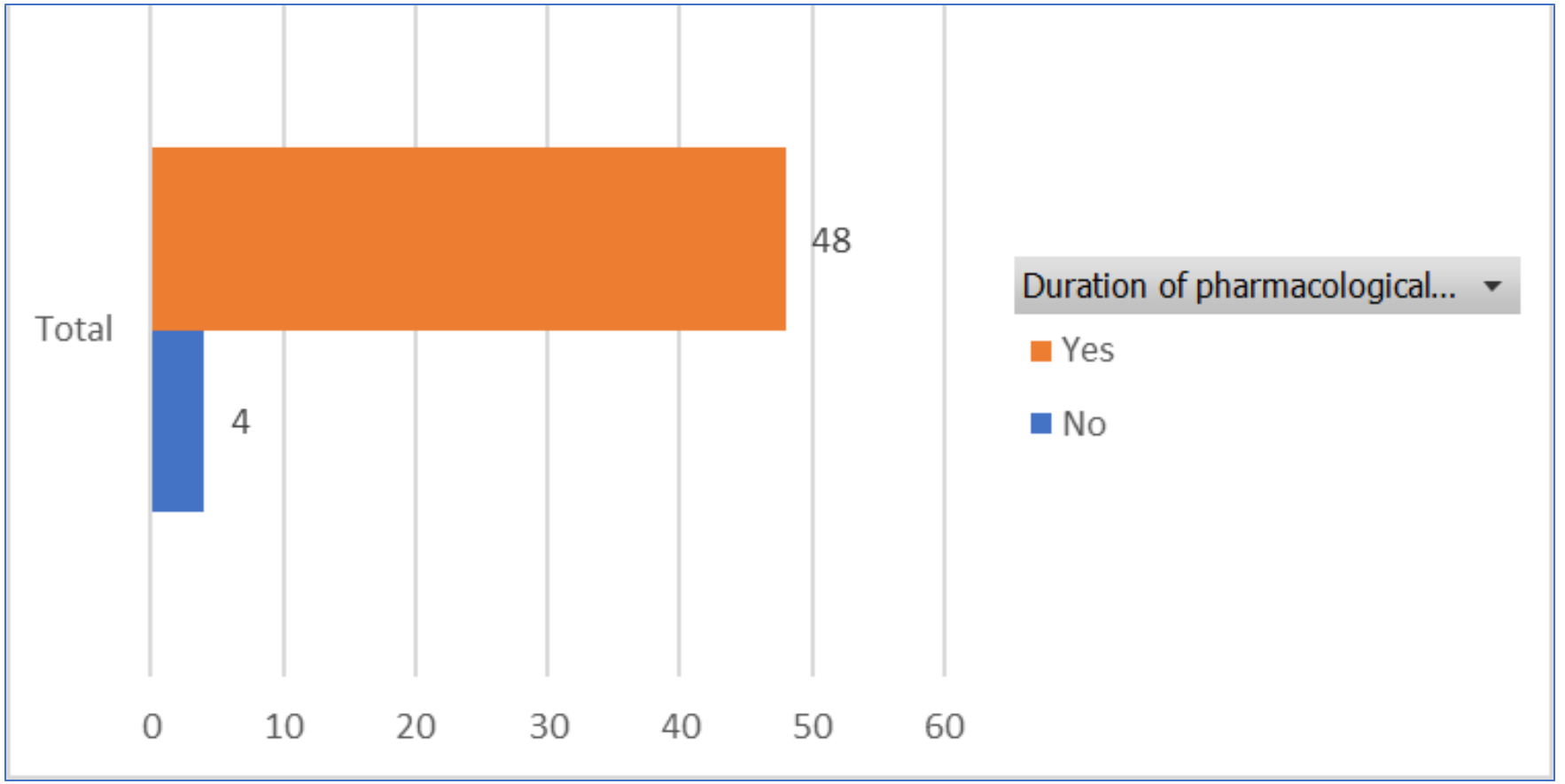
Do you think the following is an important topic?

Timing of starting pharmacotherapy for thromboprophylaxis

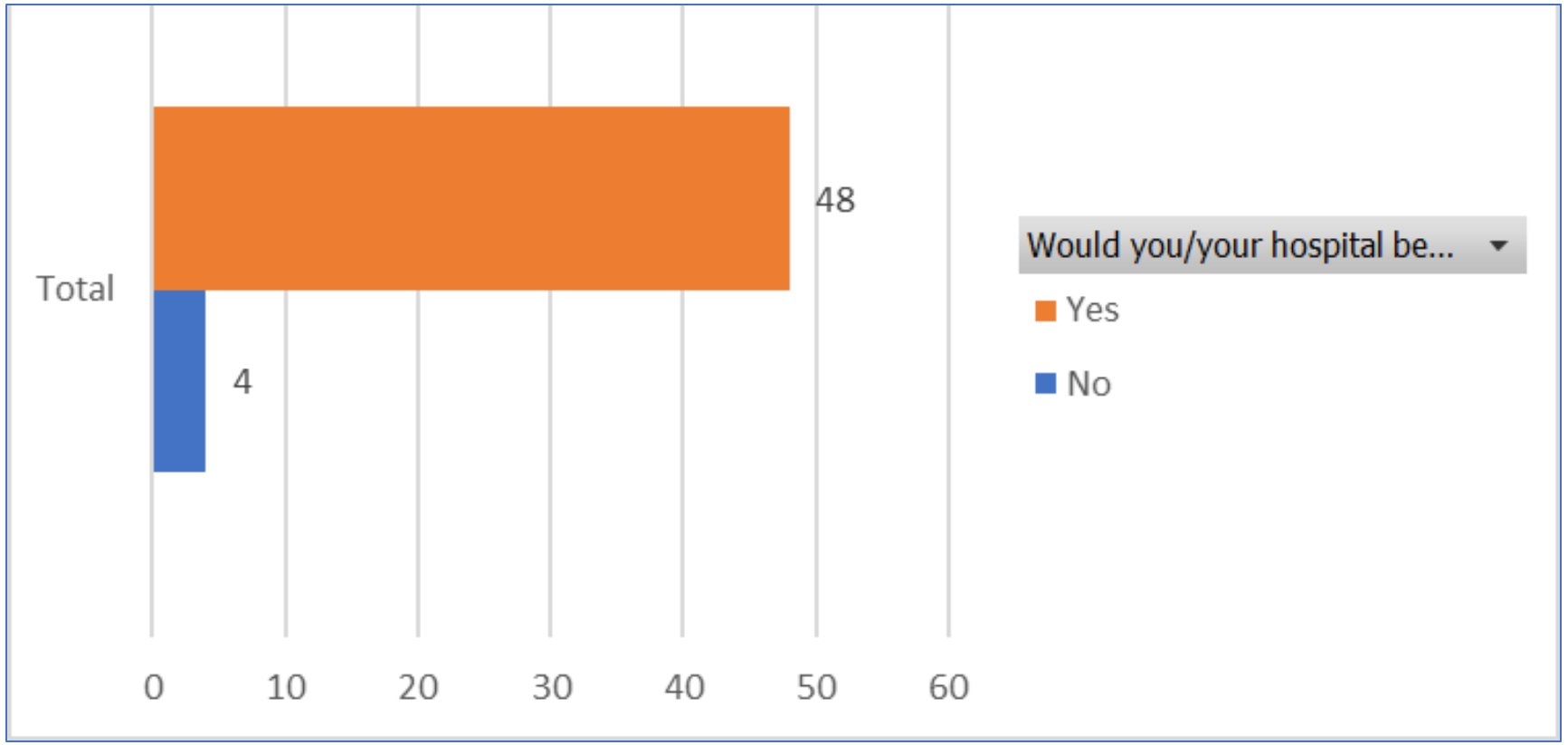


Do you think the following is an important topic?

Duration of pharmacotherapy for VTE

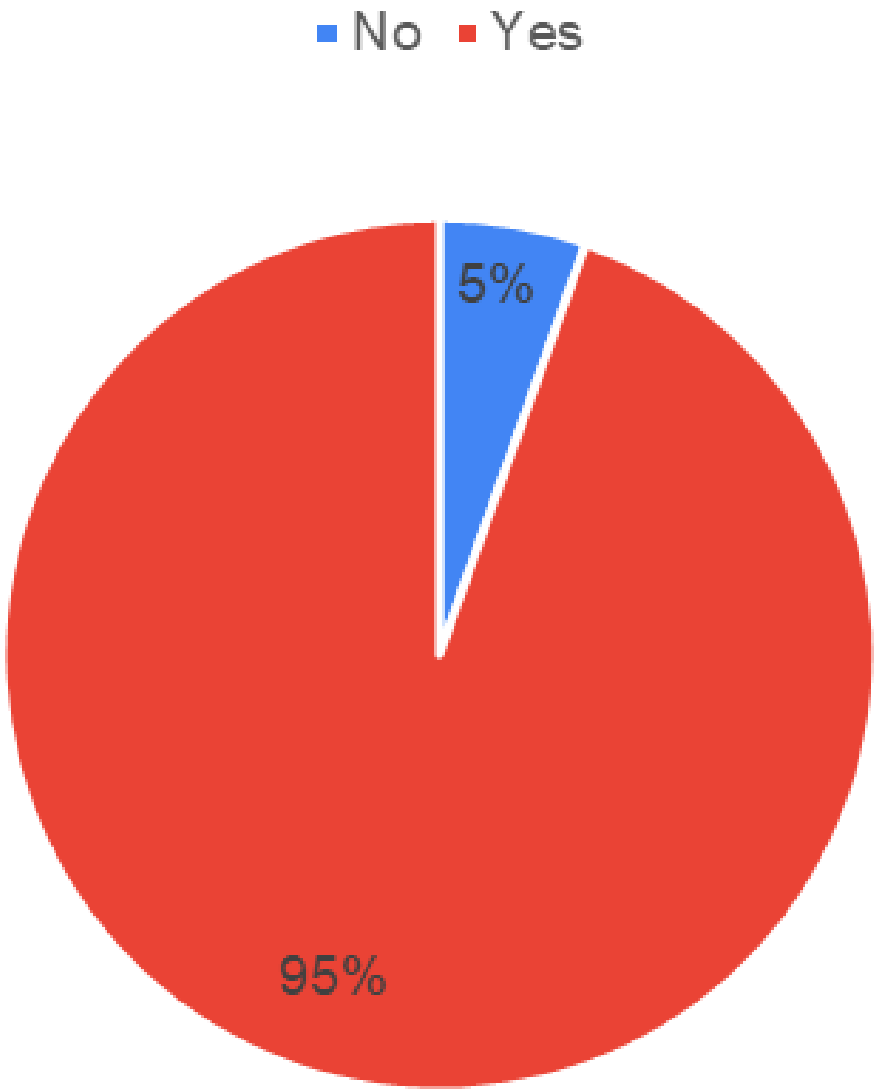


Willingness to participate

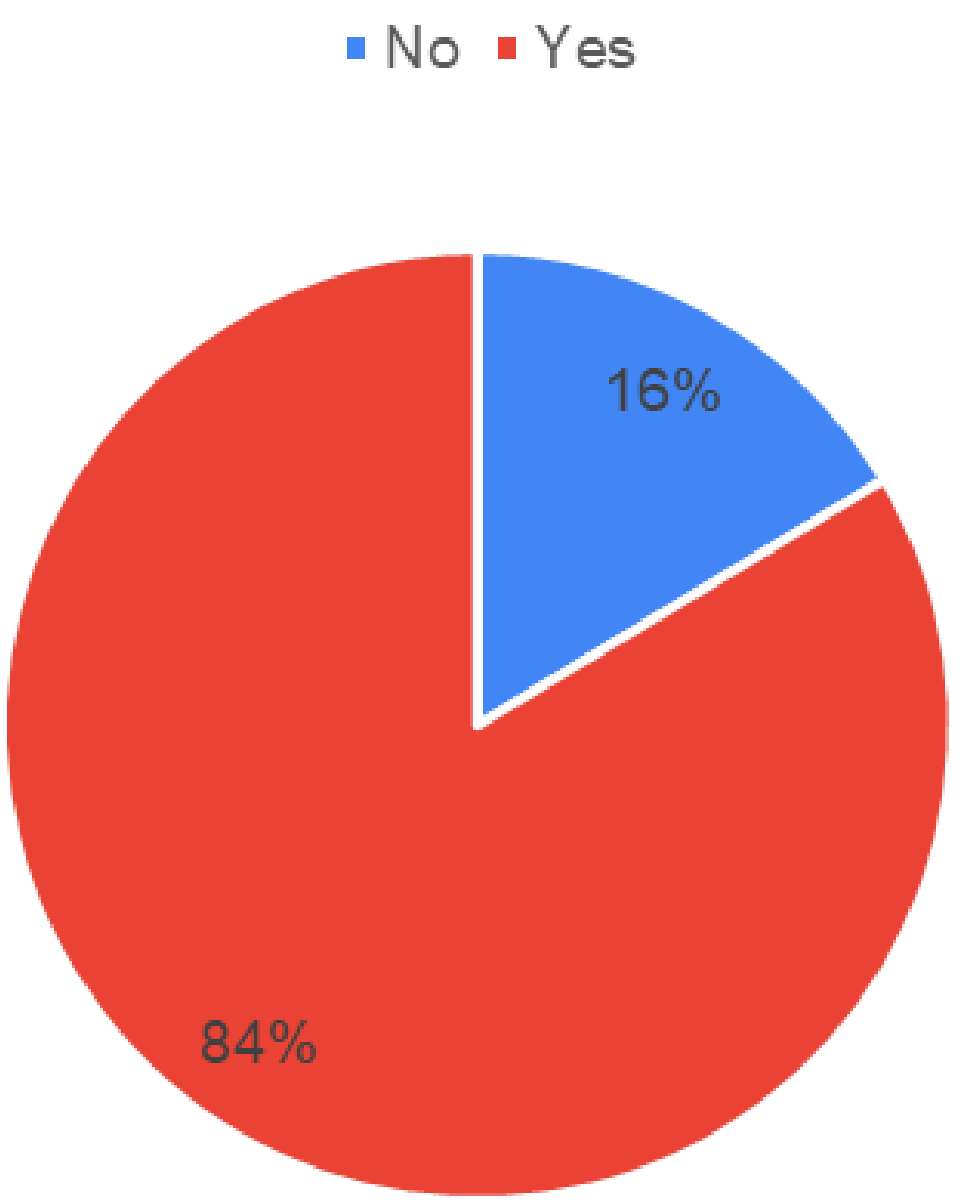


6,025 pa

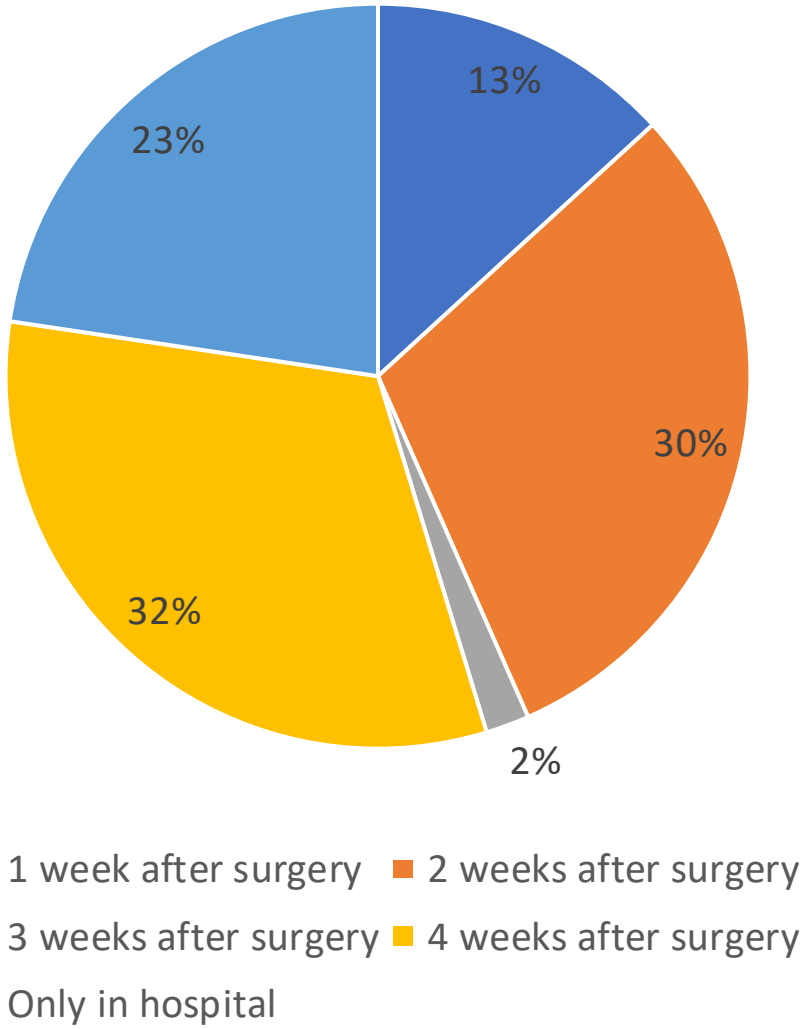
If you were to have a bariatric surgical procedure would you be willing to have a daily injection under your skin to thin out your blood and prevent blood clots/DVT/PE?



Would you be willing to self-administer daily injections to prevent blood clots/DVT/PE?

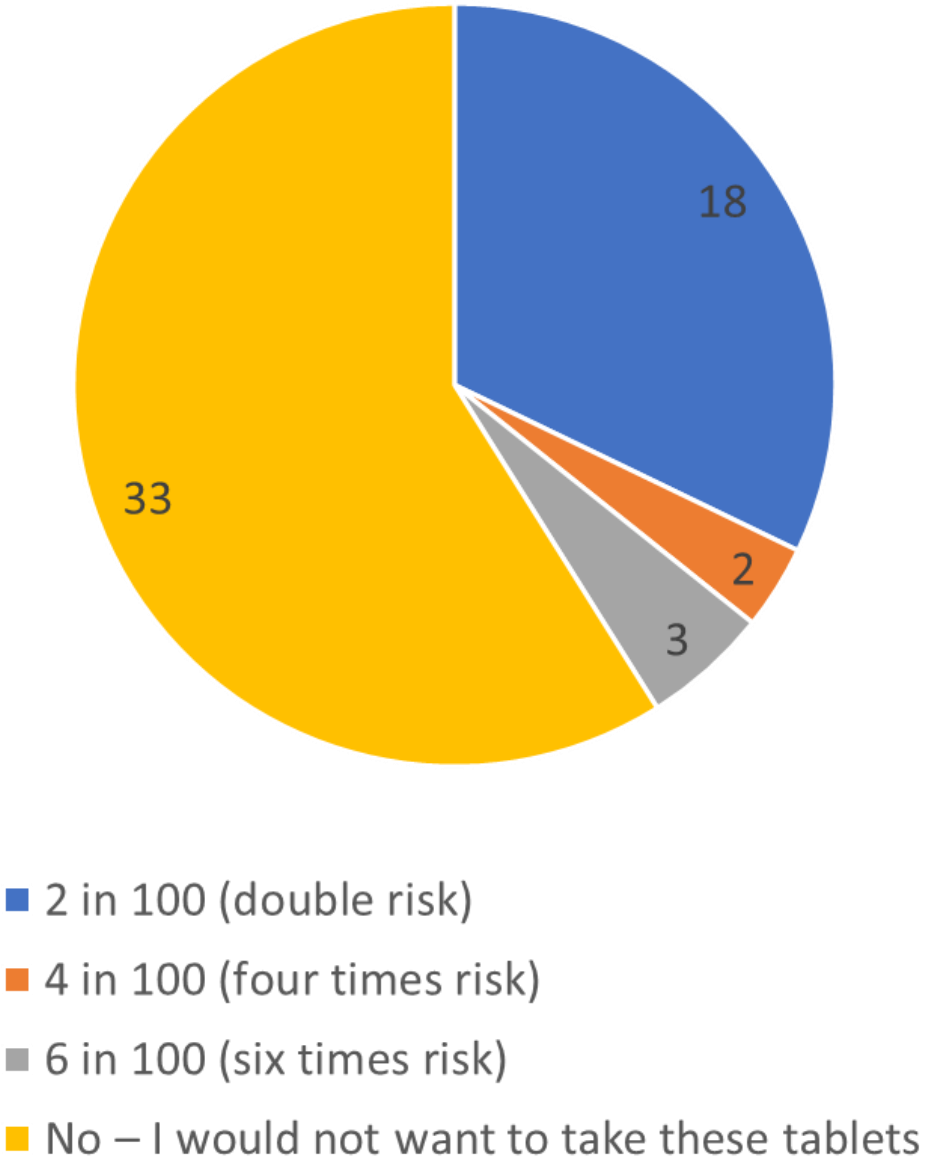


For how long would you be willing to have a daily injection under your skin to prevent blood clots/DVT/PE after an operation?



There are new tablets that can thin out the blood after surgery. There is potentially a role for these tablets in preventing blood clots/DVT/PE after bariatric surgery, however, once taken their effect is not easily reversed. This means that there is possibly a higher risk of bleeding after bariatric surgery. Normally around 1 in 100 patients who have a bariatric surgery need to return to theater.

Would you be willing to take these tablets if the risk of bleeding was:



Australia	22.2% of deaths 2.5% defined AE

Country	Rate of symptomatic VTE
Israel	0.08%
Netherlands	0.08%
Michigan	0.13%
Ontario	0.9%
SOReg-Sweden	0.11%
SOR Reg Norway	0.09%

No consistency in regime

Incidence, group 1	3%
Incidence, group 2	1.2%
Alpha	0.05
Beta	0.2
Power	0.8

N=1,990 per group

Incidence, group 1	1%
Incidence, group 2	0.4%
Alpha	0.05
Beta	0.2
Power	0.8

N=6,060 per group

Incidence, group 1	0.1%
Incidence, group 2	0.06%
Alpha	0.05
Beta	0.2
Power	0.8

N=78,425 per group

Summary

- Symptomatic VTE is an infrequent event after MBS
  - Expected 0.2-3% from literature
  - Registry data from around the world suggests 0.1% more likely incidence
  - This is despite the pharma regimes used around the world being very variable
    - All include some sort of pharma
    - All include mechanical prophylaxis
- When VTE occur they are a major source of mortality
- Surgeons see VTE management as an important topic and willing to participate in trial
- Patients happy to look at injecting self but NOT tablets if they increase risk of bleeding

RCT

Do we need chemothromboprophylaxis [illegible] MBS to pr[illegible]

Feasible?
N=75,000

- Rationale:
  - there is a broad variance in practice regarding the u[illegible]
  - Despite this the rates of VTE are very low 0.1%
  - Perhaps it is the other factors that are more important than chemoprophylaxis?

Mechanical
Hydration
Early mobilisation

VS

Non-inferiority

Mechanical
Hydration
Early mobilization
Chemoprophylaxis

CONCLUSIONS

- RCTs are the gold standard – but difficult to achieve in surgery
- In-Registry RCT are a pragmatic way to answer clinical research questions
  - *Efficient*
  - *Relatively cheap*
  - *Adaptable*
- What should be the first IFSO In-Registry RCT?
  - *Important question to practitioners and consumers*
  - *Likely to change practice*
  - *Feasible numbers*
  - *Funding*

Acknowledgements

BSR Steering Committee

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AANZGOSA Mr Ross Roberts
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