



Only one-third of Ruptured AAA patients in the 3 RCTs comparing EVAR with open repair were randomized: why does this and other flaws invalidate the RCT conclusions: RCTs can be misleading


Thomas L. Forbes, MD
 Surgeon-in-Chief & James Wallace McCutcheon Chair
 Sproul Department of Surgery, University Health Network
 Professor & Vice-Chair, Department of Surgery
 Temerty Faculty of Medicine, University of Toronto




Pyramid of Evidence Based Medicine



Ann Thorac Surg 2017;103:351-60




Pyramid of Evidence Based Medicine




Powerful test of cause and effect
 Randomization minimizes allocation or selection, and confounding bias to provide high internal validity for the study.
 Can facilitate double blinding of participants to limit bias from researchers or participants behaving differentially.
 Data collected prospectively for both groups allow consistent collection and measurement of data compared to retrospective studies.
 Outcome measures can be determined by intention to treat analyses to limit bias from loss of participants

Ann Thorac Surg 2017;103:351-60




Randomized Controlled Trials

- Results relevant to those who meet inclusion criteria
- Inclusion depends on clinical equipoise
- Results valid to specific centers & practitioners
- Lower event rates in experimental & control group
- Issues of Study Interpretation




Randomized Controlled Trials

- Results relevant to those who meet inclusion criteria
- **? External Validity**
- Inclusion depends on clinical equipoise
- Results valid to specific centers & practitioners
- Lower event rates in experimental & control group
- Issues of Study Interpretation








Randomized Controlled Trials

- Results relevant to those who meet inclusion criteria
- Inclusion depends on clinical equipoise
- Results valid to specific centers & practitioners
- Lower event rates in experimental & control group
- Issues of Study Interpretation



What patients are included?
RCT's for Open vs Endovascular Repair for RAAAs


-  Nottingham
-  AJAX
-  ECAR
-  IMPROVE



RCT's for Open vs Endovascular Repair for RAAAs

Early Mortality


	OSR	EVAR	P-value
Nottingham	53%	53%	N.S.
AJAX	25%	21%	0.56
ECAR	24%	18%	0.24
IMPROVE	37.4%	35.4%	0.62



RCT's for Open vs Endovascular Repair for RAAAs

Early Mortality

	OSR	EVAR	P-value
Nottingham	But ... Differences in Study Design & Randomization What patients were included?		
AJAX			
ECAR			
IMPROVE			




RCT's for Open vs Endovascular Repair for RAAAs

Differences in Study Design

```

    graph LR
      RAAA[RAAA] --> CD[Clinical Diagnosis]
      CD --> CT["+/- CT"]
      CT --> OSREVAR[OSR EVAR]
    
```




RCT's for Open vs Endovascular Repair for RAAAs

Differences in Study Design

```

    graph LR
      RAAA[RAAA] --> CD[Clinical Diagnosis]
      CD --> CT["+/- CT"]
      CT --> OSREVAR[OSR EVAR]
      subgraph Group1 [AJAX ECAR]
        CT
      end
    
```




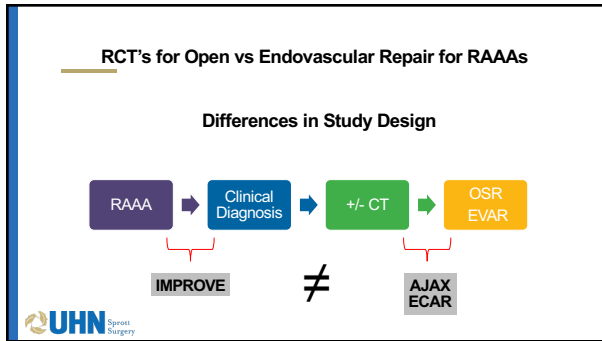
RCT's for Open vs Endovascular Repair for RAAAs

Differences in Study Design

```

    graph LR
      RAAA[RAAA] --> CD[Clinical Diagnosis]
      CD --> CT["+/- CT"]
      CT --> OSREVAR[OSR EVAR]
      subgraph Group2 [IMPROVE]
        CD
      end
      subgraph Group3 [AJAX ECAR]
        OSREVAR
      end
    
```





RCT's for Open vs Endovascular Repair for RAAAs

What patients were included?

	Nottingham	AJAX	ECAR	IMPROVE
# RAAAs ID'ed	103	520	524	1275
# Randomized	32	116	107	613
% Randomized	31%	22%	20%	48%

UHN Spinal Surgery

RCT's for Open vs Endovascular Repair for RAAAs

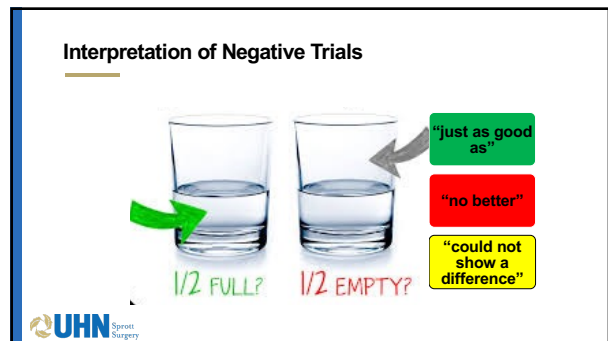
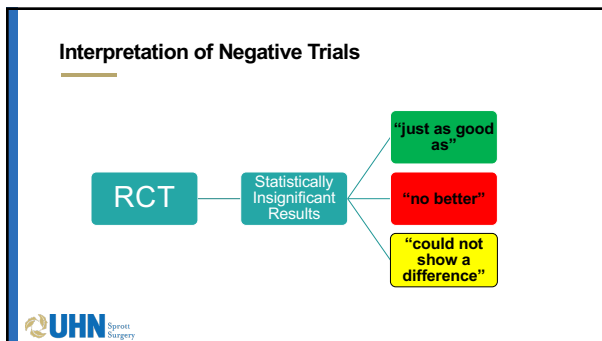
What patients were included?

	Nottingham	AJAX	ECAR	IMPROVE
# RAAAs ID'ed	103	520	524	1275
# Randomized	32	116	107	613
% Randomized	31%	22%	20%	48%

36%

UHN Spinal Surgery

- ### Randomized Controlled Trials
- Results relevant to those who meet inclusion criteria
 - Inclusion depends on clinical equipoise
 - Results valid to specific centers & practitioners
 - Lower event rates in experimental & control group
 - Issues of Study Interpretation
- UHN Spinal Surgery



RCT's for Open vs Endovascular Repair for RAAAs

Early Mortality

	OSR	EVAR	P-value	Interpretation
AJAX	25%	21%	0.58	"did not show significant difference ..."
ECAR	24%	18%	0.24	"EVAR was found to be equal ..."
IMPROVE	37.4%	35.4%	0.62	"not associated with significant reduction ..."



Randomized Controlled Trials

- Results relevant to those who meet inclusion criteria
- Inclusion depends on clinical equipoise
- Results valid to specific centers & practitioners
- Lower event rates in experimental & control group
- Issues of Study Interpretation

