Will Current Stentgrafts Offer Better Results Than Those Used In RCT's?

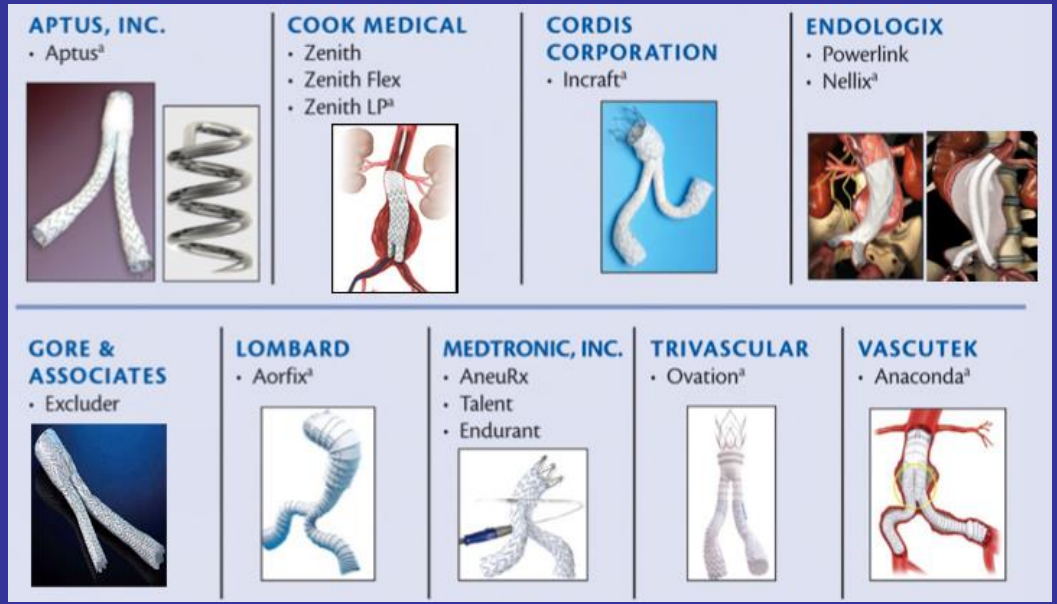
NO! RCT CONCLUSIONS REMAIN VALID

dream

ACE

OVER

EVAR



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“Who needs proof a parachute works?”

Randomized Trials

1. United Kingdom **EVAR** Trial Investigators, Greenhalgh RM, Brown LC, Powell JT, Thompson SG, Epstein D, Sculpher MJ. Endovascular versus open repair of abdominal aortic aneurysm.
   N Engl J Med. 2010;362:1863-71

2. De Bruin JL, Baas AF, Buth J, Prinssen M, Verhoeven EL, Cuypers PW, van Sambeek MR, Balm R, Grobbee DE, Blankensteijn JD; **DREAM** Study Group. Long-term outcome of open or endovascular repair of abdominal aortic aneurysm.
   N Engl J Med. 2010;362:1881-9

3. Becquemin JP, Pillet JC, Lescalie F, Sapoval M, Goueffic Y, Lermusiaux P, Steinmetz E, Marzelle J; **ACE** trialists. A randomized controlled trial of endovascular aneurysm repair versus open surgery for abdominal aortic aneurysms in low- to moderate-risk patients.
   J Vasc Surg. 2011;531167-1173

4. Lederle FA, Freischlag JA, Kyriakides TC, Matsumura JS, Padberg FT Jr, Kohler TR, Kougias P, Jean-Claude JM, Cikrit DF, Swanson KM; Open Versus Endovascular Repair (**OVER**) Veterans Affairs Cooperative Study Group. Long-term comparison of endovascular and open repair of abdominal aortic aneurysm.
   N Engl J Med. 2012;367:1988-97

How valid are the RCT's currently?

Generalizability:

- Trials included patients with infrarenal AAA suitable for both open and endovascular repair
- Available devices in first half of previous decade

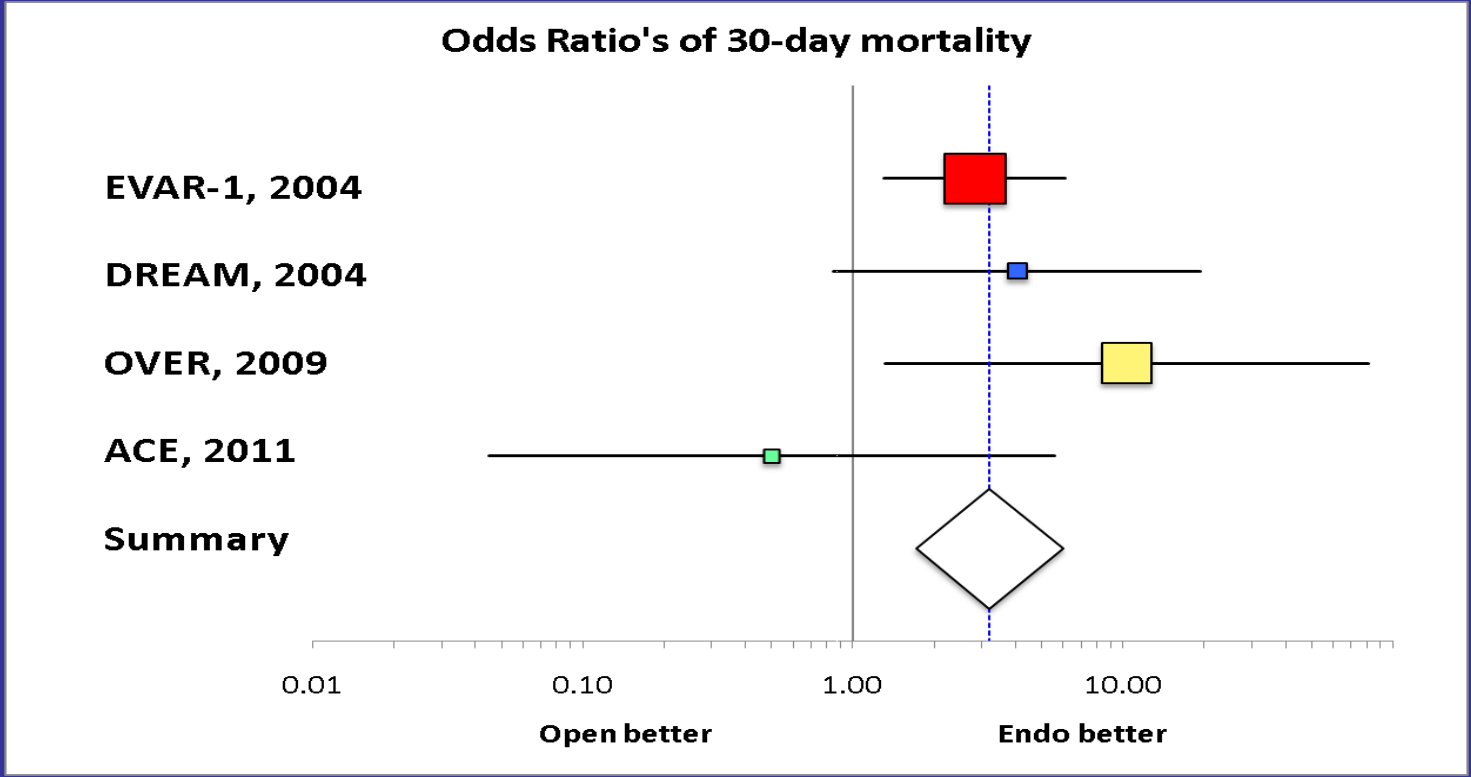
Endpoints:

- Primary: Short and long-term overall survival
- Secondary:
  - Aneurysm-related mortality
  - Re-interventions
  - Quality of Life

Short-term survival

Trial	30-day mortality		
	Open	Endo	
EVAR	4,7%	1,7%	P=0.009
dream	4,6%	1,2%	P=0.1
EVAR	3,0%	0,5%	P=0.004
ACE	0,6%	1,3%	NS

Short-term survival



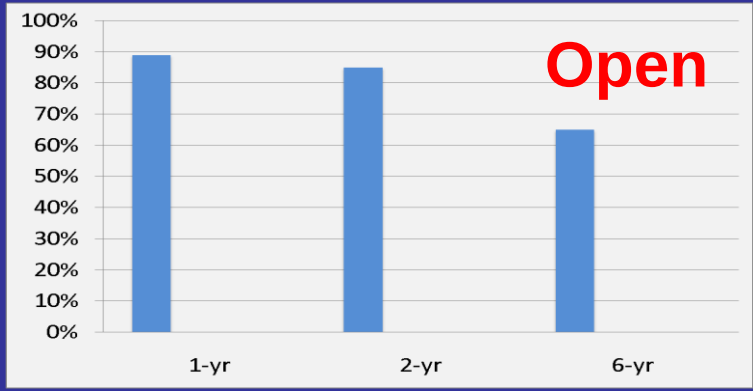
Short-term survival

- **Repeat RCT but now include:**
  - Patients suitable for current EVAR
    - Allow Branched/Chimps? - No
    - Allow Fenestrated? -Maybe
- **Will the new stentgrafts really drive the operative mortality after EVAR?**
- **What will be the effect on operative mortality?**
  - Probably predominantly driven by different risk-status of patients included (more advanced disease)
  - Probably higher for open and endo but more short-term benefit for (f)-EVAR

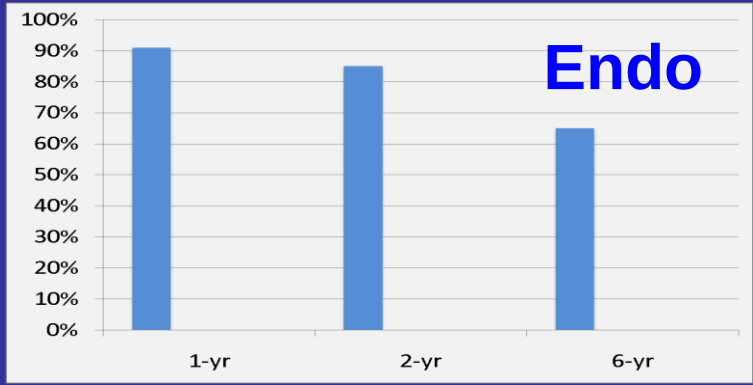
Long-term Survival

		EVAR-1
Open	1-yr	89%
	2-yr	85%
	6-yr	65%

EVAR1-survival: 90% @1-yr
losing 5% per yr



		EVAR-1
Endo	1-yr	91%
	2-yr	85%
	6-yr	65%



Long-term Survival

		EVAR-1	DREAM	OVER	ACE
Open	1-yr	89%	93%	95%	97%
	2-yr	85%	89%	89%	96%
	6-yr	65%	69%	68%	

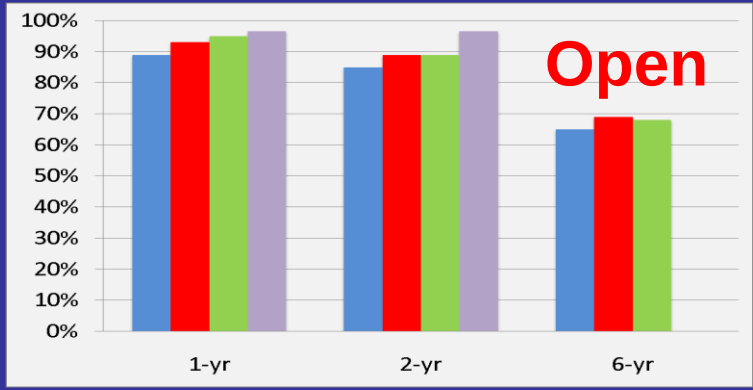
EVAR1-survival: 90% @1-yr
losing 5% per yr

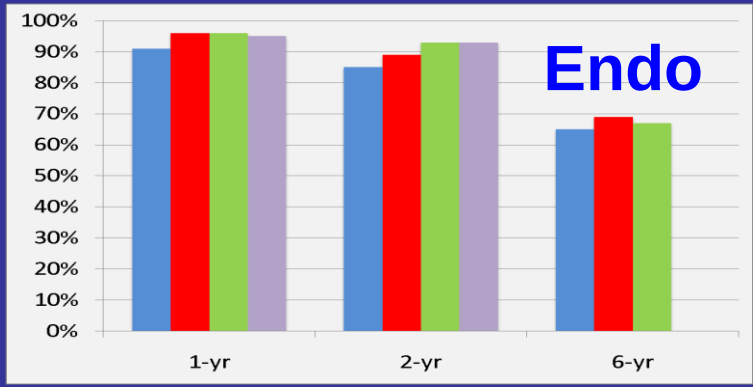
Other trials-survival: EVAR1, +4%

/X for OVER/ACE-endo: +8% @2-yr <@6-yr

/X for ACE-open: +8% @1-yr +11% @2-yr

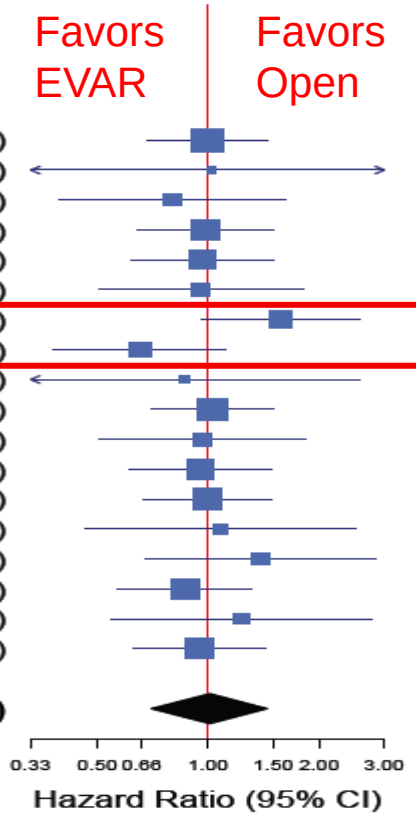
		EVAR-1	DREAM	OVER	ACE
Endo	1-yr	91%	96%	96%	95%
	2-yr	85%	89%	93%	93%
	6-yr	65%	69%	67%	



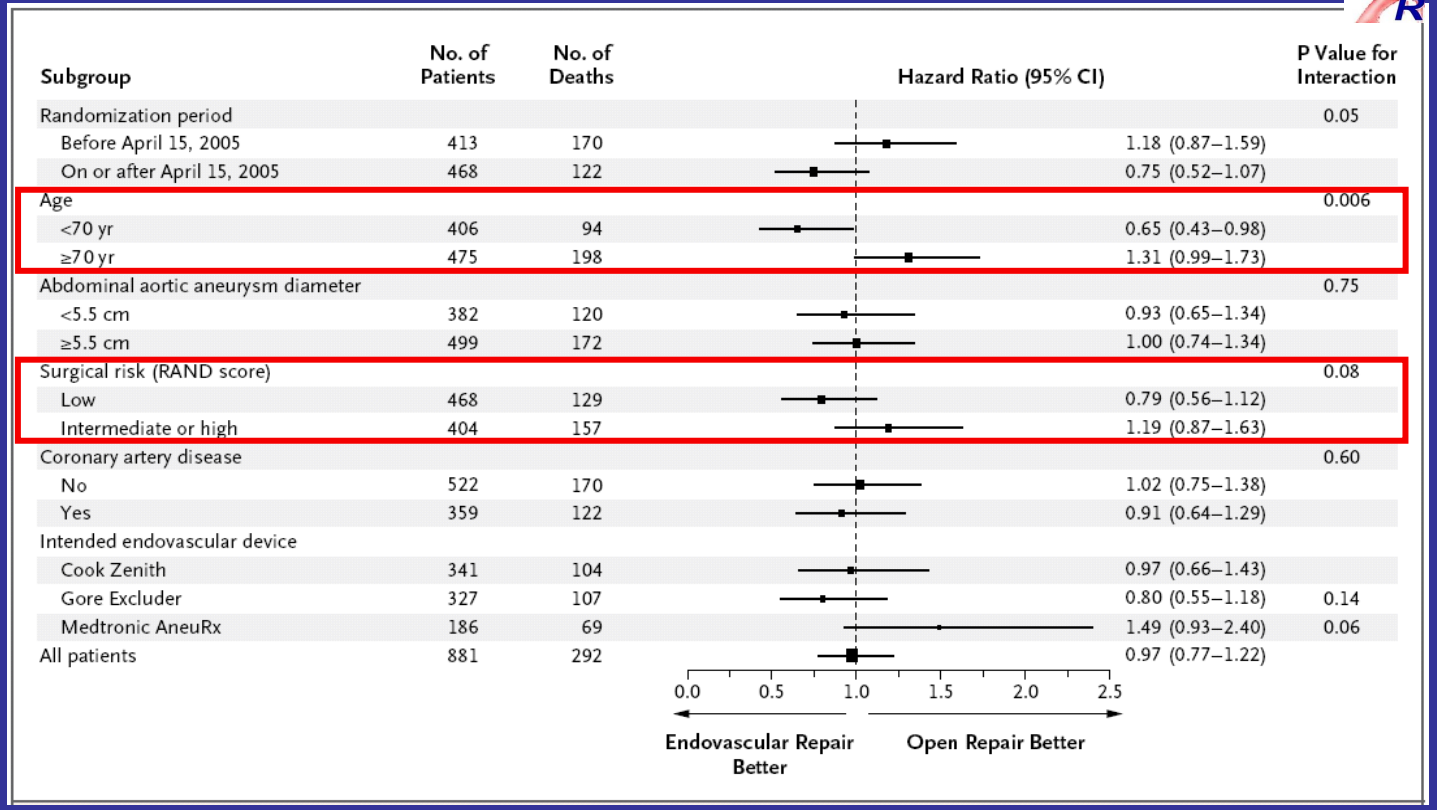


Hazard Ratios for Death

Variable	Subgroup	Pat (N)	Dth (N)	HR (95% CI)
Gender	male	322	109	0.99 (0.68-1.45)
	female	29	9	1.02 (0.27-3.82)
Age	<70	177	32	0.80 (0.40-1.62)
	>70	174	86	0.98 (0.64-1.50)
Tobacco	yes	209	79	0.97 (0.62-1.50)
	no	142	39	0.95 (0.50-1.80)
Cardiac dis	yes	154	64	1.57 (0.96-2.57)
	no	197	54	0.65 (0.38-1.12)
Renal dis	yes	28	13	0.86 (0.29-2.57)
	no	323	105	1.03 (0.70-1.51)
Pulmonary dis	yes	81	38	0.96 (0.51-1.84)
	no	270	80	0.95 (0.61-1.48)
AAA size	<70mm	300	96	0.99 (0.66-1.48)
	>70mm	51	22	1.08 (0.46-2.50)
Statin use	yes	133	30	1.39 (0.68-2.84)
	no	218	88	0.86 (0.59-1.31)
Reintervention	yes	78	26	1.23 (0.55-2.76)
	no	273	92	0.95 (0.63-1.43)
OVERALL		**351**	**118**	**1.01 (0.70-1.44)**



Hazard Ratios for Death



Subgroup	No. of Patients	No. of Deaths	Hazard Ratio (95% CI)	P Value for Interaction
Randomization period				0.05
Before April 15, 2005	413	170	1.18 (0.87–1.59)	
On or after April 15, 2005	468	122	0.75 (0.52–1.07)	
Age				0.006
<70 yr	406	94	0.65 (0.43–0.98)	
≥70 yr	475	198	1.31 (0.99–1.73)	
Abdominal aortic aneurysm diameter				0.75
<5.5 cm	382	120	0.93 (0.65–1.34)	
≥5.5 cm	499	172	1.00 (0.74–1.34)	
Surgical risk (RAND score)				0.08
Low	468	129	0.79 (0.56–1.12)	
Intermediate or high	404	157	1.19 (0.87–1.63)	
Coronary artery disease				0.60
No	522	170	1.02 (0.75–1.38)	
Yes	359	122	0.91 (0.64–1.29)	
Intended endovascular device				
Cook Zenith	341	104	0.97 (0.66–1.43)	
Gore Excluder	327	107	0.80 (0.55–1.18)	0.14
Medtronic AneuRx	186	69	1.49 (0.93–2.40)	0.06
All patients	881	292	0.97 (0.77–1.22)	

Trials in a nutshell

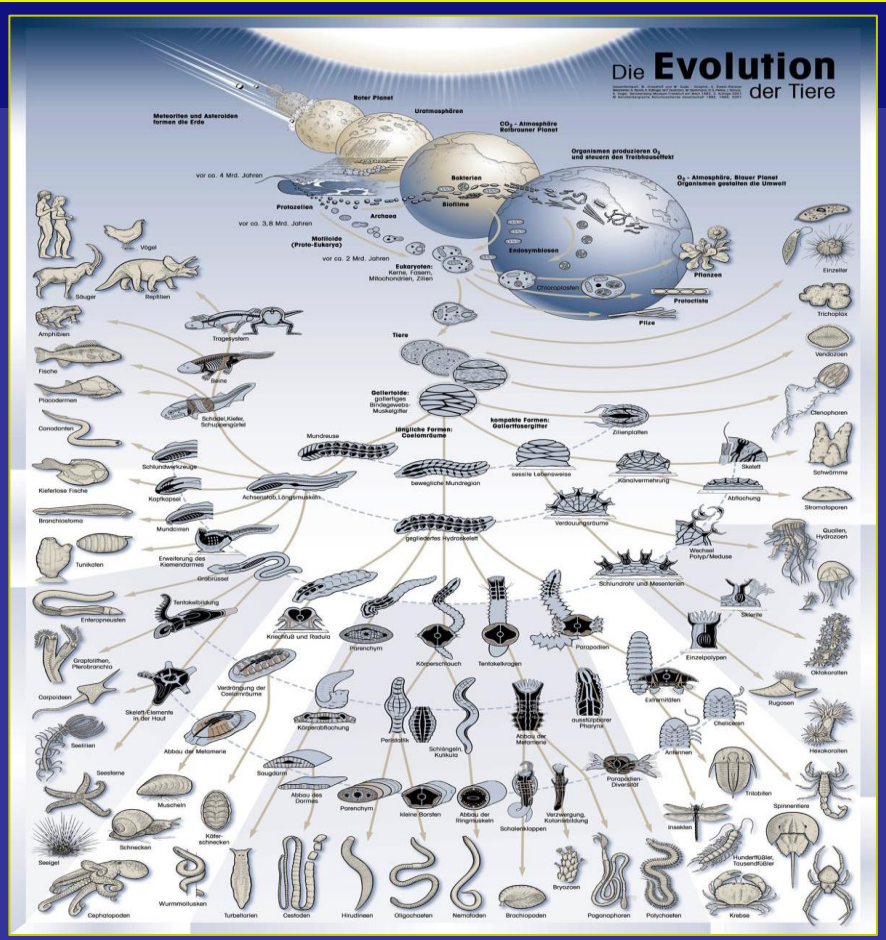
- **Short-term survival benefit 3%**
- **Lost in subsequent 1-3 years**

- **This “lag-time” depends on risk-status:**
  - Lower risk preoperatively yields longer survival benefit from EVAR

Long-term survival

- **Main drivers of survival**
  - Patient age and risk status
  - Not type/brand of endograft
  - (Except for possible effect of reinterventions)
- **Main driver of reintervention rate**
  - Anatomical suitability for EVAR
  - Newer devices may help reduce reinterventions

  <u>Counteracted by:</u>
  - Possibly less durable devices (lower profile, unproven technology)
  - More challenging anatomy, shorter more angulated necks



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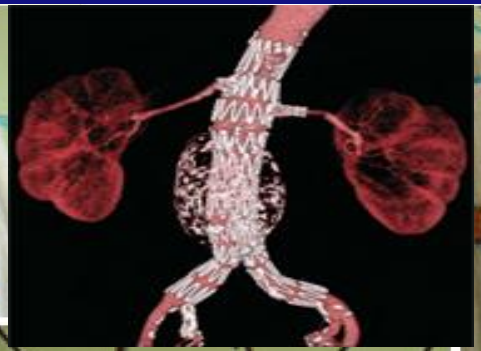

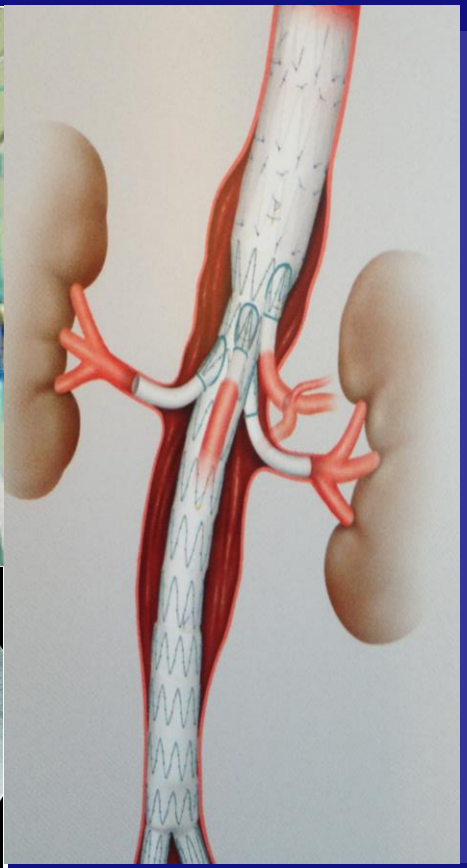


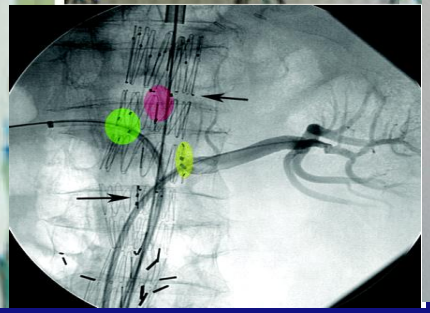

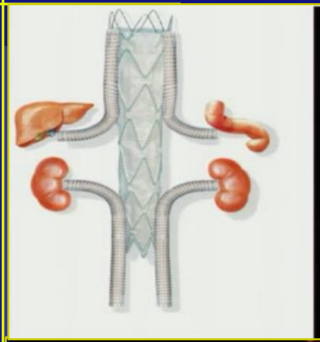

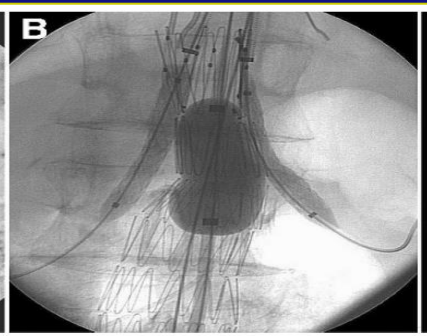

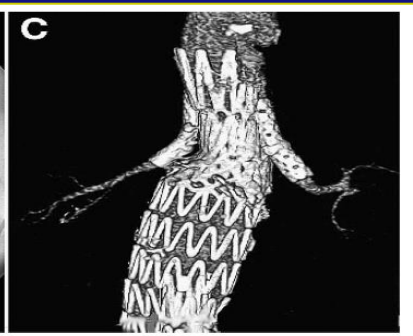

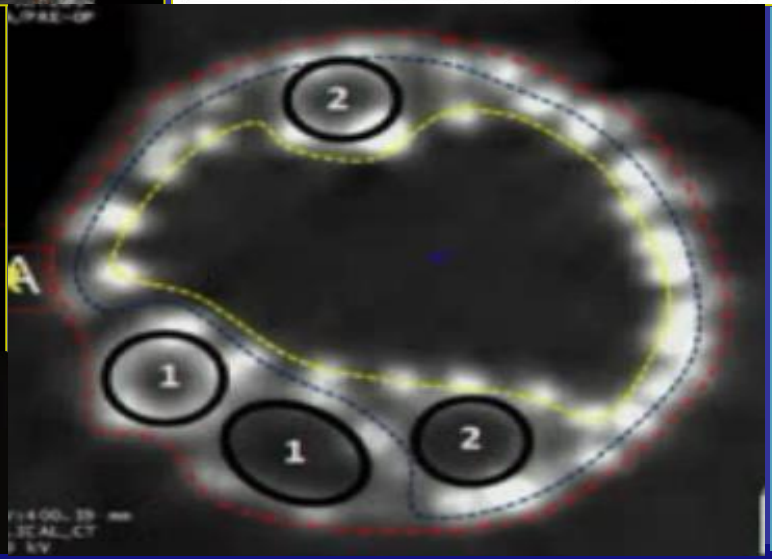

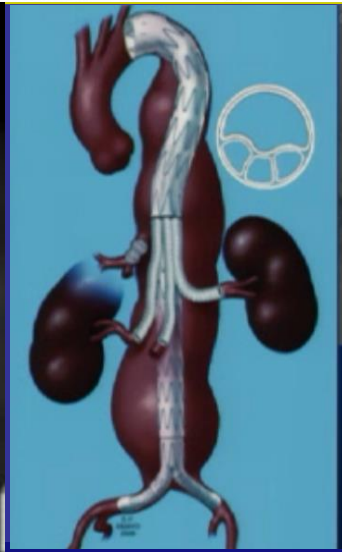

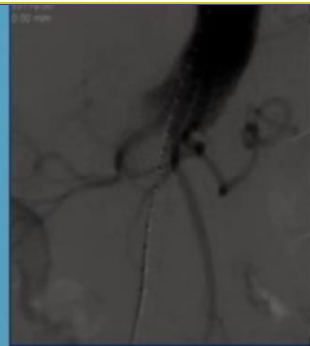

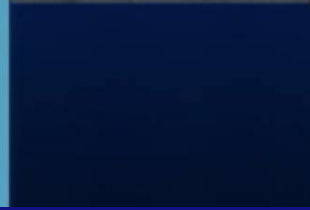

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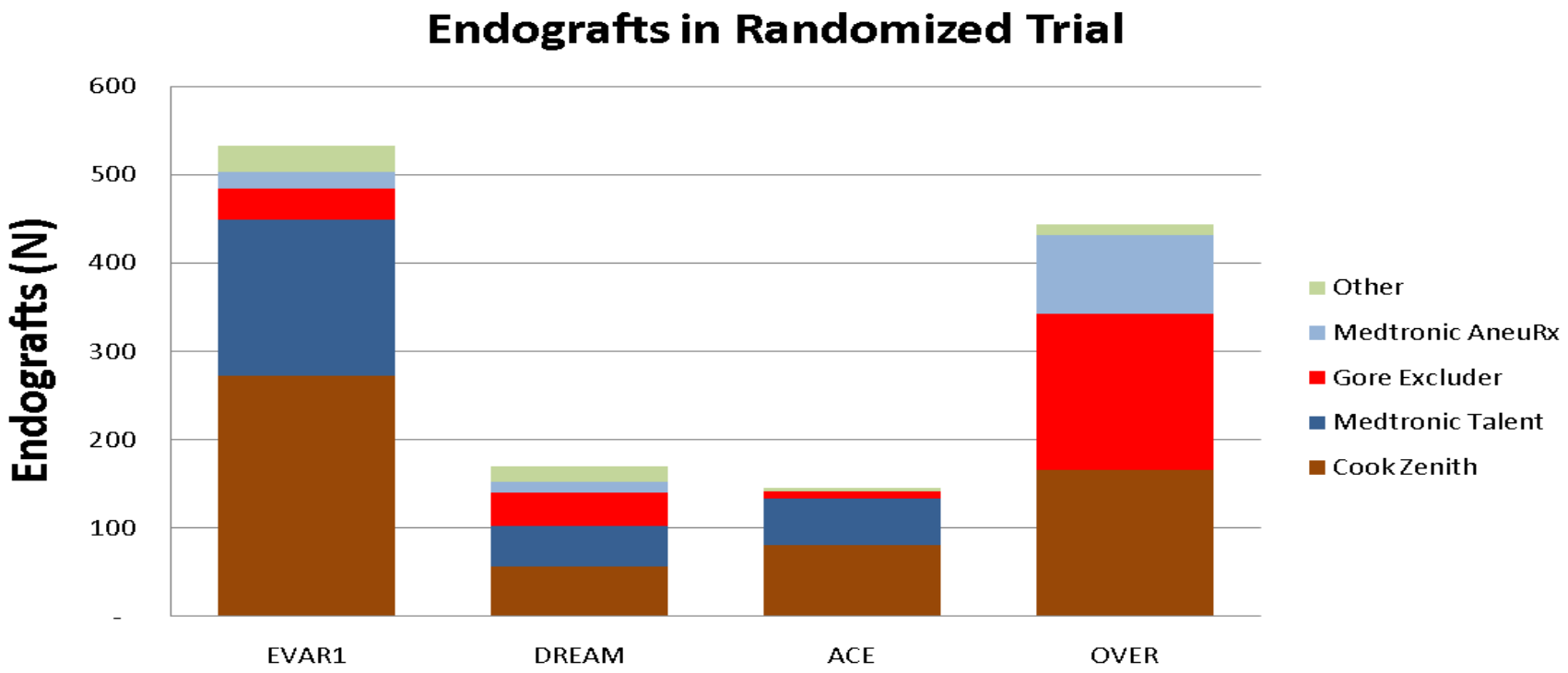


Inclusion:	1999-2003	2000-2003	2003-2008	2002-2008

Complications & Reinterventions

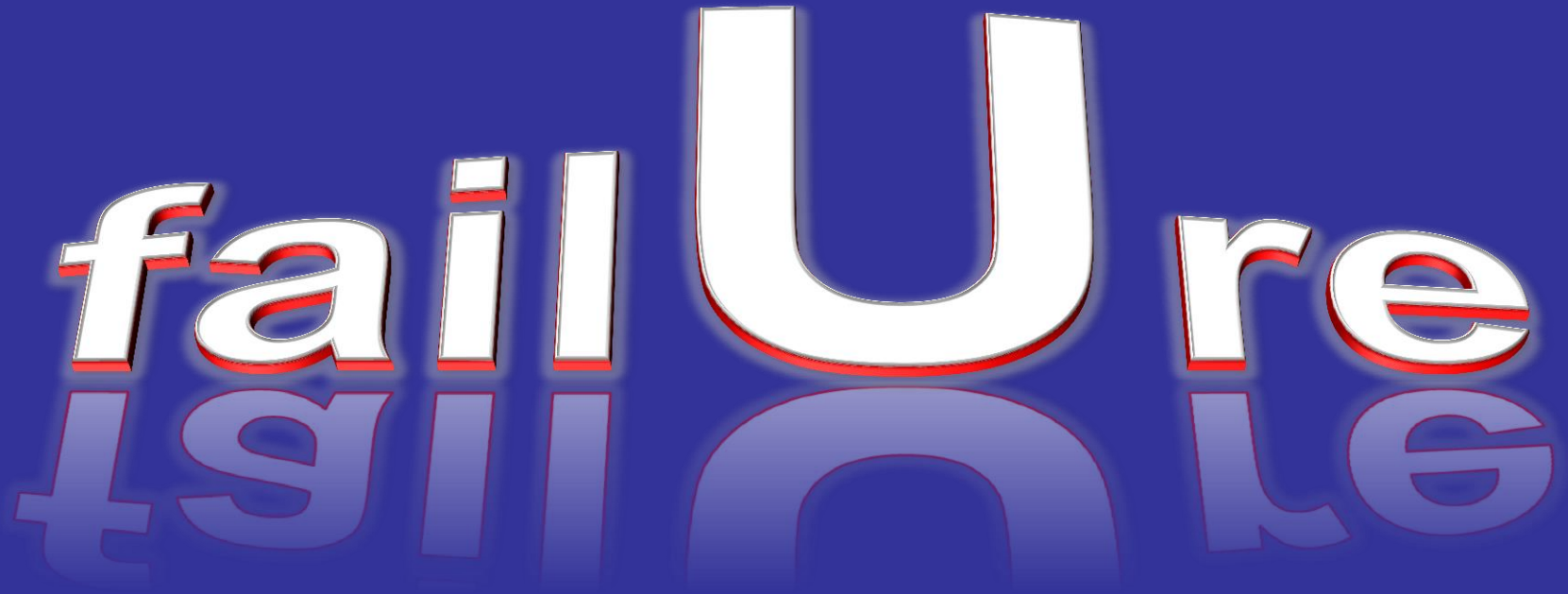
New device technology

Advantages:

- Lower profile
- Better seal/fixation
- Higher endo treatment rates
- Graft-placement more easy
- Less kinking/deformation

Disadvantages:

- Less durable?
- More complex anatomy
- Higher risk patients
- Graft-placement more difficult
- Follow-up parameters lost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Are the RCTs still useful

when we are informing our patients?

Conclusions

- **Short-term survival benefit of EVAR over open repair and its gradual loss over time is largely INdependent of endograft evolution**
- **Patient-selection drift may limit generalizability, but risk ratio of open versus EVAR may stay the same**
- **Device-related failures and reinterventions will :**
  - decrease with better EVAR-device technology
  - increase with more complex and lower profile devices, more difficult anatomy

Take-home message

THE RANDOMIZED EVAR TRIALS ARE STILL VALID !!!!!!!


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