

**HTA BASED ON HEALTH CARE SYSTEM EFFICIENCY: USING REAL-LIFE DATA TO IMPROVE HEALTH CARE MANAGEMENT**

**SETTING THE GROUND**

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**IECS**  
INSTITUTO DE EFECTIVIDAD  
CLÍNICA Y SANITARIA

# A RACE WITH HURDLES



**Seguridad**



**Eficacia**



**Calidad**



**Costo-  
Efectividad**



**Impacto  
Presupuestario**

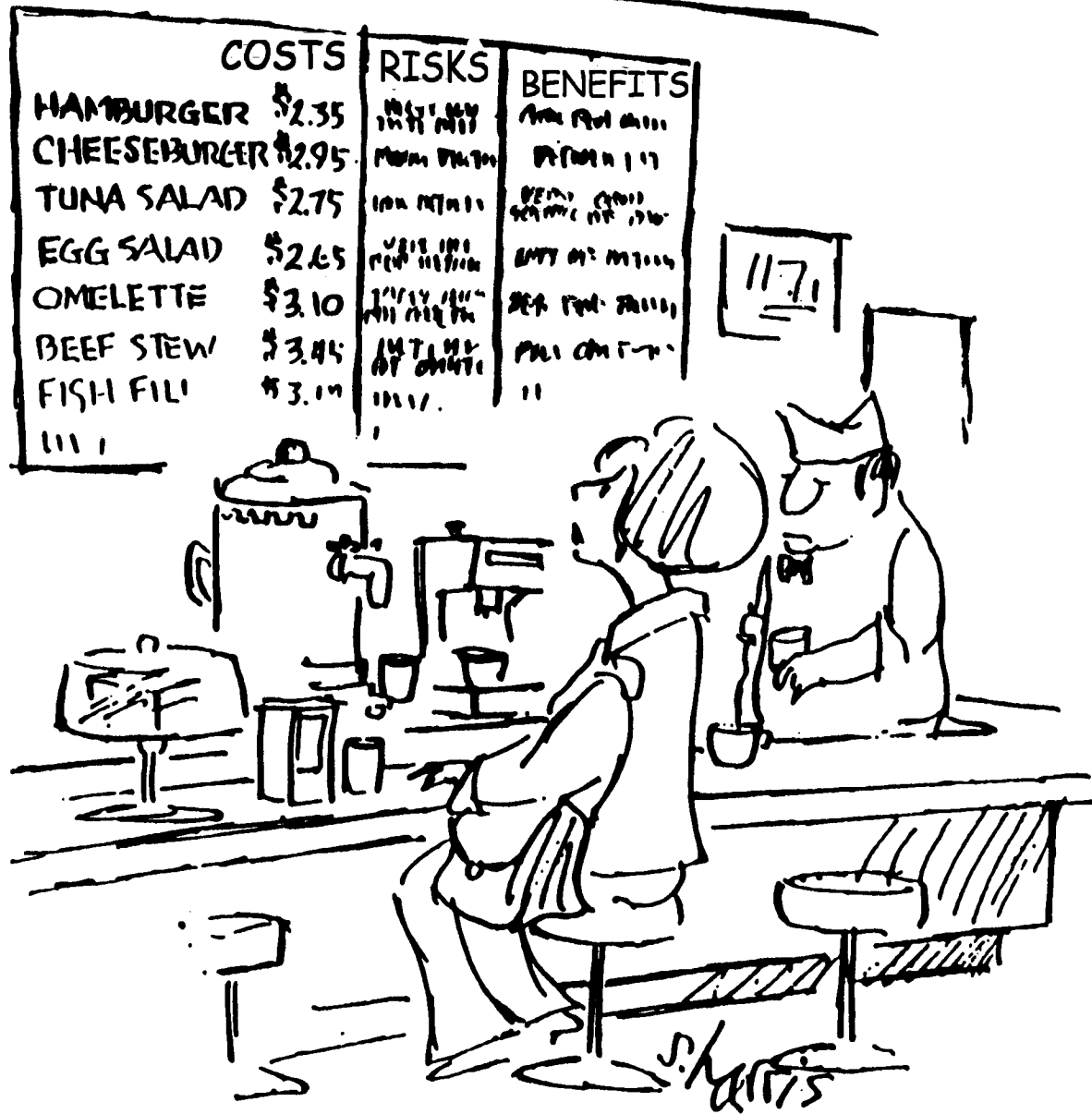
Usually 3..

Then 4... ...& 5?

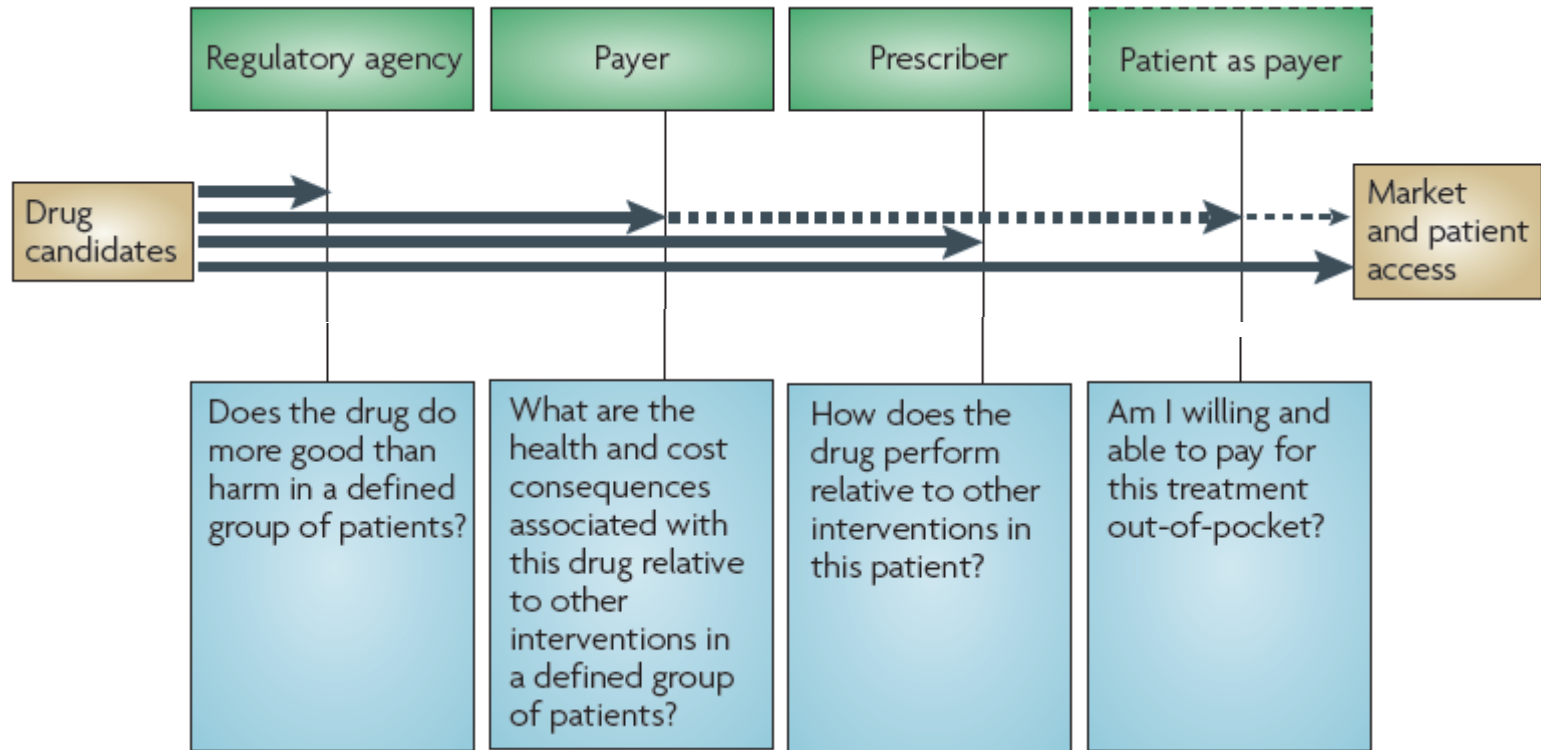


BMJ 2011;342:d2175 doi: 10.1136/bmj.d2175

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# DECISION MAKERS: PROXIMAL AND DISTAL



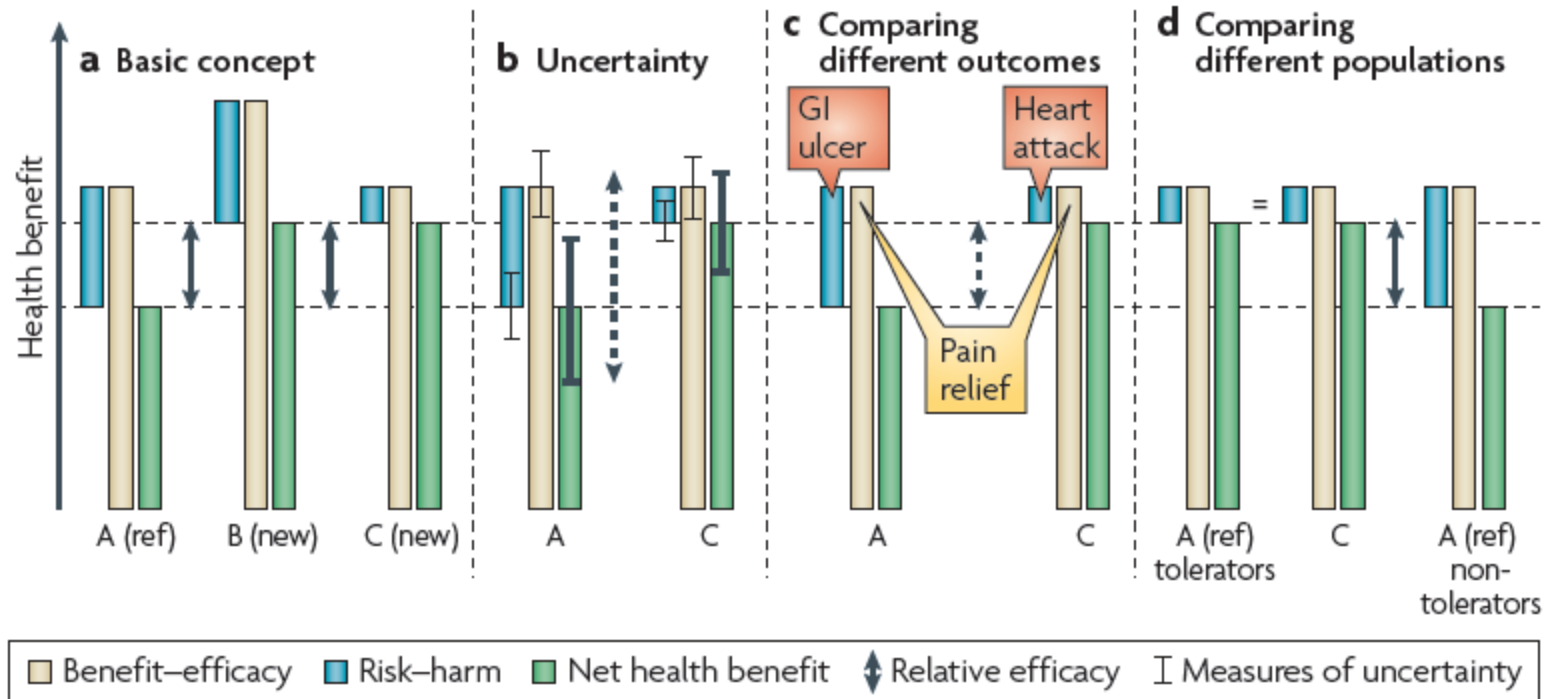
Eichler HG. NATURE REVIEWS. April 2010.

# SOME DEFINITIONS

TERM	EFFICACY	RELATIVE EFFICACY	EFFECTIVENES S	RELATIVE EFFECTIVENESS
DEFINITION: EXTENT TO WHICH AN INTERVENTION DOES MORE GOOD THAN HARM...	UNDER <b>IDEAL</b> CIRCUMSTANCES	UNDER <b>IDEAL</b> CIRCUMSTANCES , <b>COMPARED TO</b> ONE OR MORE ALTERNATIVE INTERVENTONS	WHEN PROVIDED UNDER THE <b>USUAL</b> CIRCUMSTANCES OF HEALTH CARE PRACTICE	<b>COMPARED TO</b> ONE OR MORE INTERVENTION ALTERNATIVES WHEN PROVIDED UNDER THE <b>USUAL</b> CIRCUMSTANCES OF HEALTH CARE PRACTICE
KEY FEATURES	RANDOMIZATION (EXPLANATORY RCTs)	RANDOMIZATION (EXPLANATORY RCTs)	OBSERVATIONAL	OBSERVATIONAL PRAGMATIC / NATURALISTIC <b>RCT</b>

High Level Pharmaceutical Forum of the European Commission. Core principles on relative effectiveness. *EC Pharmacuetical Forum website [online]*, [http://ec.europa.eu/pharmaforum/docs/rea\\_principles\\_en.pdf](http://ec.europa.eu/pharmaforum/docs/rea_principles_en.pdf) (2008).

# CONCEPT AND PITFALLS OF RELATIVE EFFICACY ASSESSMENT



Eichler HG. NATURE REVIEWS. April 2010.

# SOME "NOT SO NUANCES" IN RCTs

## **Superiority, non-inferiority or equivalence trials**

The International Conference on Harmonisation document on statistical principles for clinical

**Superiority trial:** A trial with the primary objective of showing that the response to the investigational product is superior to a comparative agent (active or placebo control)

**Non-inferiority trial:** A trial with the primary objective of showing that the response to the investigational product is not clinically inferior to a comparative agent (active or placebo control)

**Equivalence trial:** A trial with the primary objective of showing that the response to two or more treatments differs by an amount which is clinically unimportant. This is usually demonstrated by showing that the true treatment difference is likely to lie between a lower and an upper equivalence margin of clinically acceptable differences

Eichler HG. NATURE REVIEWS. April 2010.



# ADVANTAGES AND DISADVANTAGES OF KEY STUDY DESIGN

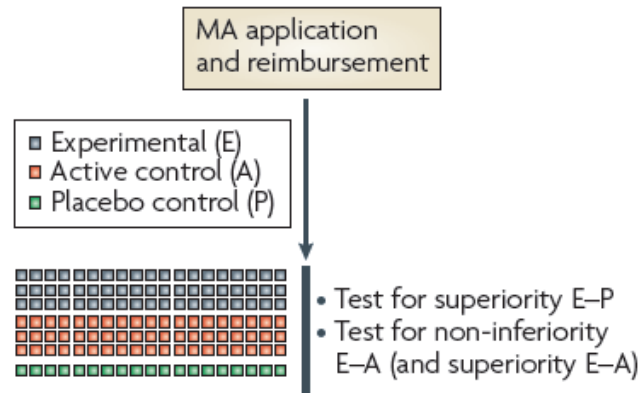
Type of study	Advantages	Disadvantages
Active-controlled superiority- showing randomized controlled trial (RCT)	<ul style="list-style-type: none"> <li>• High internal validity</li> <li>• May provide relevant relative efficacy (RE) information if comparator deemed appropriate</li> </ul>	<ul style="list-style-type: none"> <li>• Often requires large sample size</li> <li>• Only one comparator can usually be studied</li> </ul>
Two-arm non-inferiority-showing RCT	<ul style="list-style-type: none"> <li>• May be the only alternative available for demonstration of efficacy if placebo-controlled RCT considered unethical</li> <li>• Provides limited RE information</li> </ul>	<ul style="list-style-type: none"> <li>• May lack assay sensitivity and therefore internal validity</li> </ul>
Active- and placebo-controlled RCT	<ul style="list-style-type: none"> <li>• Most informative trial design</li> <li>• High internal validity</li> </ul>	<ul style="list-style-type: none"> <li>• Not achievable if placebo control considered unethical</li> <li>• Often requires large sample size</li> </ul>
Pragmatic clinical trial	<ul style="list-style-type: none"> <li>• High external validity</li> <li>• Demonstrates relative effectiveness</li> </ul>	<ul style="list-style-type: none"> <li>• Lower signal-to-noise ratio than conventional RCTs</li> <li>• Requires larger sample size</li> <li>• May mask small true differences between treatments</li> </ul>
Common reference indirect comparison based on RCT information (network meta-analysis)	<ul style="list-style-type: none"> <li>• Relatively easy and less expensive than RCTs</li> <li>• Useful in the absence of head-to-head RCTs</li> </ul>	<ul style="list-style-type: none"> <li>• Essentially non-randomized methodology</li> <li>• May be subject to unknown confounding variables</li> </ul>
Observational studies	<ul style="list-style-type: none"> <li>• May be conducted retrospectively or prospectively</li> <li>• Less expensive and time-consuming than RCTs</li> <li>• Large patient numbers can be observed</li> </ul>	<ul style="list-style-type: none"> <li>• Non-randomized information</li> <li>• Subject to high risk of confounding variables</li> </ul>

Eichler HG. NATURE REVIEWS. April 2010.

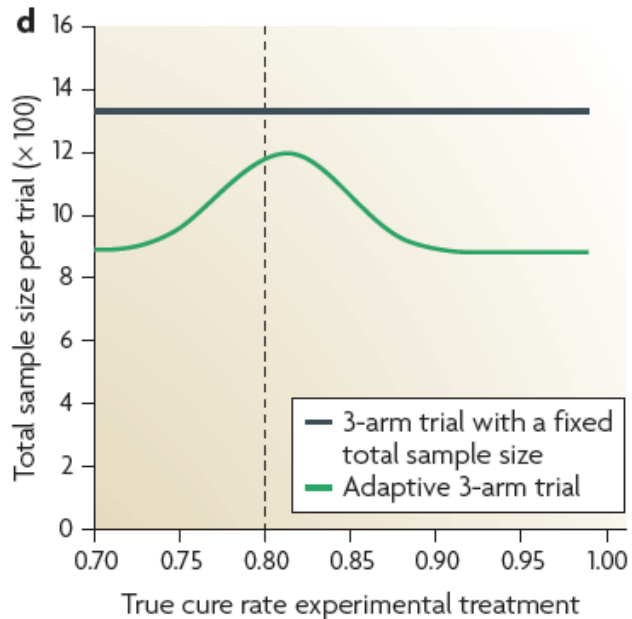
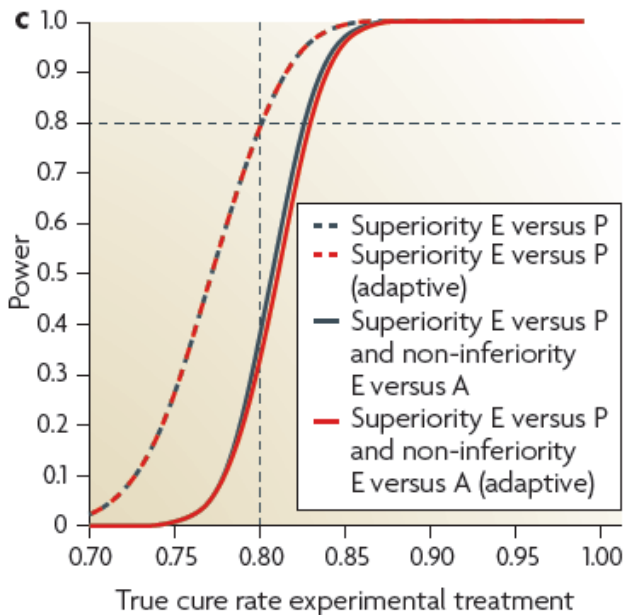
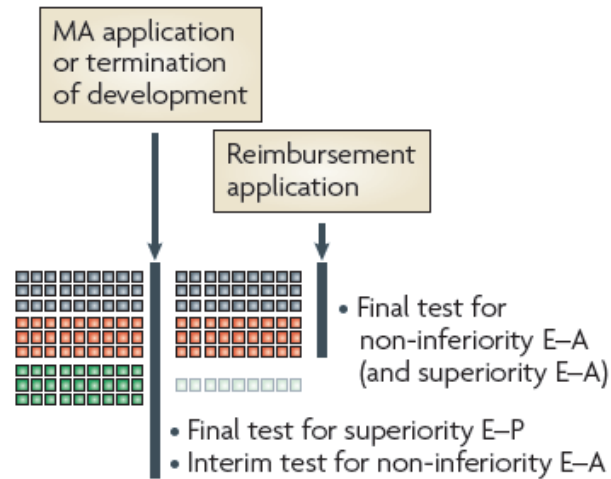
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# POTENTIAL GAINS FROM ADAPTIVE DESIGN TRIALS

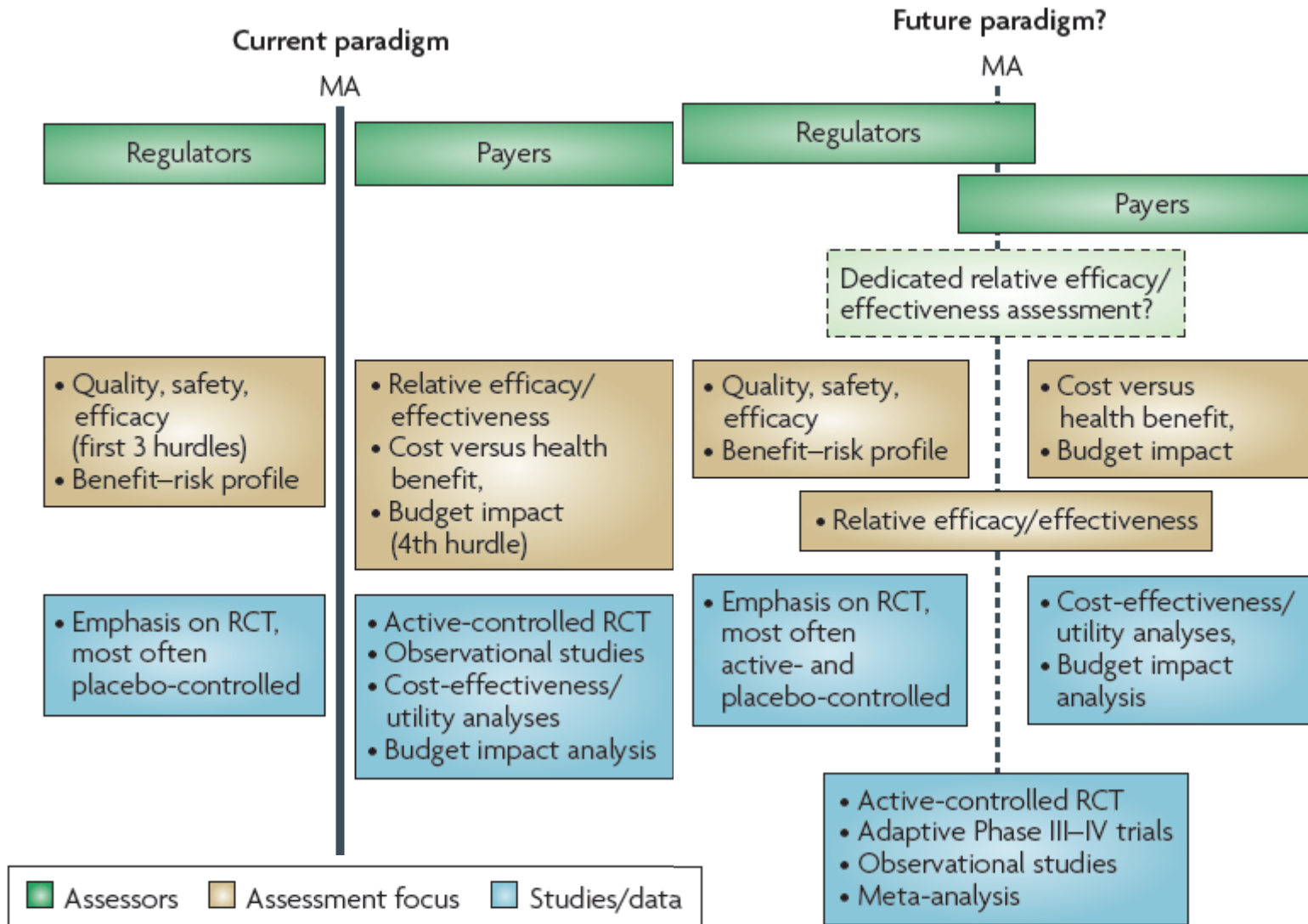
**a Fixed sample size**



**b Adaptive design**



# PARADIGM SHIFT?



# REAL LIFE EXAMPLE 1: ECONOMIC EVALUATION OF PNEUMOCOCCAL VACCINE FOR IMSS

## (INSTITUTO MEXICANO SEGURO SOCIAL)

<i>Costos vacunales</i>			
Estructura (por año quinquagenero)	Costo por dosis.		Costo para el IMSS.
	Costo de administración por dosis.		Costos para el IMSS.
	Pérdida por desperdicio.		
Probabilidad	Cobertura de la vacunación sobre los niños en edad de vacunarse.		Puede considerarse el 100% de la población blanco.
<i>Otros costos directos</i>			
Espera	Costo promedio por episodio agudo: internación por neumonía (en niños y adultos).	Micro-costeo o macro-costeo.	Costos para el IMSS.
	Costo promedio por episodio agudo: caso ambulatorio de neumonía (en niños y adultos).	Micro-costeo o macro-costeo.	Costos para el IMSS.
	Costo promedio por episodio agudo: Miringotomía (en niños y adultos).	Micro-costeo o macro-costeo.	Costos para el IMSS.
	Costo promedio por episodio agudo: manejo ambulatorio de caso de OMA (en niños y adultos)	Micro-costeo o macro-costeo.	Costos para el IMSS.
	Costo promedio por episodio agudo: internación por Meningitis (en niños y adultos).	Micro-costeo o macro-costeo.	Costos para el IMSS.

# REAL LIFE EXAMPLE 2: HEMODIALYSIS AND PERITONEAL DIALYSIS

Modalidad	Clasificación	Total Intern	LOS (Días)				Costo Internación			
			Prom	Min	Max	DS	Prom	Min	Max	DS
HD	Acceso Vascular	40	1,98	0,00	15,00	2,52	\$3.089,06	\$220,75	\$10.913,62	\$2.756,37
HD	Enf Cardiovascular	63	4,90	0,00	23,00	4,24	\$6.662,37	\$260,61	\$73.194,34	\$11.445,74
HD	Infección	151	8,74	0,00	94,00	14,23	\$5.686,08	\$350,37	\$55.359,29	\$8.719,81
HD	Peritonitis	6	6,50	2,00	15,00	4,85	\$3.337,46	\$190,00	\$10.887,41	\$5.079,66
PD	Acceso Vascular	6	1,50	1,00	2,00	0,55	\$1.330,59	\$651,41	\$2.651,30	\$726,82
PD	Enf Cardiovascular	19	8,47	1,00	31,00	7,88	\$9.762,74	\$1.778,00	\$20.042,01	\$6.226,75
PD	Infección	47	6,70	1,00	42,00	7,65	\$13.279,45	\$385,26	\$117.645,25	\$28.435,77
PD	Peritonitis	14	6,93	1,00	16,00	4,87	\$3.882,31	\$426,76	\$14.137,51	\$4.666,20

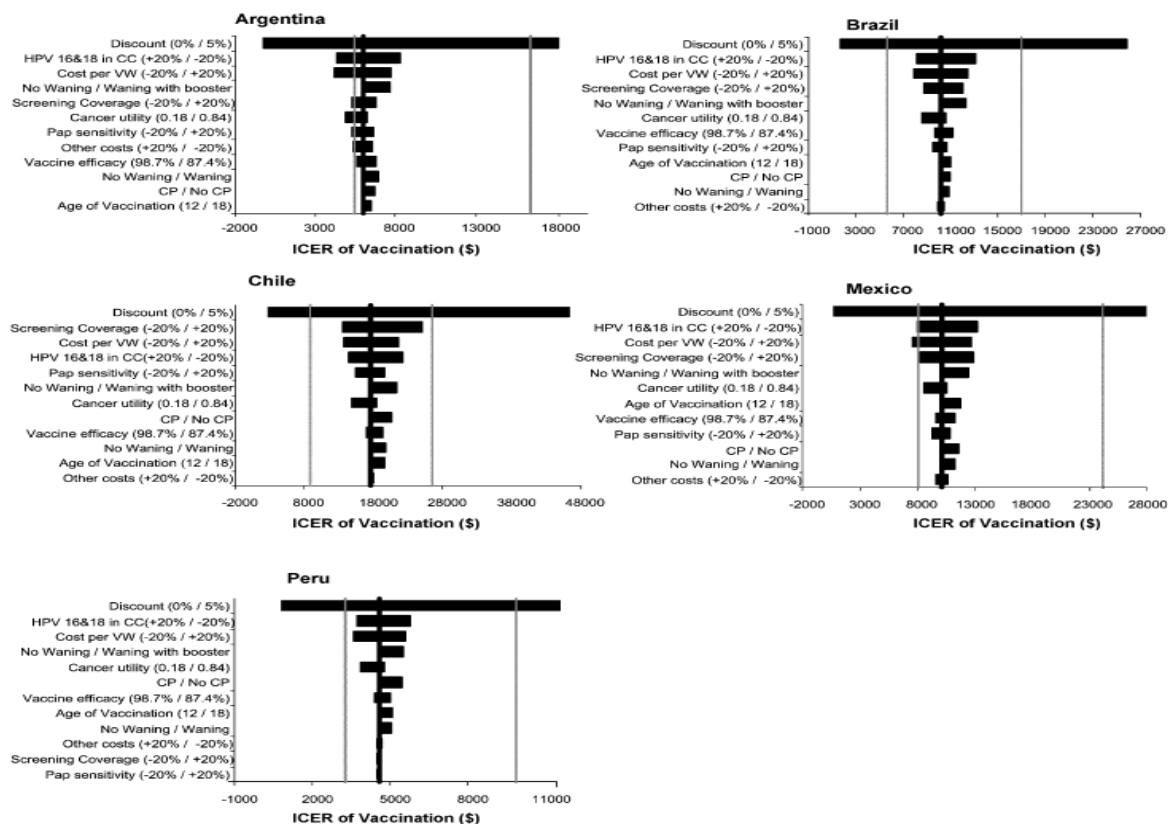
Modalidad	Clasificación	Consultas Especialistas				Consultas Guardi				Consultas MC			
		Prom	Min	Max	DS	Prom	Min	Max	DS	Prom	Min	Max	DS
HD	Acceso Vascular	2,75	0,00	23,00	4,36	0,60	0,00	3,00	0,84	0,00	0,00	0,00	0,00
HD	Enf Cardiovascular	2,35	0,00	12,00	2,81	1,10	0,00	7,00	1,58	0,10	0,00	2,00	0,35
HD	Infección	2,99	0,00	21,00	4,15	0,73	0,00	6,00	1,14	0,09	0,00	3,00	0,38
HD	Peritonitis	2,33	0,00	7,00	2,50	0,33	0,00	2,00	0,82	0,00	0,00	0,00	0,00
PD	Acceso Vascular	0,50	0,00	1,00	0,55	1,00	0,00	2,00	0,63	0,00	0,00	0,00	0,00
PD	Enf Cardiovascular	1,89	0,00	7,00	1,85	0,79	0,00	4,00	1,13	0,00	0,00	0,00	0,00
PD	Infección	3,51	0,00	14,00	3,84	0,89	0,00	5,00	1,22	0,02	0,00	1,00	0,15
PD	Peritonitis	0,71	0,00	3,00	0,99	0,57	0,00	3,00	1,09	0,07	0,00	1,00	0,27



# Cost-effectiveness analysis of a cervical cancer vaccine in five Latin American countries

Lisandro Colantonio<sup>a,b,\*</sup>, Jorge A. Gómez<sup>c</sup>, Nadia Demarteau<sup>d,e</sup>, Baudouin Standaert<sup>e</sup>, Andrés Pichón-Rivière<sup>a,b</sup>, Federico Augustovski<sup>a,b,f</sup>

# REAL LIFE EXAMPLE: ECONOMIC EVALUATION OF HPV VACCINE IN 5 LA COUNTRIES



# OBSERVATIONAL/REAL LIFE VS. EXPERIMENTAL...

## Observations Proved True

- Lower blood pressure with drugs
- Lower LDL with statins
- Aspirin to prevent MI
- Mammography for breast cancer

## ...and Not

- Hormonal Replacement Therapy (breast cancer, failed)
- Vitamins to prevent cancer/CVD (failed)
- Bone marrow transplant for breast cancer (higher death)
- Back surgery, kyphoplasty (marginal benefit)

Thank you to Andrew Epstein and Michael Lauer

# CONCLUSIONS

- DIFFERENT DATA AND REQUIREMENTS BY DIFFERENT HEALTHCARE DECISION MAKERS
- EXPERIMENTAL DATA STILL KEY TO ACCOUNT FOR ISSUES SUCH AS UNMEASURED CONFOUNDING
- EXCEPTIONS (HUGE EFFECT SIZES)

• INCREASING IMPORTANCE OF REAL LIFE OBSERVATIONAL +/- EXPERIMENTAL DATA TO INFORM HEALTH DECISIONS

Hazardous journeys

Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials

Gordon C S Smith, Jill P Pell



Parachutes reduce the risk of injury after gravitational challenge, but their effectiveness has not been proved with randomised controlled trials