Kan AI en big data ons aan verantwoordbare zorg helpen?

W. Van Biesen
Ghent University Hospital

Artificial Intelligence (A.I.)

Output

DIAL MOVE:6
DIAL MOVE:1
DIAL MOVE:2
DIAL MOVE:7
DIAL MOVE:9
DRAWN GAME...

EDSAC/USER FIRST (DIAL
DIA

Clear   Reset
Start   Stop
Single E.P

SCR   Order Tank   LongTank   0
                Multiplier
                Multiplicand   ☑ Short Tan
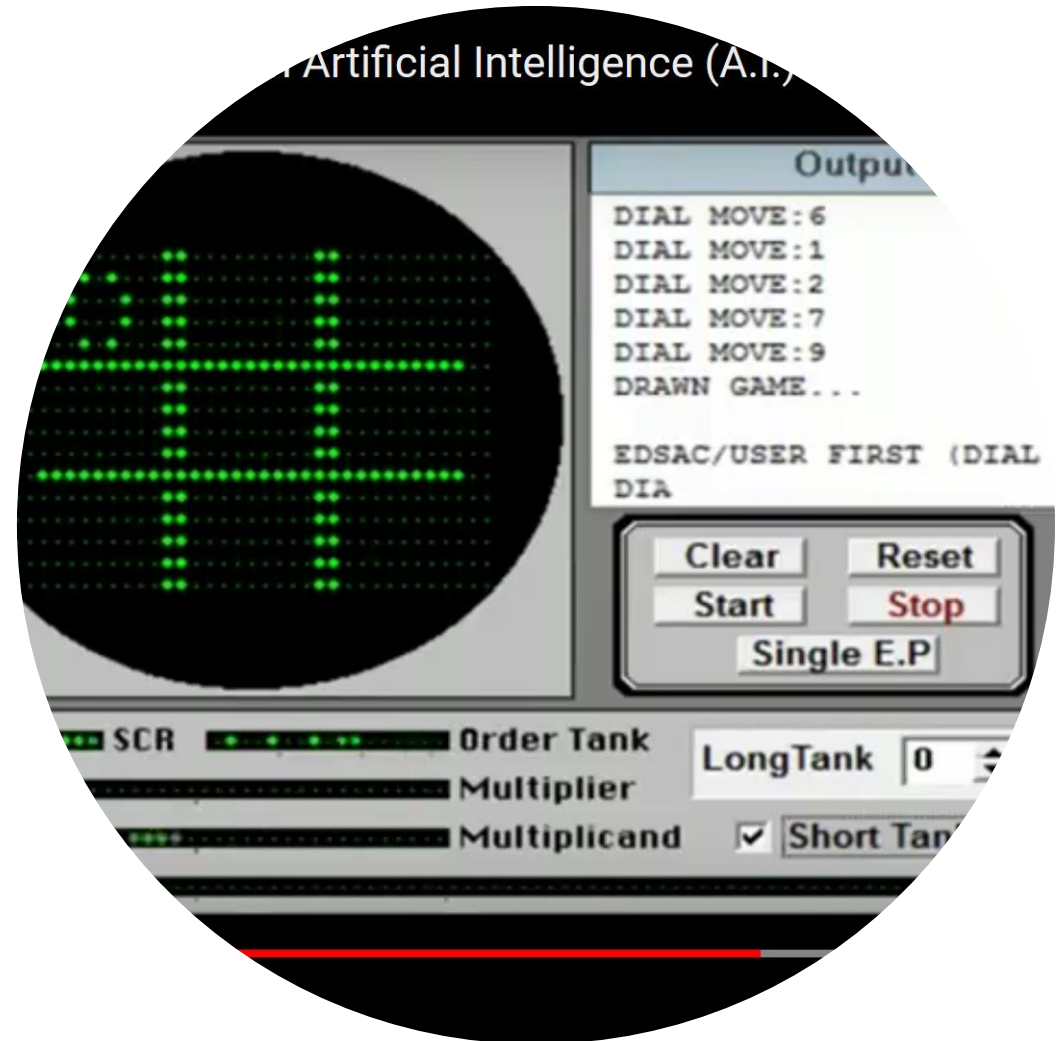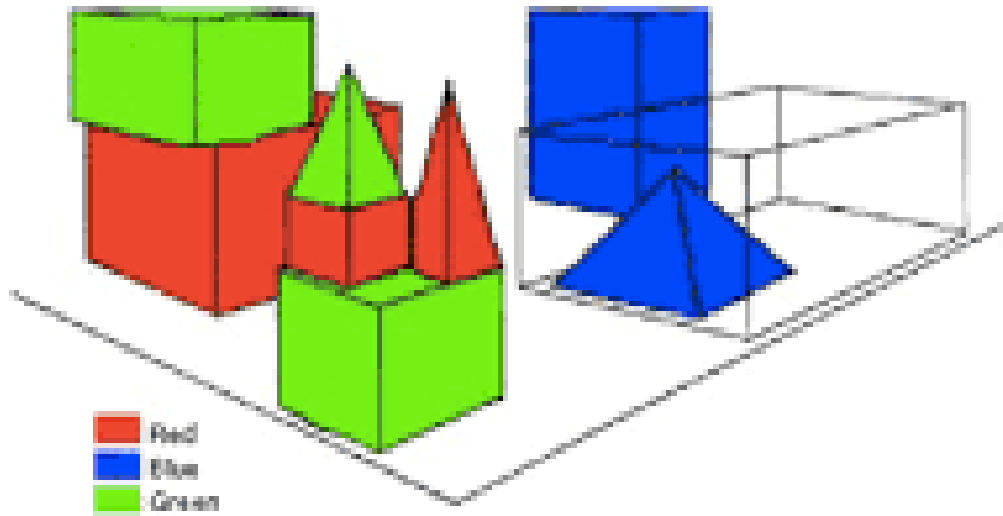
Person: Pick up a big red block.
Computer: OK.
Person: Grasp the pyramid.
Computer: I don't understand which pyramid you mean.

SHRDLU language

Conceptualisation of the world

Manipulating symbols:
2+2=4; 4+2=6;
2+2+2=6
$*£%; %$£M;
$*$ $£M

Creating "meaning"
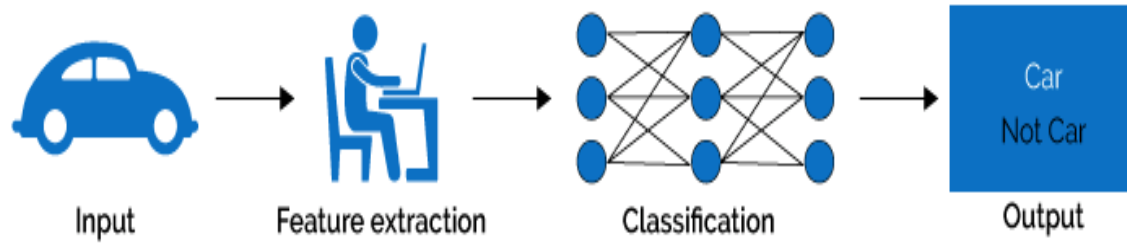
Machine Learning

Input → Feature extraction → Classification → Output

Car
Not Car

Deep Learning

Input → Feature extraction + Classification → Output

Car
Not Car

Train

Errors

FEATURES

Deploy

FEATURES

Intervention

Basic science

Can it work?
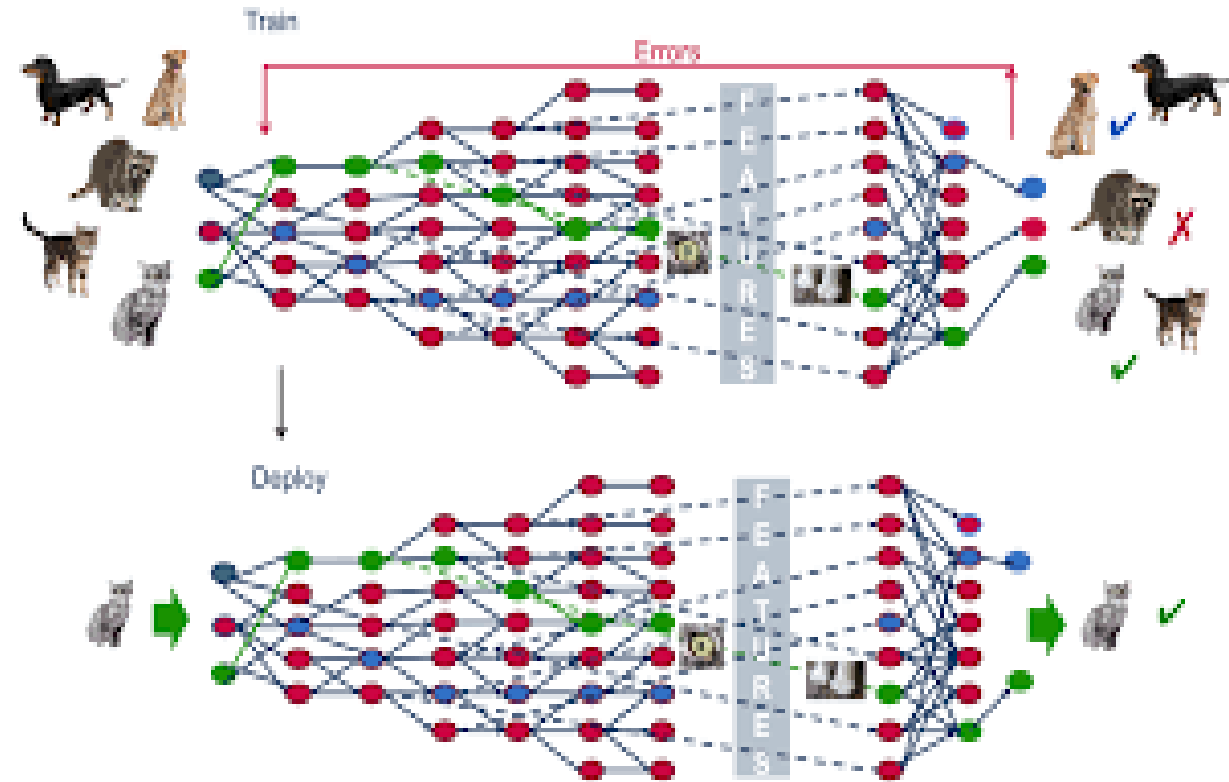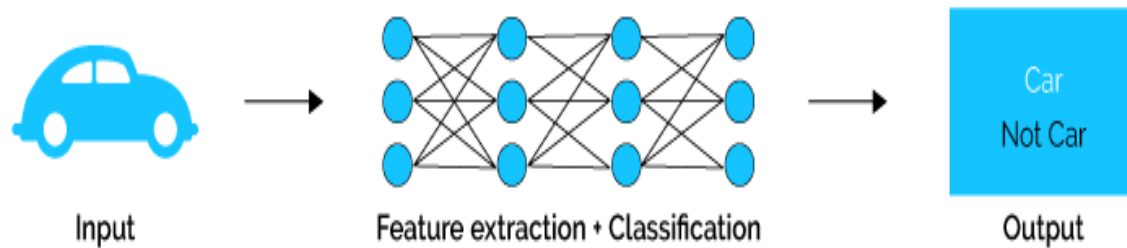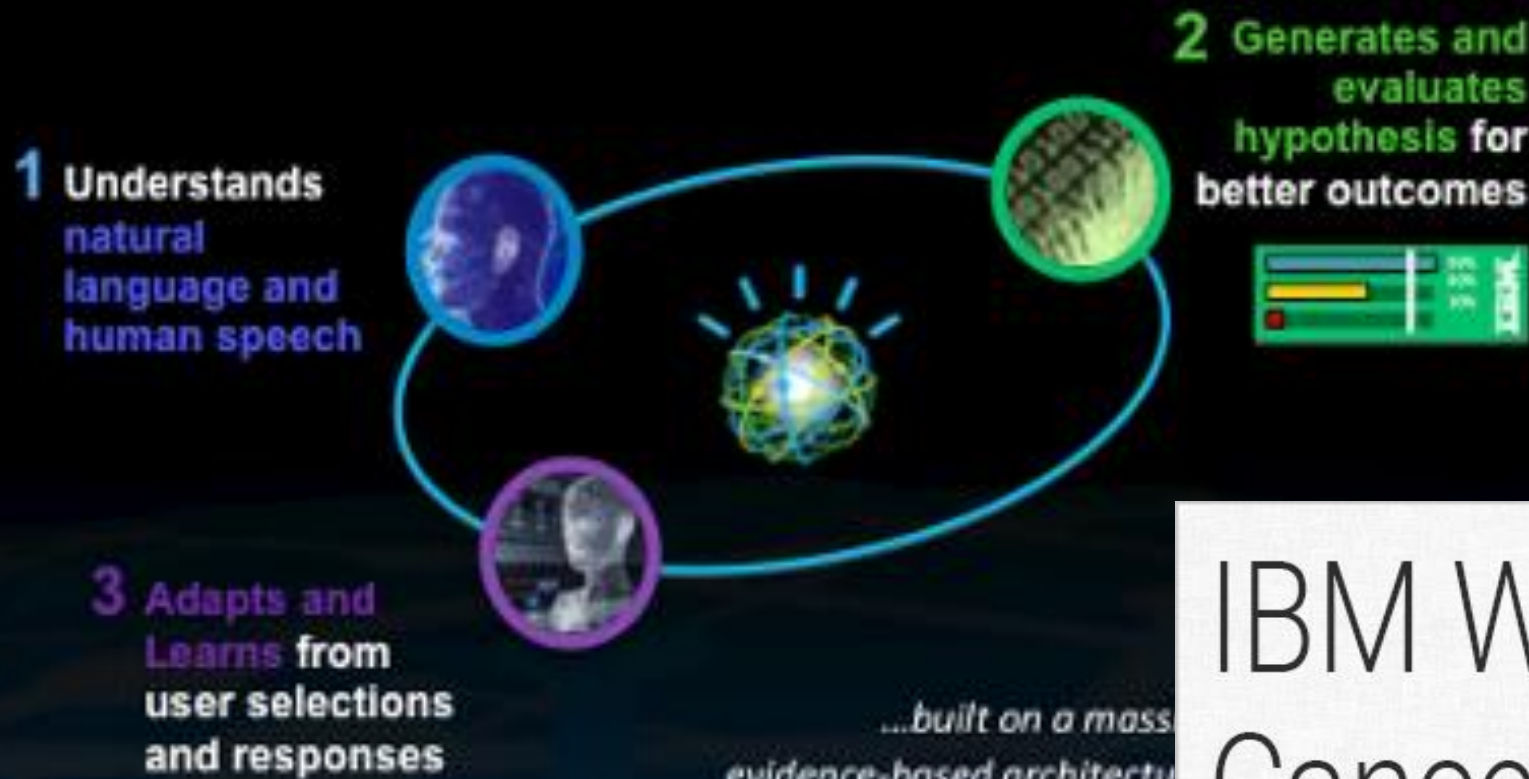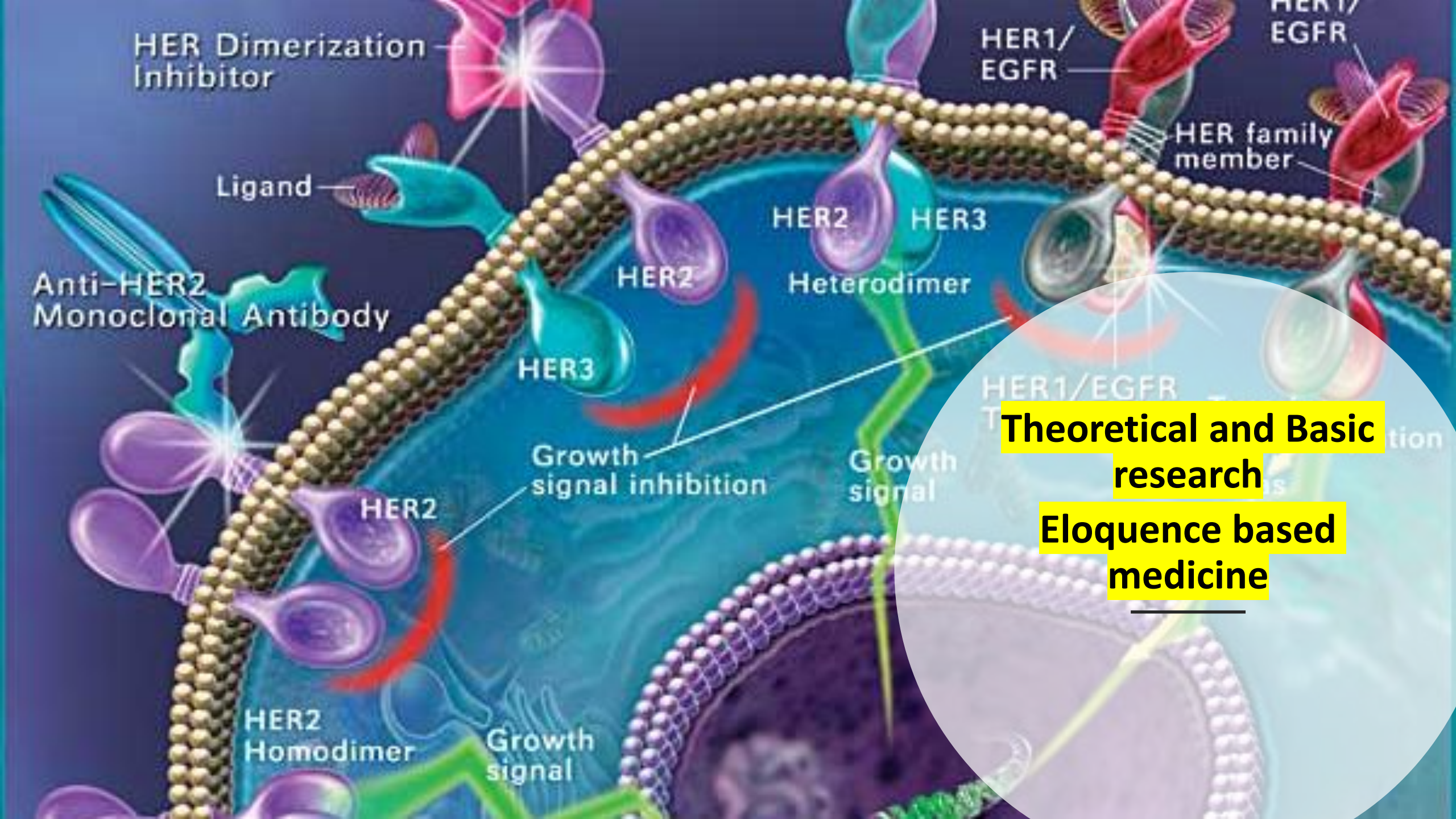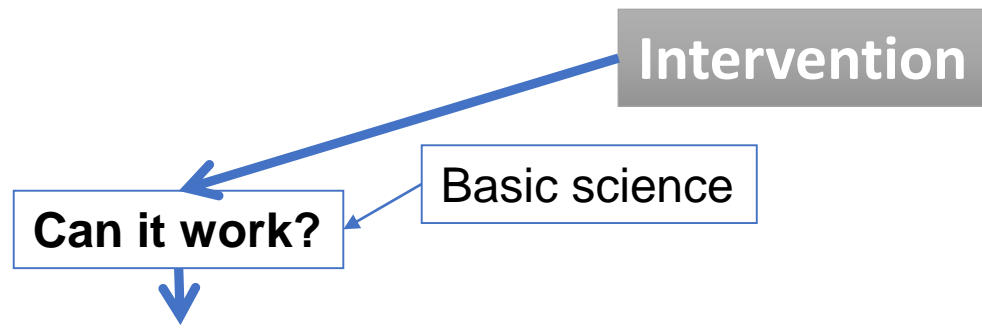
Evidence Based Medicine

Decision making on (medical) actions, intentionally based on a transparant and systematic analysis of available evidence, and this applied to a real-life clinical context

**With the goal to decrease the
DISCREPANCY
between
medical actions
And
Medical knowledge**

Evidence Based Medicine
Randomized Controlled Trial

Randomisation to ensure that the only difference between two experimental groups is the intervention under scrutiny

Causality

Automated, electronic alerts for acute kidney injury: a single-blind, parallel-group, randomised controlled trial
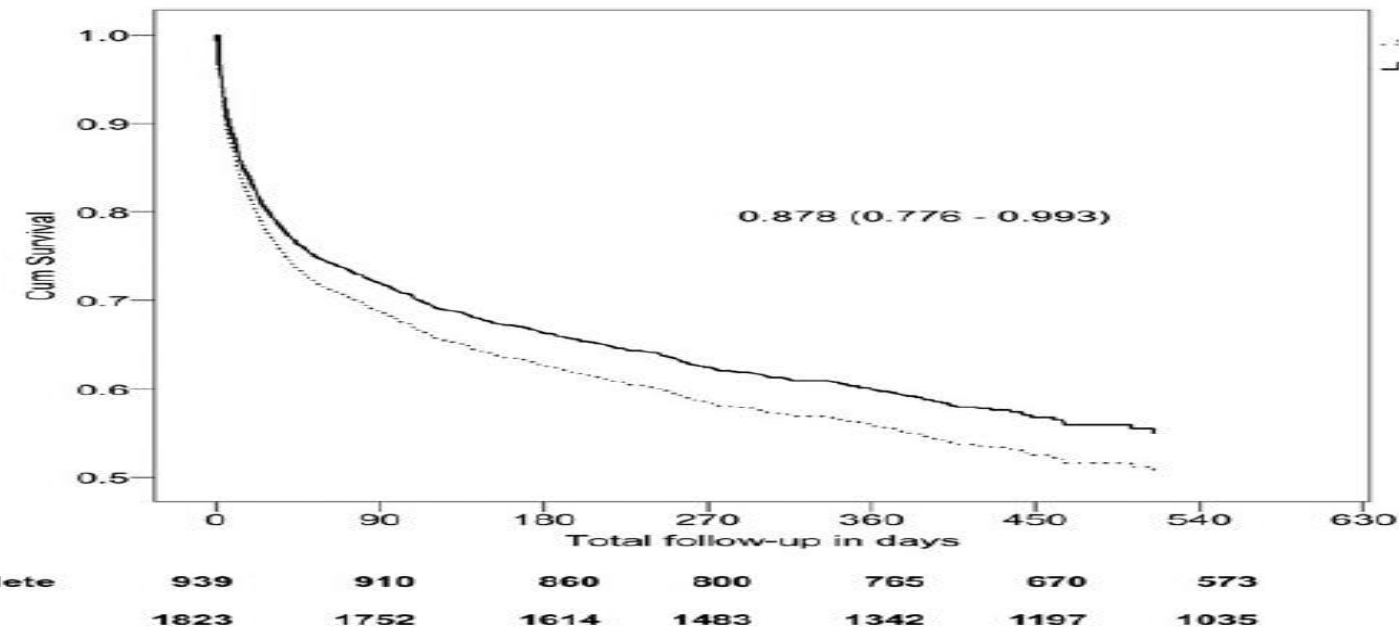
F Perry Wilson, Michael Shashaty, Jeffrey Testani, Iram Aqeel, Yuliya Borovskiy, Susan S Ellenberg, Harold I Feldman, Hilda Fernandez, Yevgeniy Gitelman, Jennie Lin, Dan Negoianu, Chirag R Parikh, Peter P Reese, Richard Urbani, Barry Fuchs

Original Article

A simple care bundle for use in acute kidney injury: a propensity score matched cohort study

No at risk						
AKI-CB complete	939	910	860	800	765	670	573
AKI-CB not completed	1823	1752	1614	1483	1342	1197	1035

Cochrane review Hemmingsen et al, BMJ, 2011

Study	No of events/total		Risk ratio (Mantel-Haenszel, random) (95% CI)	Weight (%)	Risk ratio (Mantel-Haenszel, random) (95% CI)
	Intensive control	Conventional control			
UGDP 1978	52/204	52/210		8.6	1.03 (0.74 to 1.44)
Service 1983	0/10	0/10		0.0	Not estimable
VA CSDM 1995	5/75	5/78		0.8	1.04 (0.31 to 3.45)
Jaber 1996	0/23	0/22		0.0	Not estimable
UKPDS 1998	539/3071	213/1138		25.9	0.94 (0.81 to 1.08)
Kumamoto 2000	3/55	6/55		0.6	0.50 (0.13 to 1.90)
Bagg 2001	0/21	0/22		0.0	Not estimable
ACCORD 2008	257/5128	203/5123		20.4	1.26 (1.06 to 1.51)
ADVANCE 2008	498/5571	533/5569		30.7	0.93 (0.83 to 1.05)
REMBO 2008	4/41	4/40		0.7	0.98 (0.26 to 3.64)
IDA 2009	0/51	0/51		0.0	Not estimable
VADT 2009	102/892	95/899		12.3	1.08 (0.83 to 1.41)
Total (95% CI)	1460/15 142	1111/13 217		100.0	1.02 (0.91 to 1.13)

Test for heterogeneity: $\tau^2=0.01$, $\chi^2=10.07$, df=7, P=0.18, $I^2=30\%$

Test for overall effect: z=0.33, P=0.74
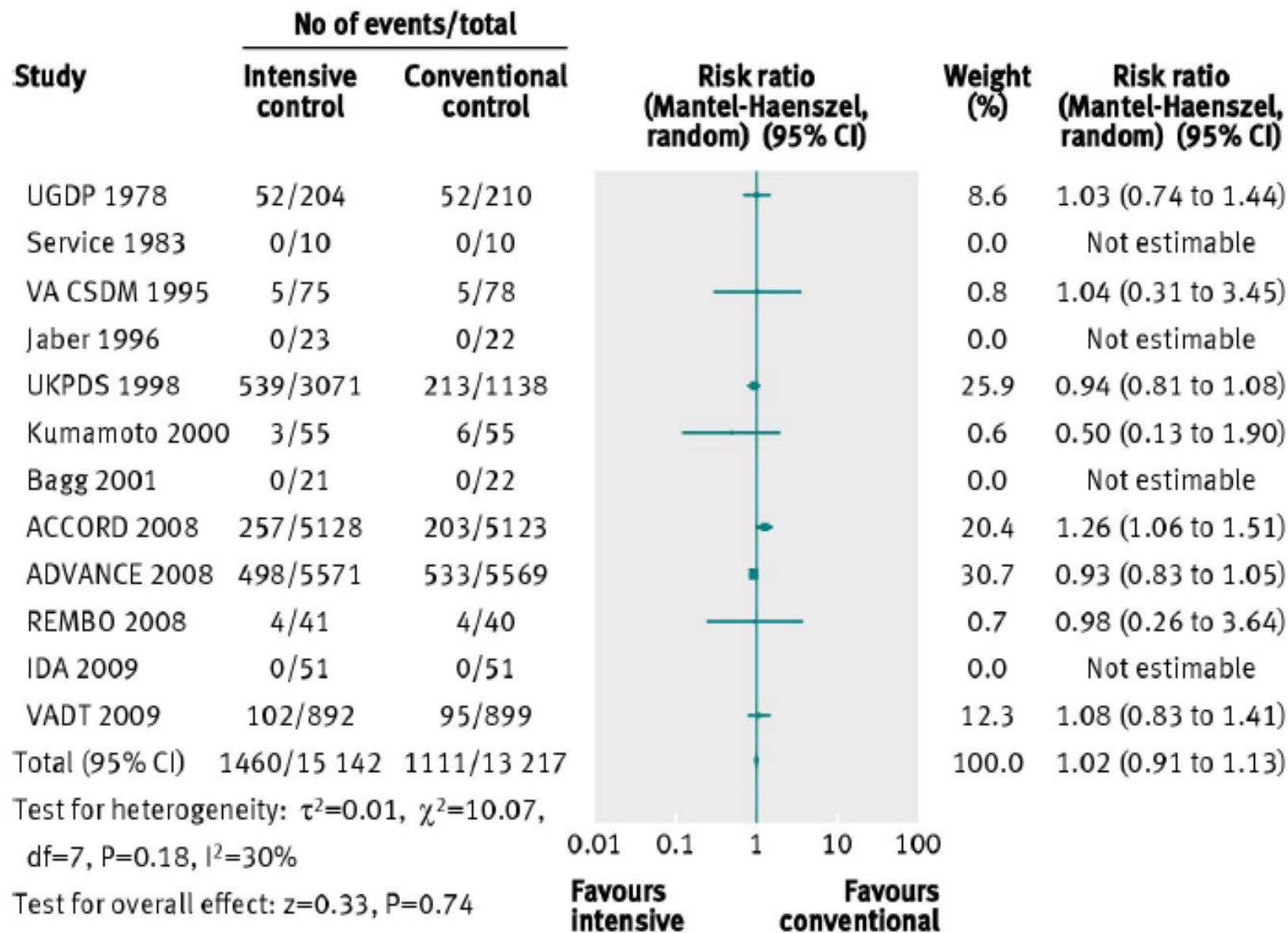
Favours intensive   Favours conventional
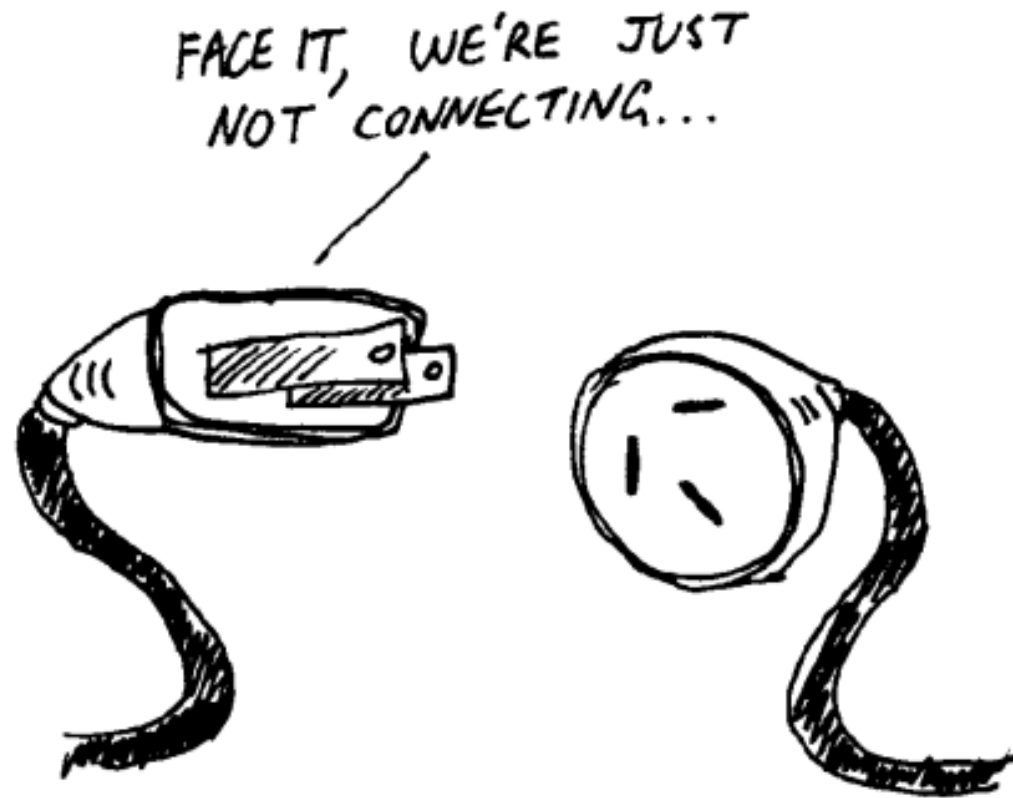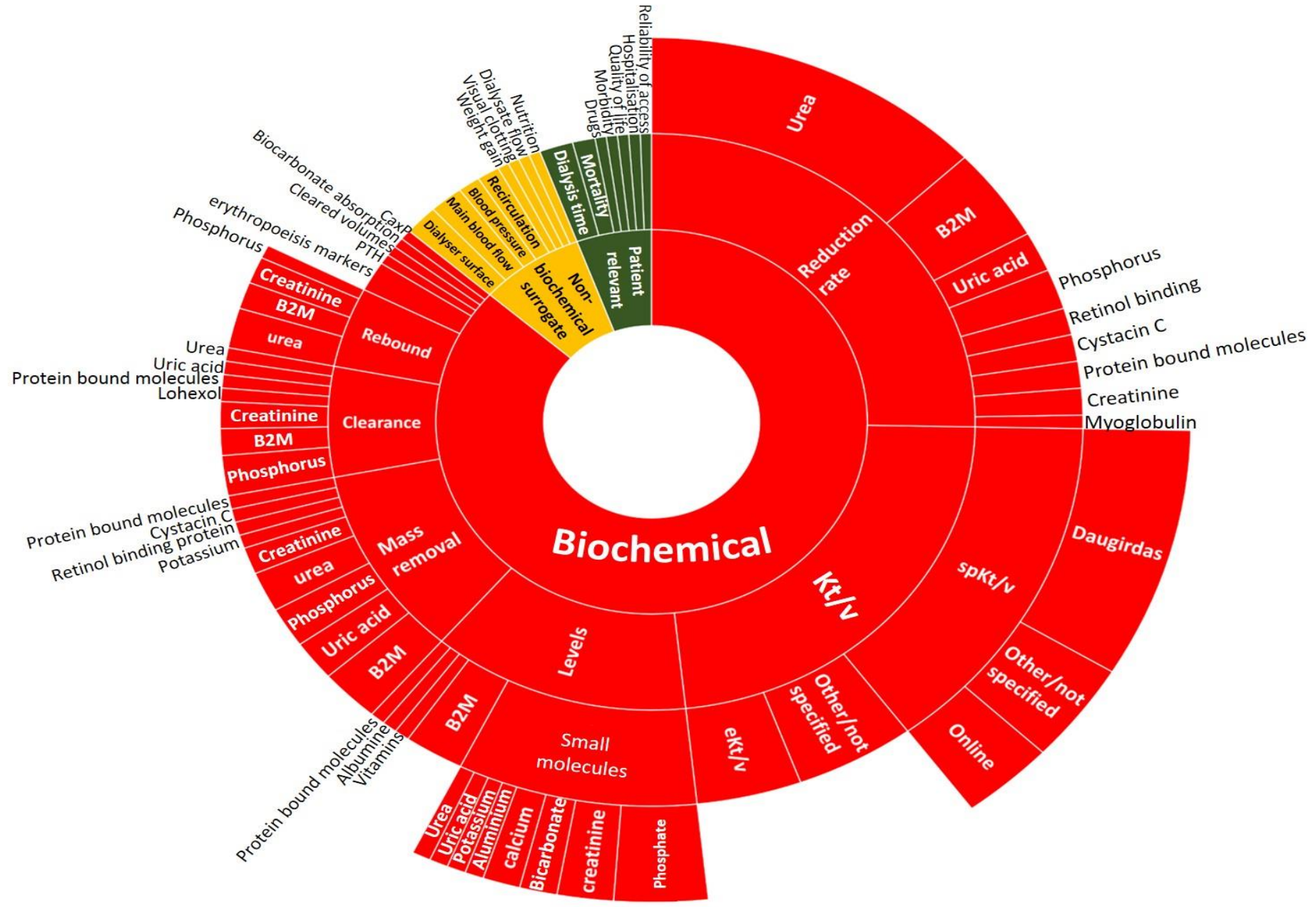
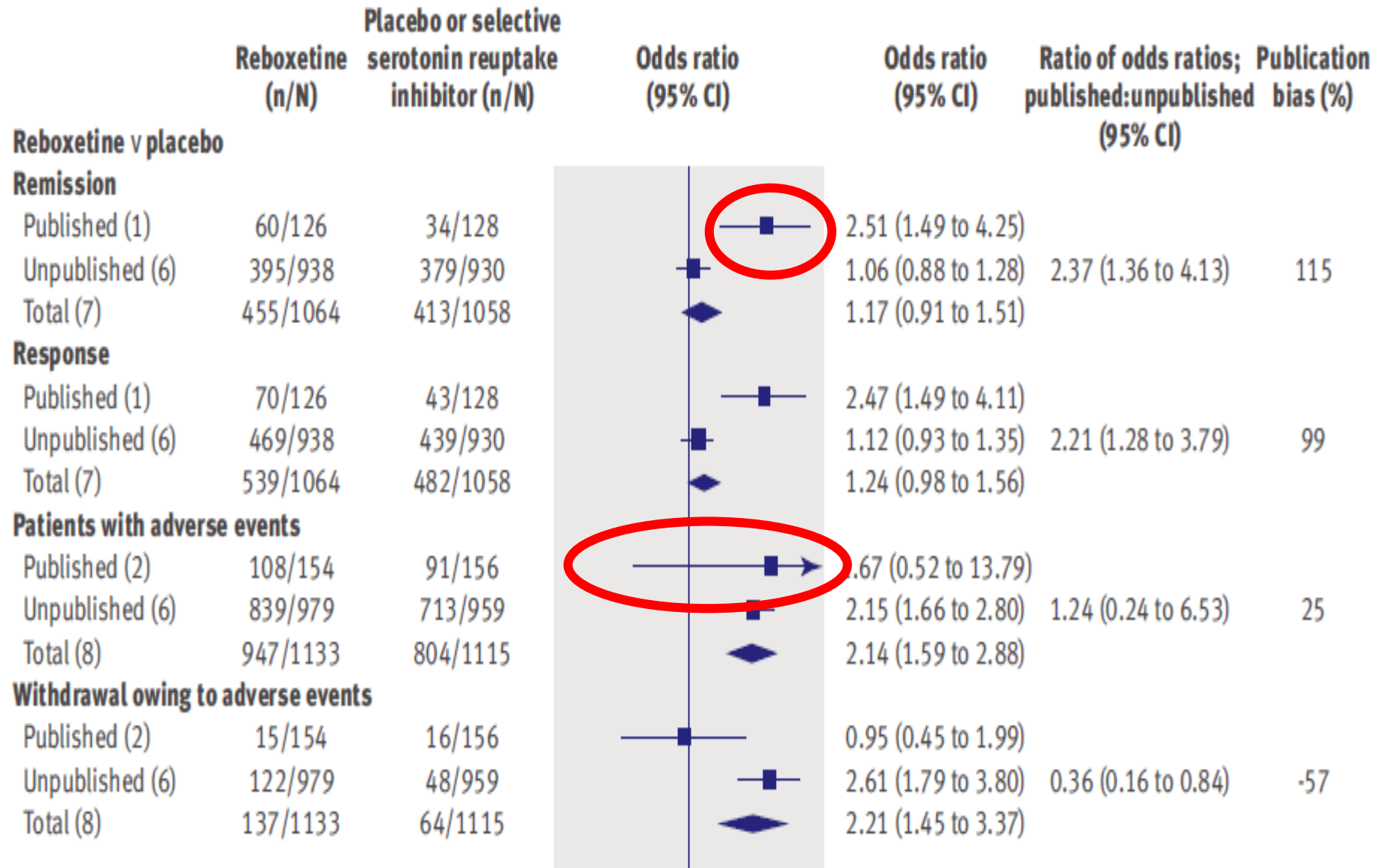**Fig 2** Forest plot for all cause mortality

Wrong outcomes impede meta-analysis

Adequacy of dialysis: definitions in RCTs: a systematic review

Impact of non-published evidence: the reboxetine case

	Reboxetine (n/N)	Placebo or selective serotonin reuptake inhibitor (n/N)	Odds ratio (95% CI)	Odds ratio (95% CI)	Ratio of odds ratios; published:unpublished (95% CI)	Publication bias (%)
Reboxetine v placebo						
Remission						
Published (1)	60/126	34/128		2.51 (1.49 to 4.25)		
Unpublished (6)	395/938	379/930		1.06 (0.88 to 1.28)	2.37 (1.36 to 4.13)	115
Total (7)	455/1064	413/1058		1.17 (0.91 to 1.51)		
Response						
Published (1)	70/126	43/128		2.47 (1.49 to 4.11)		
Unpublished (6)	469/938	439/930		1.12 (0.93 to 1.35)	2.21 (1.28 to 3.79)	99
Total (7)	539/1064	482/1058		1.24 (0.98 to 1.56)		
Patients with adverse events						
Published (2)	108/154	91/156		.67 (0.52 to 13.79)		
Unpublished (6)	839/979	713/959		2.15 (1.66 to 2.80)	1.24 (0.24 to 6.53)	25
Total (8)	947/1133	804/1115		2.14 (1.59 to 2.88)		
Withdrawal owing to adverse events						
Published (2)	15/154	16/156		0.95 (0.45 to 1.99)		
Unpublished (6)	122/979	48/959		2.61 (1.79 to 3.80)	0.36 (0.16 to 0.84)	-57
Total (8)	137/1133	64/1115		2.21 (1.45 to 3.37)		

www.european-real-best-practice.org

Eyding et al, BMJ, 2010

Evaluation of the Inclusion of Studies Identified by the FDA as Having Falsified Data in the Results of Meta-analyses: The Example of the Apixaban Trials

Our sensitivity analysis results showed that conclusions may be altered in meta-analyses by the inclusion of publications with falsified data. This study should add impetus for robust sensitivity analyses and stronger protections against falsified data. Falsified data can affect not only the original publication, but also any subsequent meta-analyses and any resulting clinical or policy changes resulting from the findings of these studies.

Biases in electronic health record data due to processes within the healthcare system: retrospective observational study

Denis Agniel,[1] Isaac S Kohane,[1,2] Griffin M Weber[1,3]

WHAT IS ALREADY KNOWN ON THIS TOPIC

Dynamic processes within the healthcare system, such as the hours when clinics are open and when patients are scheduled to be seen, leave an imprint on electronic health record data

WHAT THIS STUDY ADDS

An evaluation of using the effects of healthcare processes on 272 laboratory tests to predict three year survival in the full patient populations seen over a year at two large hospitals

The hour of the day the test was ordered, the day of the week, and the amount of time between consecutive tests is more predictive of three year survival than the actual value of the test result, for most tests

Polysaccharide Conjugate Vaccine against Pneumococcal Pneumonia in Adults

M.J.M. Bonten, S.M. Huijts, M. Bolkenbaas, C. Webber, S. Patterson, S.
C.H. van Werkhoven, A.M.M. van Deursen, E.A.M. Sanders, T.J.M. V
M. Patton, A. McDonough, A. Moradoghli-Haftvani, H. Smith, T. M
M.W. Pride, G. Crowther, B. Schmoele-Thoma, D.A. Scott, K.U.
R. Lobatto, B. Oosterman, N. Visser, E. Caspers, A. Smorenburg
W.C. Gruber, and D.E. Grobbee

FRAMING

80% relative risk reduction
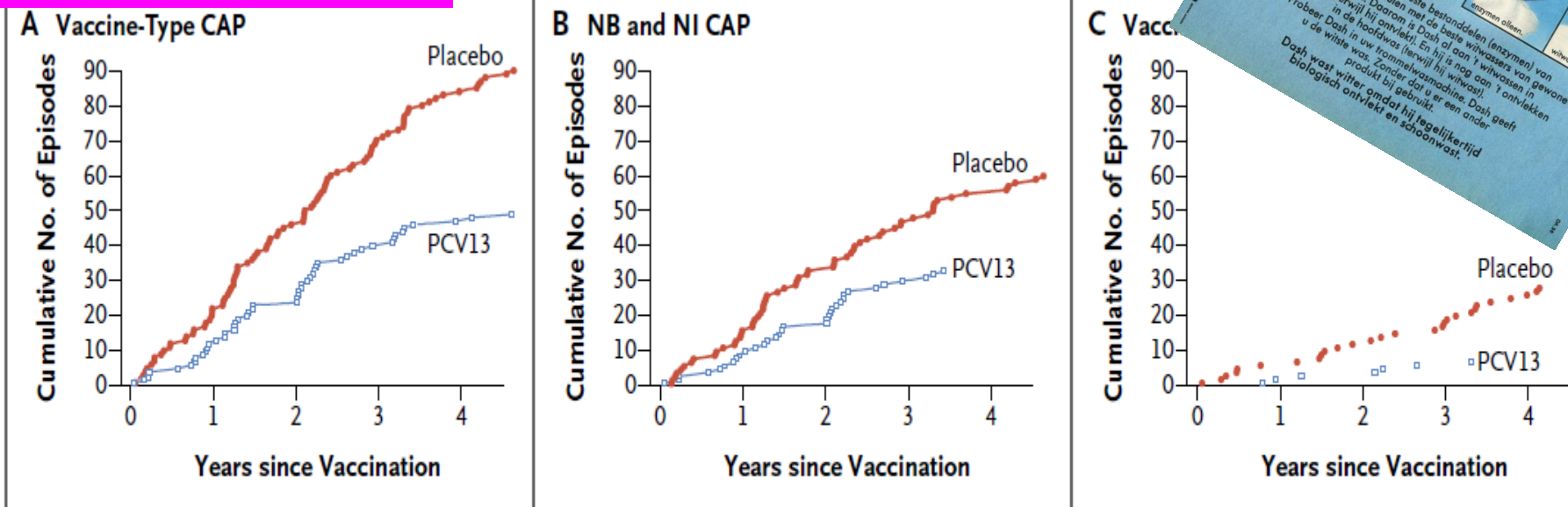
Figure 2. Post Hoc Analysis of the Cumulative Episodes of the Primary and Secondary Efficacy End Points in the Per-Protocol Population.

Polysaccharide Conjugate Vaccine against Pneumococcal Pneumonia in Adults

M.J.M. Bonten, S.M. Huijts, M. Bolkenbaas, C. Webber, S. Patterson, S. Gault,
C.H. van Werkhoven, A.M.M. van Deursen, E.A.M. Sanders, T.J.M. Verheij,
M. Patton, A. McDonough, A. Moradoghli-Haftvani, H. Smith, T. Mellelieu,
M.W. Pride, G. Crowther, B. Schmoele-Thoma, D.A. Scott, K.U. Jansen,
R. Lobatto, B. Oosterman, N. Visser, E. Caspers, A. Smorenburg, E.A. Emini,
W.C. Gruber, and D.E. Grobbee

PER 84000 patients!!!!

49 vs 90 infection with vaccine type strai
100 vs 144 Pneumococcal CAP

NNT: 51/42000 => 1/823

Mortality from pneumococcal pneumonia: 2 vs 2

Overall mortality: 3006 vs 3005

Overall CAP: 747 vs 787

External validity

RALES-study

Juurlink et al N Engl J Med
2004, 351:543-551
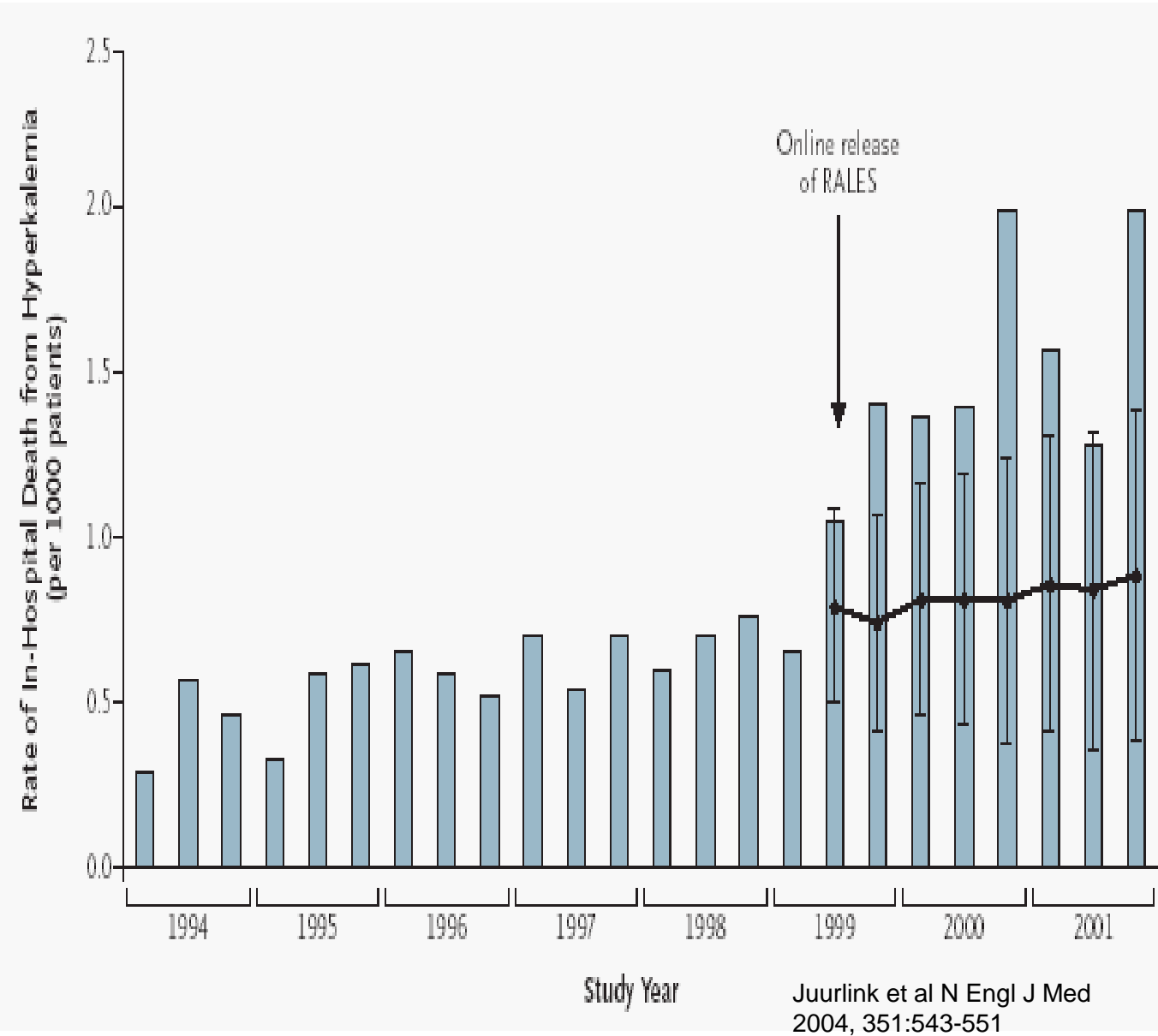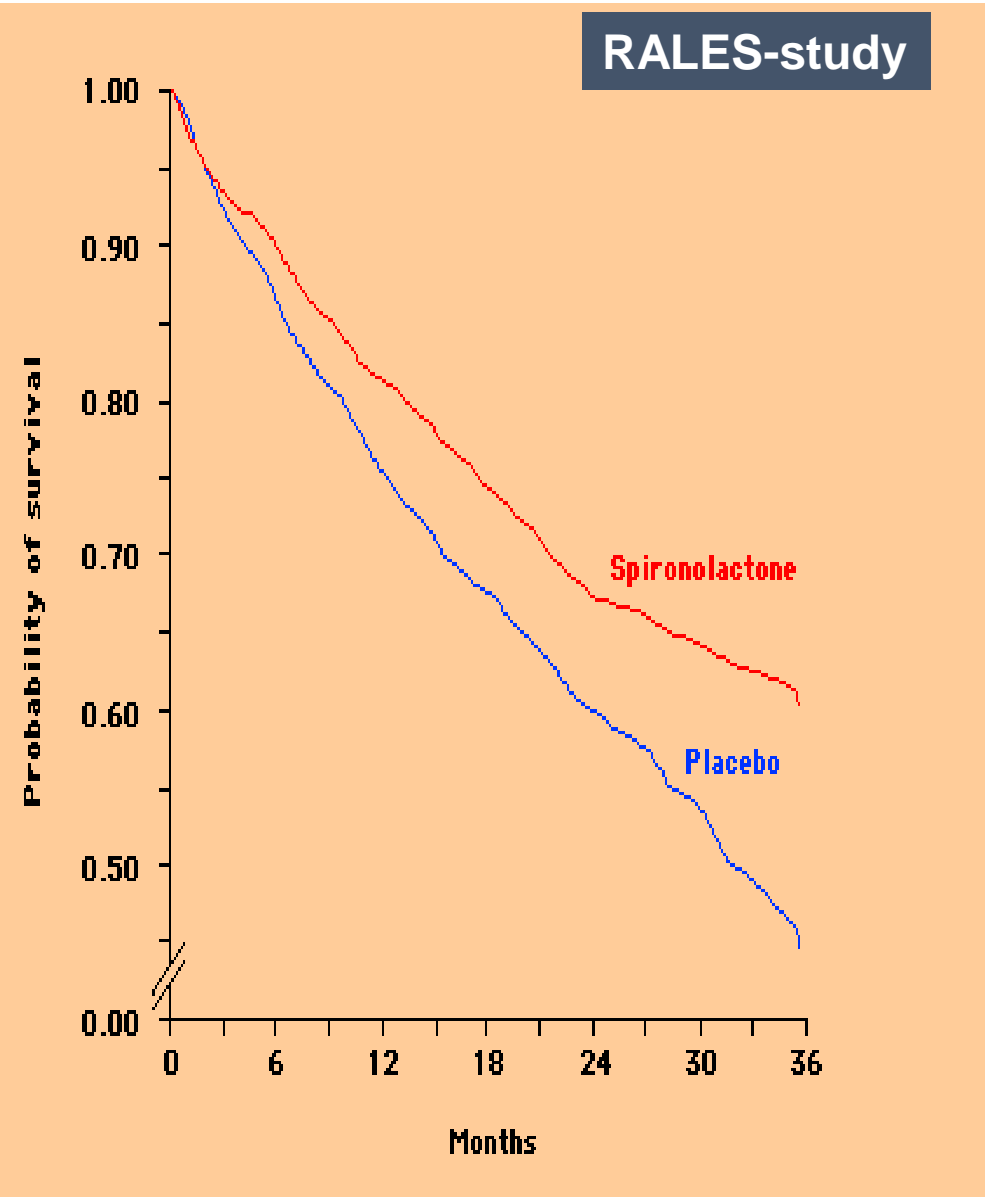
Target population

RCT sample
(random selection)

Generalisibility
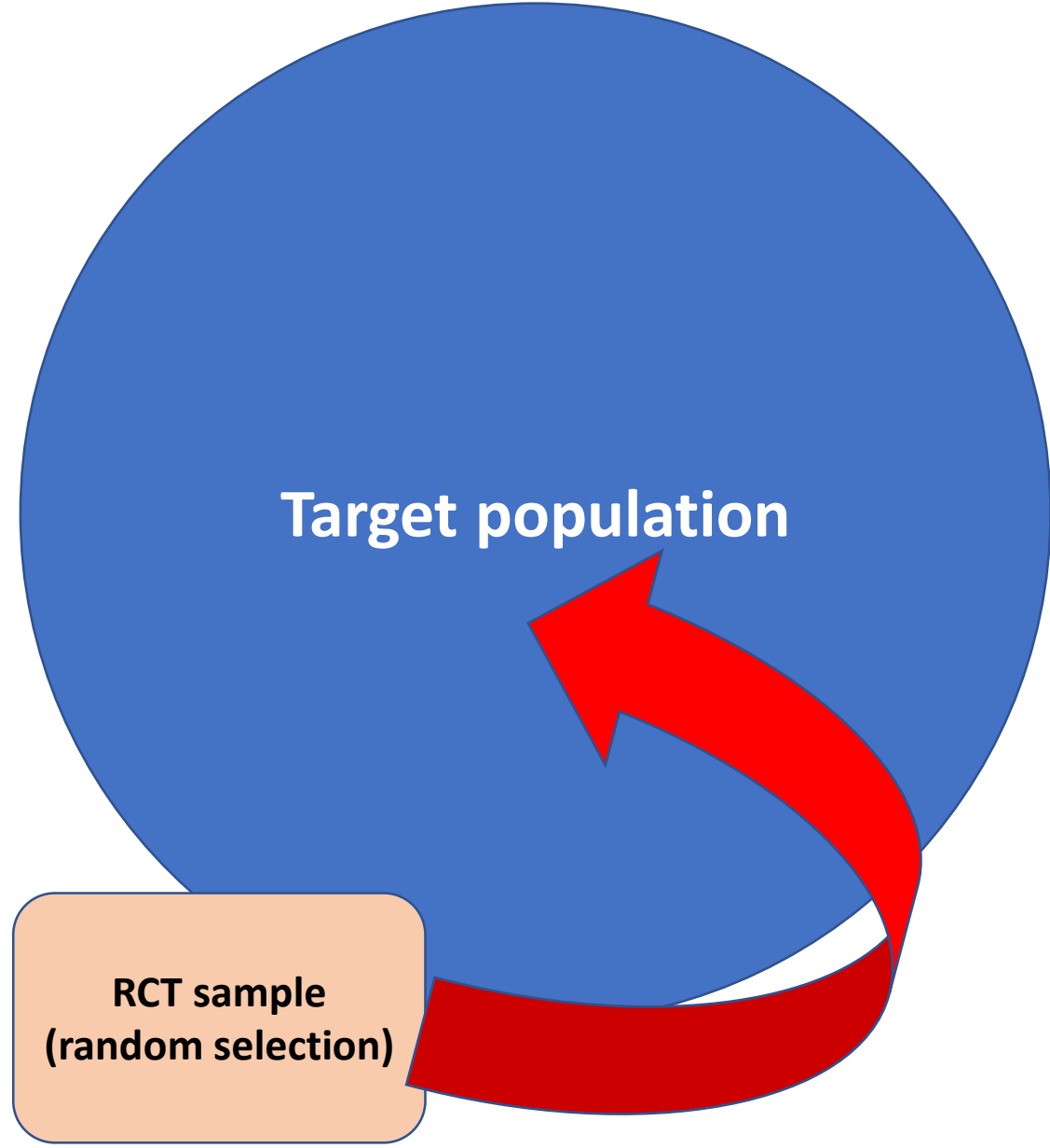
Target population

RCT sample
(random selection)
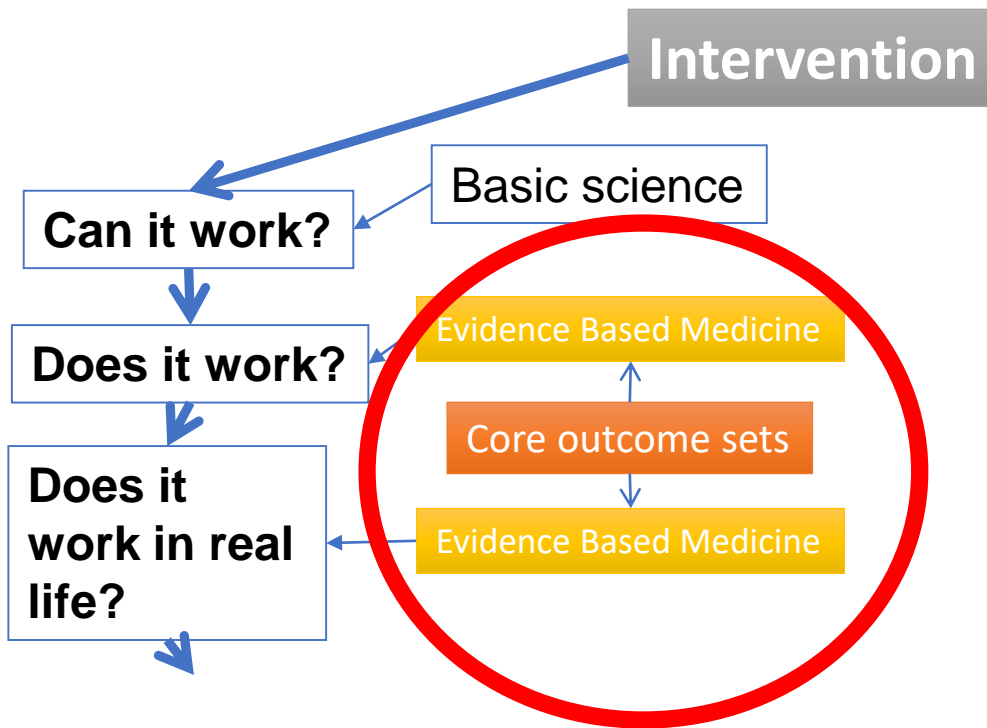
Transportability
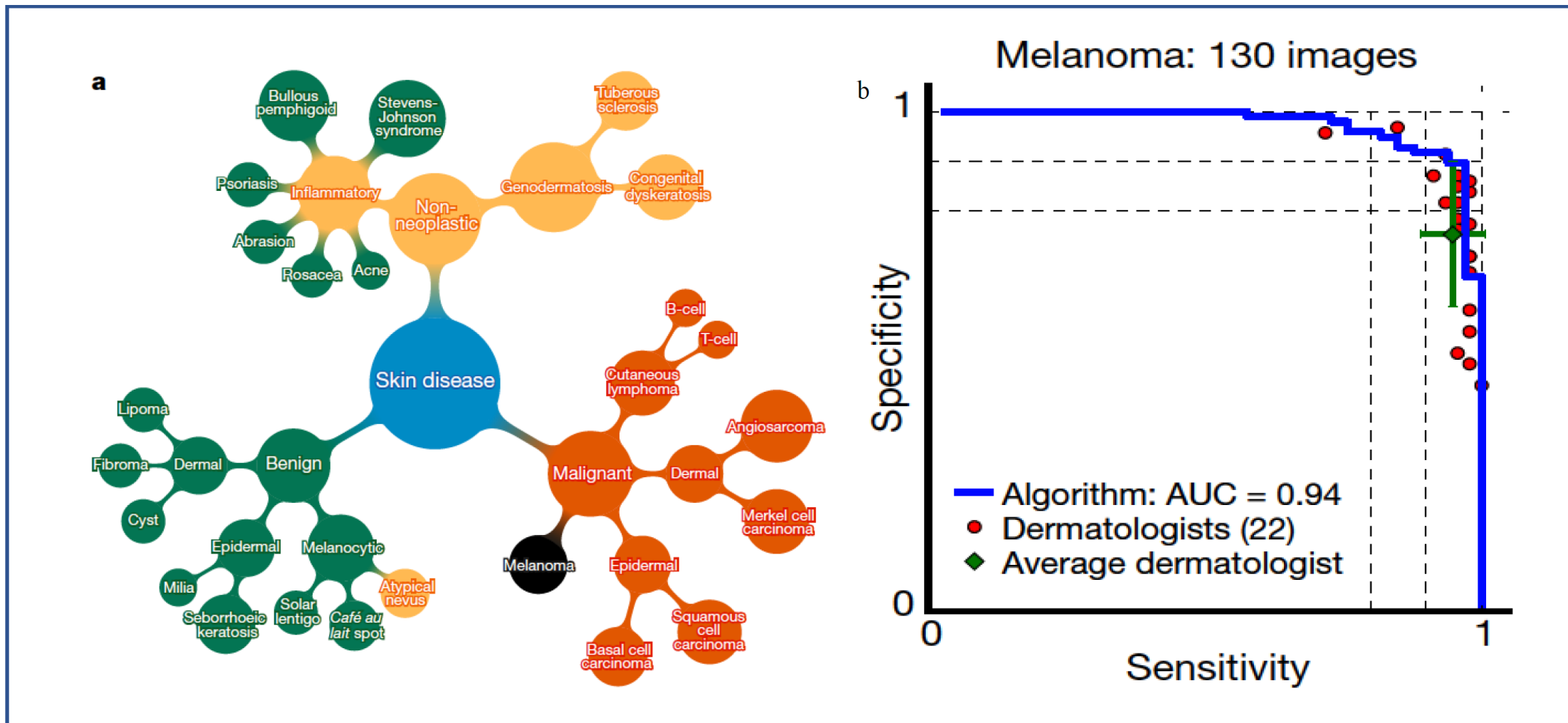
Figure 3: a) (left panel) Illustration of the top levels of the tree-structured taxonomy. The full set of 2032 diseases are leaf nodes and were used for the developing the algorithm. b) (right panel) Classification results for a set of 130 images of melanocytic lesions, blue curve from the algorithm, red dots from individual dermatologists. Images taken from Esteva et al. 2017 [30].

How much does Herceptin cost?

28000 euro/year

Herceptin® 150 mg
powder for concentrate for
solution for infusion

Trastuzumab

Primary endpoint effect size: disease free survival at 2 year:

7,6 %(85,5% vs 78,2%).

powder for concentrate for
solution for infusion

Trastuzumab

1 vial

Roche

Trastuzumab

1 vial

Roche

Table 1 Cost and potential benefits of adjuvant cancer treatments in Norfolk and Norwich University Hospital Trust

Treatment	No of patients given treatment	Drug cost (£000)	Proven benefit	Potential benefit at our hospital	Cost per patient cured (£000)
Adjuvant chemotherapy for lung cancer	15	23	5-15% improved 5 year overall survival[w3]	1 extra patient cured	23
Oxaliplatin as adjuvant therapy for colon cancer compared with fluorouracil alone	20	137	5% improved 3 year disease-free survival; no benefit to overall survival[w4]	1 extra patient without recurrence at 3 years	137
Neoadjuvant chemotherapy for oesophageal cancer	25	8	9% improved 5 year survival[w5]	3 extra patients cured	2.67
Rituximab in addition to CHOP for non-Hodgkin lymphoma in patients over 60	25	215	13% improved 2 year overall survival[w6]	3 extra patients cured	71.67
Adjuvant aromatase inhibitors in postmenopausal breast cancer	270	120	3.7% improved disease-free survival compared with tamoxifen; no benefit to overall survival[w7]	8 extra patients without recurrence at 3 years	15
Total	355	503		16 extra patients cured	
Herceptin for early stage breast cancer	75	1940	0-4% improved 4 year overall survival[w1 w2]	3 extra patients cured	650

CHOP=cyclophosphamide, doxorubicin, vincristine, and prednisolone.

Barett et al, BMJ, 2006
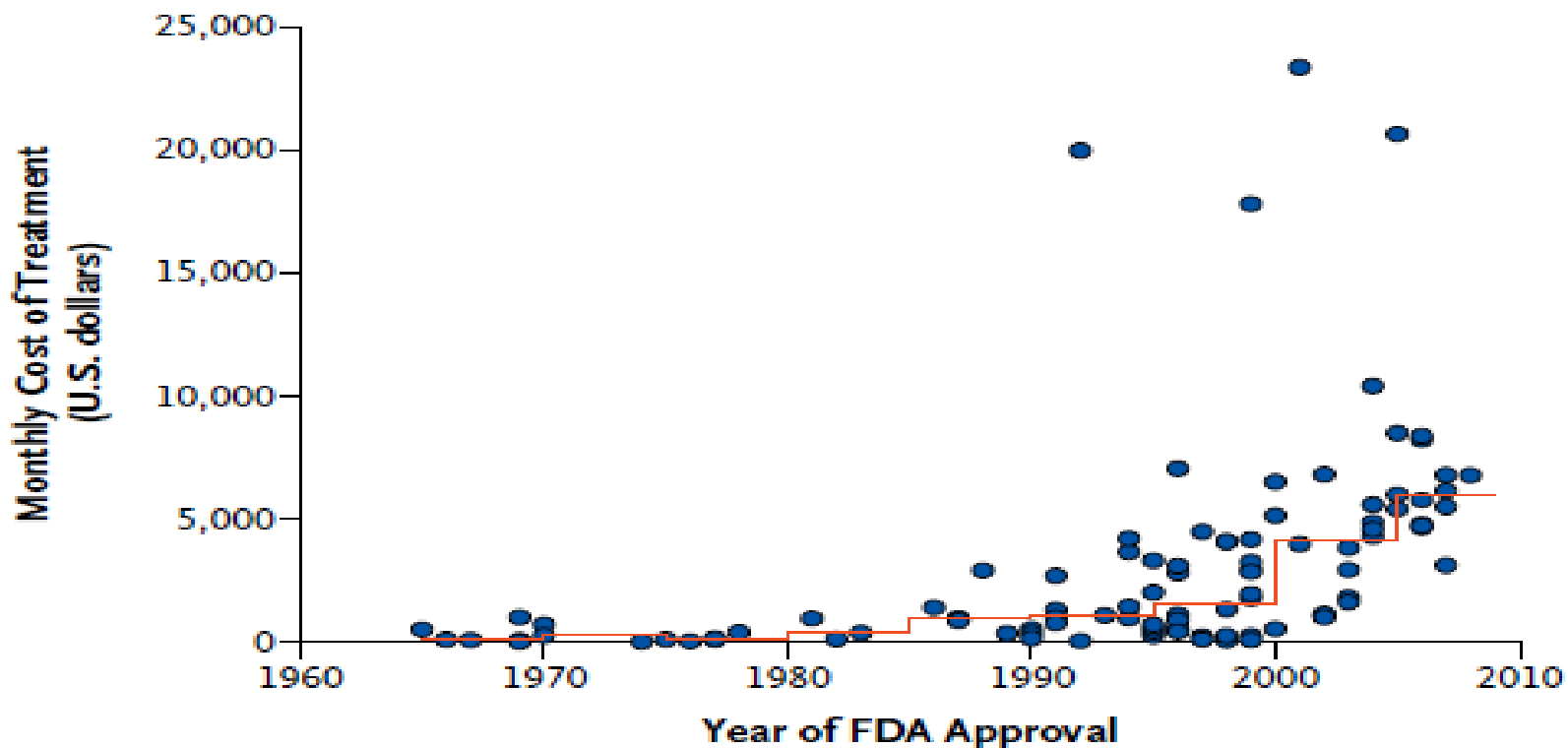
Figure 1. Monthly and Median Costs of Cancer Drugs at the Time of Approval by the Food and Drug Administration (FDA), from 1965 through 2008.

Shown are costs for 1 month of cancer treatment for a person who weighs 70 kg or has a body-surface area of 1.7 m². The red line indicates median prices during a 5-year period. Prices have been adjusted to 2007 dollars and reflect the total price for the drug at the time of approval, including both the amount of Medicare reimbursement and the amount paid by the patient or by a secondary payer. (For details about the costs of individual drugs, see the Supplementary Appendix, available with the full text of this article at NEJM.org.)

R-RCT vs. RCT
STEMI Thrombectomy Story

TASTE (R-RCT)
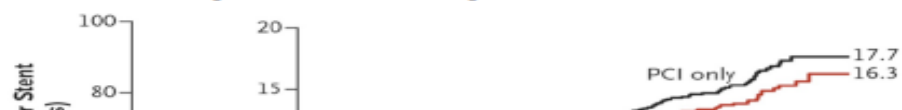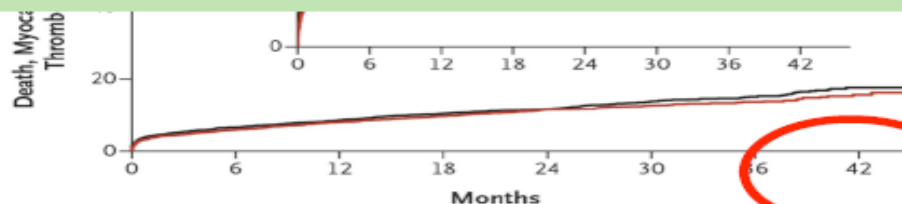
TOTAL (tradtionell RCT)

500,000 €   **15,000,000 €**

1st patient: June 2010
30 centers
33 months to full enrollment
7,244 patients

1st patient: August 2010
87 centers
48 months to full enrollment
10,732 patients

Lagerqvist B et al. N Engl J Med 2014;371:1111-1120

Jolly SS et al. N Engl J Med 2015;372:1389-1398

UCR

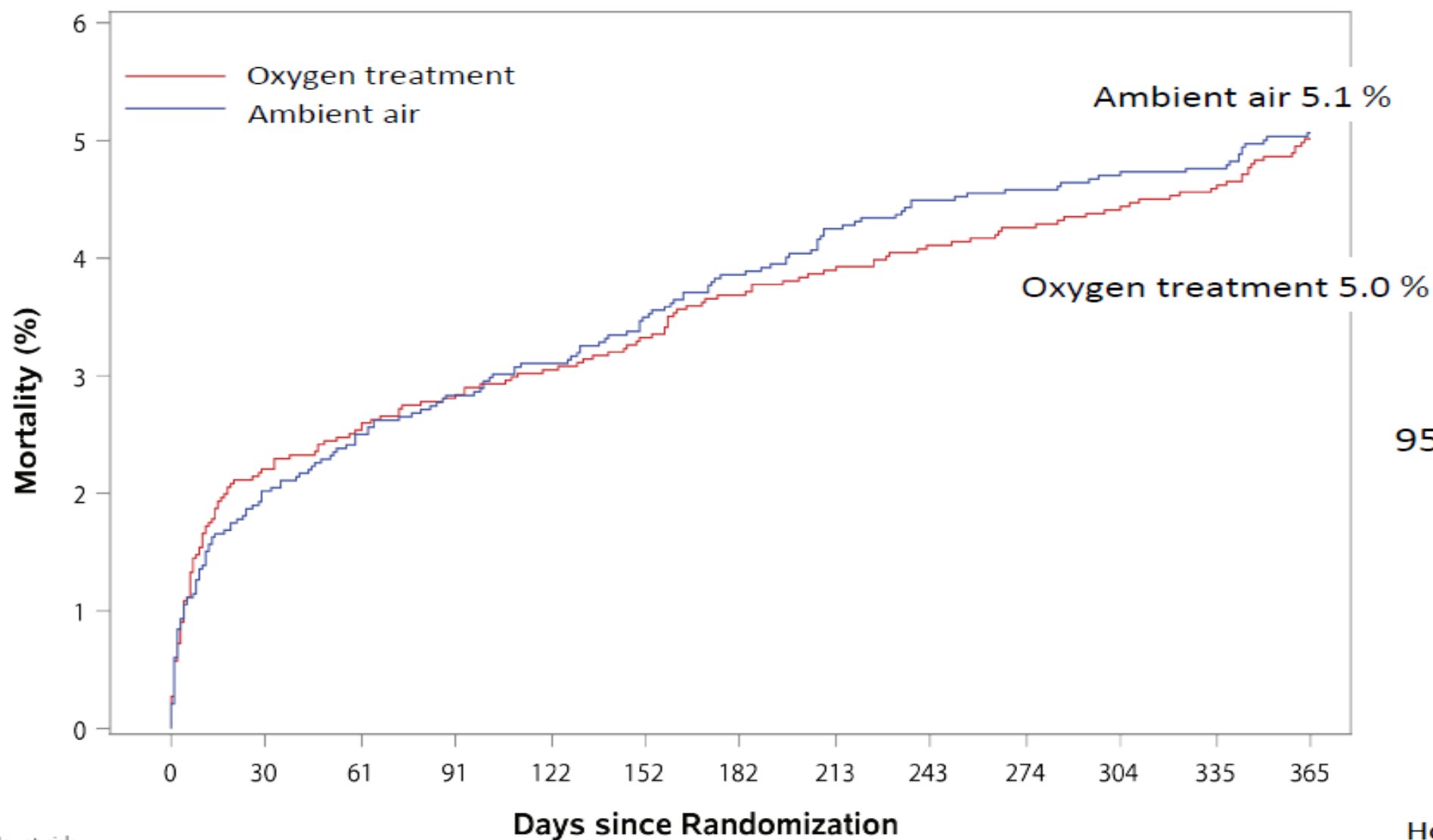# DETermination of the role of OXygen in suspected Acute Myocardial Infarction

Robin Hofmann, MD
Karolinska Institutet
Department of Clinical Science and Education
Division of Cardiology, Södersjukhuset
Stockholm, Sweden

DETO2X-AMI compared to other studies

Number of randomized patients with suspected AMI

- Hofmann, DETO2X-AMI (2017)
- COCHRANE Meta-analysis (2016)
- Stub, AVOID (2015)
- Ranchord (2012)
- Ukholkina (2005)
- Rawles (1976)
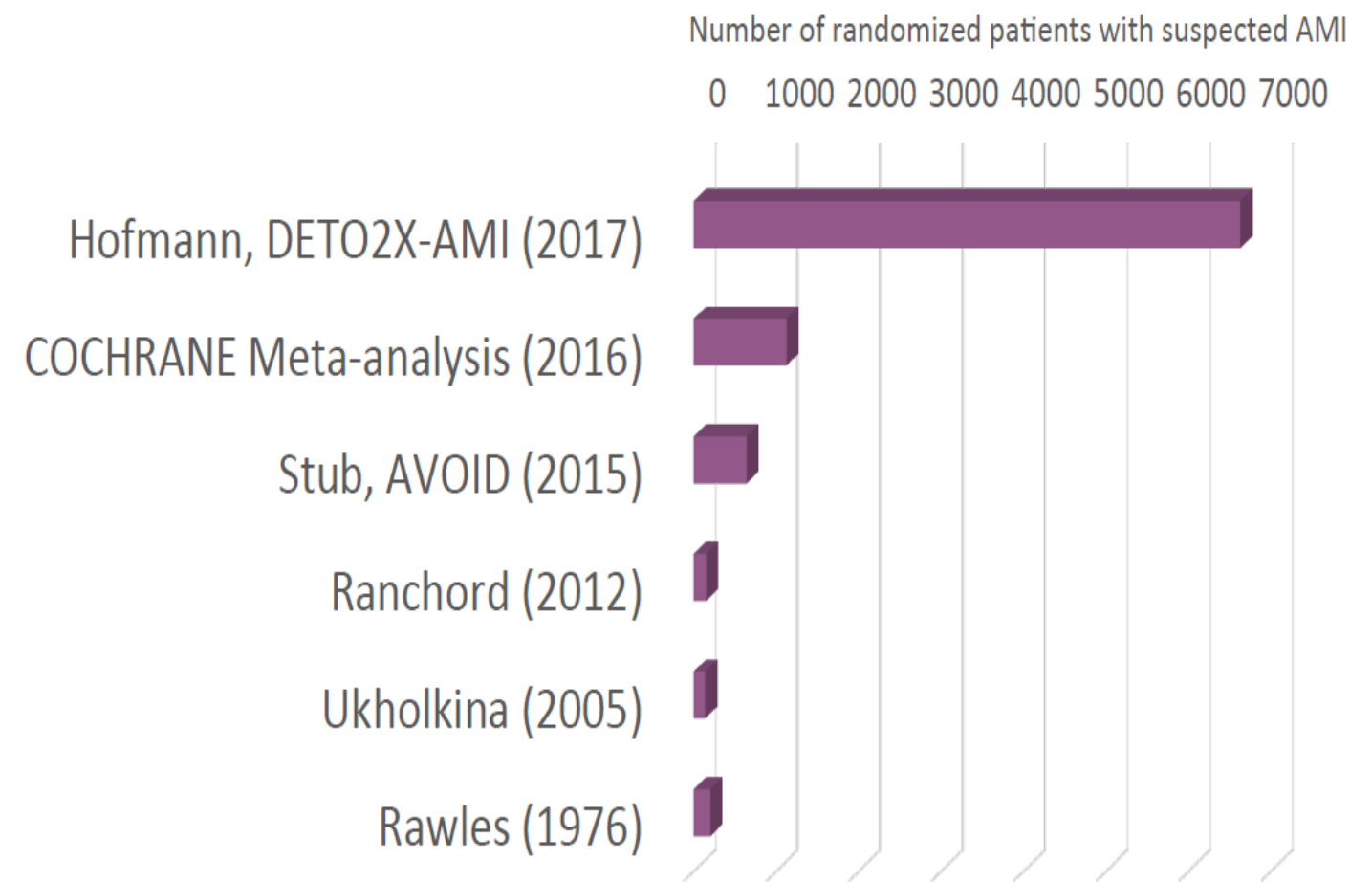
Primary Endpoint up to 365 days

No. at risk

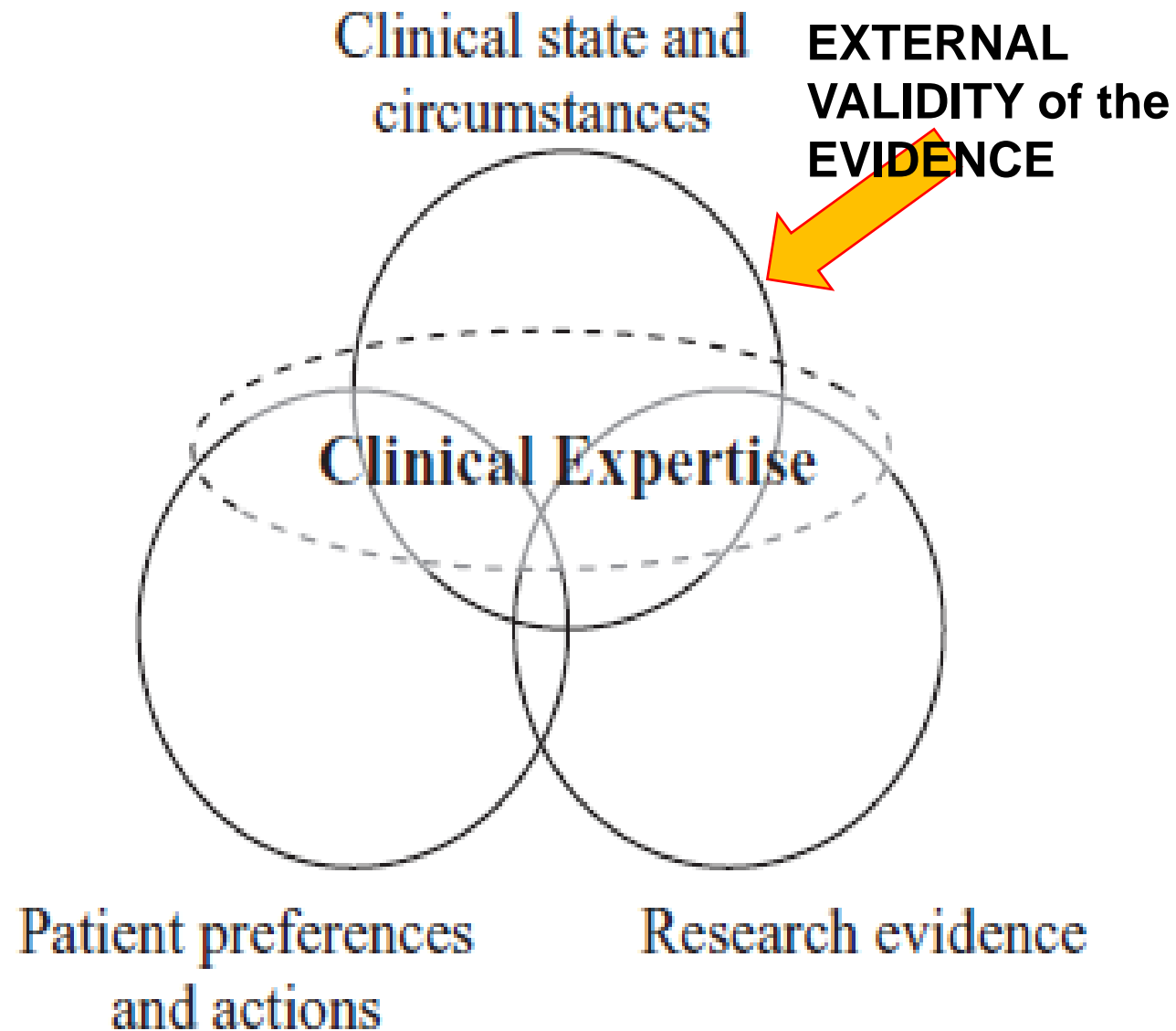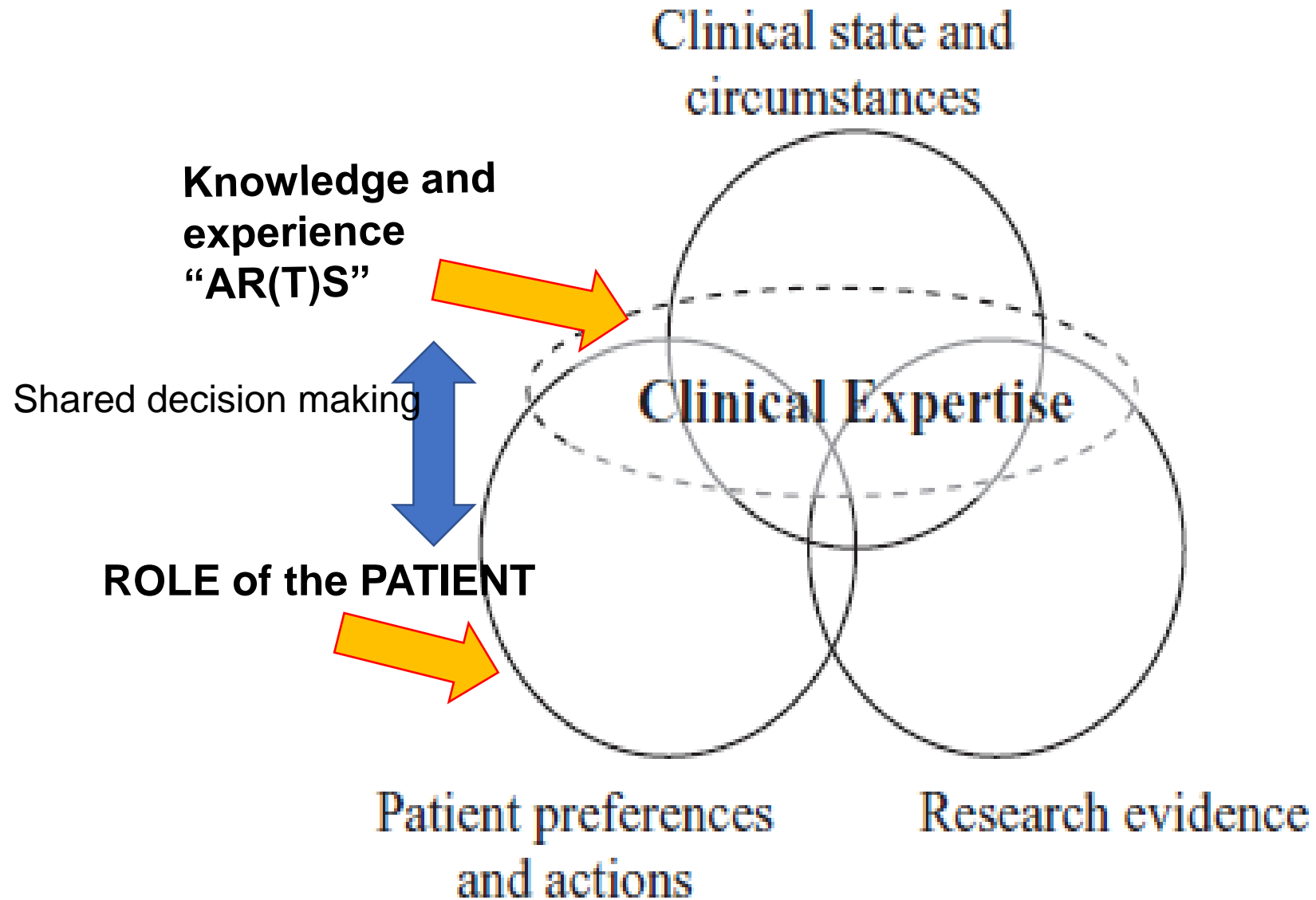|												
Oxygen treatment	3311	3238	3227	3218	3210	3201	3189	3182	3175	3170	3165	3159	3145
Ambient air	3318	3251	3235	3224	3215	3202	3190	3177	3169	3166	3162	3160	3150

Hofmann, et al.
N Engl J Med. 2017 Aug 28
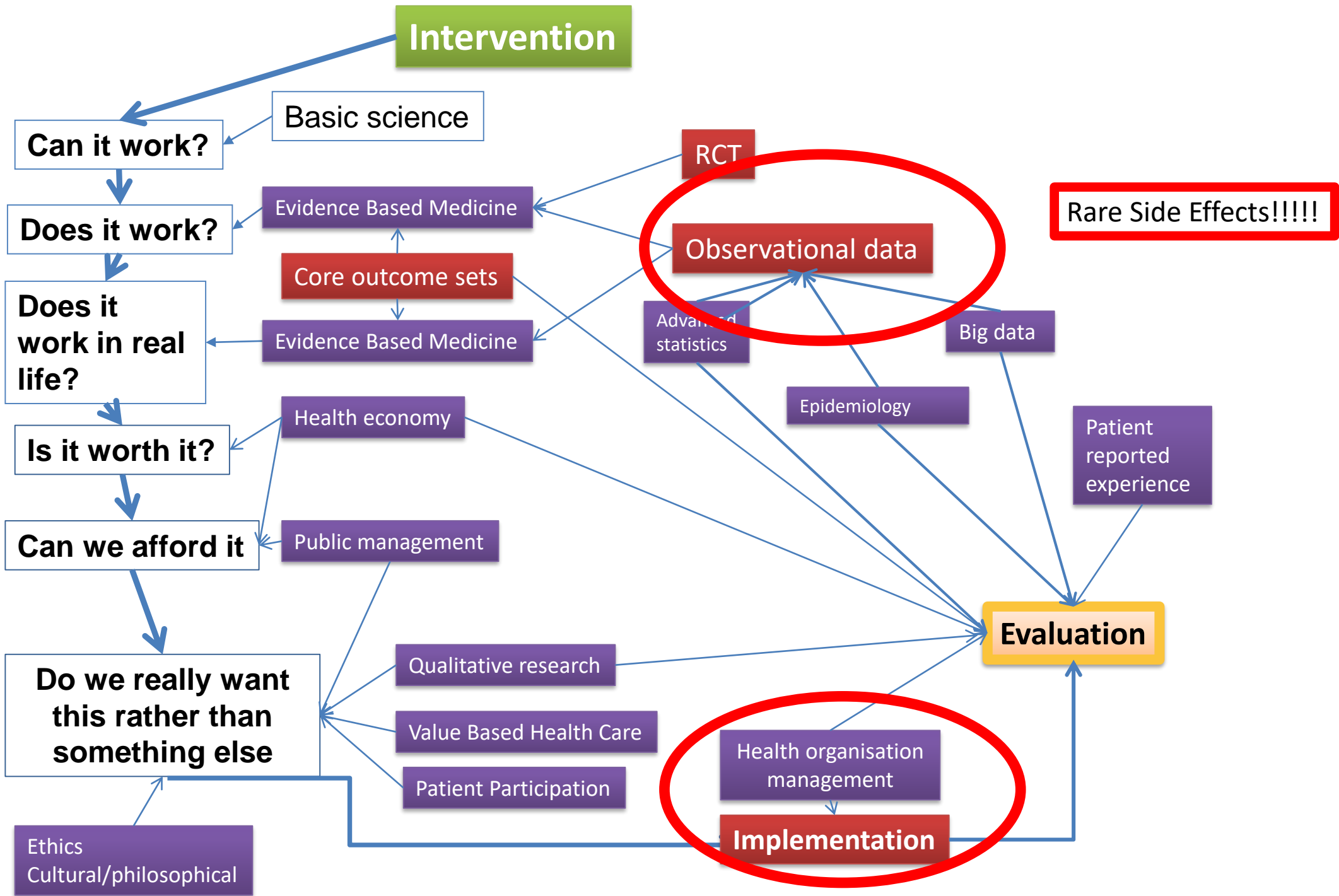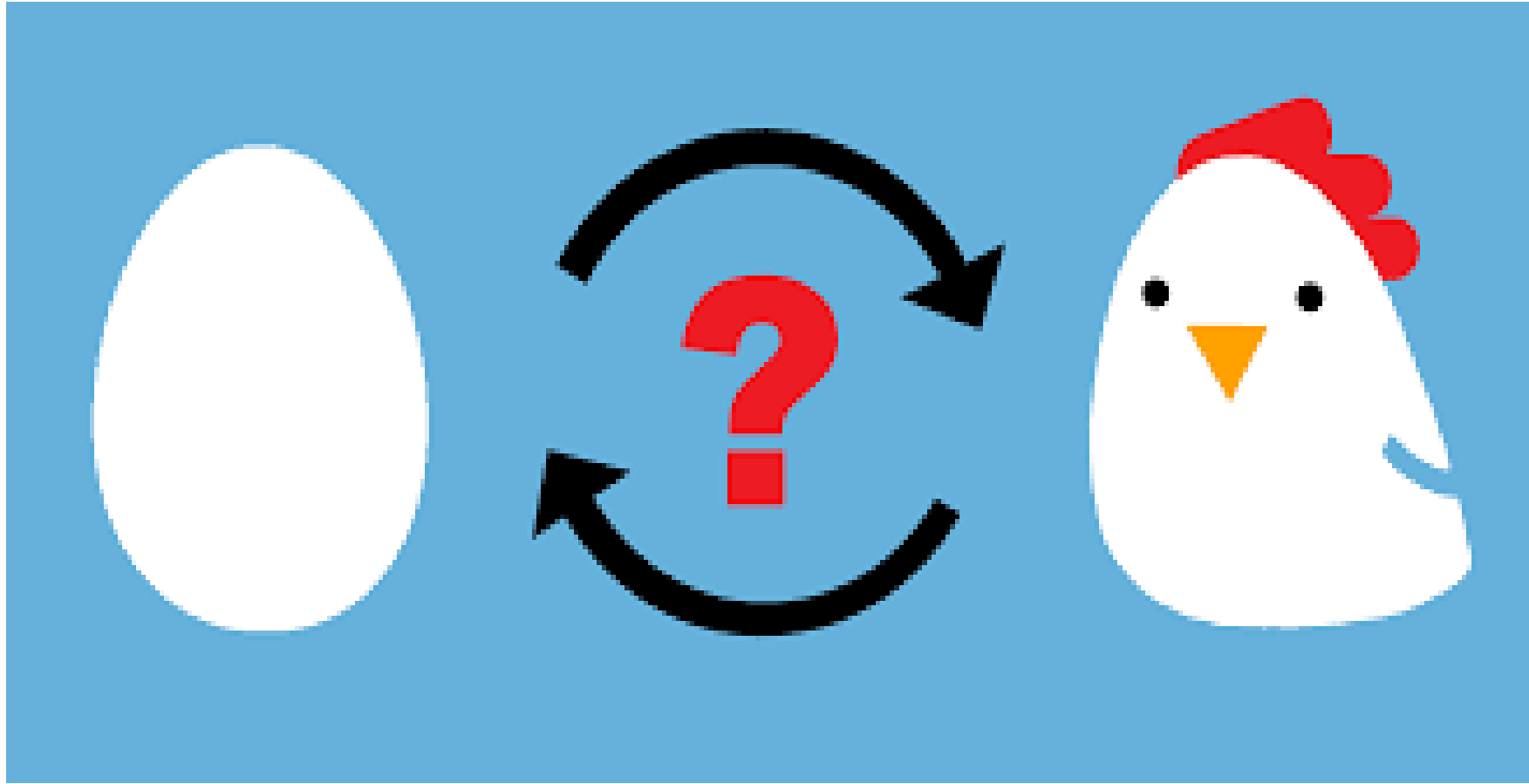
Causality
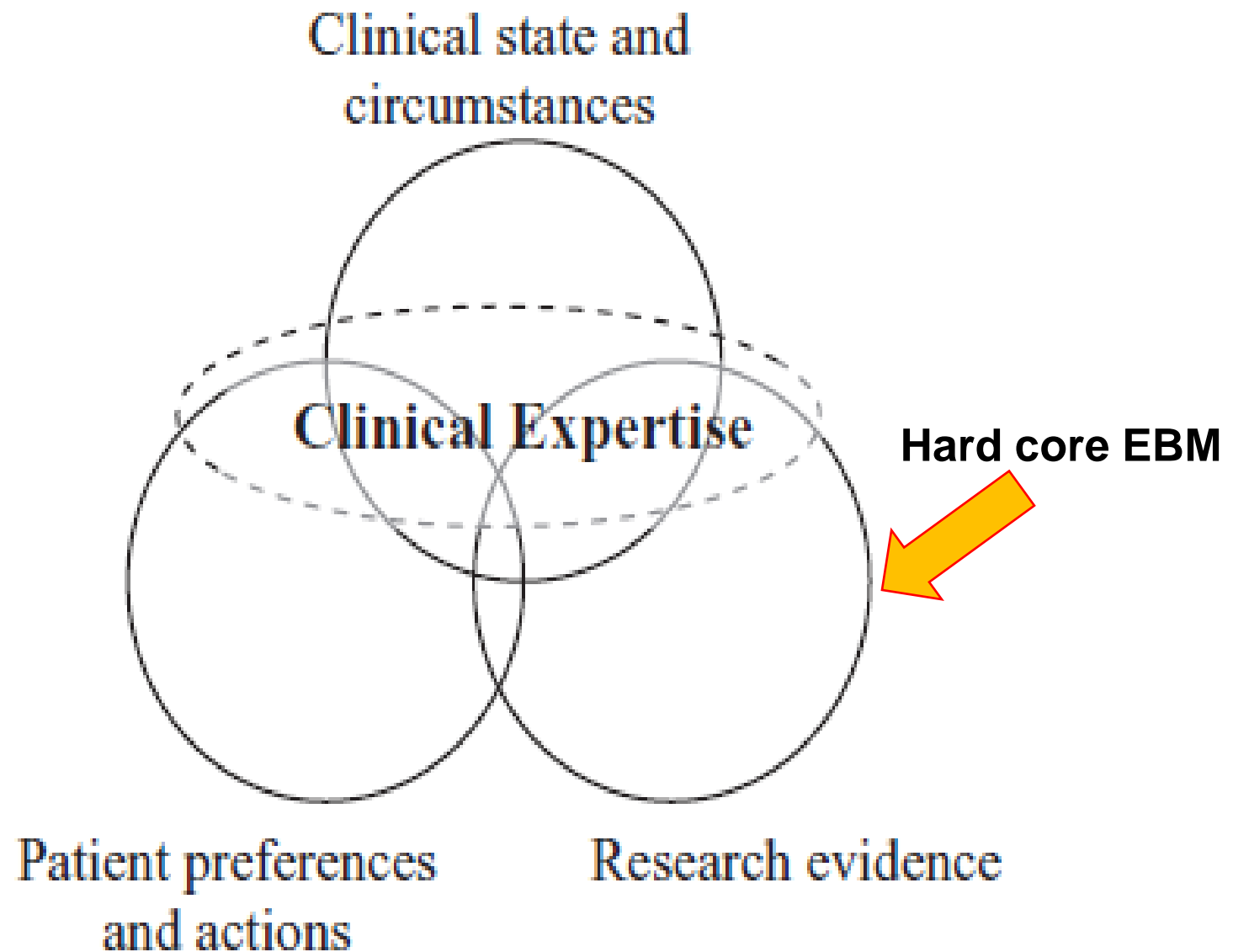
Figure 1 Evidence-based decision-making for clinical contexts.

Figure 1 Evidence-based decision-making for clinical contexts.

Figure 1 Evidence-based decision-making for clinical contexts.

Hormonal Therapy
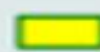
Chemotherapy and Hormonal Therapy

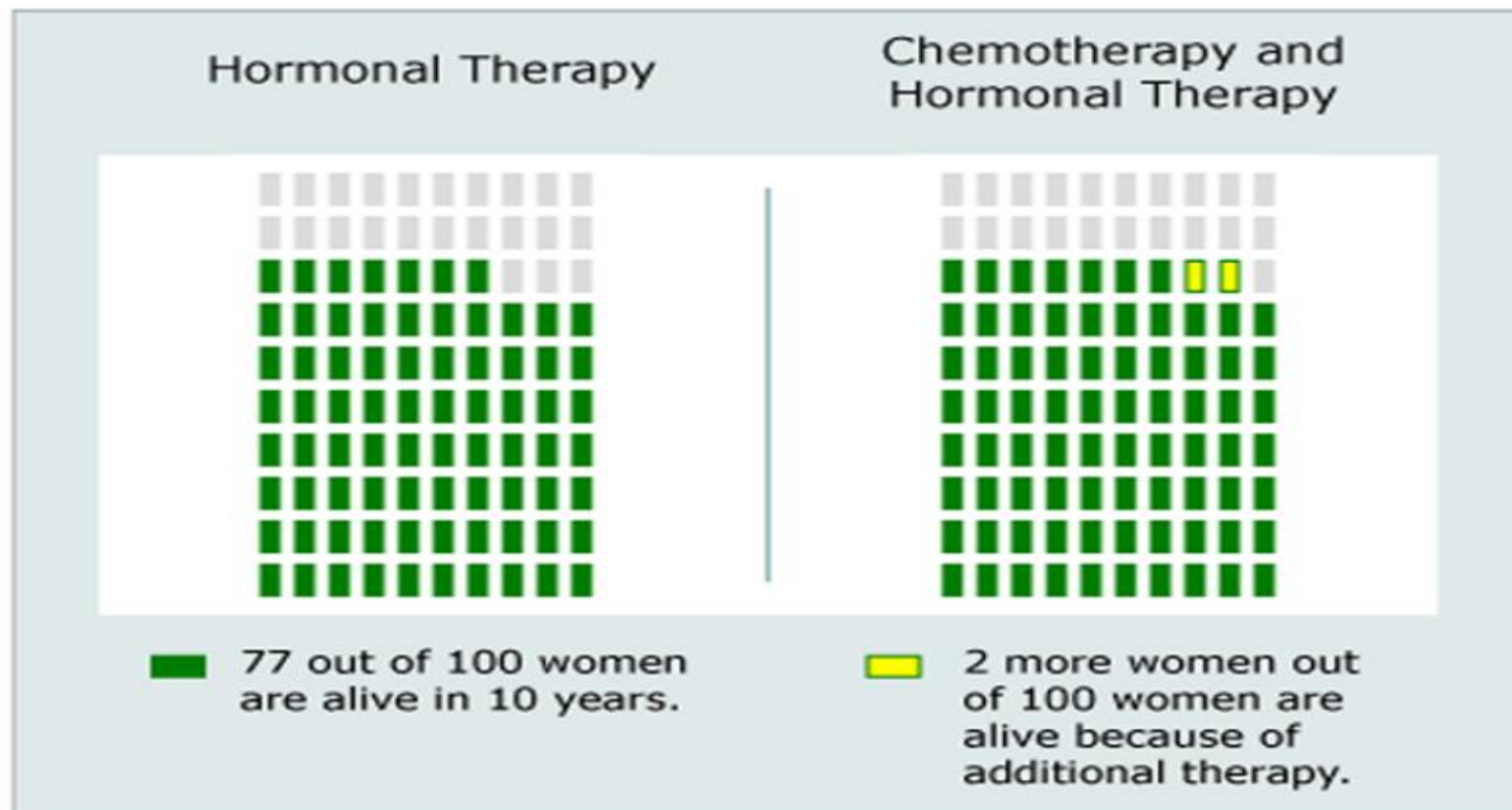|	
🟩	77 out of 100 women are alive in 10 years.
🟥	23 out of 100 women die because of cancer.
🟦	7 out of 100 women die of other causes.
🟨	2 more women out of 100 women are alive because of additional therapy.

Figure 2.
Survival-only pictographs from primary study
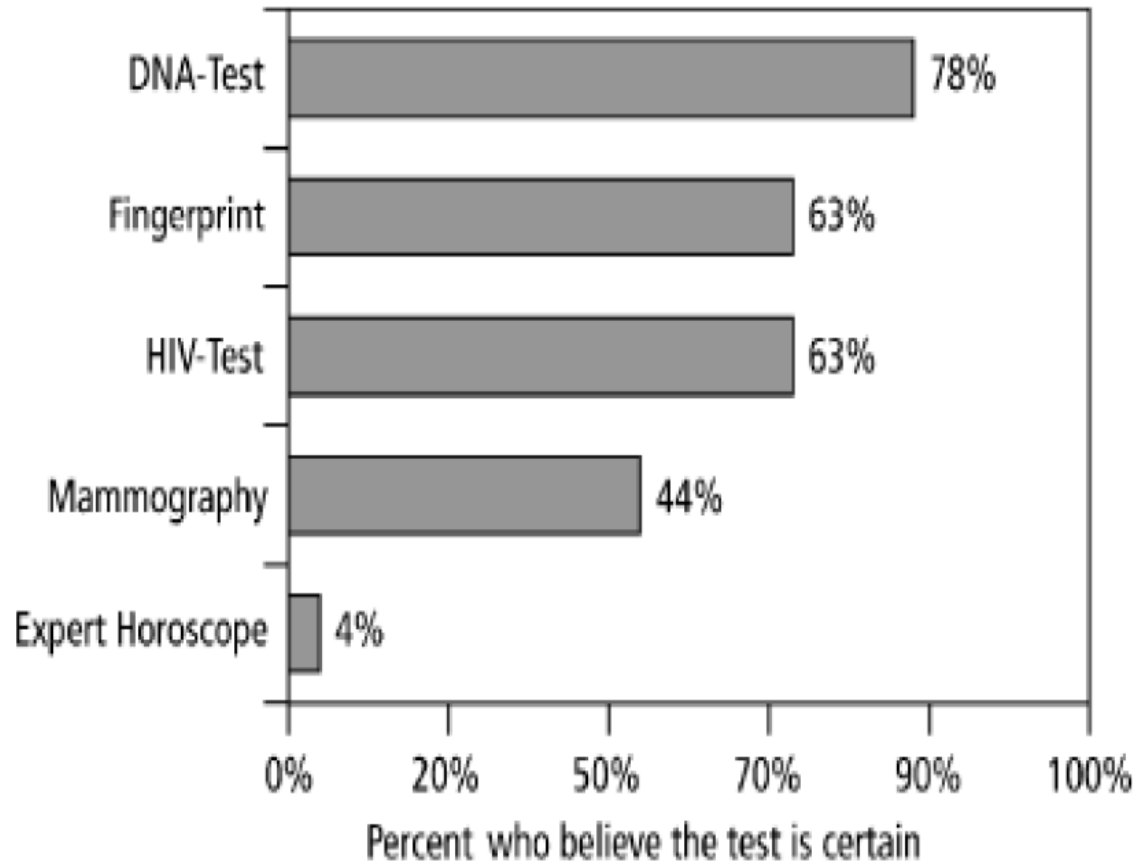
Statistical illiteracy: uncertainty

Fig. 6. The illusion of certainty. Shown are results from face-to-face interviews conducted in 2006, in which a representative sample of 1,016 German citizens was asked: "Which of the following tests are absolutely certain?" (Gigerenzer, 2008).

TABLE 8

Answers by 20 AIDS Counselors to the Client's Question: "If One Is Not Infected With HIV, Is It Possible to Have a Positive Test Result?"

1	"No, certainly not"	11	"False positives never happen"
2	"Absolutely impossible"	12	"With absolute certainty, no"
3	"With absolute certainty, no"	13	"With absolute certainty, no"
4	"No, absolutely not"	14	"Definitely not" . . . "extremely rare"
5	"Never"	15	"Absolutely not" . . . "99.7% specificity"
6	"Absolutely impossible"	16	"Absolutely not" . . . "99.9% specificity"
7	"Absolutely impossible"	17	"More than 99% specificity"
8	"With absolute certainty, no"	18	"More than 99.9% specificity"
9	"The test is absolutely certain"	19	"99.9% specificity"
10	"No, only in France, not here"	20	"Don't worry, trust me"