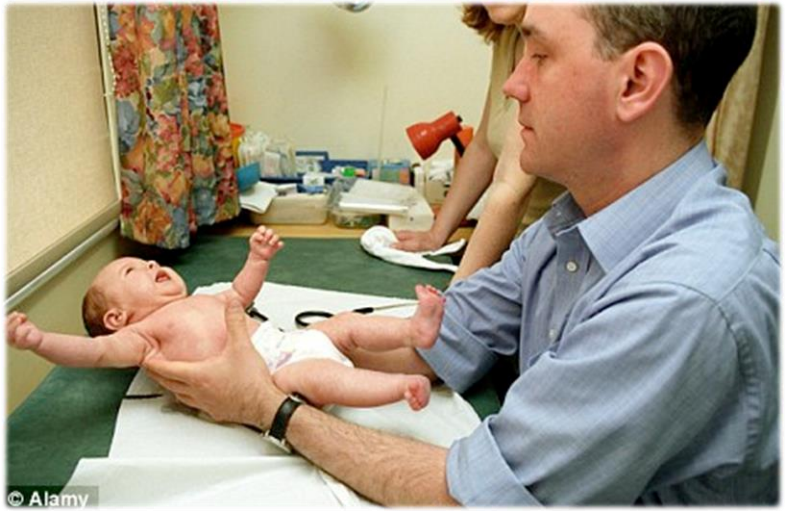
"Healthcare decision making – who should be round the table?"

Dr. Amanda Adler
Chair, National Institute of Care Excellent (NICE)
Technology Appraisal Committee B
Physician, Cambridge University Hospitals Foundation Trust

National Health Service



- ‘Universal health care’
- Free at point of care
- ‘Cradle to grave’
- Funded by taxation
- Funds are limited

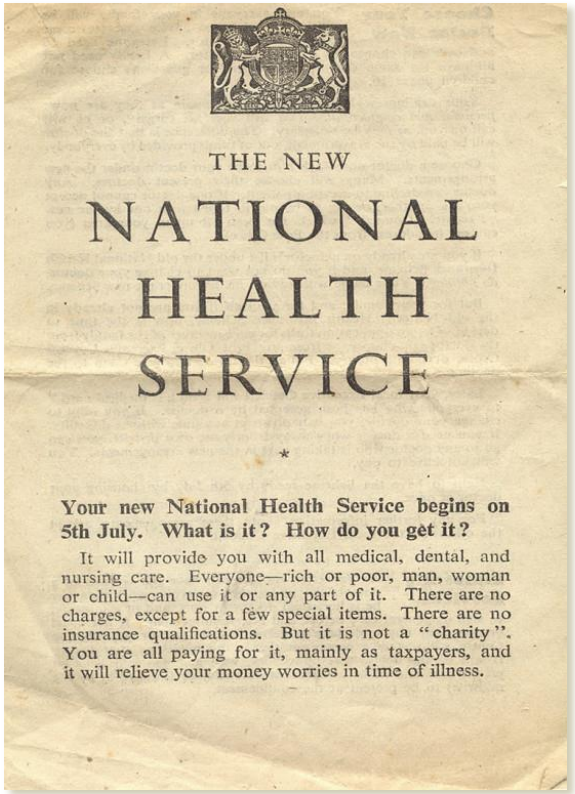
Many choices, limited resources

Maximise ‘utility’ (well-being)

NICE in England handles these decisions

https://fthmb.tqn.com/iohHY0mQXDNbxDbCXYf3yflCJO4=/768x0/filters:no_upscale()/about/GettyImages-499636577-1--58b9df955f9b58af5cbc1a14.jpg

NHS has made these decisions even more important



THE NEW

NATIONAL HEALTH SERVICE

*

Your new National Health Service begins on 5th July. What is it? How do you get it?

It will provide you with all medical, dental, and nursing care. Everyone—rich or poor, man, woman or child—can use it or any part of it. There are no charges, except for a few special items. There are no insurance qualifications. But it is not a "charity". You are all paying for it, mainly as taxpayers, and it will relieve your money worries in time of illness.

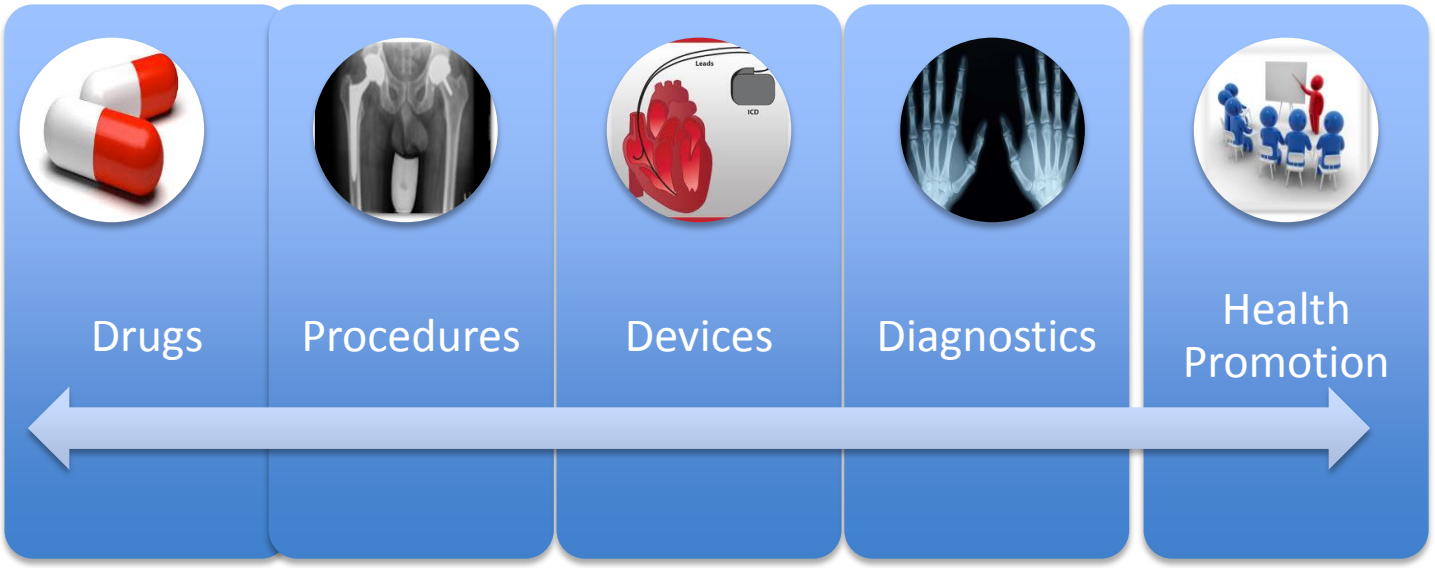
'..the NHS was founded on a fallacy: that there was a finite amount of ill-health….which, once removed, would result in …health care becoming cheaper as the need for it dropped off. What has happened is the success in health care has resulted in people living longer potentially to be ill more often and consume more resources' - David Hunter

1948

*David Hunter

Adler 2019

NICE oversees Health Technology Appraisal
How does NICE define a ‘technology’?



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When a new drug ('technology') comes to England Regulators and NICE ask different questions

1. Does the drug work?
2. Is the drug safe?

1. How well does the drug work compared with what the NHS currently offers ?
2. Does the drug reflect a good use of limited health care resources?

Fixed budgets and 'opportunity costs'

Need for a common measure of effectiveness

New diabetes drug

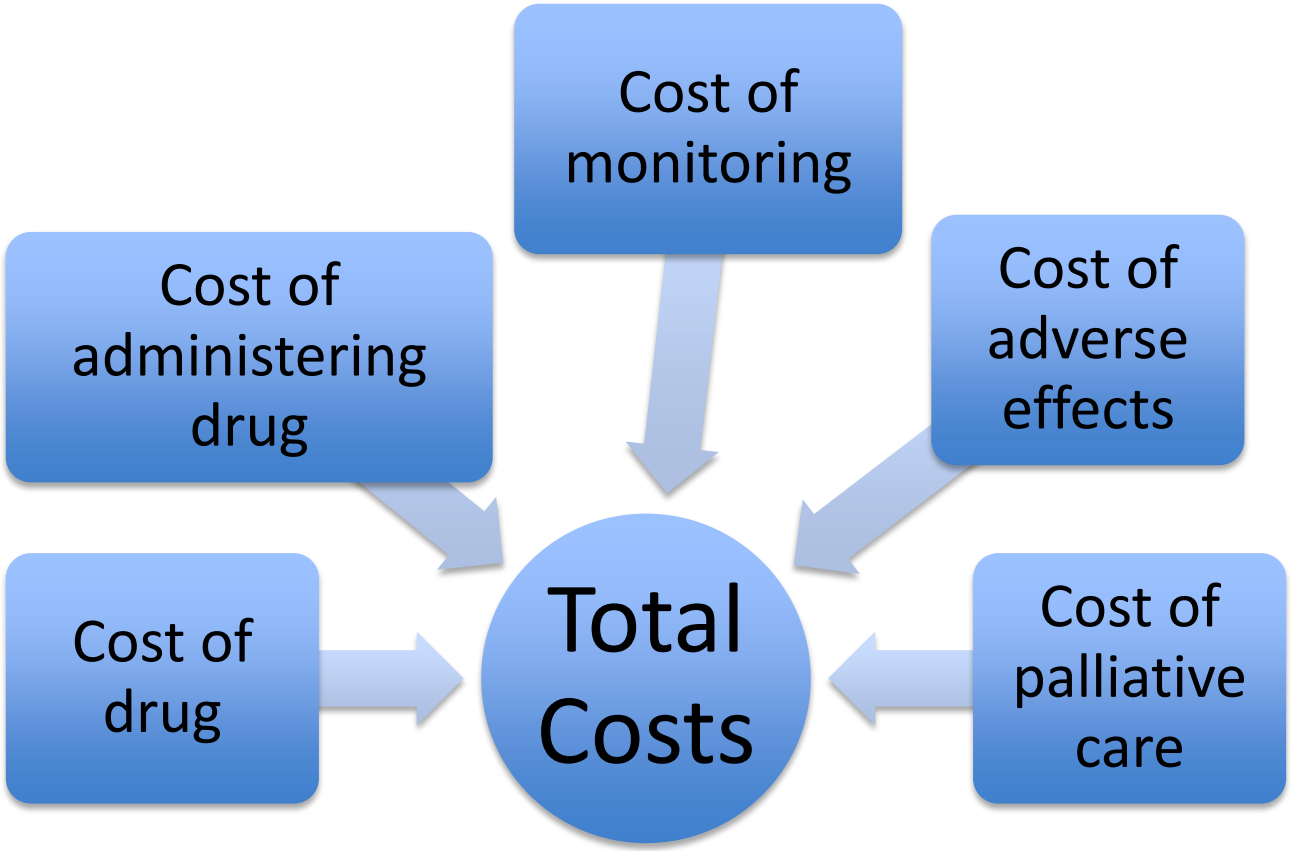
Other diabetes drug?
Diabetes education?
Alzheimer's drugs?
Childhood vaccines?
Cancer drugs?
Hospice?

Willett, BMJ

Effectiveness common to all diseases

Adler 2019

Calculating Costs
Example: new vs. older cancer drug



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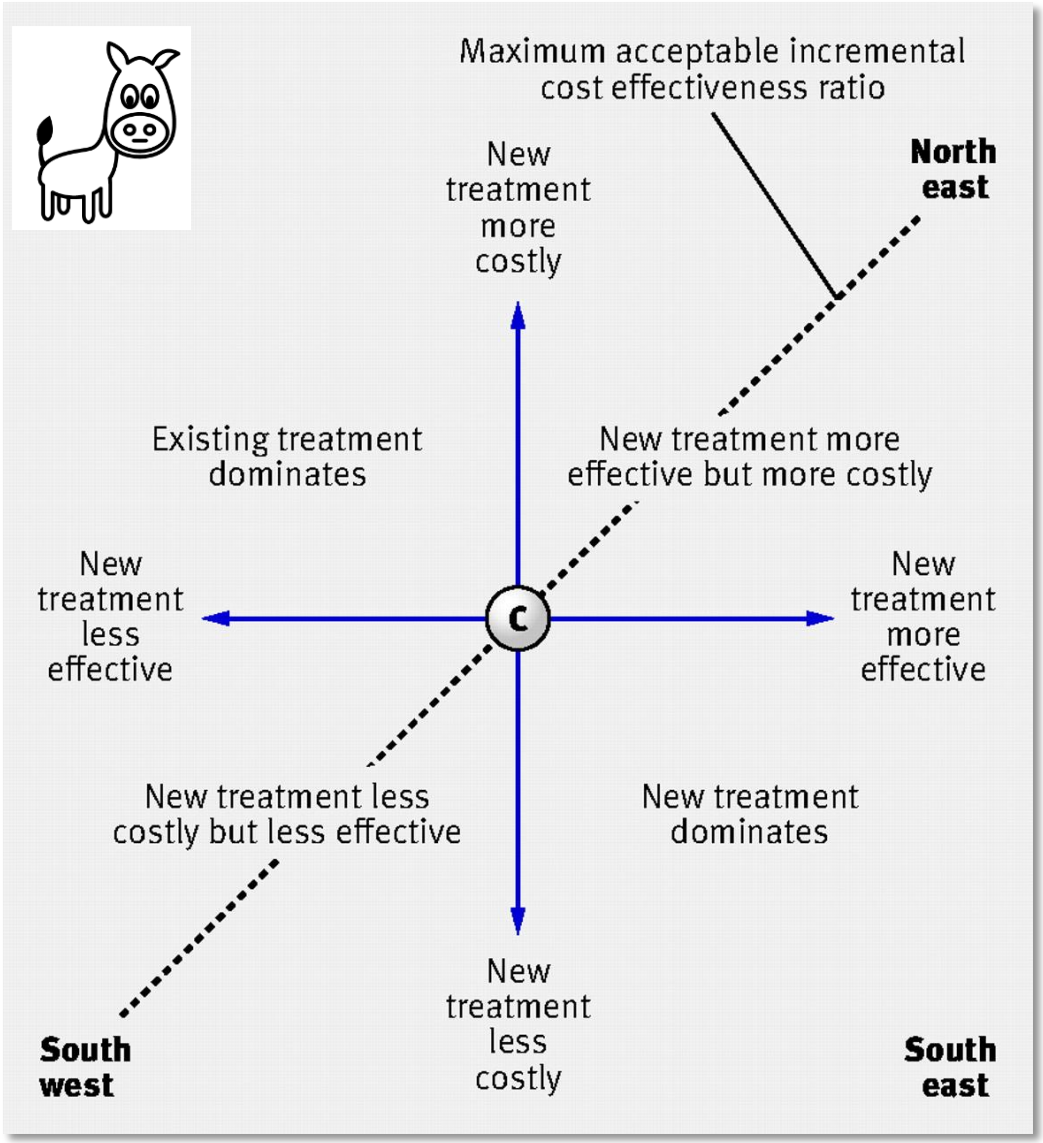
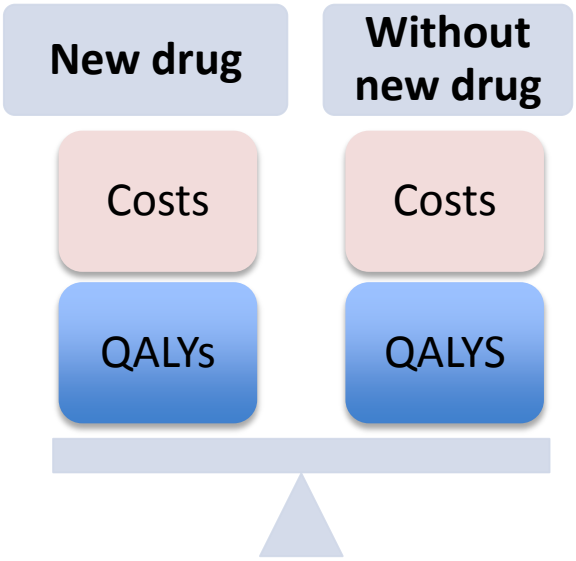
Cost effectiveness plane

C= what NHS currently offers

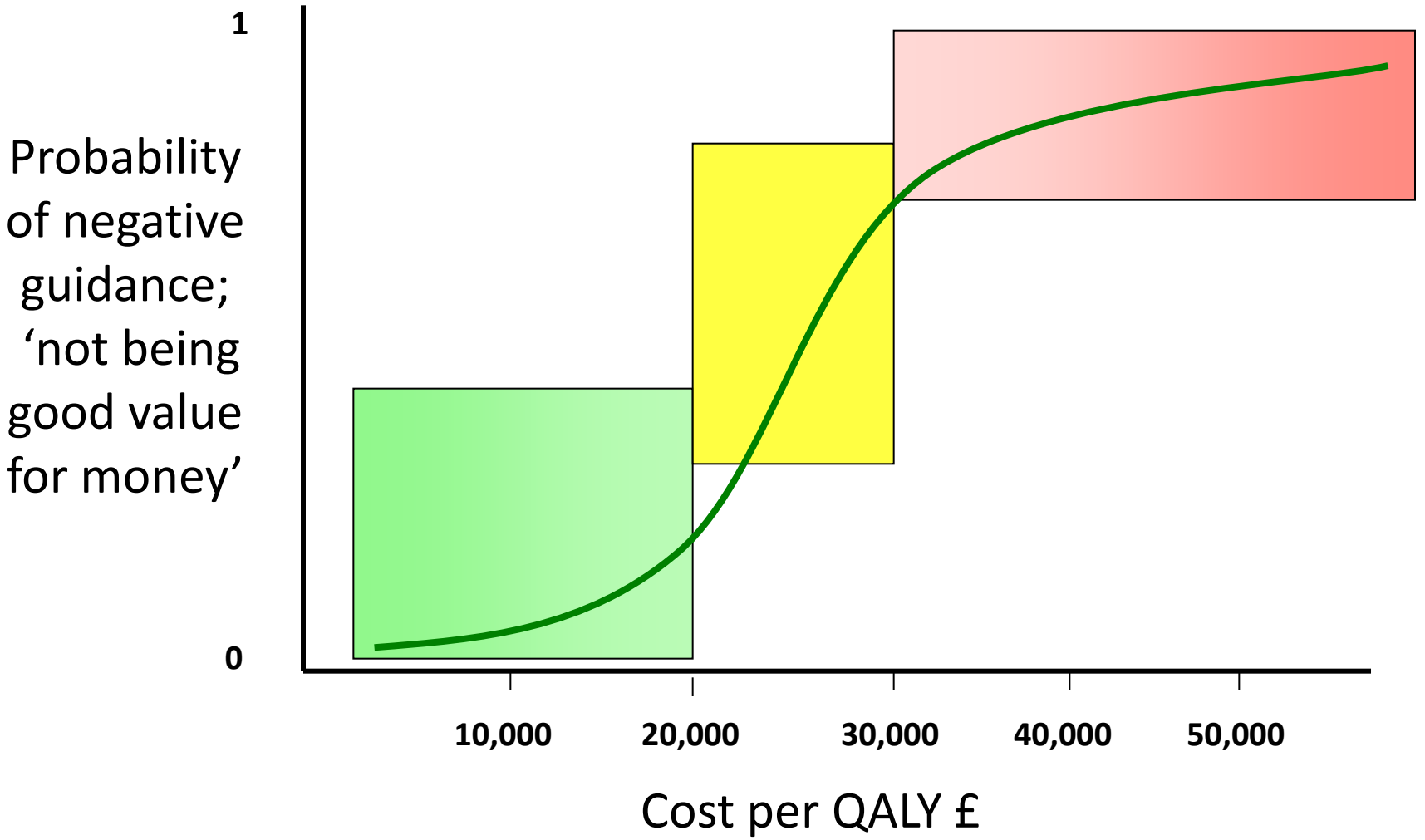


Incremental Cost Effectiveness Ratio
Δ Cost/ΔQALY



BMJ 2011;342:d1548; S Shah, S Chakravarty;

What is the willingness to pay for a QALY?



‘Reference’ Case

Element of health technology assessment	Reference
Defining the decision problem	Scope developed by NICE
Comparator(s)	Offered in the NHS
Perspective costs	NHS and PSS
Perspective benefits	All health effects on individuals
Measure of health effects	QALYs
Type of economic evaluation	Cost-effectiveness estimated by an incremental cost effectiveness ratio (ICER = Δ cost/Δ QALY)
Synthesis of evidence on outcomes	Systematic review
Source for measuring health-related quality of life	Reported by patients and carers
Source of preference data for valuing changes in health-related quality of life	General public
Discount rate	Annual rate of 3.5% on both costs and effects
Equity weighting	An additional QALY has same weight regardless of the characteristics of individuals receiving the health benefit

To make decisions,
who should be around the table and why?

Who makes decisions for NICE?

Technology Appraisal Committees

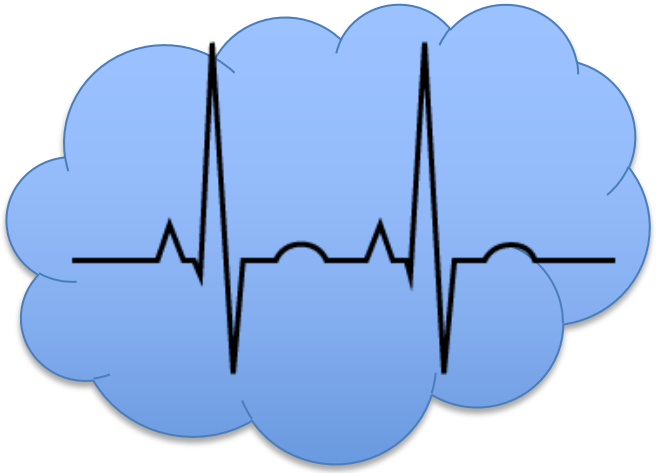
‘independent’, ‘transparent’, ‘managed conflicts’

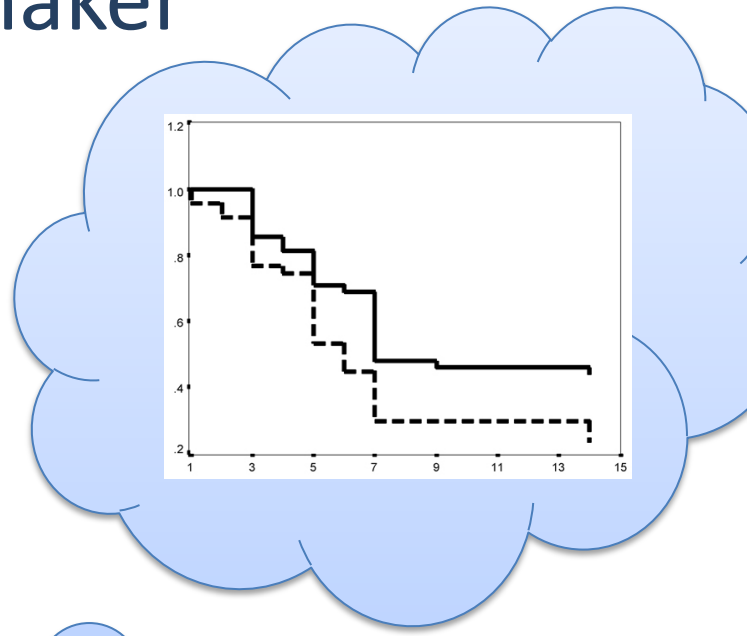
- Chair and vice-chair
- ‘Consultants’ (senior doctors)
- Statistician
- Health economists
- Clinical pharmacologist
- Paediatrician
- Psychiatrist
- Nurse
- Managers
- Pharmacist
- Ancillary NHS
- General Practitioners
- Public health physicians
- Lay members
- Industry representatives

Adam Wishart, BBC2, “Price of Life”

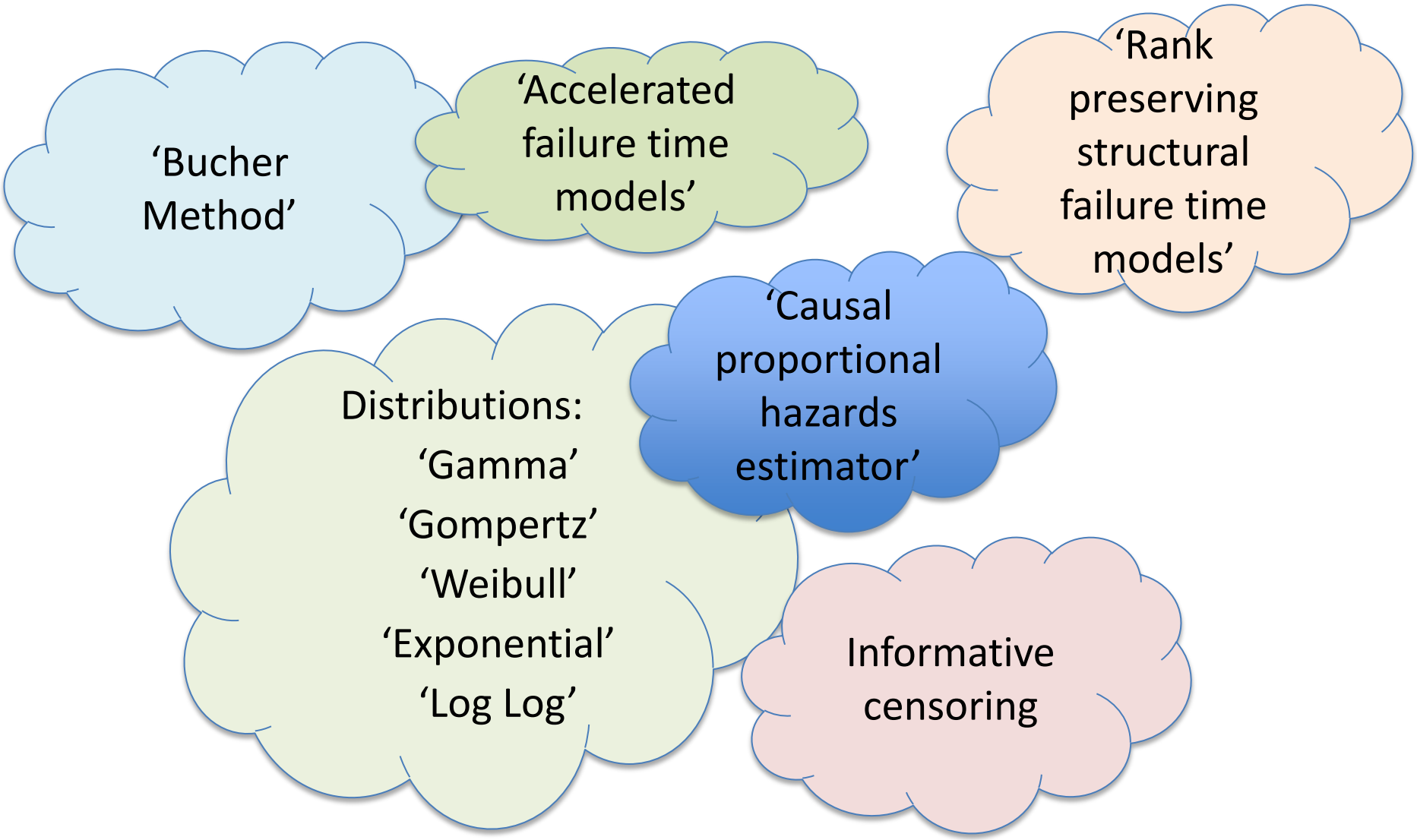
Clinicians …
who understand statistics

Ideal decision maker



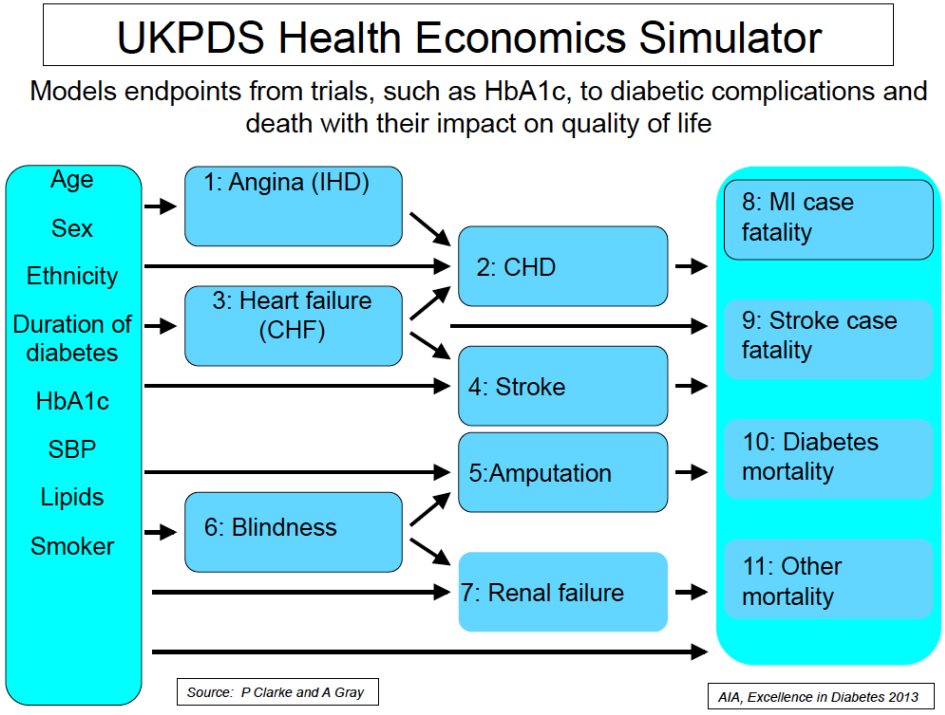


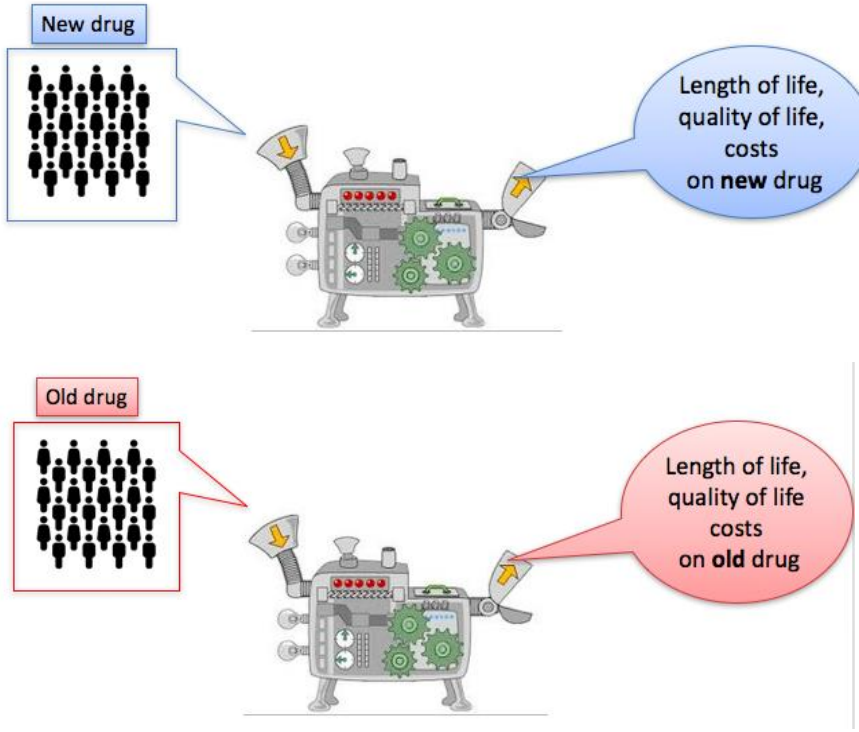
Technically demanding



People who can build and understand disease models

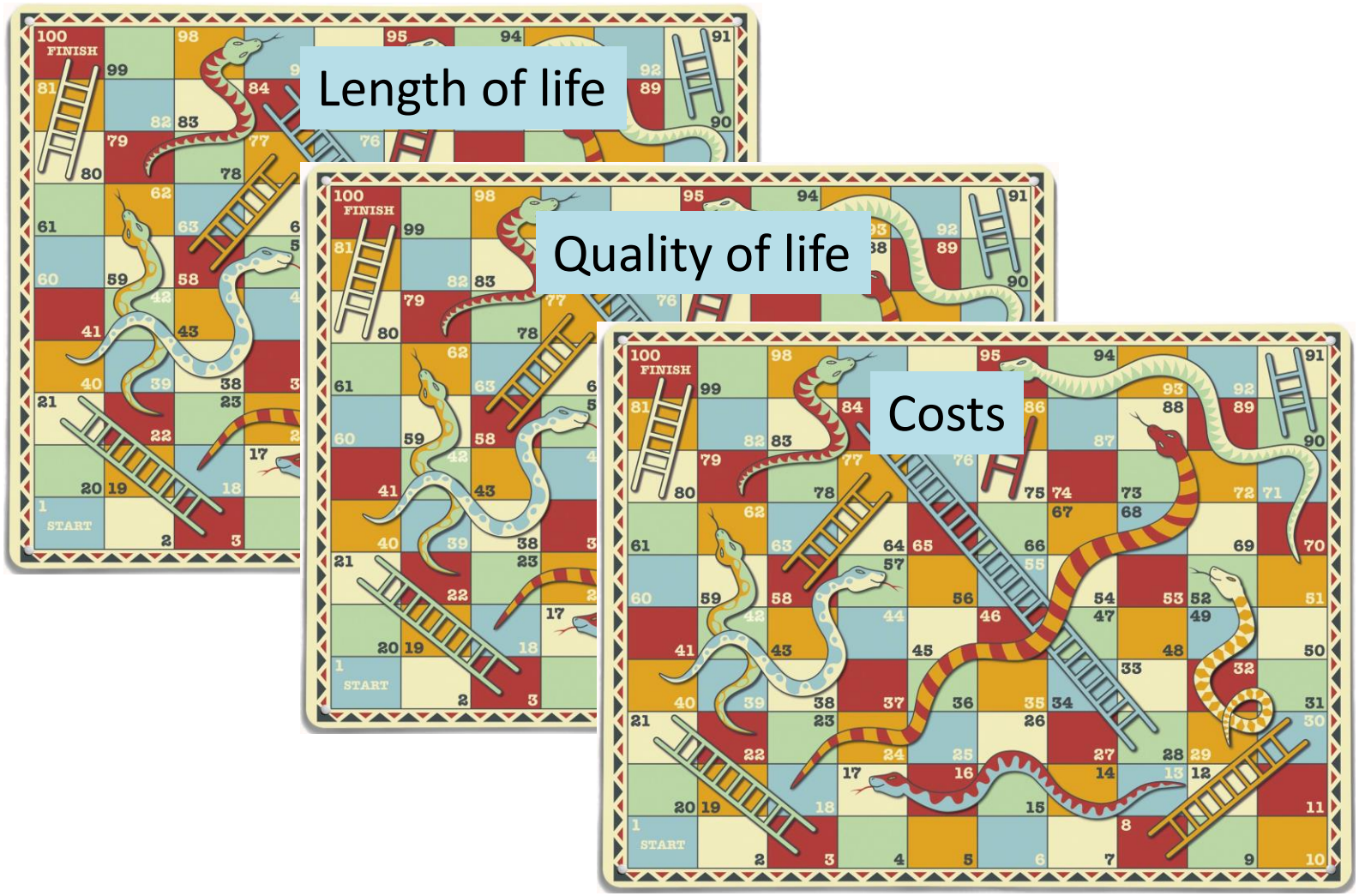
Trials infrequently measure length or quality of life as the 1◦endpoint necessitating modelling



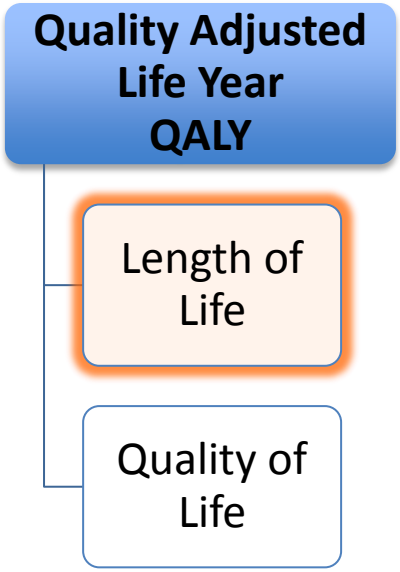


P. M. Clarke, A. M. Gray · A. Briggs et al. UKPDS 68 Diabetologia (2004) 47:1747–1759

Diabetes snakes and ladders

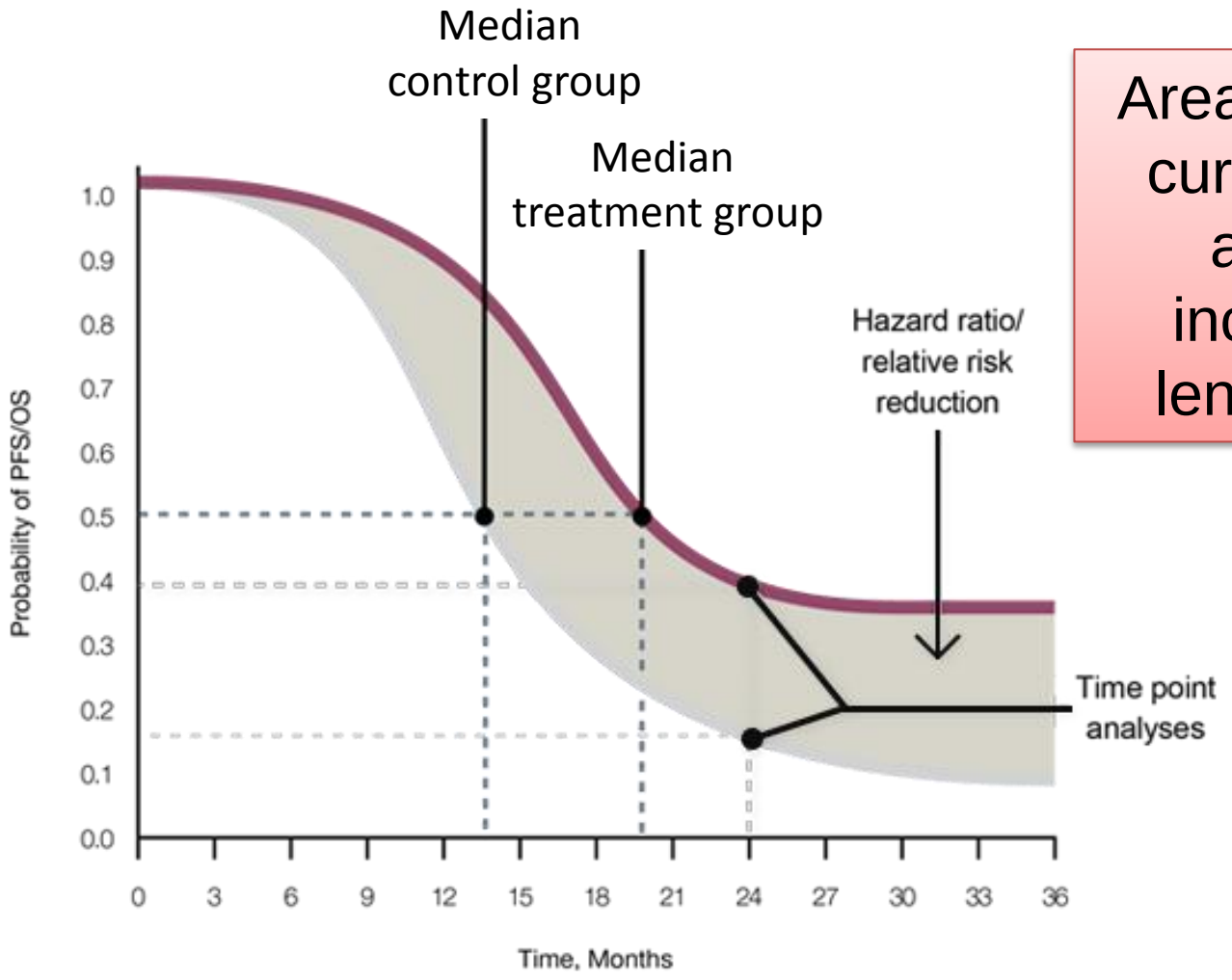


People who understand survival modelling – trials are short, life is long



How much longer - on average – do people live?

Health economists need averages

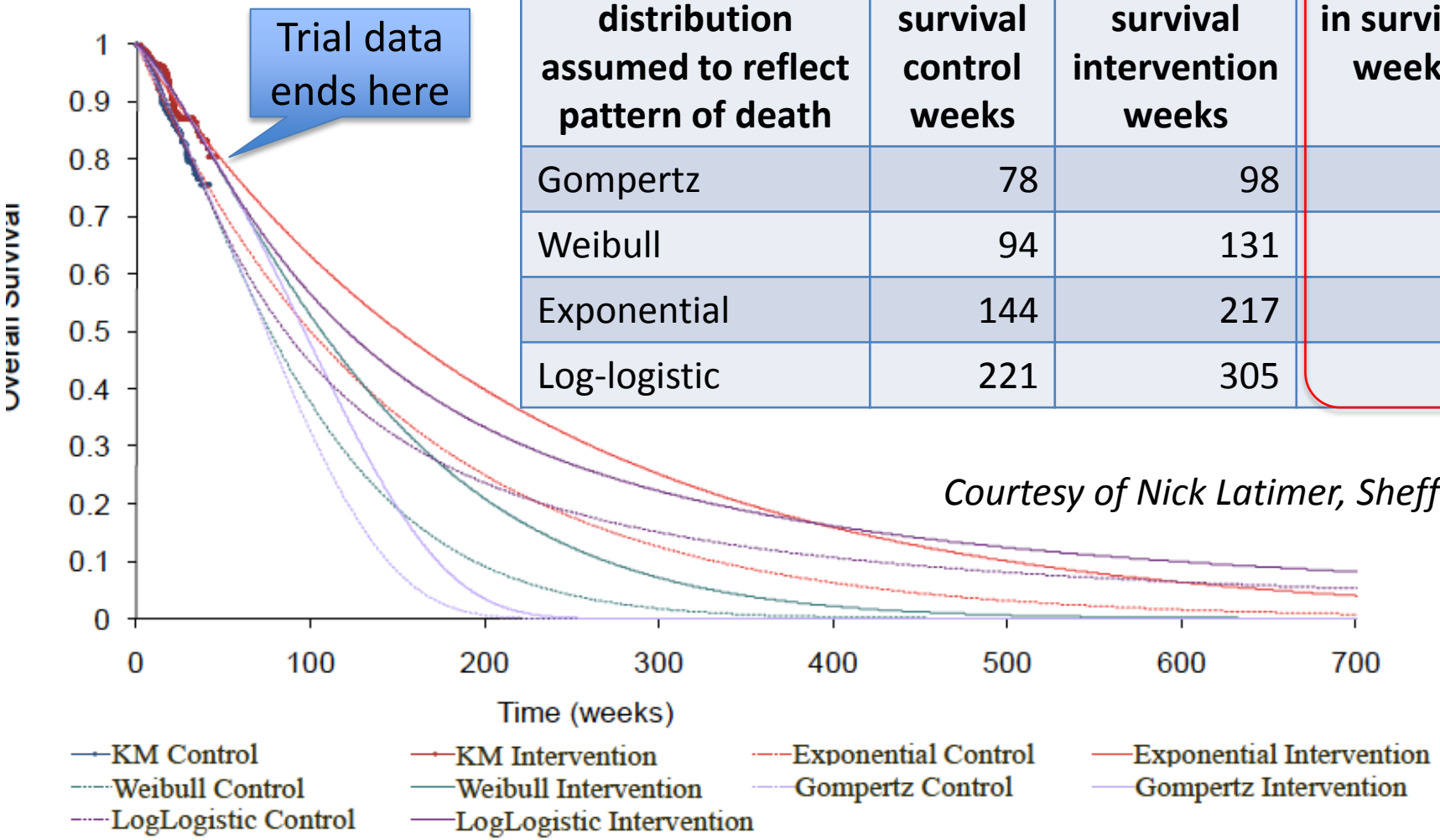


Area under the curve equals average increase in length of life

http://www.rethinkmultiplemyeloma.bmsinformation.com/Measures-of-Progression

Requires extrapolating survival – effects of choosing different distributions

Statistical distribution assumed to reflect pattern of death	Mean survival control weeks	Mean survival intervention weeks	Mean gain in survival weeks
Gompertz	78	98	**20**
Weibull	94	131	**37**
Exponential	144	217	**73**
Log-logistic	221	305	**85**

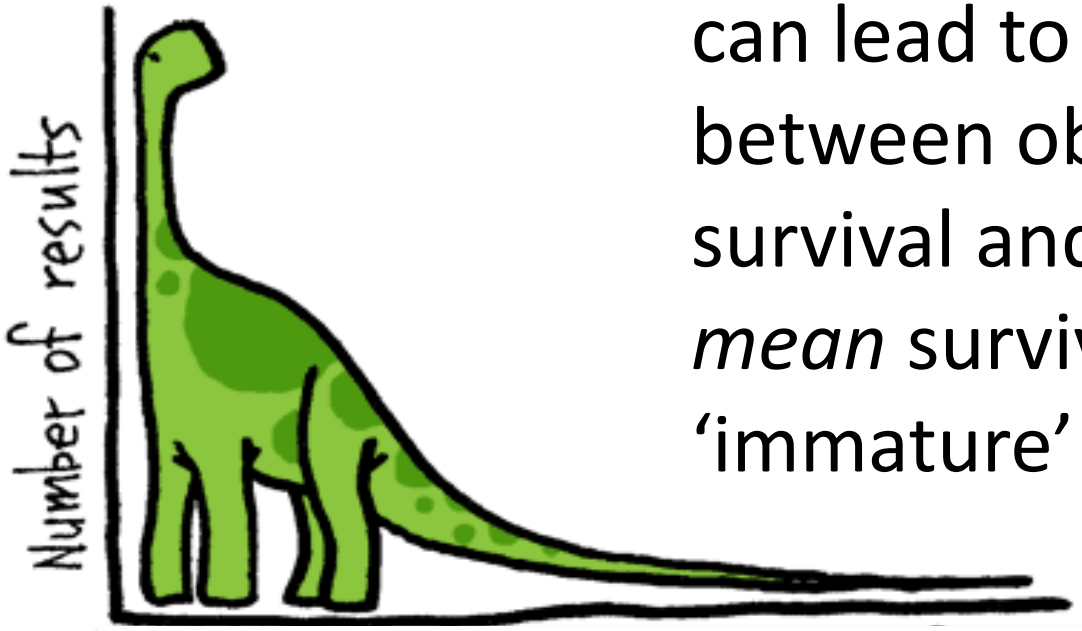


Courtesy of Nick Latimer, Sheffield

Survival Analyses – Methods often used in HTA - accessed Aug 2015

Statistical distributions with heavy tails

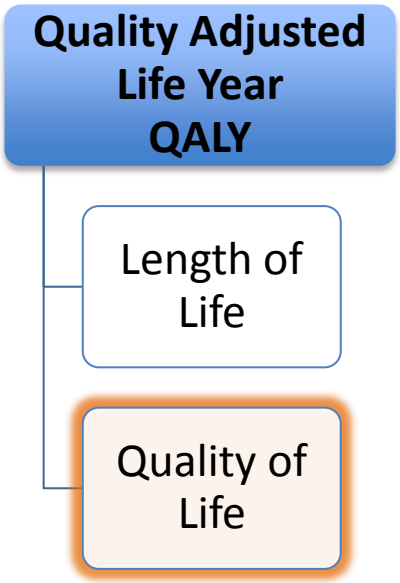
'the tail wags the curve'



Number of patients remaining at risk

can lead to big differences between observed *median* survival and estimated *mean* survival when data 'immature'

People who understand quality of life



Example: Hypoglycaemia

Example: Company X has a new drug for diabetes. Compared to a current drug, it does not lower complications or make people live longer, but it lowers the rate of hypoglycaemia (without increasing glycaemia). It costs more than the current drug. What is it worth to the NHS to avoid hypoglycaemia and improve quality of life?

Luis Prado Noun Project

Hypoglycaemia – what's it 'worth' to prevent?

https://haam.org/2015/04/24/taste-of-torah-rich-man-poor-man/

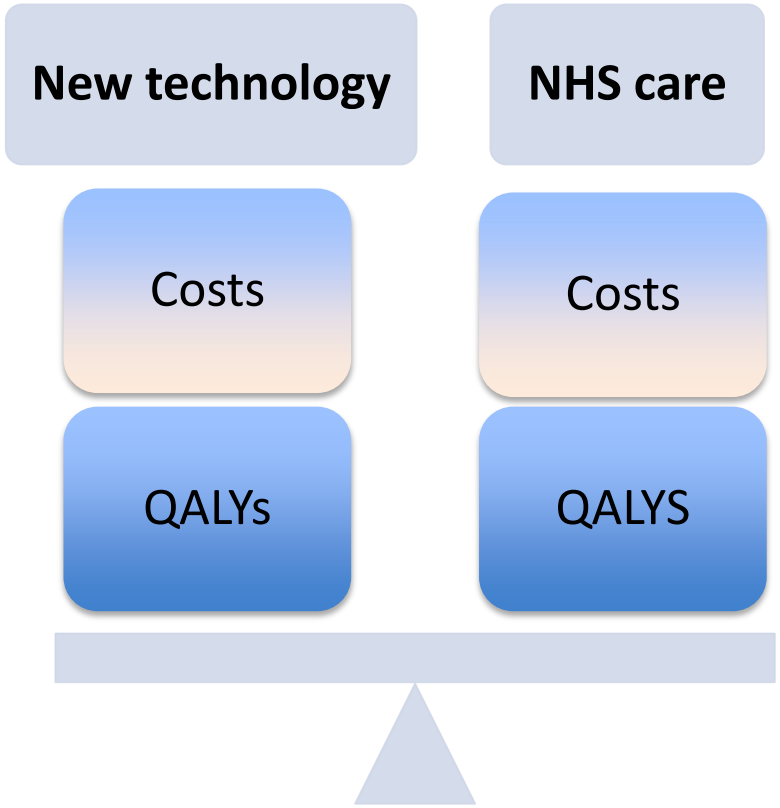
Time trade off

40 years left of life with hypoglycaemia , willing to forego 20 years for perfect health; perfect health is 1.0 and death is 0.

Utility with hypoglycaemia = 0.5

Jantoo.com

People who understand costs



Vinflunine for Bladder Cancer

- Drug cost mainly based on:
  - body surface area
  - number of treatment cycles
  - intravenous infusion every 21 days as an outpatient
- Total treatment costs
  - £21,714 for vinflunine + best supportive care
  - £8,642 for best supportive care
- ICER > £100,000 per QALY
- Sensitivity analyses:
  - **even when drug has £0 price, ICER £27,478**

Reference: Vinflunine for the treatment of advanced or metastatic transitional cell carcinoma of the urothelial tract NICE technology appraisal guidance [TA272]

Adler 2016

People who appreciate short-comings of observational data including residual confounding

Company's argument

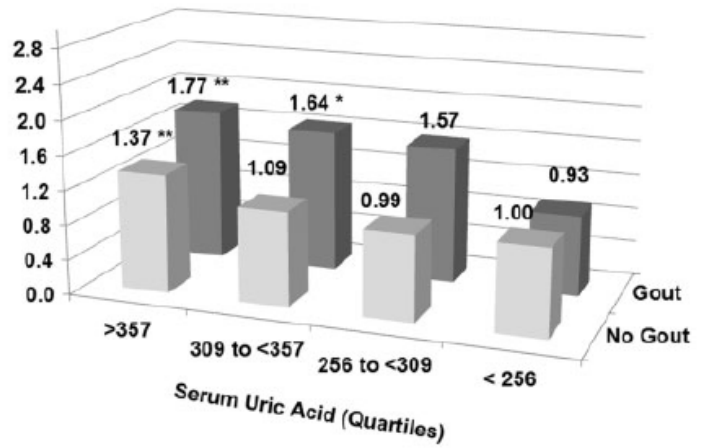


Figure 1. Joint associations of serum uric acid and gout with total mortality in the general population. $^{**}P<0.01$, $^{*}P<0.05$ vs. referent group (uric acid < 256 µmol/l and no gout). Adjusted for age, sex, race, comorbid conditions and body mass index.

- "Company used the study by Stack et al. to model the decrease in mortality risk when lowering serum uric acid levels with treatment."
- "Committee noted that the analysis by Stack et al. did not control for, among other potential confounders, poor renal function, which increases the risk of dying and was itself highly associated with serum uric acid levels in the same study."
- Was done in the general population therefore would imply that whole population needs treatment.
- Company presented pharmacoepidemiological data.
- Also potentially confounded

Stack et al. Q J Med 2013; 106:647–658
Final Appraisal Consultation Document NICE

Recommendation

Lesinurad for treating chronic hyperuricaemia in people with gout (TA506)

1 Recommendations

1.1 Lesinurad is not recommended within its marketing authorisation, that is, with a xanthine oxidase inhibitor for treating hyperuricaemia in adults with gout whose serum uric acid is above the target level despite an adequate dose of a xanthine oxidase inhibitor alone.

The main factors affecting the cost effectiveness of lesinurad are the assumptions that lowering serum uric acid levels in people with gout improves quality of life and that it prolongs life. Results from observational studies suggest that people with chronic gout have a shorter life expectancy than people without gout. However, there is no robust evidence from randomised trials to show that lowering serum uric acid levels extends life.

People who appreciate short-comings of observational data including confounding by indication

Insulin in type 2 diabetes
Not safe? Safe?

"In people with T2DM, exogenous insulin therapy was associated with an increased risk of diabetes-related complications, cancer, and all-cause mortality."

Currie et al. Mortality and other important diabetes-related outcomes with insulin vs. other antihyperglycemic therapies in type 2 diabetes.

Outcome of expert advisor panel

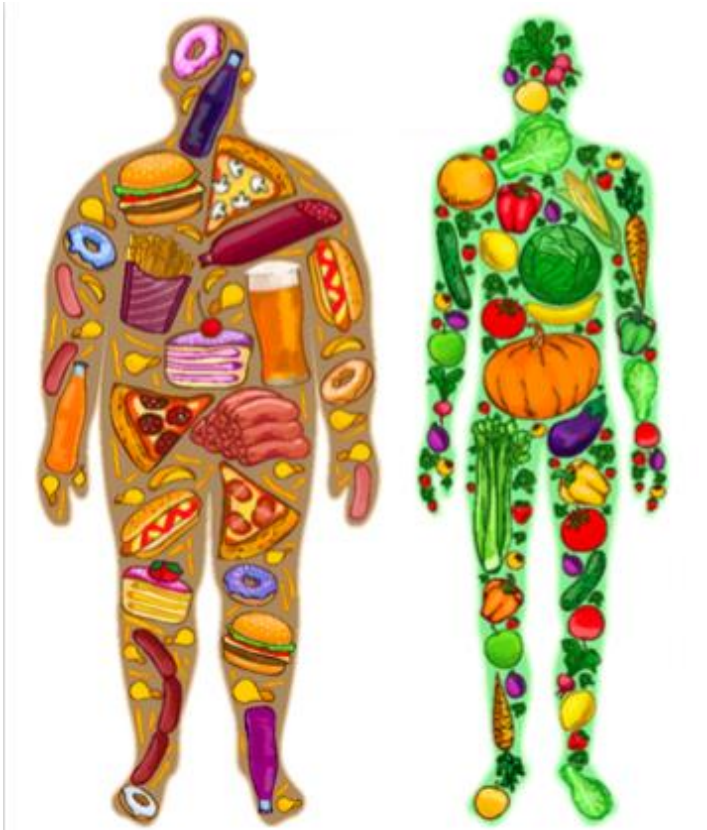
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

31 May 2013
EMA/329790/2013
EMEA/H/C/000309

Outcome of review of new safety data on insulin glargine

Data from population-based studies and the scientific literature do not indicate an increased risk of cancer

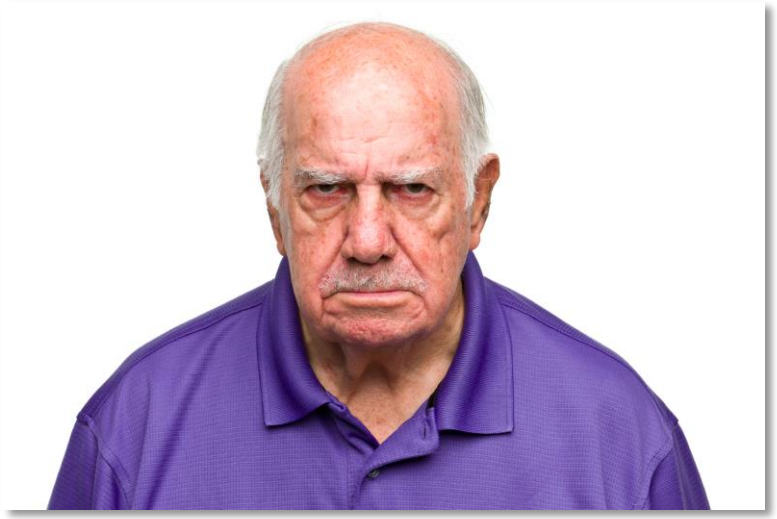
Does insulin kill people with type 2 diabetes?



Takes insulin

Does not take insulin

Patients who share their experience….



Tell about the experience of living with the condition or about the drug…

‘Methuselah’ bias

Bible (Genesis): ‘And all the days of Methuselah were nine hundred sixty and nine years: and he died’

Few patients appreciate that for fatal diseases, decision makers are aware that the patient is one of the lucky few.

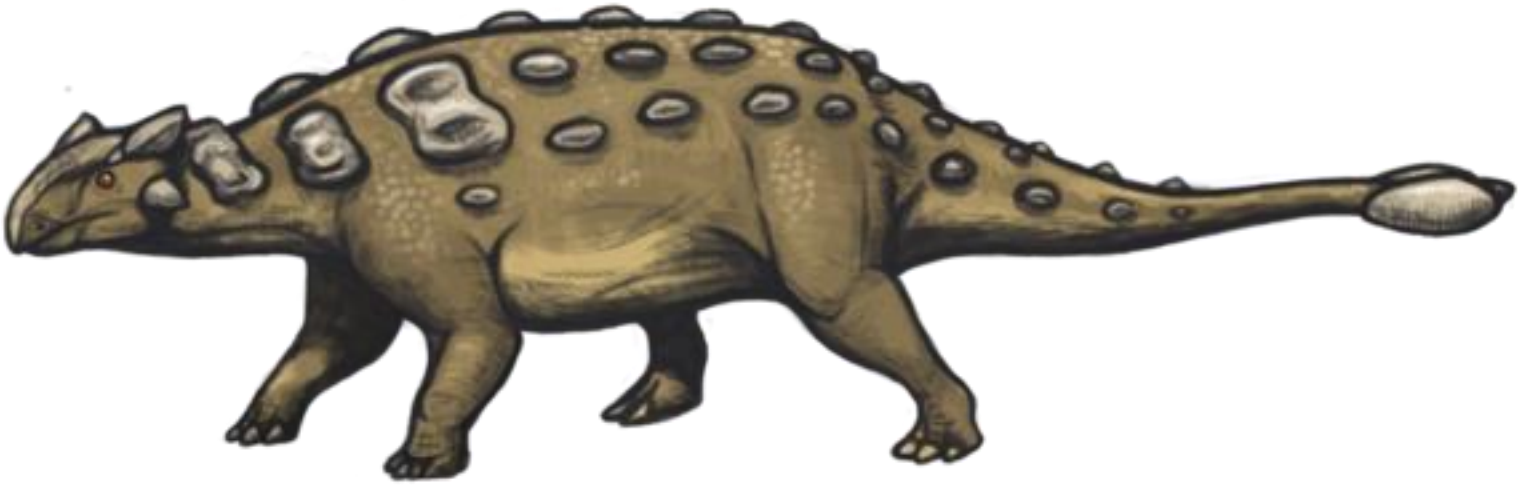
People who minimize their conflicts of interest

Conflicts are ‘subconscious’, and not all conflicts are financial

When Evidence Says No, but Doctors Say Yes

https://www.theatlantic.com/health/archive/2017/02/when-evidence-says-no-but-doctors-say-yes/517368/

People with ‘thick skins’



NICE bows to pressure to re-open consultation on 'bonkers' diabetes guidelines

Partha Kar
@parthaskar

Follow

Met >15 diabetes specialists over last few days. Not a single person thinks the draft Type 2 diabetes @NICEcomms document makes any sense

Sentenced to death by NICE

Doctors Outraged by NICE Draft Guidance on Drug Treatments for Type 2 Diabetes, Online Study Shows

Thank you and enjoy the course
It could change your life!

July 1996
Attending Cambridge Course

Dec 1996
Working in Oxford with
Prof Robert Turner