

Applying an economic framework to the evaluation and valuation of pharmacogenetic tests

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Targeting treatment?

Pharmacogenetic testing

- More information for prescribers and decision-makers
- Predict all side effects?
- Perfectly predict 'a responder'?
- Additional BUT not **perfect** information

Targeting treatment?

Economic methods can provide information on

- Relative effectiveness of medicine
 - fewer ADRs or better response?
- Relative accuracy of the pharmacogenetic test
- Impact of benefits to patients (health status)
- Impact of costs to the health service (and society)
- Preferences for models of service delivery
- Population (not individual) level decision-making

Providing healthcare

- Finite health budget
- NHS budget in England
 - £33 bn in 1996/7
 - £96 bn in 2008/9
- Average expenditure per person
 - £426 in 1996
 - £1,612 in 2010
- Each Primary Care Trust funding calculated using a resource allocation formula
- 80% of the total NHS budget now allocated directly to PCTs
 - ‘...allowing them to tailor health services locally to meet local patient needs’.

Making healthcare choices

Finite budget → have to make choices about how to use NHS resources

Locally

- Service commissioners: Primary Care Trusts
- Specialised Commissioning Groups
- Hospitals eg. Drug formularies
- Clinicians (management options/treatment choices)

Nationally

- National Specialised Commissioning Group (was NSCAG)
- National Institute for Health and Clinical Excellence (NICE)

How are these decisions made?

Making choices: use of evidence

- Epidemiological data
- Evidence of clinical effectiveness
- Healthcare need (capacity to benefit)
- Costs of treatment (opportunity costs)
- Evidence of cost effectiveness
- Patient and expert views
- Needs of the community
- Policy drivers
- (Exceptional need)

Efficiency

- How do we allocate the healthcare budget so that we get the most benefit from the medicines?
 - Maximum clinical effectiveness eg. response rate
 - Minimum side effects
 - Maximise health gain
 - Maximise efficiency (best value for money)
- *Allocative*: using resources, across the whole economy, so that benefit is maximised (or the opportunity cost is minimised).
- *Technical*: means producing a given output for the least cost, or maximising output for a given cost.

Q: How do we measure 'efficiency'?

.....Opportunity Cost

Is the benefit that would be derived from using a resource in its best alternative use



A fabulous family holiday?
A flashy sports car?
Lifetimes supply of pizza

Over one-year.....

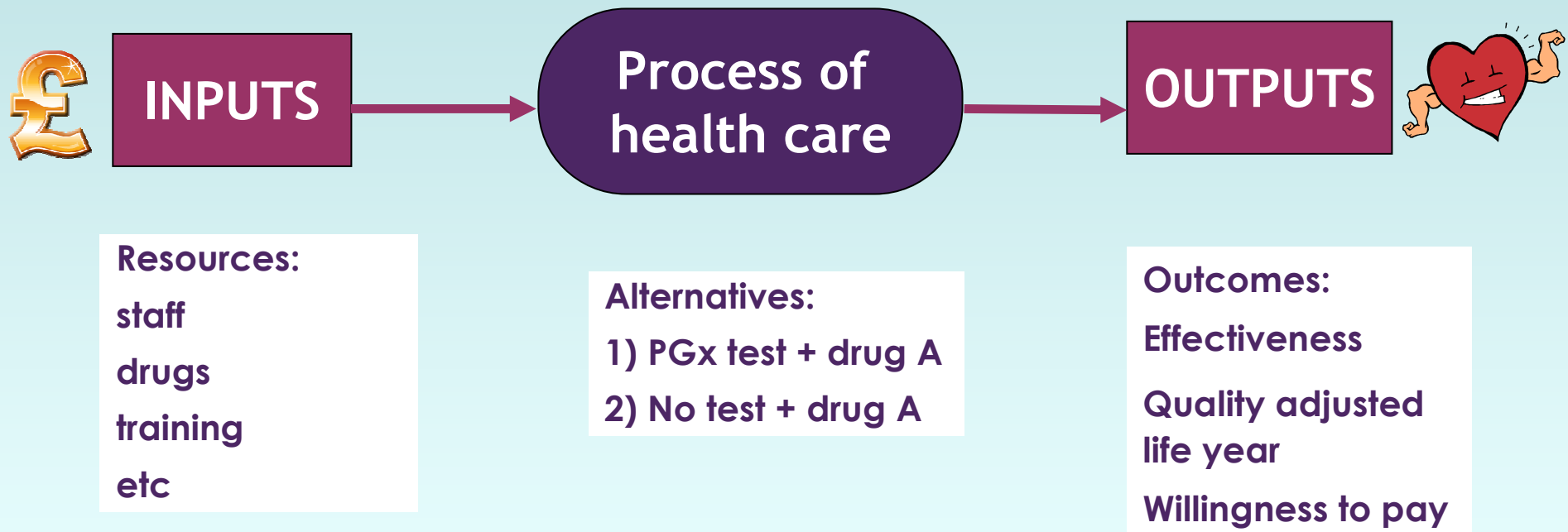
57 people offered diagnostic test for a single gene

6 people have hip replacements

1 person gets Herceptin for breast cancer

Economic evaluations

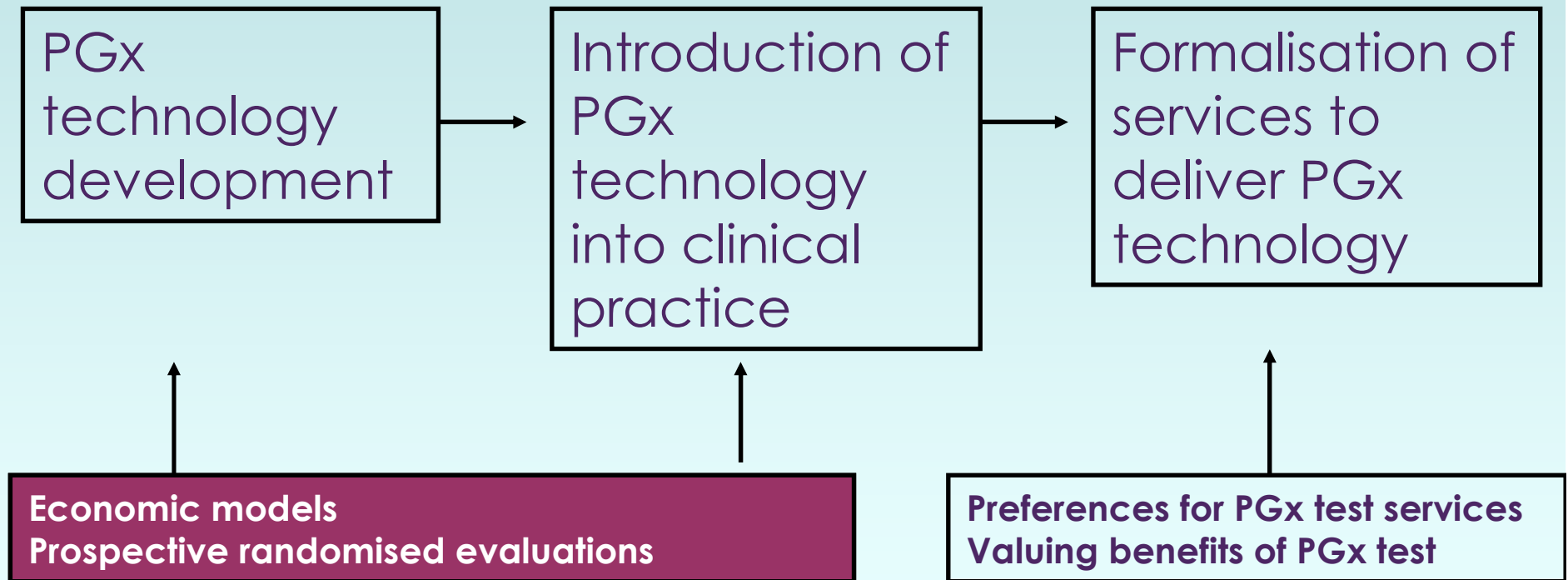
- One of a number of methods used by health economists
- Provide evidence about (technical) efficiency



Types of Economic Evaluation

- Cost-minimisation analysis
- Cost-effectiveness (utility) analysis
- Cost-benefit analysis

Pharmacogenetic diffusion process



Developing the evaluation framework

- Define the (research) question: identify and describe the interventions under evaluation
- Structure the evaluation (trial/model) based on the intervention process: describe each clinical care pathway
- ‘Collect’ outcome and resource (cost) evidence
 - Maximising health gain: link between clinical improvement and health status (The EQ-5D)
- The economic analysis:
 - incremental costs and incremental benefit
 - Quantify the uncertainty in your answer (sensitivity analysis)
- Present the results

What is the (research) question?

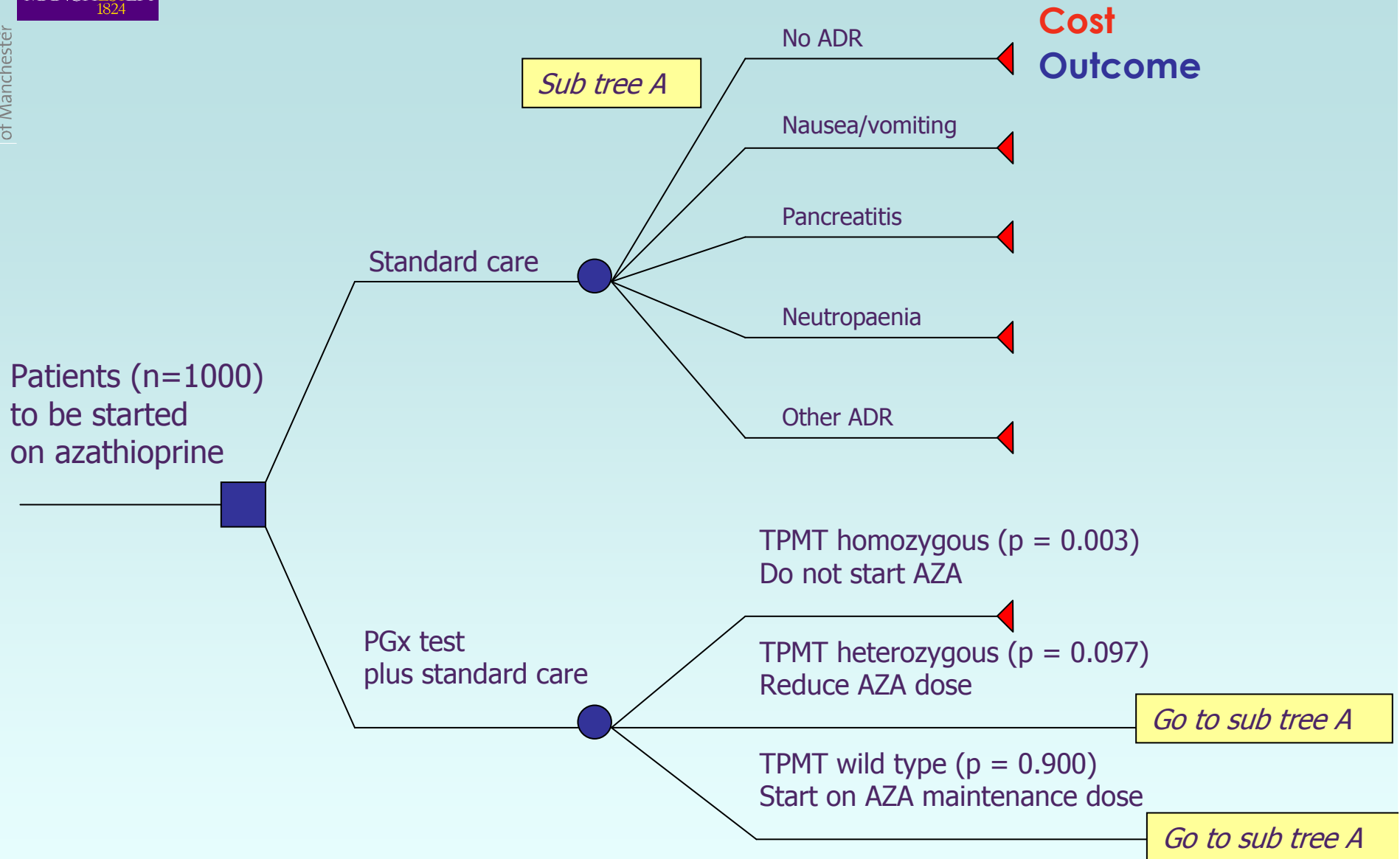
- Describing the intervention or service under investigation: the scope of the evaluation
- Process of intervention/service (inputs and outputs):
 - What happens when a patient presents to the NHS
 - Outcome of the process
 - Resource use and cost of the process

Q: How well has this been done?

- Perspective (viewpoint) of the study: dependent on who will be funding the intervention/using the information from the evaluation

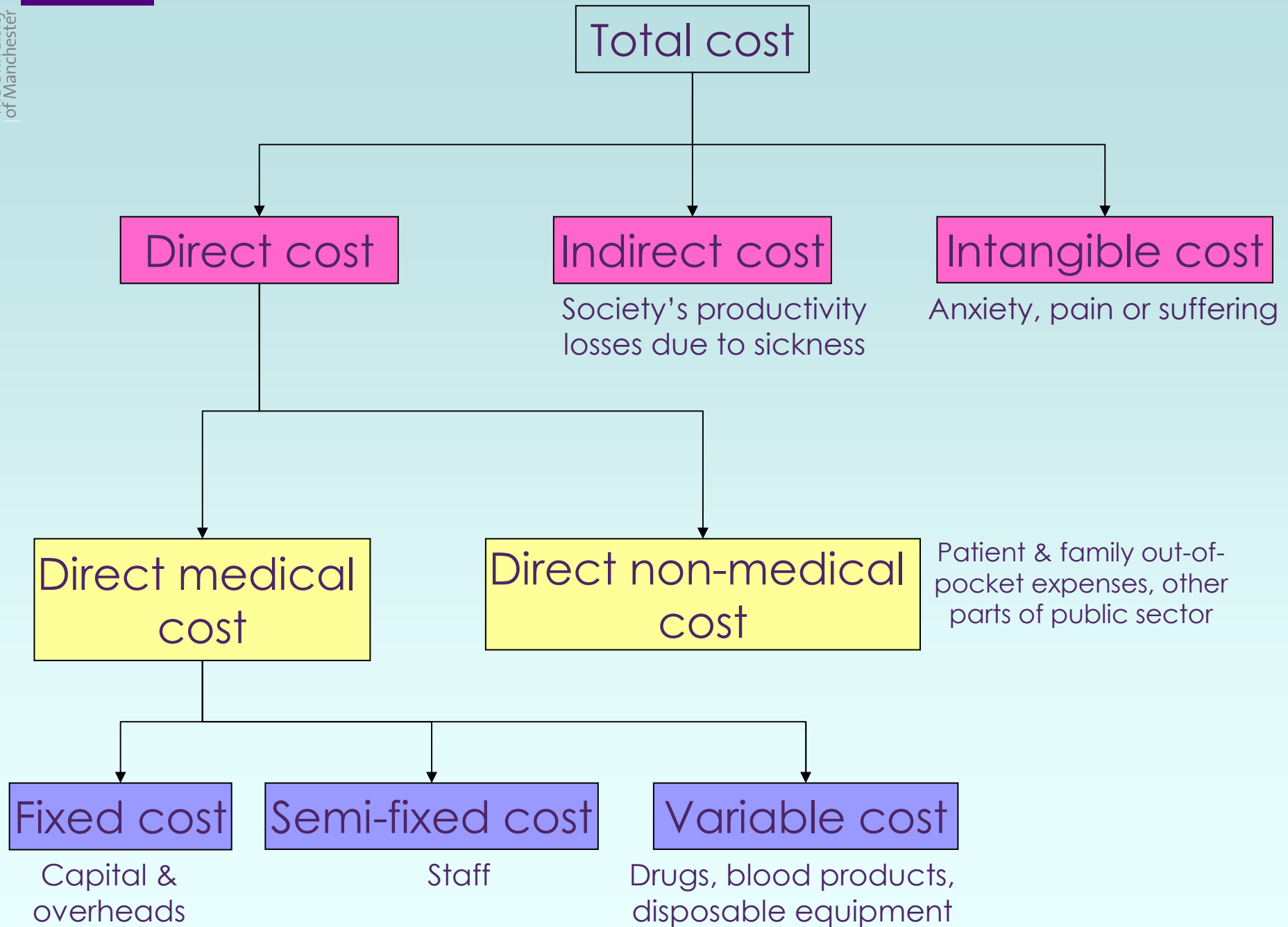
Find economic and clinical evidence

1. Describe the clinical pathways for PGx test compared with current practice
 2. Identify probabilities to the chance events in the model (clinical evidence) and attach costs and patient benefits to each pathway (economic evidence)
- Primary economic evaluation
 - Data from a randomised controlled trial
 - Secondary economic evaluation
 - Economic & clinical data combined from many sources
 - Systematic review and meta-analysis
 - Decision analytic model



What should be costed?

- True economic cost takes into account all the cost associated with an intervention.
- In an economic evaluation, the costs included depend on:
 - the perspective (viewpoint) of the evaluation
 - Society (everyone)
 - NHS and Personal Social Services
 - Hospital
 - the time horizon (follow-up) of the evaluation
 - 1 year
 - 10 years
 - Lifetime



Incremental costs and marginal costs

Incremental cost: difference in overall cost between providing an intervention (A) and the alternative intervention (B).

For example, the incremental cost of gemcitabine compared to standard care for pancreatic cancer

Marginal cost: the cost of doing one more intervention.

For example, the marginal cost of doing one more screening test for cervical cancer

Measuring the benefit of interventions

Benefits, outcomes and consequences refer to the effect on the patient, not the effect on the people providing the service.

Cost is not an outcome measure.

The principal outcome categories used in economic evaluation are:

- effectiveness
 - eg. cases successfully diagnosed
 - life-years gained
- utility and health-related quality of life
- expressing benefits as monetary values

Measuring Health Related Quality of Life

- Most modern medicines improves quality, rather than quantity of life
- Using clinical indicators implies that changes in these will link directly to an effect on the patient's quality of life.
- Measuring quality of life is hard and methods still being developed!
- Many functional, social, psychological, cognitive and subjective factors that impact on quality of life.
- Quality of life measures can be divided into generic and disease-specific measures.

The EuroQoL (EQ-5D)

Mobility

Self-care

Usual activities

Pain/discomfort

Anxiety/depression

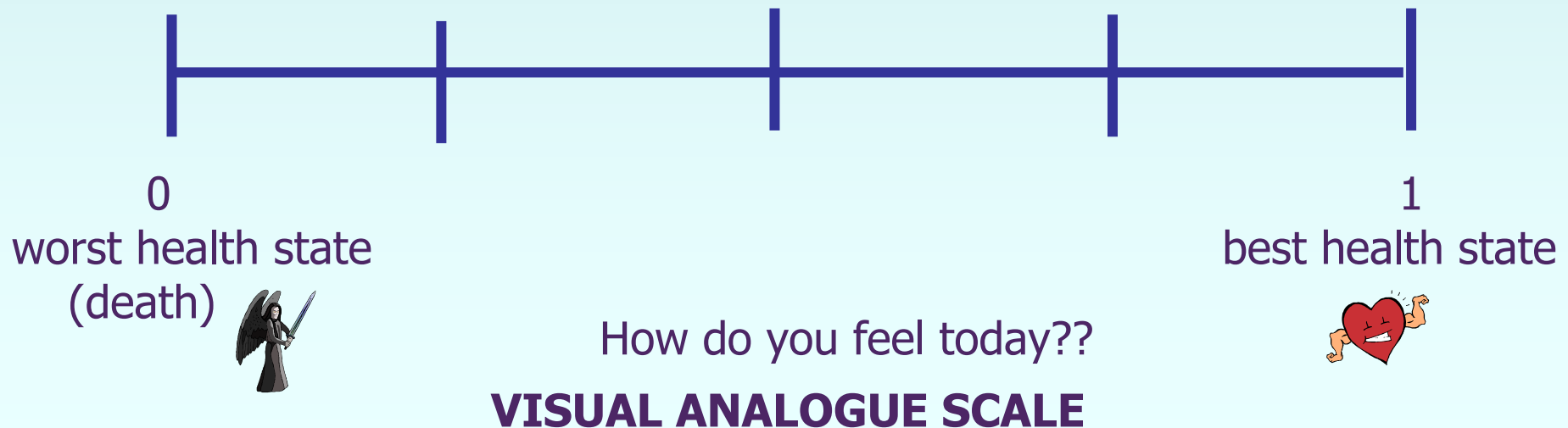
No problems (1) Some problems (2) Major problems (3)

Perfect health = 11111 = 1.0 utility score

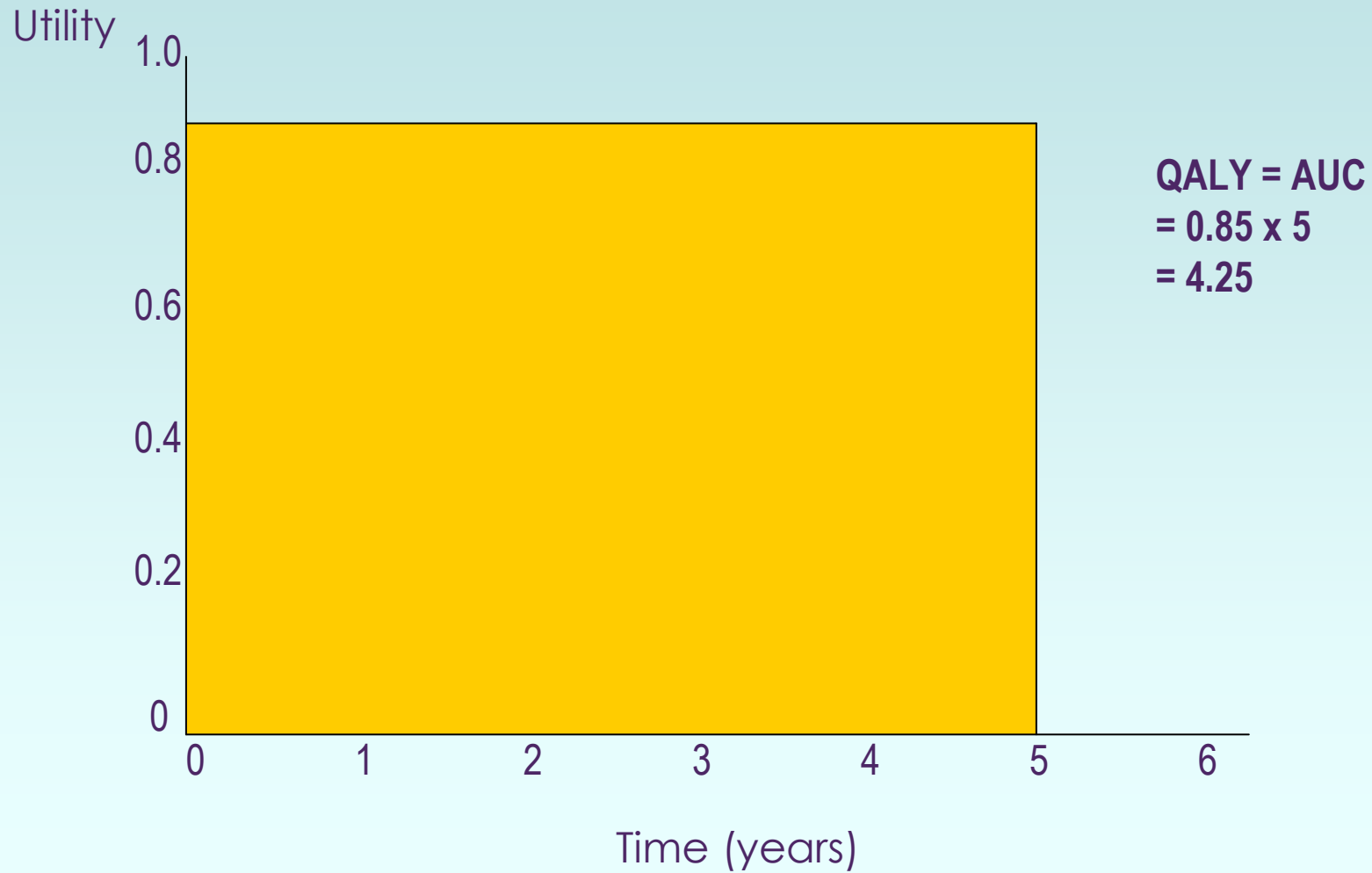
Some problems walking = 21111 = 0.85 utility score

Valuing Benefit (utility)

- A value attached by an individual for a specific level of health status or a specific health outcome.
- Different individuals may attach different values to the same health state.
- Compare between groups of patients with different illnesses or outcomes in different patient groups.
- Methods: standard gamble, time trade off, visual analogue scale



The Quality Adjusted Life Year (QALY)



Valuing benefit: contingent valuation

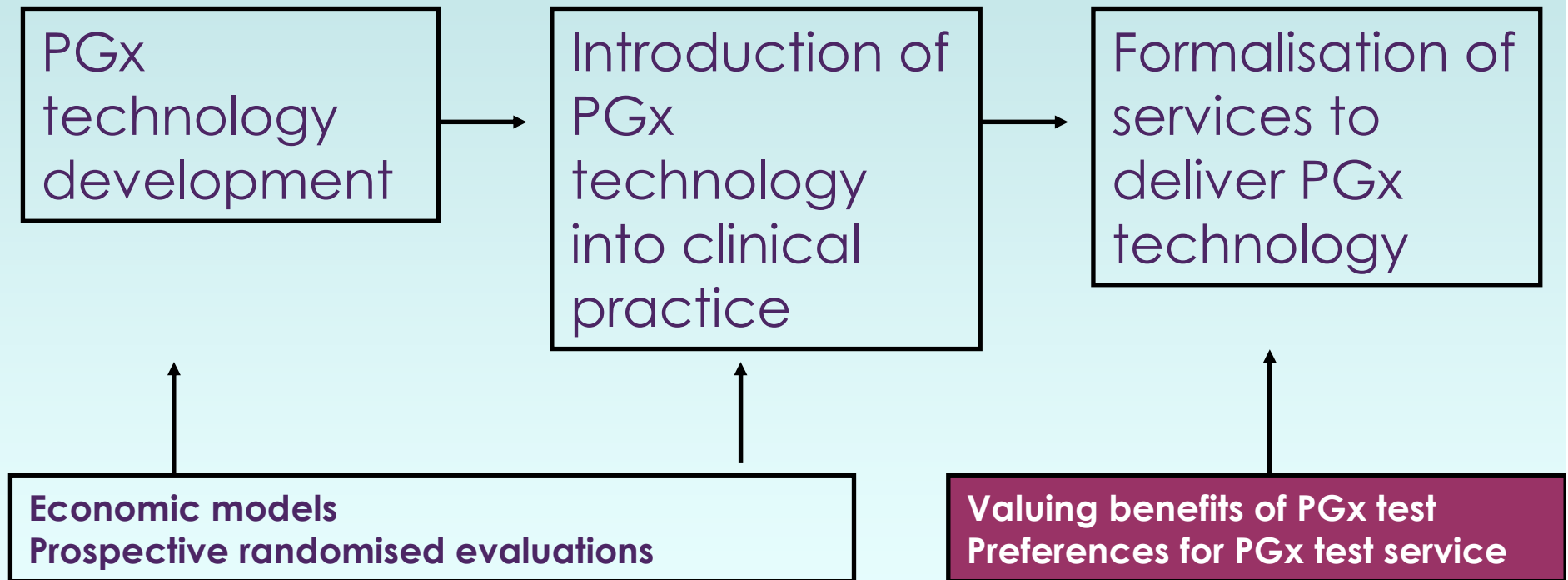
This method seeks to elicit how much an individual would be willing to pay (WTP) to avoid an illness or obtain the benefits of a treatment (or test).

You are taking a medicine for Crohns disease. There is a risk you will develop a side effect that reduces the number of white blood cells to fight infection in your body. There is a common chance (1 in 1,000) you will develop this side effect. Alternatively there is a test you can take that may predict your risk of this side effect. The test is not perfect.

1. Would you take the test?
2. How much would you be 'willing to pay' to take this test?

What value do you attach to this test to reduce this ADR?

Pharmacogenetic diffusion process



Incorporating patient preferences

- Qualitative exploration of peoples' views about PGx services
- Observe 'market behaviour' ie. Use of PGx testing (revealed preference)
- Ask individuals to state a preference (stated preference) for a possible future service
- Ranking services: gets harder and less reliable with more options
- Rating services: makes strong assumptions that humans can report 'degrees' of preference differences
- Discrete choices: reflects how people make daily decisions and relies on fewer assumptions about cognitive ability

Valuing stated preferences

- The aim: to measure preferences, choices and trade-offs
 - Process: how the service is provided
 - Outcome: the measure of benefit to the patient
- The methods:
 - contingent valuation (for whole service)
 - conjoint analysis and discrete choice experiments (individual attributes)
- How much do people value the potential risk reduction offered by a PGx test?
- What are the preferred characteristics of a PGx service?

Which characteristics of a pharmacogenetic service are valued most highly?

- Describe the hypothetical (virtual) service to be valued
- Frame the choice question
- Describe the service in terms of
 - attributes (process and outcome)
 - levels that each attribute can take
- Use mathematical design theory to produce a set of ‘choices’
- Identify the sampling frame: current (& future) patients
- Field the survey (on-line or postal)
- Analyse the data: regression methods

Pharmacogenetic testing: key issues

- Clinically valid: Sensitivity (true +) and specificity (true -) and predictive value
- Economical: Maximum patient health gain given the cost of PGx test compared with current practice (no PGx test)
- Practical: Get the result to the patient at the right time
- Paucity of evidence on
 - relative costs and benefits of pharmacogenetic tests
 - preferences for providing pharmacogenetic services
 - factors stimulating demand (barriers)

Future challenges

- Efficiency: How do we allocate scarce resources so that benefit is maximised from pharmacogenetic testing?
- Generating robust evidence of patient value from pharmacogenetic testing services for commissioners
- Patient preferences for models of service delivery:
 - do patients value the process or outcome most highly?
- Develop good quality clinical and economic evaluations of models of pharmacogenetic tests and services
- *Economics* can be used to inform the decision making process about the allocation of scarce resources