Health Technology Assessment: can Japan learn from England’s successes and mistakes?

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Professor of Practice in Global Health, Imperial College London
Outline of today’s lecture

- HTA and priority setting: defining the terms
- HTA: global momentum growing
- NICE in the UK: an overview
- Health service costs matter!
- NICE and drug pricing
- Vertical funds: more trouble than they are worth?
- HTA, strategic purchasing and quality improvement
- Reflections on Japan
DEFINING THE TERMS
What is Health Technology Assessment?

• HTA is a multidisciplinary process that summarises information about the medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, robust manner. HTA answers clinical questions of new, potential innovative, healthcare technologies such as: How well does a new technology work compared with existing alternative health technologies? For which population group does it work best? HTA can also answer economic questions like: What costs are entailed for the health system? It is therefore a considered key tool for decision makers to ensure the accessibility, quality and sustainability of healthcare.

• A health technology is defined as an intervention that may be used to promote health, to prevent, diagnose or treat acute or chronic disease, or for rehabilitation. Health technologies include pharmaceuticals, devices, procedures and organizational systems used in health care.”

• OR...

• “Health technology assessment (HTA) is a tool to review technologies and provide evidence of the value these technologies can deliver to patients and their families, health system stakeholders, and to society more broadly.”
Using HTA to inform priority setting

HTA can form an integral part of a process for considering scientific evidence, economic evidence and social values, to directly inform coverage and policy decisions relating to healthcare interventions.

- drugs, devices, diagnostics, surgical interventions and services, both preventative and curative/palliative
- but also service delivery models, programmatic reforms, health and public policy interventions (e.g. smoking cessation).

Should include economic evaluation (EE)/ cost-effectiveness analysis (CEA); not just clinical effectiveness as waste costs lives

- drawing comparisons: compared to the status quo, what do we gain out of the new intervention, and at what extra cost?

Not just a technical exercise: the process and social values are equally important

it must carry budgetary implications; ie it must have teeth to make a positive difference
Using Economic evaluation

“... the comparative analysis of alternative courses of action in terms of both their costs and consequences.”

Drummond, Stoddart & Torrance, 1987

Analysis should be conducted separately for each subgroup of patients.
The HTA Process

What is the Decision problem?
Topic identification and Prioritisation

How do we decide if the evidence is strong enough to support a decision? What are our recommendations?

How is the decision implemented and monitored?

Defining Decision Space / Topic Selection

Analysis

Appraisal

Decision Making

Implementation

What is the required analysis needed to help answer the decision problem?

What is the decision to be taken?

Source: PRICELESS, South Africa
The HTA process in more detail...

- Topic Selection
- Scoping and Decision Problem Formulation
- Evidence Submission
- Preparation of an ‘Evaluation Report’ (Internal or External Group)
- Stakeholder Consultation
- Independent Advisory Committee develops Preliminary Recommendations
- Decision Making
  - Final Recommendations Formulated
  - Stakeholder Consultation

- Review
HTA IS NOW A GLOBAL MOVEMENT…
“to integrate health intervention and technology assessment concepts and principles into relevant strategies and areas...including, but not limited to, universal health coverage, health financing, access to and rational use of quality-assured medicines, vaccines and other health technologies, the prevention and management of non-communicable and communicable diseases, mother and child care, and the formulation of evidence-based health policy”
"Evidence helps when negotiating price and rules on reimbursement, which in turn affect access. Health technology assessment is a routine part of the decision-making process for adding medicines to the national benefit package in Thailand, and other countries such as Indonesia and India are introducing this approach."
HTA is becoming a major tool for priority setting and price negotiations for national governments in emerging markets...

**National Health Insurance Act of 2013, Section 11- Excluded Personal Health Services**

**Philippines:** “The Corporation shall not cover expenses for health services which the Corporation and the DOH consider cost-ineffective through health technology assessment...”

**Indonesia: Minister of Health’s Decree No. 71 /2013 Article 34**

(5) Health Technology Assessment Committee provide policy recommendation to the Minister on the feasibility of the health service as referred to in paragraph (4) to be included as benefit package of National Health Insurance

“the India Medical Technology Assessment Board for evaluation and appropriateness and cost effectiveness of the available and new Health Technologies in India...standardized cost effective interventions that will reduce the cost and variations in care, expenditure on medical equipment...overall cost of treatment, reduction in out of pocket expenditure of patients...”. Ref: MTAB, Ministry of Health & Family Welfare, Government of India

**Service coverage (5.3): South Africa** “Detailed treatment guidelines, based on available evidence about cost-effective interventions, will be used to guide the delivery of comprehensive health entitlements. Treatment guidelines will be based on evidence regarding the most cost-effective interventions.”

HTA unit budgeted @R368m in 2018 budget by country’s Treasury
October 2018: China legislates HTA and launches National Centre of Medicine and Health Technology Assessment

4. Knowledge translation and Decision Making

- Pricing Negotiation for 18 Generic Cancer Drug
- Updating National Essential Drug List
- Comprehensive Drug Assessment
- Reviewing Public Health Service Package
- Setting Up the List of Appropriate Technologies in County Level Hospitals

“We have fully utilized HTA...to balance financially sustainability and access to new cancer drugs...up to 30% price reductions compared to nearby countries”
Director of Chinese Medical Insurance Bureau, Beijing, October 2018
and in high income economies in the EU...

“The outcome of HTA is used to inform decisions concerning the allocation of budgetary resources in the field of health, for example, in relation to establishing the pricing or reimbursement levels of health technologies. HTA can therefore assist Member States in creating and maintaining sustainable healthcare systems and to stimulate innovation that delivers better outcomes for patients”

…who use HTA to decide listing and pricing of new technologies

Table 1. Summary of European Collaborations in Procurement of Health Innovations

<table>
<thead>
<tr>
<th>Alliance</th>
<th>Member Countries</th>
<th>Initiation Date</th>
<th>Areas of cooperation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valetta Declaration*</td>
<td>Malta, Cyprus, Greece, Italy, Spain, Portugal, Slovenia, Croatia, Ireland, Romania</td>
<td>May 2017</td>
<td>Information sharing on prices and markets, joint negotiation for purchasing to ensure affordability</td>
</tr>
<tr>
<td>Central Eastern European and</td>
<td>Romania, Bulgaria, Croatia, Latvia, Poland, Sebia, Slovakia, Slovenia, Republic of Moldova, FYR Macedonia</td>
<td>November 2016</td>
<td>Price negotiation</td>
</tr>
<tr>
<td>South Eastern European Countries Initiative</td>
<td>Greece, Bulgaria, Spain, Cyprus, Malta, Italy, Portugal</td>
<td>June 2016</td>
<td>Information sharing on prices and markets, collaboration on R&amp;D</td>
</tr>
<tr>
<td>Southern European initiative</td>
<td>Bulgaria, Croatia, Estonia, Hungary, Latvia, FYR Macedonia, Romania, Serbia, Slovakia, Slovenia</td>
<td>June 2016</td>
<td>Information sharing on prices and markets, with potential for joint purchasing in the future</td>
</tr>
<tr>
<td>Nordic Pharmaceutical Alliance</td>
<td>Denmark, Iceland, Norway, Sweden</td>
<td>June 2015</td>
<td>Horizon scanning, information sharing on prices and markets</td>
</tr>
<tr>
<td>Romanian and Bulgarian Initiative</td>
<td>Romania, Bulgaria</td>
<td>June 2015</td>
<td>Joint negotiations in purchasing to get lower prices for pharmaceuticals and cross-border exchange of medicines in short supply to ensure continuity of access</td>
</tr>
<tr>
<td>Beneluxa initiative of Pharmaceutical Policy</td>
<td>Belgium, Netherlands, Luxembourg, Austria, Ireland**</td>
<td>April 2015</td>
<td>HTA, horizon scanning, information sharing on prices and markets, joint negotiation for purchasing to ensure affordability</td>
</tr>
<tr>
<td>Baltic Partnership Agreement</td>
<td>Latvia, Lithuania, Estonia</td>
<td>May 2012</td>
<td>Centralized joint purchasing (tenders, negotiation, payment and distribution) to reduce expenditure and ensure continuity of access</td>
</tr>
</tbody>
</table>

* Michalopoulos, 2017, 2018; ** Ireland recently joined (An Ronn Slaine, 2018; Beneluxa, 2018a)

**Outcome Report**

On

“Health Technology Assessment of Intraocular Lenses for treatment of Age-related Cataracts in India”

“The benefit packages for Phacoemulsification with foldable lens and small incision cataract surgery with rigid PMMA lenses may cost as 9606 INR and 7405 INR respectively”

Health Technology Assessment In India (HTAin) Secretariat, Department of Health Research, Ministry of Health and Family Welfare

July-2018
New Delhi
**HTA informs pricing across EU**

“While some countries systematically apply HTA for all new medicines (such as Denmark, France and Poland), others only assess those causing certain concerns due to, for instance, uncertain effectiveness, high prices or high budget impact (such as United Kingdom). Of the 45 countries surveyed, 34 have at least one HTA agency in place, primarily in the public sector.”

<table>
<thead>
<tr>
<th>Branded Name</th>
<th>Company</th>
<th>Therapeutic Area</th>
<th>Year</th>
<th>HTA Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lojuxta</td>
<td>Aegerion</td>
<td>Hyper-cholesterolemia</td>
<td>2015</td>
<td>Belgium re-used Dutch HTA work</td>
</tr>
<tr>
<td>Orkambi</td>
<td>Vertex</td>
<td>Cystic fibrosis</td>
<td>2016</td>
<td>First submission – Joint HTA (Belgium and Netherlands); external referee (Dutch Zorginstituut); Luxembourg used final report</td>
</tr>
<tr>
<td>Praluent</td>
<td>Sanofi</td>
<td>Dyslipidemias</td>
<td>2016</td>
<td>External referee (Dutch Zorginstituut for Belgium)</td>
</tr>
<tr>
<td>Orkambi</td>
<td>Vertex</td>
<td>Cystic fibrosis</td>
<td>2017</td>
<td>Second submission - Joint HTA (Belgium Netherlands); external referee (Dutch Zorginstituut); final report sent to Luxembourg and Austria</td>
</tr>
<tr>
<td>Vyndaqel</td>
<td>Pfizer</td>
<td>Amyloidosis</td>
<td>2017</td>
<td>External referee (Dutch Zorginstituut for Belgium); Luxembourg used final report</td>
</tr>
<tr>
<td>Ocaliva</td>
<td>Intercept</td>
<td>Primary biliary cholangitis</td>
<td>2018</td>
<td>Joint HTA (Belgium and Netherlands)</td>
</tr>
<tr>
<td>Spinraza</td>
<td>Biogen</td>
<td>Spinal Muscular Atrophy</td>
<td>2018</td>
<td>Joint HTA (Belgium and Netherlands)</td>
</tr>
</tbody>
</table>

And even in the USA private insurers adopt HTA…

- “CVS Caremark is initiating a program that allows clients to exclude any drug launched at a price of greater than $100,000 per QALY from their plan. The QALY ratio is determined based on publicly available analyses from the Institute for Clinical and Economic Review (ICER), an organization skilled in the development of comparative effectiveness analyses.

- Medications deemed “breakthrough” therapies by the U.S. Food and Drug Administration will be excluded from this program, which will focus on expensive, “me-too” medications that are not cost effective, helping put pressure on manufacturers to reduce launch prices to a reasonable level.”

NICE IN THE UK: PAST, PRESENT AND FUTURE
The role of NICE in the UK

The National Institute for Health and Care Excellence (NICE) provides national guidance and advice to improve health and social care

- Produces *evidence-based guidance* and advice for health, public health and social care practitioners.
- Develops *quality standards and performance metrics* for those providing and commissioning health, public health and social care services;
- Provides a *range of information services* for commissioners, practitioners and managers across the spectrum of health and social care.
Background to the creation of NICE in the 90s…

- Doctors adopting new health technologies without adequate evidence of their clinical and/or cost effectiveness
- Out of date technologies and services being used even though they had been superseded by newer developments
- Lack of national clinical guidelines and many of the existing clinical guidelines not updated and of poor quality
- Postcode lottery inappropriate variation in access to care and care standards
- (later) Prospect of significant reinvestment in the NHS: plan to grow from about 6.5% to about 9% of GDP

• “The Government is determined that the services and treatment that patients receive across the NHS should be based on the best evidence of what does and does not work and what provides best value for money (clinical and cost-effectiveness).

  • ‘A new National Institute for Clinical Excellence will be established to give new coherence and prominence to information about clinical and cost-effectiveness.’

  • ‘…membership will be drawn from the health professions, the NHS, academics, health economists and patient interests.’

• All too often in the past, the same problem has been partially solved in different areas. Best practice has not been shared as it should have been. As a result patients have not had fair access to the best the NHS has to offer.”
1999: NICE is established: focus on professionals and quality, not drug prices

**Evidence-informed:** “A new National Institute for Clinical Excellence will be established to give new coherence and prominence to information about clinical and cost-effectiveness.”

**Multidisciplinary:** “The National Institute’s membership will be drawn from the health professions, the NHS, academics, health economists and patient interests.”

**Incremental:** “The Government will consider developing the role and function of the National Institute as it gathers momentum and experience.”

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"Subject to and in accordance with such directions as the Secretary of State may give, the Institute shall perform: such functions in connection with the promotion of clinical excellence, and the effective use of available resources in the health service"

Article 3 (functions of the Institute) of the principal Order (1999/amended 2005)
The Coalition government reforms, 2013: quality becomes the Law!

“The Secretary of State must...secure continuous improvement in the quality of services provided to individuals...In discharging the duty...the Secretary of State must have regard to the quality standards prepared by NICE under section 234 of the Health and Social Care Act 2012.”
NICE: changes and evolution... to 2014

- ~30 WTE; £11M
- 560 WTE; £67.2M
NICE: changes and evolution...to 2019

~30 WTE; £11M

620 WTE; £70M
NICE - “Technology Appraisals”

• “The NICE technology appraisal programme assesses the clinical- and cost-effectiveness of new medicines, significant licence extensions and other health technologies….The NHS is legally obliged* to fund and resource medicines and treatments recommended by NICE’s technology appraisals. Since April 2016, it has been agreed that all new cancer medicines and significant new licenced indications will be appraised by NICE”.

*When NICE recommends a treatment ‘as an option’, the NHS must make sure it is available within 3 months (unless otherwise specified) of the final guidance publication.

• Source: NICEimpact (2018) - Cancer
Drug development

Regulatory approval

NICE/HTA

Use in healthcare system

Under controlled conditions and compared to placebo:
• Is the drug safe?
• Does the drug do more good than harm?

In routine clinical practice and compared with existing treatments:
• Do the additional clinical benefits justify the expected additional cost?

Incorporating consideration of relevant social value judgements

Why is NICE needed alongside regulation?
HBP of an imaginary country where the Ministry of Health (many years ago) defined a cost-effectiveness threshold of USD 10,000 per QALY in order to consider a technology as cost-effective and allow its incorporation into the benefit plan.

This limit is imposed by the constrained health care budget.

New health technology with a cost-effectiveness ratio of USD 25,000/QALY

New Technology

Technologies that will be displaced offered less “value for money”. The benefit gain from the new treatment is greater than the benefit foregone

Cost-saving (e.g. polio-Sabin vaccine)

Very cost-effective (e.g. USD 1,000 per QAL)

Relatively good cost-effectiveness (e.g. USD 5,000 per QALY)

Cost-effective (e.g. USD 7,500 per QALY)

Cost-effective (but at the limit, e.g. USD 8,000 or 10,000 per QALY)

Is the benefit gain from the new treatment greater than the benefit foregone through displacement?

No. Displaced technologies offered better “value for money” (the healthcare system loses “health” and efficiency)

Opportunity costs matter!

Source: Andrés Pichon-Riviére, 2013. La aplicación de la evaluación de Tecnologías de Salud y las evaluaciones económicas en la definición de los Planes de Beneficios en Latinoamérica
The NICE process

Horizon scanning and topic selection → working closely with industry for Technology Appraisals

- Notify NICE on health technologies 3-5 years before UK licence that may be suitable for NICE topic selection and ultimately NICE Technology appraisal or Highly Specialised Technologies evaluation.

- Companies cannot access the NICE TA process without contacting NIHRIO first.

- Once a new or repurposed technology is approximately 3 years prior to licence, the NICE topic selection team are notified. Work with companies to ensure that the information passed to NICE is accurate and timely.

- Rely on pharmaceutical companies providing us with regular updates on estimated regulatory and marketing authorisation plans. NIHRIO respects confidential and commercially sensitive information.

Cost effectiveness –

*Incremental cost-effectiveness ratio (ICER):*

\[
\frac{\text{cost}_{\text{new}} - \text{cost}_{\text{current}}}{\text{health gain}_{\text{new}} - \text{health gain}_{\text{current}}}
\]

At NICE, health gain is expressed as quality adjusted life years (QALYs) which allows us to calculate the **cost per QALY** for any technology under consideration.
COSTS MATTER!!!
NHS Reference Costs

• "Reference costs are the average unit cost to the NHS of providing defined services to NHS patients in England in a given financial year. They show how NHS providers spend money to provide healthcare to patients."
  - In 2017/18 – 232 NHS providers spending £68 Billion delivering healthcare to patients
  - Reference costs collection is the **nationally mandated** collection of cost data from all NHS providers – began in 1997
  - It is NHS providers’ **responsibility** to improve their internal costing processes and systems
  - National bodies (Dept. Health, NHS England, NHS Improvement) have a responsibility to ensure the costs collected are useful – provide comprehensive and clear guidance on cost collection for providers
NHS Reference costs – some uses

- Helps NHS providers better understand the cost of their services
- Improves accountability to government
- Informs the national pricing of services --> National Tariff Payment System
- Supports HTA by providing unit costs for cost-effectiveness calculations
The NHS National Tariff

- Informed by average costs (NHS Reference Costs)
- Covers >60% of acute hospital income
- Driven by HRGs (the "currency" - clinical grouping classification system)
- NICE guidance informs tariff

Source: DH (2011)
**Hospital Episode Statistics (HES)**

- **Responsibility of NHS Digital**
  

- HES is a data warehouse containing details of all admissions, outpatient appointments and Emergency attendances at NHS hospitals in England

- Data are collected during a patient's time at hospital, submitted to NHS Digital for processing and returned to the providers → allows hospitals to be paid for the care they deliver

- HES data also needed as an input into the National Tariff

- Can also be used for research and planning health services

### Summary HES Outpatient Data by Month of Activity, for final data from 2007-08 to 2018-19 and Provisional*, 2019-20

<table>
<thead>
<tr>
<th>Rolling 12 month period comparison</th>
<th>October 2017 to September 2018</th>
<th>October 2018 to September 2019</th>
<th>% change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Appointments**(1)(2)(3)</td>
<td>121,171,819</td>
<td>123,497,385</td>
<td>2.3%</td>
</tr>
<tr>
<td>Attended Appointments</td>
<td>84,816,372</td>
<td>86,428,936</td>
<td>2.3%</td>
</tr>
<tr>
<td>% of all appointments</td>
<td>78.1%</td>
<td>76.5%</td>
<td>-</td>
</tr>
<tr>
<td>Did not attend appointment</td>
<td>7,965,018</td>
<td>7,749,888</td>
<td>-2.0%</td>
</tr>
<tr>
<td>% of all appointments</td>
<td>6.6%</td>
<td>6.3%</td>
<td>-</td>
</tr>
<tr>
<td>Follow-up attendances for each first attendance</td>
<td>2.18</td>
<td>2.17</td>
<td>-</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Year to date comparison</th>
<th>April 2018 to September 2018</th>
<th>April 2019 to September 2019</th>
<th>% change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Appointments</td>
<td>47,805,148</td>
<td>47,848,336</td>
<td>0.9%</td>
</tr>
<tr>
<td>Attended appointments</td>
<td>47,805,148</td>
<td>47,848,336</td>
<td>0.9%</td>
</tr>
<tr>
<td>% of all appointments</td>
<td>78.1%</td>
<td>77.9%</td>
<td>-</td>
</tr>
<tr>
<td>Did not attend first appointment</td>
<td>3,957,549</td>
<td>3,822,174</td>
<td>-4.3%</td>
</tr>
<tr>
<td>% of all appointments</td>
<td>6.6%</td>
<td>6.3%</td>
<td>-</td>
</tr>
<tr>
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<td>2.17</td>
<td>2.17</td>
<td>-</td>
</tr>
</tbody>
</table>
Costs of staff time

- In the UK the Personal Social Services Research Unit (University of Kent) produces an annual “Unit Costs of Health and Social Care” (first produced in 1992) which provides detailed costing for staff time.
  - E.g. provides national information on an hour of a nurse’s or doctor’s time, in primary care or in hospital settings.
  - Costings take into account education and qualifications, and even environment costs (carbon emissions).
  - Also have costs for on-line consultation systems.

See: [https://www.pssru.ac.uk/project-pages/unit-costs/](https://www.pssru.ac.uk/project-pages/unit-costs/)
Patient Reported Outcome Measures

- NHS has recently started asking patients whether or not they feel better after certain operations: in 2009, England introduced the national PROMs programme
  - All patients having elective hip replacement, knee replacement, and up to September 2017, varicose vein and groin hernia surgery in England, have been asked to fill in standardised health questionnaires before they have surgery and once again some months afterwards.
  - Condition specific measures (Oxford Hip Score, Oxford Knee Score)
  - General health measures (EQ-5D)
  - Supports improvements in clinical practice, organisational benchmarking, research
Latest PROMs data 2017/18

Key findings

- In 2017/18, patients undergoing hip replacements reported average health gains on the Oxford Hip Score of 21.8 for males and 22.5 for females. On the Oxford Knee Score, these were 16.6 for males and 17.5 for females.
- Almost all hip replacement patients (97.0%) showed an improvement on the Oxford Hip Score.
- Of reported knee replacement patients 94.3% showed improvement on the Oxford Knee Score.

Key facts

Comparing pre- and post-operative 'EQ-5D Index' scores (a combination of five key criteria concerning patients' self-reported general health), an increase in general health was recorded for:

- 89.7 per cent of hip replacement respondents (88.8 per cent for 2016-17)
- 82.2 per cent of knee replacement respondents (81.0 per cent for 2016-17)
What data do we need?

**Resource use**
- Primary care visits, IP stays...

**Unit costs**
- e.g. $ per visit

**Test accuracy**
- Sensitivity/specificity

**Treatment effects**
- Survival, health status

**Preferences**
- QoL weights

**Epidemiology**
- Baseline risks, sub-groups

"MODEL"

"Value" estimate
Economic Evaluation and Value for Money in HTA

Kalipso Chalkidou, MD, PhD
Professor of Practice in Global Health, Imperial College London
Director of Global Health Policy and Senior Fellow, Center for Global Development
Director, international Decision Support Initiative
What type of analyses can inform HTA?

<table>
<thead>
<tr>
<th>Type of analysis</th>
<th>Where it is used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost-of-illness analysis</td>
<td>A determination of the <strong>economic impact of an illness</strong> or condition (typically on a given population, region, or country) e.g., of smoking, arthritis, or diabetes, including associated treatment costs</td>
</tr>
<tr>
<td>Cost-Effectiveness Analysis</td>
<td>A <strong>comparison of costs in monetary units with outcomes in quantitative non-monetary units</strong> such as Quality Adjusted Life Years (QALYs) or averted Disability Adjusted Life Years (DALYs), reduced mortality or morbidity. This is often termed “cost-utility analysis” (CUA) and you should give thought to whether your preferred outcome measure should be some indicator of health gain or loss or some indicator of the utility of such gains or losses. An advantage of the health gain/loss approach is that it is more readily understandable by clinicians and the public and easier to validate.</td>
</tr>
<tr>
<td>Budget Impact Analysis</td>
<td>Can be conducted in addition to a CEA to <strong>determine the impact of implementing or adopting a particular technology</strong> or technology-related policy on a <strong>designated budget</strong>, e.g., for a drug formulary or health plan.</td>
</tr>
<tr>
<td>Cost-Consequence analysis</td>
<td>A form of cost-effectiveness analysis that presents <strong>costs and outcomes in discrete categories</strong>, without aggregating or weighting them</td>
</tr>
<tr>
<td>Cost-Minimisation analysis</td>
<td>A form of analysis that <strong>assumes that the effects of two interventions are the same, but the costs differ</strong>. The analysis <strong>compares costs to identify the least costly</strong></td>
</tr>
<tr>
<td>Cost-Benefit analysis</td>
<td>compares costs and benefits, both of which are <strong>quantified in common monetary units</strong></td>
</tr>
</tbody>
</table>
Economic evaluation in HTA

“... the comparative analysis of alternative courses of action in terms of both their costs and consequences.”

Drummond, Stoddart & Torrance, 1987

<table>
<thead>
<tr>
<th>Costs</th>
<th>Current treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>value of extra resources used (loss to other patients)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>New treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>value of health gain for this patient group</td>
</tr>
</tbody>
</table>

Analysis should be conducted separately for each subgroup of patients.
Cost effectiveness –
Incremental cost-effectiveness ratio (ICER):

\[
\frac{\text{cost}_{\text{new}} - \text{cost}_{\text{current}}}{\text{health gain}_{\text{new}} - \text{health gain}_{\text{current}}}
\]

How do you express “health gain”?
A generalizable health outcome:
**Quality Adjusted Life Years**

- **What is a QALY?**
  - A QALY combines both quantity and health-related quality of life (QoL) into a single measure of health gain
  - The amount of time spent in a health state is weighted by the QoL score attached to that health state
  - QoL scores should reflect peoples’ preferences over health
  - QoL is usually scored with ‘perfect health’=1 and death=0

- **Why use QALYs?**
  - Can weigh up net effect of treatment for patients
    - Survival vs. QoL (e.g. for cancer chemotherapy)
    - Long-term QoL for chronic & recurrent conditions (e.g. arthritis)
    - Benefits vs. harms (e.g. COX II inhibitors)
  - Allows broader comparisons between patient groups
The **Quality Adjusted Life Year** (QALY) is a measure used in healthcare to compare the value of different health interventions. It takes into account both the length and quality of life. The graph illustrates the concept with two scenarios:

- **Current treatment** results in a certain length of life but with a reduced quality of life due to side effects, leading to an initial QALY loss.
- **New treatment** offers a longer life span and a higher quality of life, leading to a net gain in QALYs.

QALYs gained refer to the difference in quality-adjusted years of life between the two treatments.
“A QALY is a QALY is a QALY”

Usual value judgements used to calculate QALYs:

1 QALY = one year of ‘perfectly healthy’ life for one person
= two years of life with QoL of 0.5 for one person
= one year of life with QoL of 0.5 each for two people
Alternatives to the QALY

• Using QALYs may not always be possible
  • Because of assumptions underpinning the QALY and other factors (such as adequate data availability)
• Alternatives? Single indicators (e.g. weight loss in kg; or deaths averted; or or life years gained, and so on) – but lose benefits of using a generalizable measure
  • May be unavoidable however – use must be justified
• Disability-Adjusted Life Year: one lost year of "healthy" life
  • But like QALYs also associated with important assumptions and simplifications
Going beyond the QALY
Accounting for ‘fairness’

• Equity-adjustment (See Principle 11)
  • Weight QALY gains to different individuals according to their age, health status, socio-economic status…?
  • Research is progressing, but no usable methods yet (?)

• Deliberative approach
  • Provide decision-making panels with descriptive information about the distribution of QALYs
  • They discuss and make qualitative judgements about trade-offs
  • Current NICE method (Tony Culyer)

• Multicriteria Decision Analysis (MCDA)…
Using HTA and CEA to make decisions

• What’s important (to you…)?
  • Clinical effectiveness
  • Uncertainty
  • Disease severity
  • Special populations (e.g. children, people with cancer…)
  • “End-of-Life”
  • Legal constraints
  • Implementation issues
  • ‘Fairness’
  • Supporting ‘innovation’ by industry
  • Cost effectiveness and ‘opportunity cost’…
  • All of the above? And more?

• Cost-effectiveness thresholds (implicit/explicit)…. 
Assessing cost effectiveness
Weighing up the benefits, harms and costs

<table>
<thead>
<tr>
<th>Cost ($)</th>
<th>Effect (QALYs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>New treatment</td>
<td>New treatment</td>
</tr>
</tbody>
</table>
Assessing cost effectiveness

"Value for money"

- New treatment dominated
- Low extra cost
  - High QALY gain
  - £/QALY
- High extra cost
  - Low QALY gain

Current treatment

CE threshold

Treatment cost-effective in shaded region

New treatment dominates
### Thresholds – implicit and explicit

<table>
<thead>
<tr>
<th>Explicit</th>
<th>Implied/not stated</th>
</tr>
</thead>
</table>
| **NICE – UK (NB not Scotland)**  
  - £20 – 30,000 per QALY; £50,000 + per QALY ("End of Life" etc) | **Pharmaceuticals Benefits Advisory Committee (PBAC) – Australia**  
  - Technologies with ICERs greater than $75,000/QALY rarely recommended (OECD) |
| **National Centre for Pharmacoeconomics - Ireland (NCPE)**  
  - €45,000/QALY | **Pharmaceutical Management Agency (PHARMAC) – New Zealand**  
  - They “fund medicines within a fixed budget, and as CE is only one of its nine decision criteria used to inform decisions, thresholds cannot be inferred or calculated” |
| **Health Intervention and Technology Assessment Program (HITAP) – Thailand**  
  - 160,000 Baht per QALY (approx. 1.2 x GNI per capita) – “demand side” threshold | **Canadian Agency for Drugs and Technologies in Health (CADTH) – Canada**  
  - Use a “supply side threshold” but not stated |

Source: Thokala et al, 2018
What is your “threshold”? If the concern is to improve population health, need to consider opportunity costs – that is comparing the health benefits gained from an intervention with the health that is likely to be lost as a consequence of additional investments.
Sources of thresholds: The perils of a threshold not linked to WTP = ‘Cost Effective’ and Unaffordable

“In low and middle income countries, the World Health Organization (WHO) has recommended thresholds of 1 to 3 times gross domestic product (GDP) per capita – seemingly on the basis of recommendations from the “Commission on Macroeconomics and Health” report from 2001.”(1)

“In low and middle income countries, the World Health Organization (WHO) has recommended thresholds of 1 to 3 times gross domestic product (GDP) per capita – seemingly on the basis of recommendations from the “Commission on Macroeconomics and Health” report from 2001.”(1)

“For instance, values of £20-30,000 and US$50,000 per QALY have commonly been applied in the United Kingdom and United States, respectively; without clear rational but with some sense they reflect the consumption value of health.”(1)

“To say that an alternative is cost-effective but not affordable must mean that the (implicit or explicit) “threshold” used to judge cost-effectiveness does not reflect the opportunity costs incurred given the scale of the impact on health expenditure” (Lomas et al 2018)

1) Cost-Effectiveness Thresholds IDSI working group final report
NICE decision options

NICE can:

• Recommend for routine commissioning (either in line with marketing authorisation or “optimised”)
• Not recommend for routine commissioning
• Recommend for inclusion in the Cancer Drugs Fund or other managed access

Health professionals are expected to take NICE guidance fully into account when exercising their clinical judgment; though guidance cannot override professional autonomy

The NHS (in England) is obliged to provide funding & resources for medicines & treatments recommended by NICE –within 3 months [this has now been revised]

All NICE guidance is reviewed within 3 years and may or may not be updated
NICE’s decision making

The Committee will want to be increasingly certain of the cost-effectiveness of a technology as the impact of the adoption of the technology on NHS resources increases.

(Para 6.2.14 Guide to Methods of Technology Appraisal, NICE 2013)
NICE decisions based on value for money: 2007 – 2013: the ICER matters
NICE’s threshold

- NICE “does not use a precise maximum acceptable ICER above which a technology would automatically be defined as not cost effective or below which it would”.*
- £20,000 to £30,000 per QALY gained range
- Below £20,000 will recommend treatment, above £20,000 a case can be made e.g. the change in HRQL has been inadequately captured, or distinctive benefits not adequately captured in the QALY measure
- “Above a most plausible ICER of £30,000 per QALY gained … need to identify an increasingly stronger case”
- £50,000 for life-extending end-of-life treatments

*Guide to the Methods of Technology Appraisal, April 2013
An inherently political and social engagement process

• “Those developing clinical guidelines, technology appraisals or public health guidance must take into account the relative costs and benefits of interventions (their ‘cost effectiveness’) when deciding whether or not to recommend them.” (Principle 2, SVJ, NICE 2008)

BUT

• “Decisions about whether to recommend interventions should not be based on evidence of their relative costs and benefits alone. NICE must consider other factors when developing its guidance, including the need to distribute health resources in the fairest way within society as a whole.” (Principle 3)

• See: http://www.nice.org.uk/media/C18/30/SVJ2PUBLICATION2008.pdf
## Application of ‘special circumstances’

### Table 1

Application of ‘special circumstances’ in the appraisal of some products with incremental cost-effectiveness above £30 000 per quality adjusted life year

<table>
<thead>
<tr>
<th>Topic</th>
<th>ICER ('000s)</th>
<th>Severity</th>
<th>End of life*</th>
<th>Stakeholder persuasion</th>
<th>Significant innovation</th>
<th>Disadvantaged population</th>
<th>Children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Riluzole (motor neurone disease)</td>
<td>38–42</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trastuzumab (advanced breast cancer)</td>
<td>37.5</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Imatinib (chronic myeloid leukaemia)</td>
<td>36–65</td>
<td>✓</td>
<td></td>
<td></td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Imatinib (gastrointestinal stromal tumour)</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pemetrexed (malignant mesothelioma)</td>
<td>34.5</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Ranizumab (age-related macular degeneration)</td>
<td>&gt;&gt;30</td>
<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omalizumab (severe asthma)</td>
<td>&gt;30</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sunitinib (advanced renal cancer)</td>
<td>50</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lenalidomide (multiple myeloma)</td>
<td>43</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Somatotropin (growth hormone deficiency)</td>
<td>n/a</td>
<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic subcutaneous insulin infusion (childhood Type 1 diabetes)</td>
<td>n/a</td>
<td></td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*End-of-life considerations have only been explicitly taken into account since January 2009 on the basis of supplementary advice from the Institute to the Appraisals Committee.

ICER, incremental cost-effectiveness ratio (£ per quality-adjusted life year).

Rawlins, Barnett, Stevens Br J Clin Pharmacol 2010
NICE processes

- **Multiple Technology Appraisal (MTA)**
  - First appraisal completed Apr 2000
  - Normally covers more than one technology, or one technology for more than one indication
  - An extensive review of the evidence (planned to be completed in 62 weeks)

- **Single Technology Appraisal (STA)**
  - “rapid” review process first guidance issued Aug 2006
  - STA can only cover a single technology for a single indication
  - New STA process since 2018

- **Fast Track Appraisal (FTA) from 1 Apr 2017**
  - “those technologies that NICE can be confident would fall below £10,000 per QALY”
  - e.g. aflibercept for treating myopic choroidal neovascularisation

Reproduced: Professor John Cairns, LSHTM
But increasingly NICE’s threshold has been going up...

<table>
<thead>
<tr>
<th>Threshold</th>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>£20,000/QALY</td>
<td>Certainty of the ICER</td>
<td>HTA committees should be more cautious about recommending a technology if there is considerable uncertainty about its clinical- and/or cost-effectiveness.</td>
</tr>
<tr>
<td>Additional health benefits</td>
<td>HTA committees should take account of additional health benefits if there are strong reasons to indicate that these have not been fully captured in the calculation of a technology’s ICER.</td>
<td></td>
</tr>
<tr>
<td>Non-health objectives of the NHS</td>
<td>HTA committees should take account of the wider effects and social considerations relating to technologies under assessment. This includes consideration of: significant non-health effects; costs/benefits incurred outside the NHS; special account for the needs of disabled people, relief of stigma, and distribution of benefits to the most disadvantaged so as to reduce health inequalities. This excludes consideration of: individual choice or individuals values; cultural attitudes and religious views; race/ethnicity; personal responsibility for health; age; sex/gender and sexual orientation; socioeconomic status and social roles.</td>
<td></td>
</tr>
<tr>
<td>Innovative nature of the technology</td>
<td>HTA committees should take account of a technology’s innovative nature, specifically if the innovation adds demonstrable and distinctive benefits that are substantial and may not have been fully captured in the calculation of a technology’s cost-effectiveness.</td>
<td></td>
</tr>
<tr>
<td>£30,000/QALY</td>
<td>Life-extending end-of-life technologies</td>
<td>HTA committees may give greater weight to QALYs offered by technologies indicated for patients with a short life expectancy (&lt;24 months) and which offer the potential to extend life (normally by &gt;3 months, compared with current NHS treatment).</td>
</tr>
<tr>
<td>£50,000/QALY</td>
<td>Highly specialized technologies</td>
<td>HTA committees may give greater weight to QALYs offered by highly specialized drugs for the treatment of chronic and severely disabling conditions affecting small groups of patients.</td>
</tr>
</tbody>
</table>

£100,000 threshold for highly specialised technologies*

* Chronic & severely disabling condition, where the technology has the potential for life long use, usually in very few centres in the NHS & likely to have a very high acquisition cost.

- Introduced QALY weights (proportional to the incremental QALYs gained) up to a maximum of 3

<table>
<thead>
<tr>
<th>Incremental QALYs gained (per patient, using lifetime horizon)</th>
<th>Weight versus £100,000/QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than or equal to 10</td>
<td>1</td>
</tr>
<tr>
<td>11-29</td>
<td>Between 1 and 3 (using equal increments)</td>
</tr>
<tr>
<td>Greater than or equal to 30</td>
<td>3</td>
</tr>
</tbody>
</table>

Reproduced: Professor John Cairns, LSHTM
Technology appraisals can be for fairly rare conditions, e.g. nusinersen for treating spinal muscular atrophy [between 1,200 & 2,500 children & adults in UK]

Criteria to be met to be highly specialised technology

- The target patient group in its licensed indication is so small that treatment will usually be concentrated in very few centres in the NHS
- The condition is chronic and severely disabling
- The technology is expected to be used exclusively in the context of a highly specialised service; is likely to have a very high acquisition cost & has the potential for lifelong use.

Reproduced: Professor John Cairns, LSHTM
NICE in the future

A number of areas of strategic interest reflecting the growing importance and potential opportunities offered by digitalisation, ‘big data’, machine learning…. 

1. Maintaining recommendations up to date
2. Rapid sequencing of new drugs and technologies
3. Integrating recommendations into IT systems
4. Improving the accessibility of NICE recommendations (putting advice and guidance into a single “integrated product” on NICE website)

…..”more and faster appraisals” (The 2019 Voluntary Scheme for Branded Medicines Pricing and Access)
NICE announces details of health technology evaluation methods review

Following approval at its recent Board meeting NICE has confirmed the details of its review of the methods it uses to develop guidance on drugs, medical devices and diagnostics.

22 July 2019  Share

The purpose of the review is to optimise NICE's evaluation methods to support the ambition of the NHS to provide high quality care that offers good value to patients and to the NHS. For medicines, the review is linked to the commitments in the 2019 Voluntary Scheme for Branded Medicines Pricing and Access.

Engagement with key stakeholders has resulted in a short-list of topics that will be

1.4 The National Institute for Health and Care Excellence (NICE) also supports the Voluntary Scheme and will have a central role in its operation.

3.20 The standard cost effectiveness threshold used by NICE will be retained at the current range (£20,000 - £30,000 per QALY) and not changed for the duration of the Voluntary Scheme.

This update is part of the regular review and refresh of our methods to ensure that they are robust and up-to-date.
NICE AND DRUG PRICING
The drugs’ market in the UK

the person who consumes the drug (the patient) neither decides nor, in most cases, pays

the person who decides which drug should be used (the prescribing doctor) neither pays nor consumes, and

the institution that pays for the drug (the NHS / Government) neither consumes nor decides.

Misaligned incentives mean market forces alone cannot fix the problem: government regulation is necessary!
Office for Fair Trading called for pricing reform but…

• “We recommend that Government reform the PPRS replacing current profit and price controls with a value based approach to pricing to ensure the price of drugs reflect their clinical and therapeutic value to patients and the broader NHS.”

OFT, February 2007

…HTA can be inflationary!
…more flexibility [should] be brought into the system to allow price negotiation, as happens in other countries.”
NICE does not do pricing but...NICE can:

01
Signal that it requires a price reduction to offer a positive recommendation and ultimately reject

02
Negotiate confidential price discounts (increasingly done by NHS England) in the context of a managed entry agreement

03
Recommend a cancer drugs enters the Cancer Drugs Fund for a limited period and re-evaluate
And its methods getting even more complex!
Its processes getting more complex

Figure 4 Summary of the appraisal process

Figure 5 Summary of the appraisal process when an ACD is produced

Further details:
Current practice: cost-effectiveness of new drugs assessed at the price set by the company

If NICE looks like saying NO at the initially proposed price companies increasingly offer a **Patient Access Scheme**.

Also all drugs entering the 2016 CDF have a commercial arrangement

These schemes involve pricing agreements designed to improve cost effectiveness & facilitate patient access to specific drugs.
### Pricing arrangements 2007-2018

- **Outcome based**
  - Patient level 1: Refund for patients who do not reach agreed target

- **Non-outcome based**
  - Patient level 21: Free stock for initial limited period or after a dose cap
  - Population level 164: Discount on list price

---

<table>
<thead>
<tr>
<th>Outcome based</th>
<th>Patient level</th>
<th>1</th>
<th>Refund for patients who do not reach agreed target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-outcome based</td>
<td>Patient level</td>
<td>21</td>
<td>Free stock for initial limited period or after a dose cap</td>
</tr>
<tr>
<td></td>
<td>Population level</td>
<td>164</td>
<td>Discount on list price</td>
</tr>
</tbody>
</table>

- About 4 per year 2007-2011 [42% discounts on list price]
- Over 12 per year 2012-2015 [94% discounts on list price]
- About 40 per year 2016-2018 [92% discounts on list price]

Reproduced: Professor John Cairns, LSHTM
Cancer not the main/only problem…
Sovaldi: “Cost-effective” but unaffordable?

Hepatitis C drug delayed by NHS due to high cost

NHS England balks at bill for dispensing sofosbuvir: £1bn for every 20,000 people treated

The price offered by Gilead in the UK is almost £35,000 for a 12-week course. Many patients will need a 24-week course, costing £70,000. In its final draft guidance on sofosbuvir, Nice said it was allowing NHS England to postpone implementation for four months, until the end of July instead the beginning of April. NHS England failed to comment.
Expensive drugs cost lives, claims report

Andrew Ward, Pharmaceuticals Correspondent

The adoption of expensive new drugs by the NHS is doing patients more harm than good, according to a study that urges a sharp reduction in the price pharmaceuticals companies are paid for their products.

Research by the University of York found that lives were being lost and quality of life diminished because spending on overpriced drugs was diverting resources from other kinds of healthcare that would produce more benefit.
Runaway threshold? Putting a break on NICE…

- Introduce a ‘fast track’ NICE technology appraisal process for the most promising new technologies, which fall below an incremental cost-effectiveness ratio of £10,000 per QALY (quality adjusted life year), to get these treatments to patients more quickly.

- Operate a ‘budget impact threshold’ of £20 million, set by NHS England, to signal the need for a dialogue with companies to agree special arrangements to better manage the introduction of new technologies recommended by NICE. This would apply to a small number of technologies that, once determined as cost effective by NICE, would have a significant impact on the NHS budget.

- Vary the timescale for the funding requirement when the budget impact threshold is reached or exceeded, and there is therefore a compelling case that the introduction of the new technology would risk disruption to the funding of other services.

- Automatically fund, from routine commissioning budgets, treatments for very rare conditions (highly specialised technologies) up to £100,000 per QALY (5 times greater than the lower end of NICE’s standard threshold range), and provide the opportunity for treatments above this range to be considered through NHS England’s process for prioritising other highly specialised technologies.
NICE has historically not considered budget impact when making recommendations.

However, since 1 April 2017 it is routinely asked whether a positive recommendation will increase spending by more than £20 million in any of the next 3 years.

If it is likely to do so, NHS England can delay implementation from 3 months (current rule) to up to 3 years.

This increases their opportunity to bargain with manufacturers (developed partly in response to the challenges of paying for NICE’s positive HCV recommendations).

Reproduced: Professor John Cairns, LSHTM
### The new PPRS: capping growth—industry reimburses the NHS

#### Table 1: forecasts and profile of annual payment percentages

<table>
<thead>
<tr>
<th>Period</th>
<th>Aggregate net sales covered by the PPRS payment Column 1</th>
<th>Resulting aggregate PPRS payments Column 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013</td>
<td>£7,901M</td>
<td>N/A</td>
</tr>
<tr>
<td>2014</td>
<td>£8,340M</td>
<td>£311M</td>
</tr>
<tr>
<td>2015</td>
<td>£8,179M</td>
<td>£847M</td>
</tr>
<tr>
<td>2016</td>
<td>£8,062M</td>
<td>£628M</td>
</tr>
<tr>
<td>2017</td>
<td>£8,147M</td>
<td>£387M</td>
</tr>
<tr>
<td>2018 Q1</td>
<td>£2,003M</td>
<td>£156M</td>
</tr>
<tr>
<td>2018 Q2</td>
<td>£2,013M</td>
<td>£157M</td>
</tr>
<tr>
<td>2018 Q3</td>
<td>£1,968M</td>
<td>£153M</td>
</tr>
<tr>
<td>2018 Q4</td>
<td>£1,903M</td>
<td>£148M</td>
</tr>
</tbody>
</table>

As the unadjusted payment percentage for 2018 falls outside the agreed range of 2.38% to 7.80%, the actual payment percentage for 2018 will be set at 7.80%.

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The new drug pricing landscape

The NHS Long Term Plan

Published 7th January 2019

The 2019 Voluntary Scheme for Branded Medicines Pricing and Access - Chapters and Glossary

Published 5th December 2018
The NHS is now in charge:
→ gene therapies: the new frontier
ENGLAND’S VERTICAL FUND FOR CANCER DRUGS: A CAUTIONARY TALE
Policies for improving timely access to new cancer drugs

- Single Technology Appraisal (2005)
- NICE End-of-Life policy (2008/9)
- Cancer Drugs Fund (2010/11)
- Orphan drugs evaluation (2013/14)
- Value Based Assessment (2014/closed down)
- CDF as part of NICE (2016)
The launch of NICE’s End-of-Life policy (2009)

• “A QALY is a QALY is a QALY” NICE Methods Manual 1999-2009

• NICE is asking that its advisory committees “consider recommending seemingly cost-ineffective treatments which are life-extending for patients with short life expectancy, and which are licensed for indications affecting small numbers of patients with incurable illnesses.” NICE Supplementary Guidance to its Advisory Committees – January 2009
End of Life decisions as of May 2014

But NICE’s committees still find some cancer drugs not to be good value for money or clinically effective.
An election promise
Cancer Drugs Fund in pre-election manifesto

“We will create a Cancer Drugs Fund to enable patients to access the cancer drugs their doctors think will help…"

Freedom
Fairness
Responsibility

The Coalition: our programme for government
Sep 2015: the country’s National Audit Office investigates

- “Did it improve outcomes? Due to a lack of data, it is not possible to evaluate the impact that the Fund has had on patient outcomes, such as survival.

- What impact did it have on prices? The cost of the Fund from 2010 to 2015 was £968 million, slightly above the allocated budget. In the early years [it] was underspent. However, taking 2013-14 and 2014-15 together… the cost of the Fund rose by £241 million – an increase of 138%. Over half of the rise was because of an increase in the average cost of treatment per patient…”
February 2016: The country’s Parliament investigates

• “There is no assurance that the Department and NHS England are using their buying power effectively to pay a fair price for cancer drugs, including drugs paid for through the Fund.

• It is unacceptable that the Department and NHS England still do not have data to evaluate the impact of the Fund on outcomes for patients five years after the Fund was set up.”
"a populist gesture that gives the impression of benefiting patients, but in fact rewards poor quality drugs while benefiting a handful of pharmaceutical companies at the expense of the taxpayer and the full range of NHS patients” Dec 2014

"This mechanism for diverting taxpayers’ money to enhance, to little or no purpose, the profits of Big Pharma might be more aptly named “the Drug Company Fund”" Dec 2014
Cancer Drugs Fund 'huge waste of money'

By Nick Triggle
Health correspondent

28 April 2017
The Payer takes back control: NHS England

• Access to promising new treatments, via managed access arrangement, while further evidence is collected to address clinical uncertainty.

• Interim funding for all newly recommended cancer drugs, giving patients access to these treatments many months earlier than before.

• The expenditure control mechanism ensures that the CDF will not overspend.
The new arrangements cap the total, set up companies and products to compete against one another and make the whole idea of the CDF “unappealing”.
Cancer Drugs Fund 2016

Based on NHS England Board Paper PB.25.02.2016/04 Appendix 2

Reproduced: Professor John Cairns, LSHTM
2016 CDF criteria

Starting point: drug not recommended for routine use due to clinical uncertainty

1. Is the model structurally robust for decision making (omitting the clinical uncertainty)?

2. Does the drug have plausible potential to be cost-effective at the offered price, taking into account end-of-life criteria?

3. Could further data collection reduce uncertainty?

4. Will ongoing studies provide useful data? and

5. Is CDF data collection via SACT relevant and feasible?

Consider recommending entry into the CDF (invite company to submit CDF proposal)

Reproduced: Professor John Cairns, LSHTM
Did the CDF deliver value for the English society?

The evidence:

- Of the 47 CDF approved indications, only 18 (38%) reported a statistically significant OS benefit, with an overall median survival of 3.1 months.
- When assessed according to clinical benefit scales, only 23 (48%) and 9 (18%) of the 47 drug indications met ASCO and ESMO criteria, respectively.
- NICE had previously rejected 26 (55%) of the CDF approved indications because they did not meet cost-effectiveness thresholds.
- Four drugs—bevacizumab, cetuximab, everolimus and lapatinib—represented the bulk of CDF applications and were approved for a total of 18 separate indications. 13 of these 18 indications were subsequently delisted by the CDF in 2015 due to insufficient evidence for clinical benefit—data which were unchanged since their initial approval.
- The majority of patients were exposed to unpleasant side effects for no benefit.
- £1.27 billion was spent on the fund during the period studied.
- No usable data was collected on what happened to patients whose treatment was funded—such as measuring how long they lived, their quality of life or side effects.

Conclusions

We conclude the CDF has not delivered meaningful value to patients or society. There is no empirical evidence to support a ‘drug only’ ring fenced cancer fund relative to concomitant investments in other cancer domains such as surgery and radiotherapy, or other noncancer medicines. Reimbursement decisions for all drugs and interventions within cancer care should be made through appropriate health technology appraisal processes.
“But the real change to help get these drugs into the market in the UK will not come from siloed funds, but rather from these drugs costing less in the first place.

Both the government and pharma play on the fear surrounding cancer for their own ends, but pricing a cancer drug artificially high simply because it treats a feared disease does not seem fair to the NHS or, more pertinently, to patients.”

LOOKING BEYOND THE ASSESSMENT OF INDIVIDUAL “TECHNOLOGIES” – WIDER HTA

Clinical guidelines and quality improvement
HTA can be part of a stepwise process getting evidence into policy and improving the quality of health services…
…informing both quality improvement and strategic purchasing and procurement

- Supporting resource allocation decisions across programmes and technologies
- Identifying best value interventions for insurance package reimbursement
- Including new items in the Essential Medicines List
- Rolling out public health programmes

Purchasing

- Strategic purchasing and procurement of drugs and devices, including price negotiation and special access schemes
- Determining fees
- Disinvestment of wasteful or harmful practices

Priority setting

- Clinical guidelines and quality standards
- Pay for performance and quality-based contracts for providers
- Clinical audit and self-regulation for providers
- Quality regulation

Quality improvement
Clinical guidelines - what are they?

• Broad guidance covering all or specific aspects of the management of a particular condition (the pathway) [development time for guidelines is usually between 12 and 27 months (from the start of scoping to publication)]

• Incorporates technology appraisals, interventional procedures and other related NICE guidance where appropriate

• Recommendations advisory only (but can be used to develop quality standards to assess clinical practice and inform payment)
From evidence to setting standards and improving quality

- Medical education and professional training
- Performance management
- Budget management
- Provider payment mechanisms incl. case-based payment
- Communication of entitlement to patients and their families
- Clinical audit and provider benchmarking
- Provider regulation and accreditation
Example: Quality standard for diabetes prevention developed from NICE guideline

**Clinical and/or cost-effectiveness evidence (NICE PH38, 2017)**
Lifestyle-change programmes are cost-effective for all people at high risk of diabetes, particularly for people with higher HbA1c or fasting plasma glucose levels.

**NICE public health guideline recommendation (NICE PH38, 2017)**
For people confirmed as being at high risk*… Offer them a referral to a local, evidence-based, quality-assured intensive lifestyle-change programme.

*a high risk score and fasting plasma glucose of 5.5–6.9 mmol/l or HbA1c of 42–47 mmol/mol [6.0–6.4%]

**Quality statement**
Adults at high risk of type 2 diabetes are offered a referral to an intensive lifestyle-change programme.
Quality measure: Process

What amount of “quality care” is being provided?

Quality measure
Proportion of adults at high risk of type 2 diabetes who are offered a referral to an intensive lifestyle-change programme

= \frac{\text{No. of adults at high risk of type 2 diabetes who are offered a referral to an intensive lifestyle-change programme (numerator)}}{\text{All adults at high risk of type 2 diabetes (denominator)}}

Implementation

Health outcomes
Weight loss of participants in lifestyle-change programmes
Incidence of type 2 diabetes
## Case study: importance of clear institutional roles – indicator development in the UK

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<th>Role</th>
<th>Description</th>
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### Case study: importance of clear institutional roles – indicator development in the UK

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Audit and benchmarking

- Monitoring and Evaluation can help provide evidence on the value of HTA and its impact on decision-making, and importantly inform learning and future quality improvement.

- At the most simple level, monitoring seeks to address the following questions:
  - Do we observe changes in health technology utilisation after the decision?
  - Which patients receive it? And in what settings?

- Surveys and clinical audits can be used to investigate the impact of an HTA driven decision at the level of provision of care, but those require specific data collection.

- In the UK, the professional associations fund and conduct national audit programmes, independently from the government, which healthcare providers and clinicians voluntarily participate in.
  - Often include questions and key performance indicators drawn from NICE guidelines and quality standards.
National Cancer Diagnosis Audit (2017)

"The findings highlight examples of good practice, identify areas for quality improvement with the aim to help health professionals to diagnose cancer earlier.

The data also provide a baseline for future audit of the impact of 2015 NICE guidance on management and referral of suspected cancer."

CRUK (2017)
http://www.cancerresearchuk.org/health-professional/diagnosis/national-cancer-diagnosis-audit
Auditing and benchmarking of providers against national standards for stroke care

Source: Sentinal Stroke National Audit Programme (SSNAP)
Using HTA Determining what to buy, from whom, how (and for how much):

- Identify comparative value of alternatives and determine a “value-based price”
- Design outcome/quality-based indicators and performance manage
THOUGHTS ABOUT THE JAPANESE SYSTEM

UK-Japan comparison…
## UK and Japanese systems: difference and similarities (i)

<table>
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<tr>
<th>System Characteristic</th>
<th>Japan</th>
<th>UK</th>
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| Drug price control mechanism| Sophisticated and complex regulation and market based controls; stable over time  
  • HTA plays a role in price adjustment on only part of the product price  
  • Complex formula for defining price for on-patent products via similar efficacy comparison and cost calculation | Complex combination of market competition and controlled margins for generics; NICE and PPRS for branded.  
  • NICE/HTA has played an increasing role on pricing using HTA (2007-2017);  
  • Now NHS England/payer gaining more power using **budget impact** criteria (2018-present) |
| Purpose of using HTA        | To adjust a proportion of price premium; complements current pricing rules | • To manage "listing"; NICE recommendation encourages (but no longer guarantees) NHS coverage  
  • Only indirect link to pricing |
| Indication pricing?         | Weighted mean of ICERs during pilot; now revised to weighted mean of price adjustment | No; NICE looks at one price put forward by manufacturer; flexible pricing means this can change but hardly ever used; system can be gamed and launch sequence matters |
# UK and Japanese systems: difference and similarities (ii)

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<td>HTA timing</td>
<td>Post launch and after companies enter system with a given price</td>
<td>Prelaunch; starts before marketing authorization and runs alongside regulatory approval process</td>
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| Target products               | • Only high budget impact products  
• Not for paediatric products or orphan products | • Increasingly universal; all new indications  
• Includes orphan but with special rules/threshold |
| Special considerations        | Cancer, rare diseases, paediatrics                                   | End of life rule and Cancer Drugs Fund favour cancer though this is reversed  
Higher threshold for rare drugs |
| Threshold                     | JPY 5m (1.2xGDP pc) *but...* Threshold used as a cut off to determine whether HTA will be used to adjust fraction of price  
If price after adjustment is less than threshold then it is adjusted upwards... | £20-30k (0.65-1xGDP pc) but higher for certain diseases |
Some possible problems...

- Not about the whole price but only part of it
- Not about all products but only a subset with cancer favoured
- Not about coverage, but about Price
- Everything gets pushed to threshold of 1.2GDP pc
- Not at launch but later
Suggestions...

Consider HTA at launch
- Align with regulatory approval process, not with reimbursement process
- If already on market, hard to revise price
- Shorten process; consider most multinationals have health econ models ready to adapt to Japanese setting!

Use HTA as a carrot and a stick
- Reconsider price raising measures as they may inflate budget
- Apply threshold to whole price, not a fraction
- Great to reward transparency (disclosure rate) but ultimately impact on health is what matters

Consider a threshold linked to budgetary constraint
- Particularly important if prices are raised to meet this threshold
- Carry out BIA and monitor trends in expenditure

Beware of inefficient comparators
- As HTA rule applied to fraction of price, pricing based on similar products which may however be not cost effective, can set negative precedent (eg hep C drugs)

Evaluate impact on spend and readjust process
To support decision making…

Need to look at the entire body of the ’best available’ evidence

Evidence is never complete

Judgement is unavoidable

Uncertainty matters – and it should be fully explored

….and always make important information part of routine data collection…
ありがとう！