Comparative effectiveness research in mental health

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Comparative effectiveness research

Health Technology Assessment

Determines:

- whether a technology works;
- for whom;
- how it compares with the alternatives; and
- at what cost.

Clinical effectiveness

Cost effectiveness

Health technologies

defined as

Methods used to:

- promote health;
- prevent and treat disease; and
- improve rehabilitation and long term care.

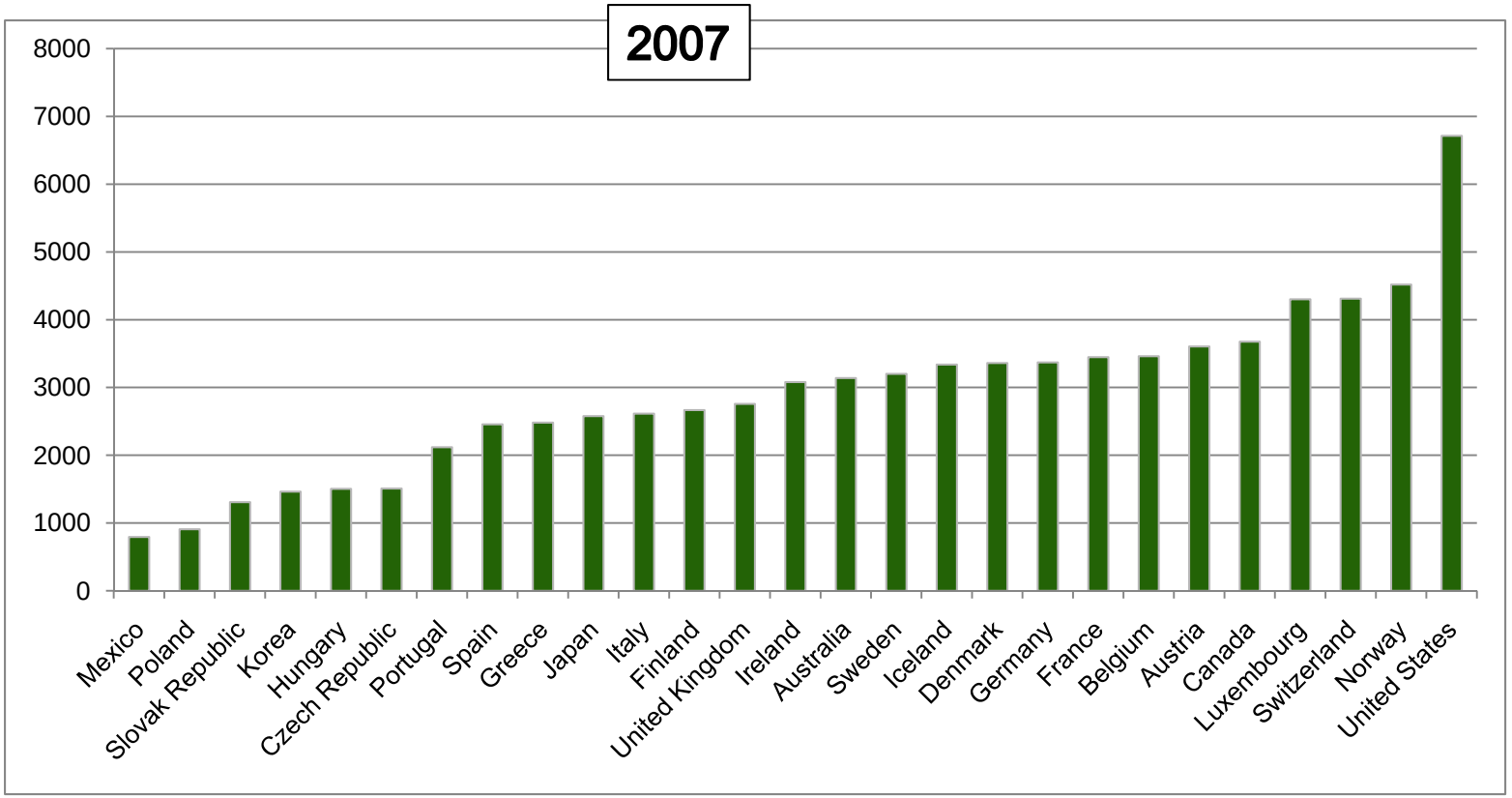
Includes:

- pharmaceuticals;
- devices and procedures;
- diagnostic methods;
- settings of care; and
- screening.

Methodological research

Resource Constraints

Healthcare Expenditure (US$ per person)



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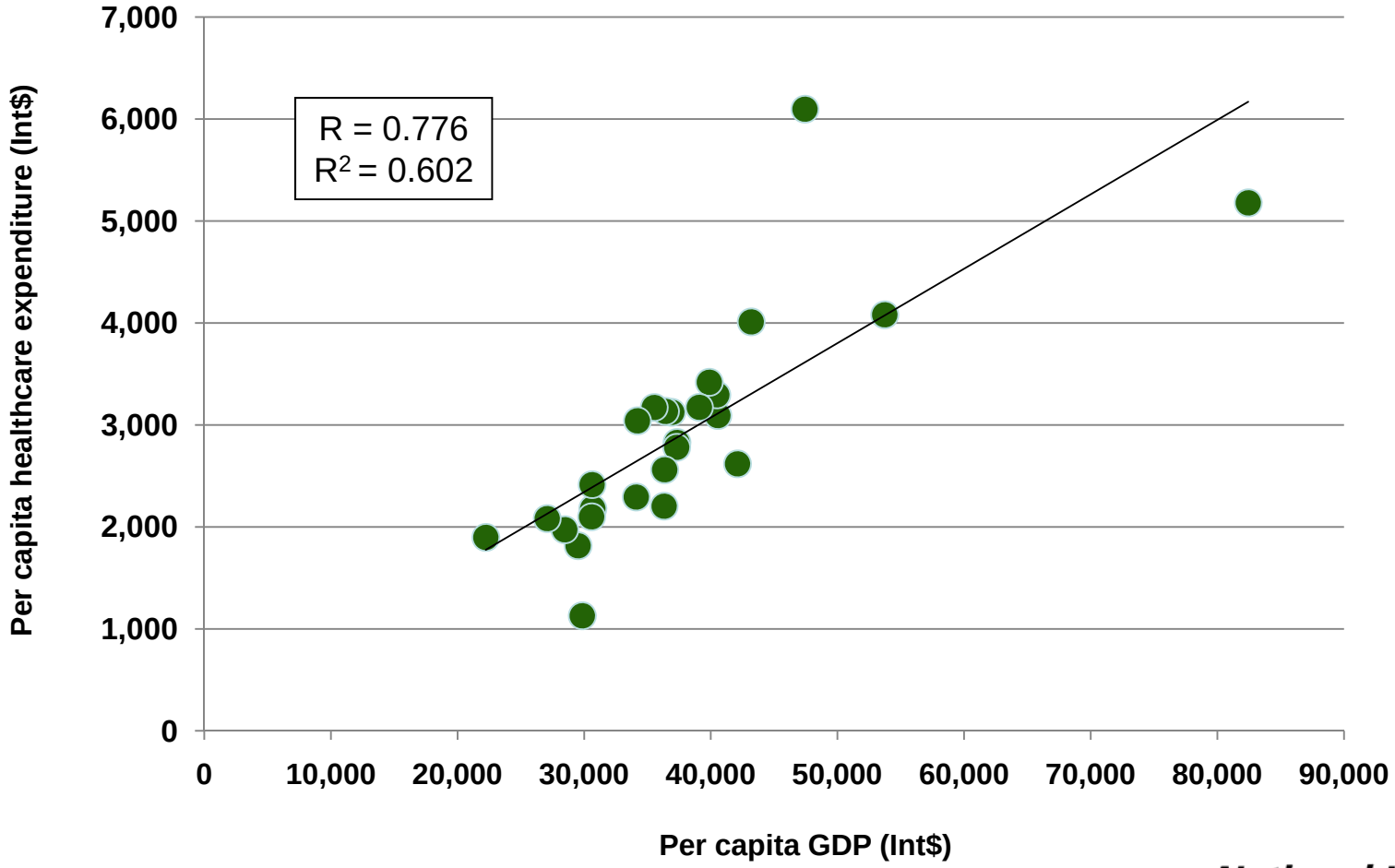
GDP and Healthcare Expenditure

2007



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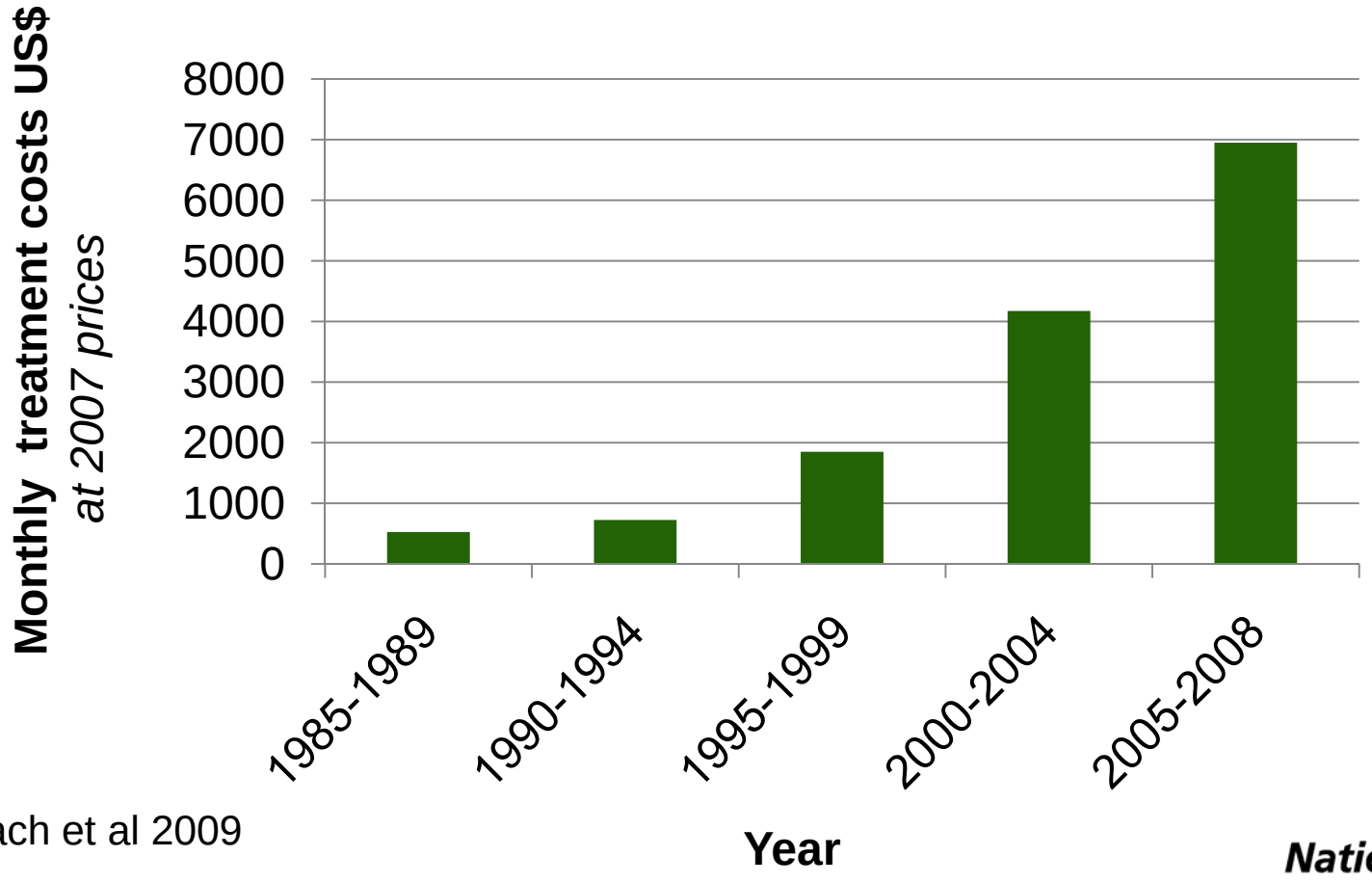
Median Monthly Costs

new anti-cancer drugs at launch



Bach et al 2009

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Clinical Evaluation

sources of evidence

1. Randomized contr[illegible]als
2. Observati[illegible]tudies
3. S[illegible]matic reviews

Avoiding "hierarchies" of evidence

Hierarchies of Evidence

Level	Description
1^{++}	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias.
1^{+}	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.
1^{-}	Meta-analyses, systematic reviews of randomized controlled trials or RCTs with a high risk of bias.
2^{++}	High quality systematic reviews of case-control or cohort studies with a low risk of confounding, bias or chance and a high probability of causality
2^{+}	Well-conducted case-control or cohort studies with a low risk of confounding, bias or chance and a significant chance that the relationship is not causal.
2^{-}	Case-control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal.
3	Non-analytical studies (for example case records, case series)
4	Expert opinion, formal consensus.

Harbour R, Miller J (2001)

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Randomized controlled trials

strengths

1. Minimizes selection bias
2. Minimizes confounding
3. Minimizes ascertainment bias
4. Minimizes random error
5. Comparative efficacy/effectiveness

Clinical effectiveness

comparisons

1. Direct comparison
    - intervention A *versus* intervention B
2. Indirect comparison
    - intervention A *versus* placebo
      intervention B *versus* placebo
    - impute intervention A *versus* intervention B
3. Mixed treatment comparisons
    - combined results of direct *plus* indirect comparisons

Randomized controlled trials

weaknesses

1. Null hypothesis
2. Generalisability
3. The problem of multiplicity
4. Assessment of safety
5. Escalating costs

Observational studies

1. Historical controlled trials
2. Case-control designs
3. Case series

Historical Controlled Trials

Evidence of Benefit

Intervention	Indication
Thyroxine (1891)	Myxoedema
Streptomycin (1948)	Tuberculous meningitis
Defibrillation (1948)	Ventricular fibrillation
Ganglion blockers (1959)	Malignant hypertension
Heimlich manoeuvre (1975)	Laryngeal obstruction
N-acetylcysteine (1979)	Paracetamol poisoning
Ganciclovir (1986)	CMV retinitis
Imiglucerase (1990)	Gaucher's disease
Laser therapy (2000)	Port wine stains
Imatinib (2002)	Chronic myeloid leukaemia
Imatinib (2005)	Gastrointestinal stromal tumours

Case-control studies

Harms

Intervention	Harm
Oral contraceptives	Venous thromboembolism
Diethylstilboestrol in pregnancy	Genital tract cancer (in offspring)
Non-steroidal anti-inflammatory drugs	Upper gastro-intestinal bleeding
Aspirin in children	Reye's syndrome
Hormone replacement therapy	Venous thromboembolism
Hormone replacement therapy	Breast cancer
Anticonvulsants	Stevens-Johnson syndrome
Olanzepine	Diabetes mellitus
Fluoroquinolones	Ruptured Achilles tendon

Case-series

1. Generalisability
2. Economic evaluation
3. Comparative efficacy/effectiveness?

More hierarchies of evidence

Level	Criteria
1a	Systematic review of RCTs with homogeneity
1a -	Systematic review of RCTs with worrisome homogeneity
1b	Individual RCTs with narrow confidence intervals
1c	All or none effects
2a	Systematic review of cohort studies with homogeneity
2a-	Systematic review of cohort studies with worrisome heterogeneity
2b	Individual cohort studies and RCTs with <80% follow-up
2c	Outcomes research or ecological studies
3a	Systematic review of case-control studies with homogeneity
3a -	Systematic review of case-control studies with worrisome heterogeneity
3b	Individual case-control studies
4	Case studies, or poor quality cohort or case control studies
5	Expert opinion without explicit critical appraisal, or based on physiology, or based on “first principles”

Economic Evaluation

Overarching principles:

1. **Economic perspective**
   - NHS and PSS
2. **Cost effectiveness**
   - Not affordability or budgetary impact
3. **Balance between:**
   - Efficiency (utilitarianism)
   - Fairness (egalitarianism)

Cost Utility Analysis

Costs (and savings)

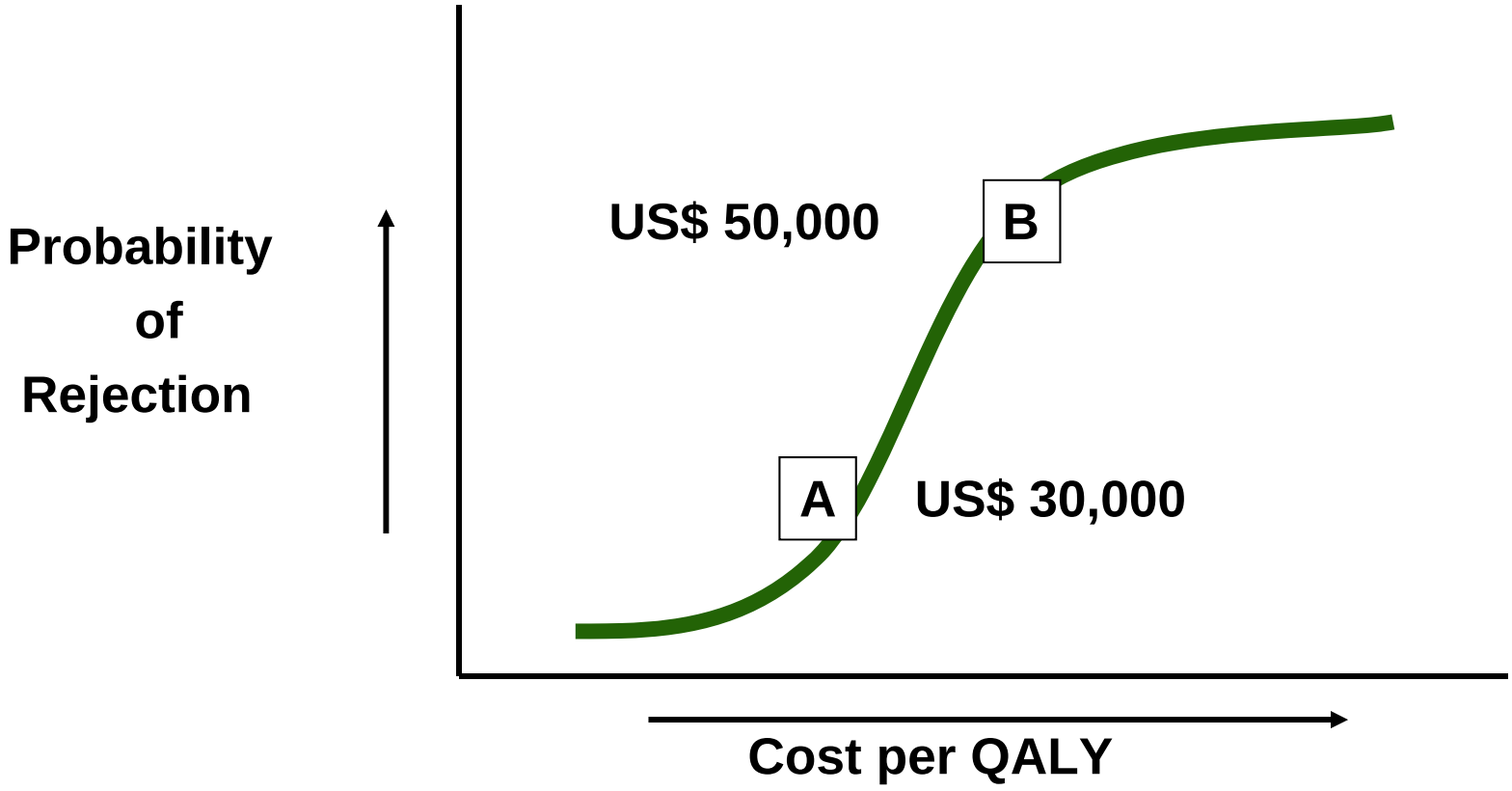
- direct
- indirect

Benefits

- in[illegible]ement (change) in HRQoL (utility)
- [illegible] for which it is “enjoyed”

Incremental cost effectiveness ratio

Cost Ineffectiveness



Decision-making

1. Scientific judgements

- Reliability of the evidence-base
- Appropriateness of sub-groups
- Generalisablity
- Capture of quality of life
- Handling uncertainty

2. Social value judgements

- Severity of disease
- End of life interventions (“rule of rescue”)
- Age
- Health inequalities

Social Value Judgements

Citizens Council:

- 30 members
- Cross-section of England and Wales
- Serve for 3 years (one third retiring annually)
- Meet twice a year – for 3 days
- Deliberative process
- Reports directly to the Board

Culturally and context specific

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Case-by-Case Decisions

Factors taken into account include:

- severity of the underlying condition
- extensions to end of life
- stakeholder persuasiveness
- significant clinical innovation
- children
- disadvantaged populations
- corporate responsibility

Recommendations >£30,000 per QALY

Topic	QALY ('000)	Severity	End of life	Significant innovation	Disadvantaged population		Corporate responsibility
Riluzole (MND)	38-42	★	★	★			
Temozolomide (glioma)	35	★	★				
Trastusumab (breast cancer)	37.5	★	★				
Imatinib (CML)	36-65	★	★	★			
Bortezomib (myeloma)	32.5	★		★			
Pemetrexed (mesothelioma)	34.5		★	★	★		★
Sunitinib (renal cancer		★	★	★			
Human growth hormone	ain					★	
Insulin	Uncertain					★	
Lenalidomide (myeloma)		★	★				

The QALY is a tool not a rule

NICE guidance

1. **Clinical:**
   - Technology appraisals
   - Clinical guidelines
   - Interventional procedures

2. **Public health**
   - Public health interventions
   - Public health guidelines

3. **Quality standards and metrics**
   - Quality & outcomes framework
   - NICE quality standards/metrics

4. **NHS Evidence**

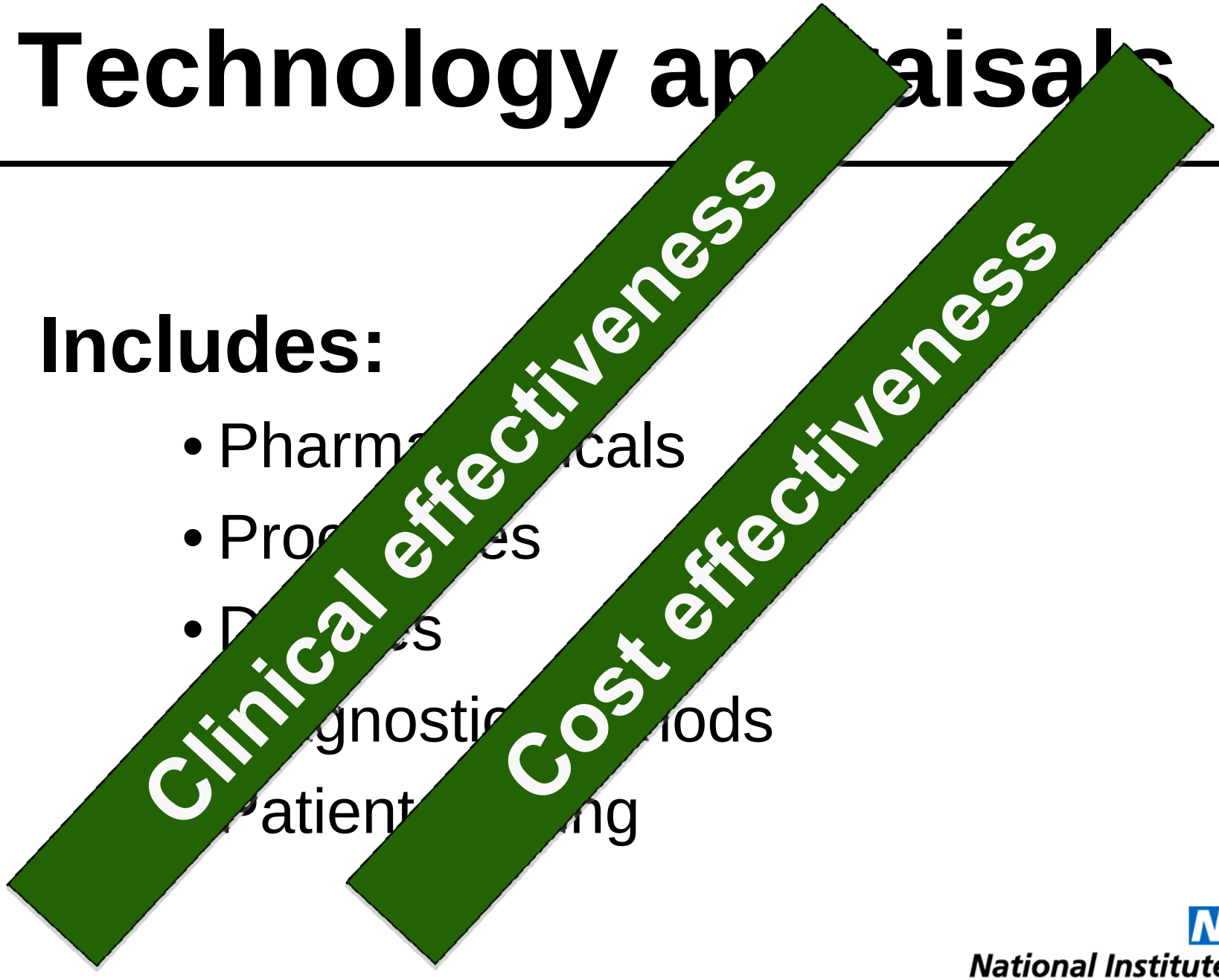
Published NICE guidance

Type 2007	Numbers
Appraisals	181
Clinical guidelines	108
Interventional procedures	314
Public health	21
Total	624

Technology appraisals

Includes:

- Pharma[illegible]icals
- Proc[illegible]es
- D[illegible]s
- [illegible]gnostic[illegible]iods
- Patient[illegible]ng



Technology appraisals

all decisions

Recommendation	Condition treatment pairs
Full use	102 (28%)
Restricted use	195 (54%)
Only in research	22 (6%)
No use	36 (10%)
Non-submission	5 (1%)
TOTAL	360 (100%)

Clinical guidelines

"Systematically develo statemen assist practitioner atient de s about appropriat h care f cific clinical circumst .

Institute of Medicine

Clinical effectiveness

Cost effectiveness

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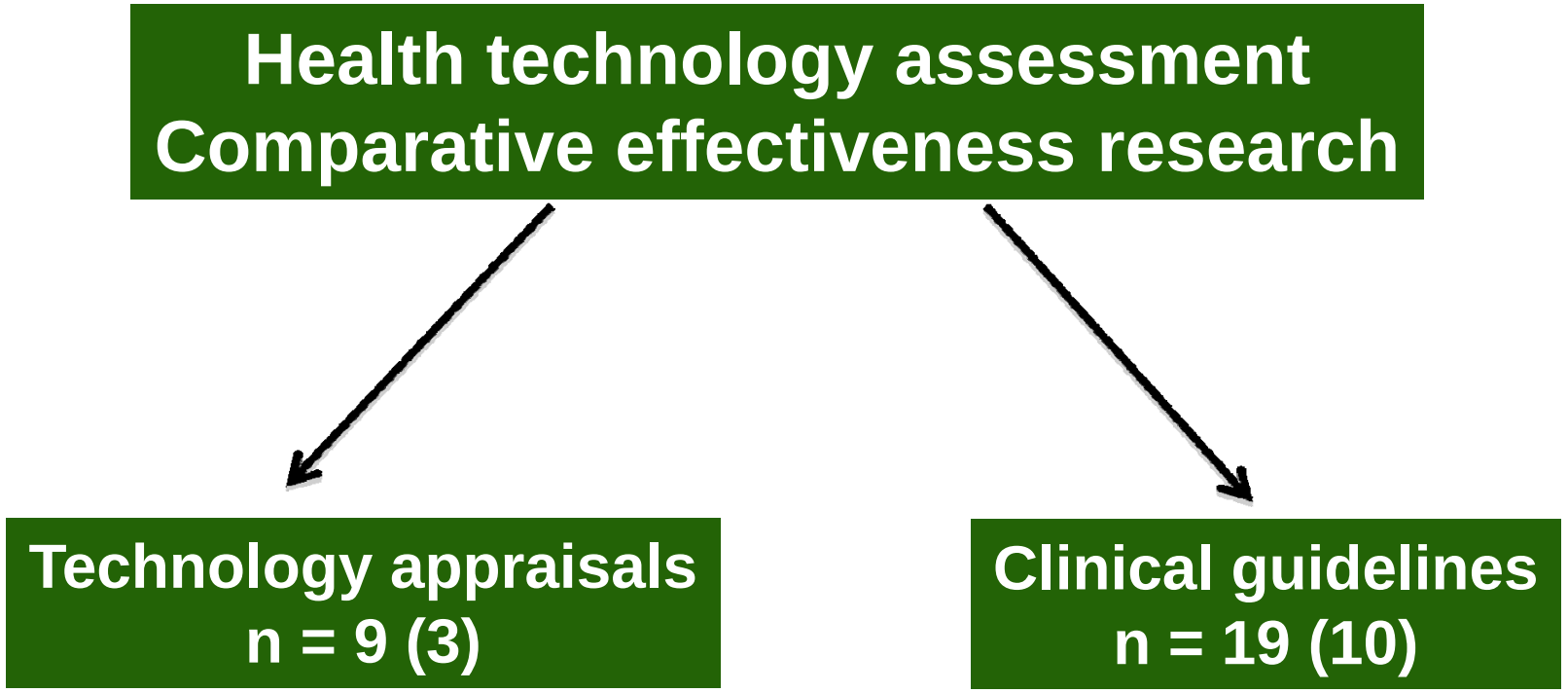
Guidelines Programme

Topic	Published
Central nervous system (inc. mental health)	24
Obstetrics & gynaecology	11
Cardiovascular	13
Metabolic	7
Cancer	17
Gastrointestinal	5
Others	37

Principles of NICE guidance

1. Robust
2. Inclusive
3. Transparent
4. Independent

Impact


Health technology assessment
Comparative effectiveness research
Technology appraisals
n = 9 (3)
Clinical guidelines
n = 19 (10)

Some examples

Technology appraisals:

- Electroconvulsive therapy
- Atypical anti-psychotic use
- Structural neuro-imagining in first episode psychosis

Clinical guidelines:

- Cognitive behavioural therapy
- Depression in children and adolescents
- Antenatal and postnatal mental health

Conclusions

1. HTA/CER has a critical part to play in ensuring high quality care.
2. Current approaches are too reliant on a restricted range of techniques
3. Methodological research is needed to increase its relevance.
4. Coupled with more (and better) primary research (and not confined to RTCs)