HTA for Cancer

Patricia Heckmann
NCCP

**Update in Pharmacoeconomics in the
Irish Healthcare Setting
March 2015**

nccp National Cancer
Control Programme

Overview

1. NCCP Structure and Functions

2. Systemic Therapy Programme

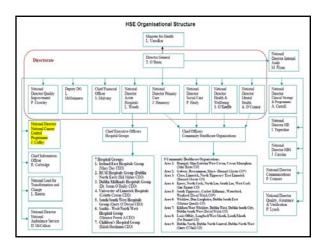3. Funding – HTAs

nccp National Cancer
Control Programme

NCCP

The National Cancer Control Programme (NCCP) was established in Ireland in 2007 to implement the National Cancer Strategy (2006)

- highlighted weakness in our approach to cancer care and relatively poor survival rates
- recommended that the NCCP be responsible for reforming and restructuring of services
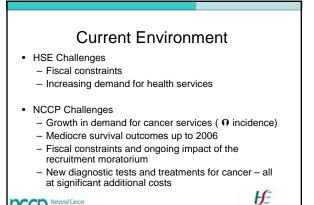
A Strategy for **Cancer Control** in Ireland

National Cancer Forum
2006

nccp National Cancer
Control Programme

Slide 1

HSE Organisational Structure

Minister for Health
L. Varadkar

Director General
T. O'Brien

Directorate

National Director Internal Audit
M. Flynn

- National Director Quality Improvement P. Crowley
- Deputy DG L. McGuinness
- Chief Financial Officer S. Mulvany
- National Director Acute Hospitals L. Woods
- National Director Primary Care J. Hennessy
- National Director Social Care P. Healy
- National Director Health & Wellbeing S. O'Keeffe
- National Director Mental Health A. O'Connor

National Director Clinical Strategy & Programmes A. Carroll

National Director National Cancer Control Programme J. Coffey

Chief Executive Officers Hospital Groups

Chief Officers Community Healthcare Organisations

National Director HR I. Tegerdine

National Director HBS J. Carolan

Chief Information Officer R. Corbridge

National Lead for Transformation and Change L. Kearns

National Director National Ambulance Service D. McCallion

National Director Communications P. Connors

National Director Quality Assurance & Verification P. Lynch

7 Hospital Groups:
1. Ireland East Hospital Group (Mary Day CEO)
2. RCSI Hospitals Group Dublin North East (Bill Maher CEO)
3. Dublin Midlands Hospitals Group (Dr. Susan O'Reilly CEO)
4. University of Limerick Hospitals (Colette Cowan CEO)
5. South/South West Hospital Group (Gerry O'Dwyer CEO)
6. Saolta - West/North West Hospital Group (Maurice Power A/CEO)
7. Children's Hospital Group (Eilísh Hardiman CEO)

9 Community Healthcare Organisations:
Area 1: Donegal, Sligo/Leitrim West Cavan, Cavan Monaghan. (John Hayes CO)
Area 2: Galway, Roscommon, Mayo. (Bernard Gloster CO*)
Area 3: Clare, Limerick, North Tipperary/ East Limerick. (Bernard Gloster CO)
Area 4: Kerry, North Cork, North Lee, South Lee, West Cork. (Ger Reaney CO)
Area 5: South Tipperary, Carlow Kilkenny, Waterford, Wexford (David Walsh CO*)
Area 6: Wicklow, Dun Laoghaire, Dublin South East (Martина Queally CO)
Area 7: Kildare West Wicklow, Dublin West, Dublin South City, Dublin South West (David Walsh CO)
Area 8: Laois Offaly, Longford West Meath, Louth Meath (Pat Bennett CO)
Area 9: Dublin North, Dublin North Central, Dublin North West (Gerry O'Neill CO)

Slide 2

Why is it important?

"One in three"

National Cancer Control Programme — NCCP

HSE

Slide 3

Scope of National Cancer Control Programme: 2007 - 2014

- Prevention
- Screening
- Diagnosis
- Surgery
- Radiation Oncology

- Systemic Therapy Programme
  - Medical Oncology
  - Haemato Oncology
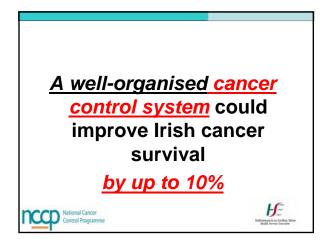- Quality Assurance
- Hereditary Cancer
- Survivorship

National Cancer Control Programme — NCCP

HSE

Current Environment

- HSE Challenges
  - Fiscal constraints
  - Increasing demand for health services

- NCCP Challenges
  - Growth in demand for cancer services (⋔ incidence)
  - Mediocre survival outcomes up to 2006
  - Fiscal constraints and ongoing impact of the recruitment moratorium
  - New diagnostic tests and treatments for cancer – all at significant additional costs

National Cancer Control Programme

Age standardised survival at 5 years for cancers diagnosed in
2000 - 2002 (all), 2002 - 2006 (Ireland)
and 2005 – 2007 (others)

	Colorectal		Lung		Breast		Ovary	
	2000-2002	2005-2007	2000-2002	2005-2007	2000-2002	2005-2007	2000-2002	2005-2007
New South Wales	65.1	66.4	16.2	17.6	87.4	87.8	39.6	39.9
Victoria	61.2	65.5	13.6	16.2	86.5	88.5	34.1	34.2
Alberta	58	58.3	13.1	15.1	84.9	82.6	34.9	36.9
British Columbia	61.5	64	14	17.7	87.5	89.1	37.8	44.1
Manitoba	59.6	63.3	19.4	20.1	83.9	86.8	37.1	28.8
Ontario	61.3	64.9	16.7	19.1	86.6	86.4	39.1	43.2
Denmark	51.7	55.8	9.6	10.9	81.5	82.4	33.7	36.1
Norway	58.8	62	11	14.4	83.8	85.5	40.2	39.7
Swedish regions	60.6	62.6	11.6	16.3	89.3	88.5	NA	NA
Ireland	54.3	54.9	10.9	11.7	76.2	80.6	NA	32.1
England	51.2	53.7	8	8.7	78.8	81.6	34.3	36.4
Northern Ireland	54.3	55.2	9.7	11	81.6	84.1	37.8	36.5
Wales	50.3	52.3	7.6	9	76.7	81	33.8	36.3

National Cancer Control Programme   Source: Irish data NCRI 2008 & international data Lancet 2010

A well-organised cancer control system **could improve Irish cancer survival** *by up to 10%*

National Cancer Control Programme

Cancer Projections for Ireland 2015 – 2040 (NCRI)
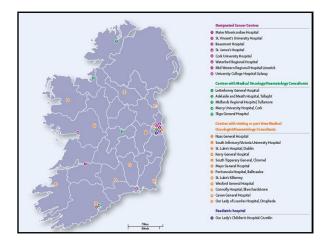
	2015	2020	2025	2030	2035	2040	% increase 2010 - 2040
Females	14322	16172	18202	20295	22368	24287	84%
Males	17008	19692	22658	25775	28855	31704	107%
All	**31330**	**35864**	**40860**	**46070**	**51223**	**55991**	**97%**

25 year growth rate 97%!

National Cancer Control Programme

Chemotherapy Use

- Projected ⬆ of 42%-45% in patients receiving chemotherapy by 2025
- Actual ⬆ in the proportion of patients by 13% between 2000-2004 and 2005-2009
  - most of this increase was in cancers where chemotherapy treatment was previously quite uncommon.

NCRI. Cancer projections for Ireland 2015-2040. 2014.

National Cancer Control Programme

Systemic Therapy Programme - Scope

- Medical Oncology and Haemato-Oncology
  - 26 hospitals delivering systemic services
- All tumour sites
- In-patient, out-patient, day case

National Cancer Control Programme

Designated Cancer Centres

1. Mater Misericordiae Hospital
2. St. Vincent's University Hospital
3. Beaumont Hospital
4. St. James's Hospital
5. Cork University Hospital
6. Waterford Regional Hospital
7. Mid-Western Regional Hospital Limerick
8. University College Hospital Galway

Centres with Medical Oncology/Haematology Consultants

9. Letterkenny General Hospital
10. Adelaide and Meath Hospital, Tallaght
11. Midlands Regional Hospital, Tullamore
12. Mercy University Hospital, Cork
13. Sligo General Hospital

Centres with visiting or part time Medical Oncologist/Haematology Consultants

14. Naas General Hospital
15. South Infirmary/Victoria University Hospital
16. St. Luke's Hospital, Dublin
17. Kerry General Hospital
18. South Tipperary General, Clonmel
19. Mayo General Hospital
20. Portiuncula Hospital, Ballinasloe
21. St. Luke's Kilkenny
22. Wexford General Hospital
23. Connolly Hospital, Blanchardstown
24. Cavan General Hospital
25. Our Lady of Lourdes Hospital, Drogheda

Paediatric hospital

26. Our Lady's Children's Hospital Crumlin

70km
40mls

Systemic Therapy Programme

Key drivers:
- Quality & Safety
- Access & Facilitators
- Coordination & Leadership

National Cancer Control Programme

Quality & Safety

- Quality & Safety
- Access & Facilitators
- Coordination & Leadership

- NCCP Oncology Medication Safety review – 2014
- Drug protocols
- National patient consent

National Cancer Control Programme

Access & Facilitators

- Cancer Drug Management Programme
- NCCP Technology Review Committee
- Key Performance Indicators
- ICT projects
- Workforce Planning

nccp National Cancer Control Programme

Coordination and Leadership

- Clinical Lead for Medical Oncology
- Clinical Advisor for Haemato-oncology
- National Systemic Therapy Strategy
- Expert Advisory Group for Haemato-oncology
- National Meeting
- Hospital Users Groups
- Website – patient and health professional information

nccp National Cancer Control Programme
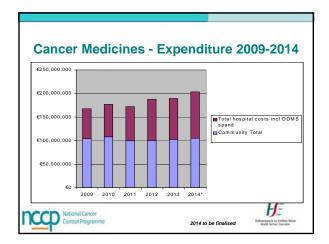
National drug protocols

- Collaborative approach
- Agreed and published on line
- Supports
  - Standardisation of practice
  - Evidence based medicine
  - Patient Safety
  - Clinical audit
  - "Money Follows the Patient" funding

nccp National Cancer Control Programme

National Cancer Drug Management Programme

- Quality & Safety
- Access & Facilitators
- Coordination & Leadership

- "Money Follows the Patient"
  - Oncology Drug Management System
  - funding for growth in oncology drugs
- Molecular diagnostics

National Cancer Control Programme

Cancer Medicines - Expenditure 2009-2014

- Total hospital costs incl ODMS spend
- Community Total

2014 to be finalised

National Cancer Control Programme

Cancer projections for Ireland 2015 – 2040

This report of cancer incidence projections shows that the incidence of cancer in Ireland is expected to double by 2040.

HSE to breach cost rules to buy new cancer drugs
Wednesday, March 13, 2013
By Dan Buckley

Skin cancer rates up 39pc in a decade

'Miracle' cancer treatment too pricey for HSE
Mark O'Regan
11/08/2014 | 02:30

Over 19,000 cancer cases diagnosed each year

HSE prepares for 'MFTP'
August 8, 2014 by Lloyd Mudiwa — Leave a Comment

Legislation/Agreements

FRAMEWORK AGREEMENT BETWEEN THE IRISH PHARMACEUTICAL HEALTHCARE ASSOCIATION LTD AND THE DEPARTMENT OF HEALTH AND THE HEALTH SERVICE EXECUTIVE ON THE SUPPLY TERMS, CONDITIONS AND PRICES OF MEDICINES

Number 14 of 2013

HEALTH (PRICING AND SUPPLY OF MEDICAL GOODS) ACT 2013

FRAMEWORK AGREEMENT BETWEEN THE ASSOCIATION OF PHARMACEUTICAL MANUFACTURERS OF IRELAND AND THE DEPARTMENT OF HEALTH AND THE HEALTH SERVICE EXECUTIVE ON THE SUPPLY TERMS, CONDITIONS AND PRICES OF GENERIC MEDICINES

Money Follows the Patient
Policy Paper on Hospital Financing

Draft for Consultation

National Cancer Control Programme

NCCP - MFTP

- •Quality & Safety
- •Access & Facilitators
- •Coordination & Leadership

- Ensures equitable access for patients to the best and most effective treatments
  - Within budgetary and regulatory boundaries
  - In line with cancer strategy
  - Facilitates treatment closer to home
- Supports clinical and financial audit
- Provides data for service planning
- Implements "Money Follows the Patient"
- Will underpin UHI and Commissioning for Cancer Services
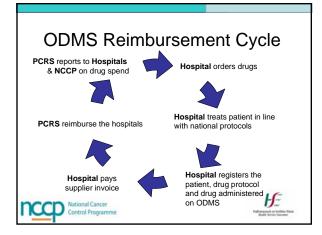
National Cancer Control Programme
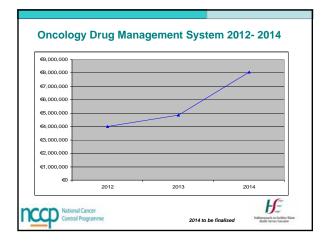
ODMS login screen

ODMS Reimbursement Cycle

PCRS reports to **Hospitals** & **NCCP** on drug spend

Hospital orders drugs

Hospital treats patient in line with national protocols

PCRS reimburse the hospitals

Hospital pays supplier invoice

Hospital registers the patient, drug protocol and drug administered on ODMS

Oncology Drug Management System 2012- 2014

2014 to be finalised

NCCP Technology Review Committee

•Quality & Safety
•Access & Facilitators
•Coordination & Leadership

- Multidisciplinary
  - Clinicians
  - Economics
  - NCCP, CPU, NCPE
- Reviews HTA and clinician guidelines
- Makes recommendations on funding priorities for cancer drugs
- 11 drugs discussed to 30/9/2014 -update

National Cancer Control Programme

HIQA - HTAs

- **14 completed – 7 cancer related**

THANK YOU

Questions??

Contact: Patricia.Heckmann@CancerControl.ie
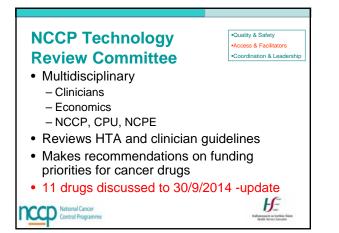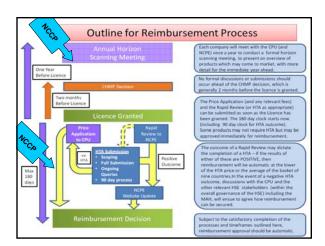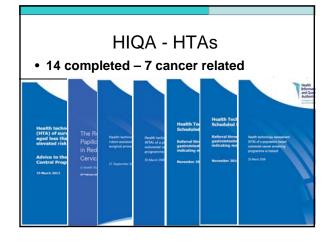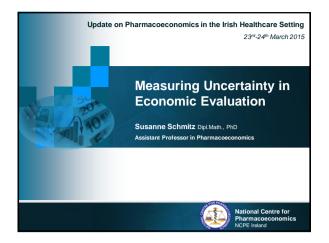
Useful documents/websites

- APMI, DOH & HSE 2012. Framework Agreement between the Association of Pharmaceutical Manufacturers of Ireland and the Department Of Health and the Health Service Executive on the Supply Terms, Conditions and Prices of Medicines.
- DOH 2013a. Health (Pricing and Supply of Medical Goods) Act.
- DOH 2013b. Money Follows the Patient: A Policy Paper on Hospital Financing.
- DOH 2013c. The Path to Universal Healthcare: A Preliminary Paper on Universal Health Insurance.
- IPHA, DOH & HSE 2012. Framework Agreement between the Irish Pharmaceutical Healthcare Association Ltd and the Department Of Health and the Health Service Executive on the Supply Terms, Conditions and Prices of Medicines.
- NCRI 2014. Cancer projections for Ireland 2015-2040.
- ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT (OECD) 2013. Cancer Care: Assuring Quality to Improve Survival.
- HIQA - http://hiqa.ie/healthcare/health-technology-assessment/guidelines

Update on Pharmacoeconomics in the Irish Healthcare Setting

23rd-24th March 2015

Measuring Uncertainty in Economic Evaluation

Susanne Schmitz Dipl.Math., PhD
Assistant Professor in Pharmacoeconomics

National Centre for Pharmacoeconomics
NCPE Ireland
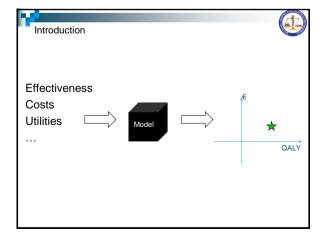
Introduction
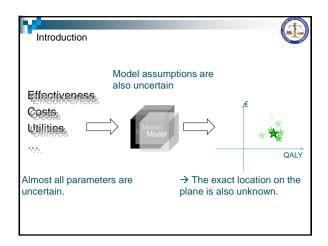
Recall

- The purpose of an economic analysis is to help in prioritising which technologies or pharmaceutical agents to introduce.
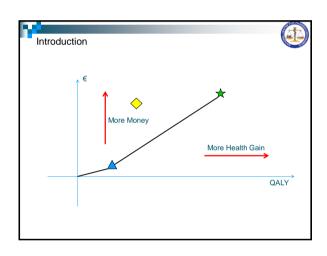
- This is done in a formal and structured way through a Health Technology Assessment. Where this is in the form of a cost-utility analysis, results can be communicated on the cost effectiveness plane.

Introduction

Effectiveness
Costs
Utilities
…

Model

€

★

QALY

Introduction

Model assumptions are also uncertain

Effectiveness
Costs
Utilities
….

€

Model

QALY

Almost all parameters are uncertain.

→ The exact location on the plane is also unknown.

Introduction

€

More Money

More Health Gain

QALY

Introduction

€

ICER = Δ€ / Δ QALY

Δ €

Δ QALY

QALY

€

Δ €

Δ QALY

QALY

€

Dominated

QALY

Are we certain this is the exact cost / gain?

€

QALY

Slide 1

Introduction

What if we could negotiate a lower price?

→ reduced ICER

€

QALY

Slide 2

Introduction

What if intervention is more effective than we thought?

→ reduced ICER

€

QALY

Slide 3

Introduction

- The ICER and the Cost Effectiveness Plane allow us to compare scenarios / interventions.

- But if we are unsure about inputs into the model, we are uncertain about the location on the plane and the ICER.

Sources of Uncertainty

- **Analytical method**
  e.g. discount rate
- **Patient sample characteristics**
  e.g. age
- **Parameters that could be sampled**
  e.g. transition rates

Parameter Uncertainty

Uncertainty

Structural Uncertainty

- **Overall Model structure**
  e.g. # Markov States
- **Structural assumptions within the model**
  e.g. functional form of transition rates

Quantifying Uncertainty

- At its simplest, not knowing may mean that there are alternative plausible 'low' and 'high' values a parameter can take.
  → This is termed 'univariate' uncertainty - OWSA

- Careful analysis of data, or elicitation from experts may allow uncertainty to be quantified probabilistically.
  → This allows 'natural' multivariate quantification of uncertainty – PSA.

  - How Valuable is the collection of further information
    → Value of information

One-Way-Sensitivity Analysis (OWSA)

Costs (local annual)	Mean	Range
Health State Costs (Healthcare payer perspective)		
EDSS 0 healthcare Cost		
EDSS 1 healthcare Cost		
EDSS 2 healthcare Cost		
Relapse Cost		
Utilities		
Health State Utilities		
EDSS 6 Utility		
EDSS 7 Utility		
EDSS 8 Utility		
EDSS 9 Utility		
Relapse disutility		
Natural History		
Annual disability progression rates		
EDSS 0-3		
EDSS 3-6		
EDSS 6-9		
EDSS 9-10		
Natural History		
EDSS 5		
EDSS 6		
EDSS 7		
EDSS 8		
EDSS 9		(0.96 - 0.99)
DMT treatment effects		
Hazard ratio of disability progression		
Alemtuzumab		
Natalizumab		
BG12 480mg		
Laquinimod		
Fingolimod		
Teriflunomide 14mg		
IFNβ / GA		
Relative ARR		
Alemtuzumab		

One-Way-Sensitivity Analysis (OWSA)

Tornado Diagram :
Natalizumab vs. IFNβ/GA

One-Way-Sensitivity Analysis (OWSA)

- Allows examination of impact of 'what if' a parameter took a different value.
- Helps analyst determine which parameters are important to decision.

- *Does not show 'what if' **all** parameters took different values.*
- *Lower/ upper values may be plausible, but not 'likely' values for the parameter – is it meaningful to decide on extremes?*

Probabilistic Analysis (PSA)

… enter probability …

Costs *(mean annual)*	Mean	Range	Distribution
EDSS 0 healthcare Cost			Gamma

Probabilistic Analysis (PSA)

… enter probability …

Costs *(mean annual)*	Mean	Range	Distribution
EDSS 0 healthcare Cost			Gamma

Probabilistic Analysis (PSA)

… enter probability …

Costs *(mean annual)*	Mean	Range	Distribution
EDSS 0 healthcare Cost			Gamma

Probabilistic Analysis (PSA)

- For all parameters in the model summarise uncertainty using probability distributions.

- Generate a realisation of the entire set of parameters and fit CE model. Record Cost and QALY.

Distribution

- Repeat many, many times.

- Draw a scatterplot to show how uncertainty in parameters affects the CE plane.

Probabilistic Analysis (PSA)

Probabilistic Analysis (PSA)

- Realistic examination of uncertainty given evidence.
- Can be used to explicitly quantify decision uncertainty.

- *Requires careful analysis to derive appropriate probability distributions.*
- *Additional computational complexity modeling support is needed.*

Probabilistic Analysis (PSA)

Threshold = 0

Threshold = Infinity

Probabilistic Analysis (PSA)

Threshold = 45K

Probabilistic Analysis (PSA)

Cost Effectiveness Acceptability Curve (CEAC)

Plots the probability of being the most cost effective treatment against the threshold.
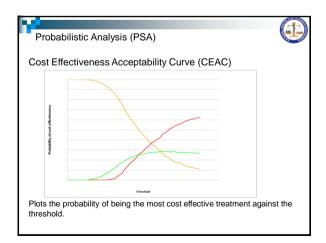
Where to go from here?

Where decision uncertainty is substantial, there may be a case for further research. (micro-costing / utility elicitation / trial)

The value of further research may be formalised using 'Value of Information'
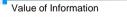
Expected Value of Perfect Information (EVPI)

The difference between optimal expected net benefit with and without perfect knowledge of the input parameters prior to the time of decision.

→Can be easily determined from the PSA outputs.
→Further research to obtain this information can be considered beneficial, if it is less costly than the EVPI.

Parameter

Expected Value of Perfect Information (EVP**PI**)

The difference between optimal expected net benefit with and without perfect knowledge of the input parameters prior to the time of decision.   a particular (group of)

→More computationally expensive.
→Indicates the direction of further research.
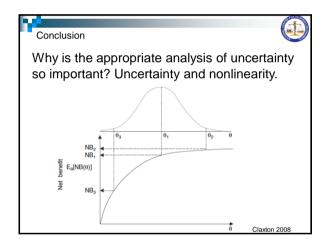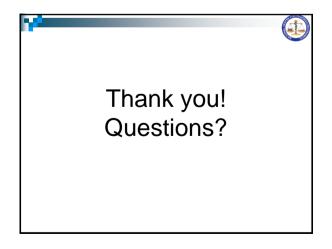
Sampling

Expected Value of ~~Perfect~~ Information (EV~~S~~I)

The difference between optimal expected net benefit with and without access to a sample of additional observations of the input parameters prior to the time of decision.

Conclusion

Why is the appropriate analysis of uncertainty so important? Uncertainty and nonlinearity.

Claxton 2008

Thank you!
Questions?

Multi-Criteria Decision Analysis, Health Technology Assessment and Uncertainty

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Trinity College Dublin

Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin
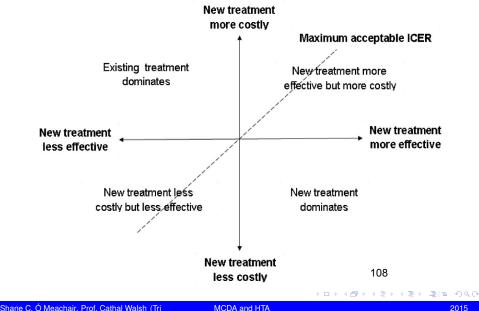
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Outline

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Decision-Making
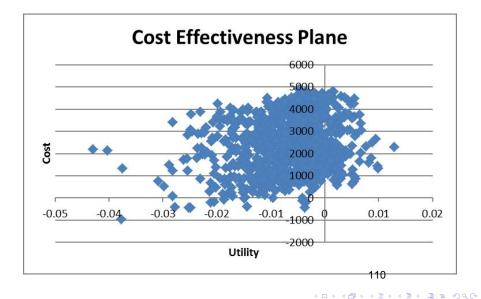
- In Ireland, threshold is €45,000 per QALY
- Uncertainty: costs and QALYs calculated from uncertain inputs.
- Probabilistic Sensitivity Analysis (PSA) - Monte Carlo simulation from input distributions.

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Cost Effectiveness Plane

THE IRISH TIMES

Fri, Feb 27, 2015

| NEWS | SPORT | BUSINESS | OPINION | LIFE & STYLE | CULTURE |

Health | Ireland | World | Politics | Crime & Law | Social Affairs | Education

HSE to provide life-saving Soliris drug despite 'astronomical' cost

Patients with rare blood diseases to get €430k drug after pressure from Government TDs

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Statistical Decision-Making

- Choose an option which maximise expected utility over uncertain states of nature.

$$\max_a E[U(\Theta, a)] = \int_\Theta U(\Theta, a) dF(\Theta)$$

- Utility function needs to include all aspects of the decision
- Can only maximise over one utility function. What if there are multiple utilities?
- $\max U(a, \Theta_1, \Theta_2 \ldots \Theta_n)$ not defined without further assumptions.

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Multi-Criteria Decision Analysis (MCDA)

- Most commonly used as a decision aid tool
- Used in industrial planning, public infrastructure investment, nuclear emergency response
- Multiple attempts to solve the MCDA problem from Operations Research and Statistics.
- Three main approaches: Outranking, Analytic Hierarchy Process, Multi-Attribute Utility Theory.
- Will look at Analytic Hierarchy Process, Multi-Attribute Utility Theory here.

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MCDA Questions

- How to obtained utilities?
- How to weight or trade-off criteria?
- How to combine criteria?

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Analytic Hierarchy Process

- Pairwise comparisons between actions on each criteria
- Specific AHP scale: max = 9, min = 1/9
- Given verbal interpretation : "equally important", "more important", "absolutely more important"

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AHP Example

	Treatment 1	Treatment 2	Treatment 3
Cost	150,000	20,000	300,000
Safety and Tolerability	No Concern	Some Concern	No Concern
Quality of Evidence	Poor	Neutral	Very Good
Innovation	None	None	Innovative

Table: Input Data

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Analytic Hierarchy Process

Example of Criteria Matrix

	Cost	Safety	Evidence	Innovation
Cost	1	1/7	5	2
Safety	7	1	7	7
Evidence	1/5	1/7	1	1/3
Innovation	1/2	1/7	3	1

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Analytic Hierarchy Process
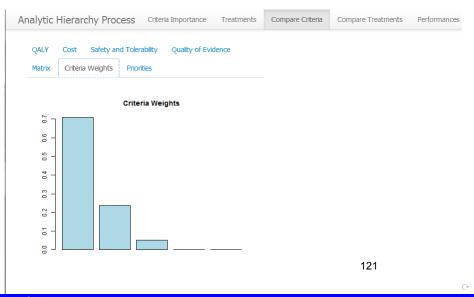
Compare each choice on each criteria, eg Cost

	Treatment 1	Treatment 2	Treatment 3
Treatment 1	1	1/9	5
Treatment 2	9	1	2
Treatment 3	1/5	1/2	1

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Analytic Hierarchy Process

Normalised criteria matrix

	Cost	Safety	Evidence	Innovation		Average
Cost	0.12	0.1	0.31	0.2		0.18
Safety	0.8	0.7	0.44	0.68		0.66
Evidence	0.02	0.1	0.06	0.3		0.05
Innovation	0.06	0.1	0.19	0.1		0.11

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AHP - Pilot study using Shiny

Analytic Hierarchy Process

Normalised cost matrix

	Treatment 1	Treatment 2	Treatment 3		Average
Treatment 1	0.1	0.07	0.63		0.26
Treatment 2	0.88	0.62	0.25		0.58
Treatment 3	0.02	0.31	0.13		0.15

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Analytic Hierarchy Process

Compare each choice on each criteria

	Cost	Safety	Evidence	Innovation
Treatment 1	0.26	0.4	0.1	0.2
Treatment 2	0.58	0.2	0.3	0.2
Treatment 3	0.15	0.4	0.6	0.6

Weights
$$\begin{pmatrix} 0.18 \\ 0.66 \\ 0.05 \\ 0.11 \end{pmatrix}$$

Multiply each row by the weights, eg for row one:

$$0.18 * 0.26 + 0.65 * 0.4 + 0.05 * 0.1 + 0.11 * 0.2 = 0.34$$

$$0.18 * 0.58 + 0.65 * 0.2 + 0.05 * 0.3 + 0.11 * 0.2 = 0.27$$

$$0.18 * 0.15 + 0.65 * 0.4 + 0.05 * 0.6 + 0.11 * 0.6 = 0.39$$

123

Analytic Hierarchy Process

$$
\begin{array}{c}
\text{Priorities} \\
\begin{array}{l}
\text{Treatment 1} \\
\text{Treatment 2} \\
\text{Treatment 3}
\end{array}
\left(
\begin{array}{c}
0.34 \\
0.27 \\
0.39
\end{array}
\right)
\end{array}
$$

124

Analytic Hierarchy Process

- Criteria and action priorities estimated from eigenvectors of comparison matrix.
- Consistency index measures consistency of preference judgements.
- Reddy et al (2014) use AHP to determine weightings of topics for NICE public guidances.

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Table 4 – Topics ranked by total weighted score.

Absolute weights	0.29	0.28	0.15	0.11	0.07	0.06	0.04	1.00
	Making a difference – Feasibility	Making a difference – Evidence available	Current variation in practice	Size of problem – Societal	Size of problem – inequality	Making a difference – range and fit	Size of problem – individually	Total score
Fluoridation of water	0.23	0.25	0.36	0.09	0.18	0.22	0.10	0.23
Tackling smoking through the media	0.22	0.29	0.05	0.36	0.16	0.16	0.13	0.22
Substance misuse	0.24	0.18	0.14	0.26	0.27	0.18	0.27	0.21
Pain as a public health problem	0.13	0.10	0.32	0.23	0.18	0.25	0.22	0.17
Sickle Cell Screening	0.18	0.17	0.14	0.06	0.21	0.19	0.29	0.17

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AHP - Pros and Cons

Advantages

- Intuitive, relatively easy elicitation. Subjective scale.
- Can be implemented quickly

Disadvantages

- \# of pairwise comparisons grows large with each additional criteria and choice option.
- May be difficult to generalise consistently over time

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Multi-Attribute Utility Theory

- Generalisation of utility/decision theory.
- Requires specification of multi-attribute utility function
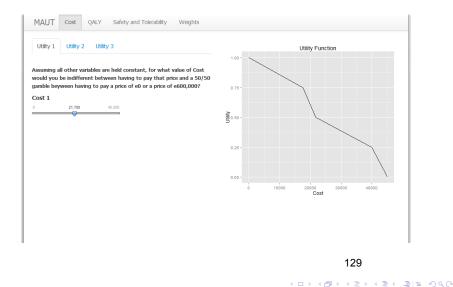
$$U(U_1(c_1), U_2(c_2), \ldots, U_n(c_n))$$

ie a joint utility function.

- Can be difficult, usually requires simplifying assumptions.
- In the simplest case, criteria are assumed utility-independent and aggregate of univariate utility functions used.

$$U(a) = U_1(a, c_1) + U_2(a, c_2) + \cdots + U_n(a, c_n)$$

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Multi-Attribute Utility Theory

129

Shane C. Ó Meachair, Prof. Cathal Walsh (Tri   MCDA and HTA   2015

MAUT - Pros and Cons

Advantages

- MAUT - established theoretical framework - rational, consistent judgements
- Elicitation can be straightforward in some circumstances, standard gamble, TTO

Disadvantages

- Joint utility function may be tricky to define, especially w/ dependencies between criteria (which there often are)

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Multi-Attribute Value Modelling

- Simplified case of MAUT
- Extension of Incremental Net Benefit

$$INB = \lambda * \Delta QALY - \Delta e$$
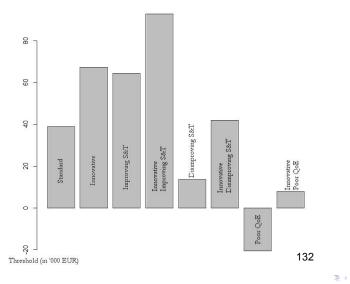
  which is a MCDA problem of two criteria, where λ is the relative trade-off between criteria.

- This can be extended to more than two criteria eg

  Benefit $= W_1(\Delta QALY) + W_2(\text{End of Life}) + W_3(Severity) + ... + W_n(N)$

- Definition of threshold changes
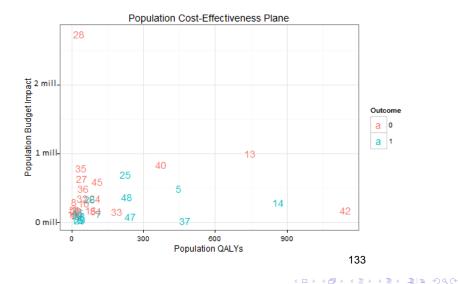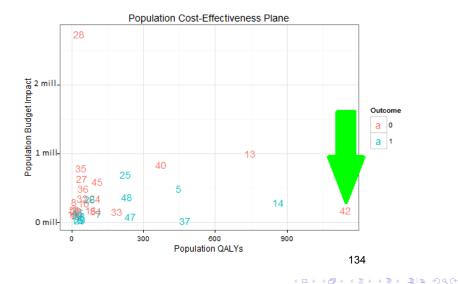
131

Threshold (in '000 EUR)

132

Benefit function: QALYs

Population Cost-Effectiveness Plane

133

Benefit function: QALYs

Population Cost-Effectiveness Plane

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Benefit function: QALYs + Evidence

Population Cost-Benefit Plane

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Population Cost-Benefit Plane

136
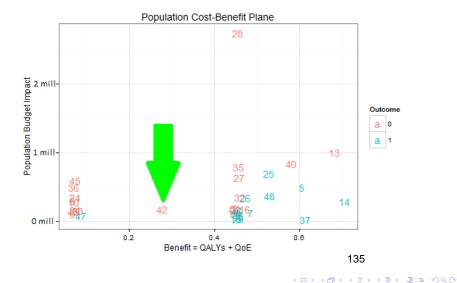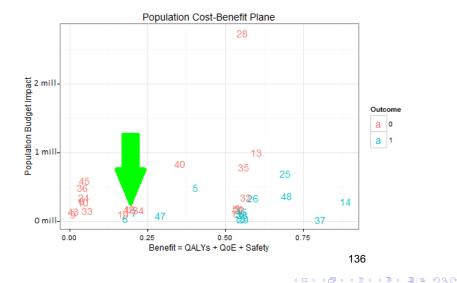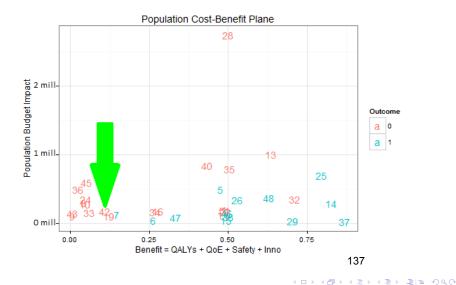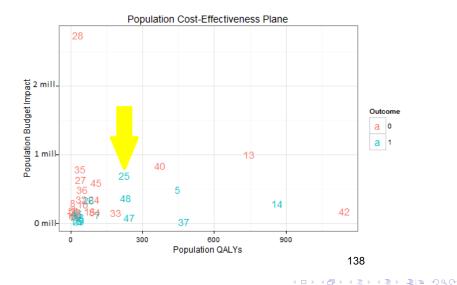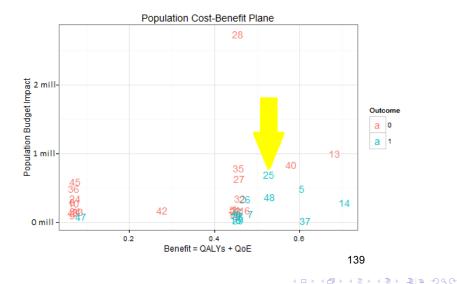
Benefit function: QALYs + QoE + Safety + Innovation

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Population Cost-Effectiveness Plane

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Benefit function: QALYs + Evidence

139

Population Cost-Benefit Plane

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Population Cost-Benefit Plane

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Uncertainty in MCDA

- AHP: fixed 'utility' judgements, inconsistency
- MAUT; uncertainty in utility functions
- All can have uncertainty in data especially when based on expert judgement (eg, social good, safety, unmet needs)rather than empirical data

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Priorities

N = 500   Bandwidth = 0.01176

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Uncertainty in Multi Attribute Utility Theory

- Can incorporate uncertainty in underlying data structure, dependencies between variables using decision theory and Bayesian modelling.
- Utility uncertainty not taken into account

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📄 Reddy B, Kelly M, Thokala P, Walters S, Duenas A
Prioritising public health guidance topics in the National Institute for Health and Care Excellence using the Analytic Hierarchy Process
Public Health, 128(10) 2014.

📄 Schmitz S. McCullagh L. Adams R. Barry M, Walsh C,
Estimating revealed weights for a multi criteria decision analysis approach to Health Technology Assessments: A case study in Ireland
SMDM Europe Proceedings 2014.

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Any questions?

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Update on Pharmacoeconomics in the Irish Healthcare Setting
23rd-24th March 2015

Combining Evidence for Economic Evaluations

Susanne Schmitz Dipl.Math., PhD
Assistant Professor in Pharmacoeconomics

National Centre for Pharmacoeconomics
NCPE Ireland
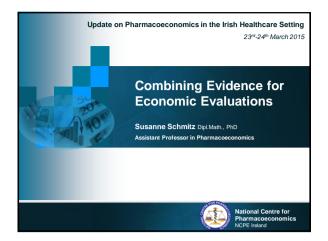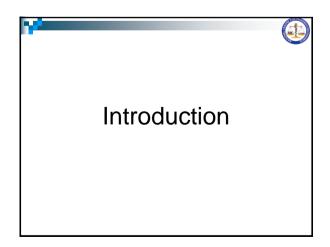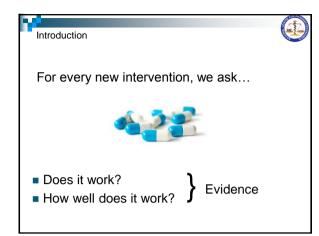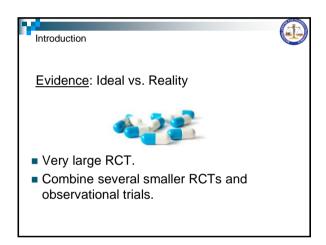
Outline

- Introduction
- Meta-Analysis
- Network Meta Analysis
- Extensions
- Summary

Introduction

For every new intervention, we ask…

- Does it work?
- How well does it work? } Evidence

Evidence: Ideal vs. Reality

- Very large RCT.
- Combine several smaller RCTs and observational trials.

Evidence Synthesis

- Combine several smaller RCTs and observational trials.
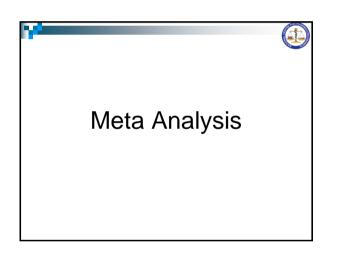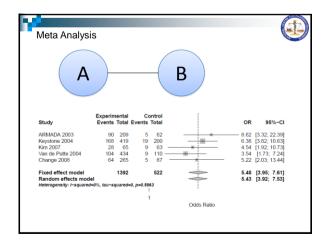
Introduction

Selecting Data

There are established methods for conducting a systematic review based on defined inclusion and exclusion criteria.
E.g. : PRISMA

www.prisma-statement.org

PRISMA 2009 Flow Diagram

Meta Analysis

Meta Analysis

Study	Experimental Events	Total	Control Events	Total		OR	95%–CI
ARMADA 2003	90	209	5	62		8.62	[3.32; 22.39]
Keystone 2004	168	419	19	200		6.38	[3.82; 10.63]
Kim 2007	28	65	9	63		4.54	[1.92; 10.73]
Van de Putte 2004	104	434	9	110		3.54	[1.73; 7.24]
Change 2008	64	265	5	87		5.22	[2.03; 13.44]
Fixed effect model		**1392**		**522**		**5.48**	**[3.95; 7.61]**
Random effects model						**5.43**	**[3.92; 7.53]**

Heterogeneity: I–squared=0%, tau–squared=0, p=0.5863

Odds Ratio

Slide 1
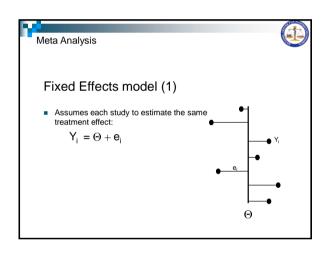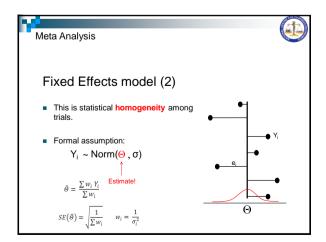
	Classical	Bayesian
Fixed Effects	I.	III.
Random Effects	II.	IV.

Slide 2

Fixed Effects model (1)

- Assumes each study to estimate the same treatment effect:

$$Y_i = \Theta + e_i$$

Y_i

e_i

Θ

Slide 3

Fixed Effects model (2)

- This is statistical **homogeneity** among trials.

- Formal assumption:

$$Y_i \sim Norm(\Theta, \sigma)$$

Estimate!

$$\hat{\theta} = \frac{\sum w_i\, Y_i}{\sum w_i}$$

$$SE(\hat{\theta}) = \sqrt{\frac{1}{\sum w_i}} \qquad w_i = \frac{1}{\sigma_i^2}$$

Y_i

e_i

Θ

150
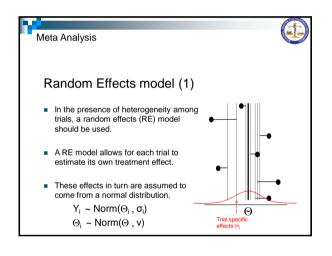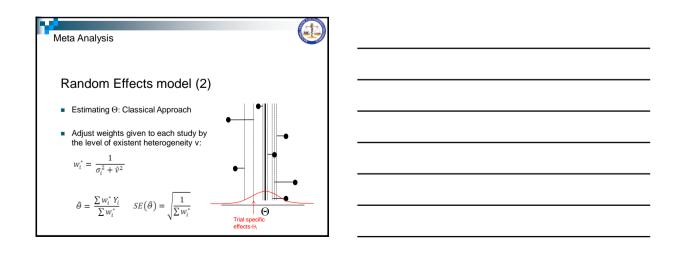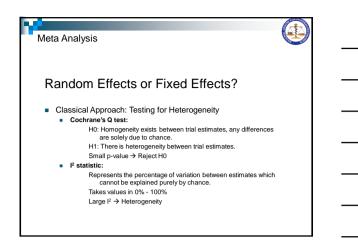
Heterogeneity
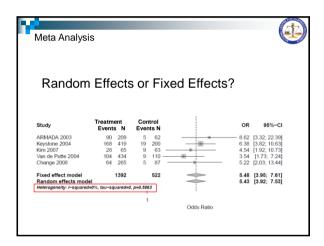
- Not all studies are the same. Studies may differ for many different reasons, for example design, conduct, patient characteristics, dosing, etc.

- Therefore, not all studies necessarily measure the exact same treatment effect.

- This is called <u>between study heterogeneity</u>.

Random Effects model (1)

- In the presence of heterogeneity among trials, a random effects (RE) model should be used.

- A RE model allows for each trial to estimate its own treatment effect.

- These effects in turn are assumed to come from a normal distribution.

$$Y_i \sim Norm(\Theta_i , \sigma_i)$$
$$\Theta_i \sim Norm(\Theta , v)$$

Θ

Trial specific effects Θ_i

Random Effects model (2)

- Estimating Θ: Classical Approach

- Adjust weights given to each study by the level of existent heterogeneity v:

$$w_i^* = \frac{1}{\sigma_i^2 + \hat{v}^2}$$

$$\hat{\theta} = \frac{\sum w_i^* Y_i}{\sum w_i^*} \qquad SE(\hat{\theta}) = \sqrt{\frac{1}{\sum w_i^*}}$$

Θ

Trial specific effects Θ_i

Meta Analysis

Random Effects or Fixed Effects?

- Classical Approach: Testing for Heterogeneity
  - **Cochrane's Q test:**
    - H0: Homogeneity exists between trial estimates, any differences are solely due to chance.
    - H1: There is heterogeneity between trial estimates.
    - Small p-value → Reject H0
  - **I² statistic:**
    - Represents the percentage of variation between estimates which cannot be explained purely by chance.
    - Takes values in 0% - 100%
    - Large I² → Heterogeneity

Meta Analysis

Random Effects or Fixed Effects?

Study	Treatment Events	N	Control Events	N		OR	95%-CI
ARMADA 2003	90	209	5	62		8.62	[3.32; 22.39]
Keystone 2004	168	419	19	200		6.38	[3.82; 10.63]
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Random effects model						**5.43**	**[3.92; 7.53]**

Heterogeneity: I−squared=0%, tau−squared=0, p=0.5863

Odds Ratio

Meta Analysis

Classical vs. Bayesian

The **Classical Analysis** is based solely on the data; the **Bayesian Analysis** includes prior knowledge.

$$\textbf{Posterior} \quad \alpha \quad \textbf{Prior * Likelihood}$$

Prior Distribution
$\Theta \sim [-,-]$, $v \sim [-,-]$

Θ

Classical vs. Bayesian

	Classical	Bayesian
Data	Combine Summary Measures	Hierarchical Model of underlying response
Parameter	Unknown, but fixed value	Random Variable
Outcome	Point Estimate + Confidence Interval	Posterior Distribution
Interpretation	Significant vs. Non-Significant	Probability Statements

---

Classical vs. Bayesian

← favours drug A   No Difference   favours drug B →

Bayesian Estimate

There is a probability of 87% that drug B is better than drug A.

87%

The 95% CI crosses the line of no differences. Therefore there is no statistically significant difference between drug A and drug B.

Classical Estimate

Fixed or Random Effects in a Bayesian Meta Analysis?

Random Effects Model

Fixed Effects Model

→ Use model fit criteria (DIC) to choose between models.

Due to the hierarchical modeling approach, the FE model is nested within the RE model.

Network Meta Analysis (NMA)

Network Meta Analysis

When comparing 2 treatments…
➢ Direct Evidence is preferable, but not always available or sufficient.
➢ Indirect Evidence also contains information and should be considered in an analysis.
➢ NMA provides a tool combining direct and indirect evidence.
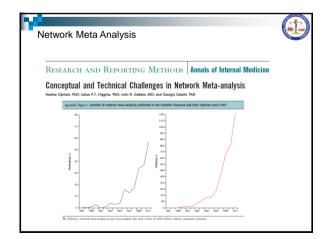
When comparing 3 or more treatments…
➢ NMA allows the estimation of relative efficacy between treatments in a larger network of treatments.

Network Meta Analysis

RESEARCH AND REPORTING METHODS | Annals of Internal Medicine

Conceptual and Technical Challenges in Network Meta-analysis
Andrea Cipriani, PhD; Julian P.T. Higgins, PhD; John R. Geddes, MD; and Georgia Salanti, PhD

Appendix Figure 1. Number of network meta-analyses published in the scientific literature and their citations since 1997.

We defined a network meta-analysis as any meta-analysis that used a form of valid indirect relative treatment estimates.

Evidence Networks

Star Design   Ladder Design   Any connected Network

Connected Networks

Any **connected Network**

Connected Networks

Any **connected Network**

Connected Networks

Considering this as one network, **it is not a connected Network!**

Closed Loops

Closed Loops

No closed Loops

Model features and Assumptions:

- ➢ Adjusted Method
- ➢ Uncertainty

- ➢ Treatment Exchangeability
- ➢ Consistency

- ➢ Hierarchical Model

Adjusted Method

Study 1

Drug A   Drug B

Study 2

Drug A   Drug C

Evidence Network:
Simplest Case Scenario

Treatment Exchangeability

Study 1

Drug A   Drug B

Study 2

Drug A   Drug C

Similarity Assumption between trials.

Effect of Drug B:
3 responders more
than in Placebo Arm.

Effect of Drug C:
7 responders more
than in Placebo Arm.

Treatment Exchangeability

Study 1

Similarity Assumption between trials.

Drug A | Drug B

Effect of Drug B:
3 responders more
than in Placebo Arm.

Study 2

Drug A | Drug B

Expected effect if we replaced Drug C by Drug B:
3 responders more than in Placebo Arm.

Consistency Assumption

Direct and Indirect evidence estimate the same parameter [A vs. B].

- Consistency for a comparison [A vs. B] can only be checked, if at least 2 alternative network pathways between the drugs exist.

- Clinical expertise is very important in the data selection process, as multiple pathways are not always available.

Consistency Assumption

Checking for Consistency:

1) Is there inconsistency?
   Compare model fit of 'inconsistency model' and 'consistency model'.
2) Locate inconsistency.
   Compare deviance contributions of each data point given the 2 models.
3) Measure inconsistency
   Node split method (Dias et al. 20)

Uncertainty

Direct Evidence

$$\text{Var (A vs. B)} = \sigma^2$$

Indirect Evidence

$$\text{Var (A vs. B)} = 2\sigma^2$$

⚠ Indirect evidence is automatically down weighted.

Questions to ask…
… before combining evidence

- Are all relevant treatments included?
- Are all relevant trials included?
- Do treatments form a connected network?
- Is it appropriate to combine? (assumptions)

(D. Caldwell, MTC workshop for Nice, 2006)

Bayesian Hierarchical Model

- Simultaneously performs IC where DC is not available.
- Borrowing strength across the network ensures optimal use of data.

Study Level   Overall Level

AC 1
AC 2
AC i
→ AC

→ AB

BC 1
BC 2
BC j
→ BC

- *Multiple Treatment Arms*
- *Multiple Baseline Treatments*
- *Meta-Regression*
- *Quantify Incoherence*
- *Include all available evidence*
- *...*

Examples

1) Kieran J, Schmitz S, O'Leary A, Walsh C, Bergin C, Norris S, et al. The relative efficacy of boceprevir and telaprevir in the treatment of **hepatitis C** virus genotype 1. Clinical infectious diseases. 2013;56(2):228-35.
2) Dranitsaris G, Schmitz S, Broom RJ. Small molecule targeted therapies for the second-line treatment for **metastatic renal cell carcinoma**: a systematic review and indirect comparison of safety and efficacy. Journal of cancer research and clinical oncology. 2013;139(11):1917-26.
3) Schmitz S, Adams R, Walsh CD, Barry M, FitzGerald O. A mixed treatment comparison of the efficacy of anti-TNF agents in **rheumatoid arthritis** for methotrexate non-responders demonstrates differences between treatments: a Bayesian approach. Annals of the rheumatic diseases. 2012;71(2):225-30.
4) Mesgarpour B, Heidinger BH, Schwameis M, Kienbacher C, Walsh C, Schmitz S, et al. Safety of off-label **erythropoiesis stimulating agents** in critically ill patients: a meta-analysis. Intensive care medicine. 2013;39(11):1896-908.
5) Schmitz S, Adams R, Walsh C. **Incorporating data from various trial designs** into a mixed treatment comparison model. Statistics in Medicine. 2013;32(17):2935-49.

NMA: Example (I)

Evidence Network

Evidence Network

BG-12 240mg tds
BG-12 240mg bd
Placebo
Glatiramer Acetate
Teriflunomide 14mg
IFN β-1b 250mcg SC
Teriflunomide 7mg
Fingolimod 0.5mg
Laquinimod
Fingolimod 1.25mg
Natalizumab
IFN β-1a 30mcg IM
Alemtuzumab
IFN β-1a 22mcg SC
IFN β-1a 44mcg SC

Outcome Measures

- Annualized Relapse Rate (ARR)
  ARR = #Relapses / Patient Years

- Progression Free Survival (PF)
  3 month confirmed disability progression (change in EDSS score)

NMA: Including Observational Data

Including Observational Data

Incorporating data from various trial designs into a Mixed Treatment Comparison Model

Susanne Schmitz[†,a], Roisin Adams[b], Cathal Walsh[a,b]

Bayesian approach allows the inclusion of a wide range of data sources.
In fact:
The inclusion of **ALL** available data sources is advocated.

However:
To date, all MTC analyses are based solely on RCT evidence.

Sutton (2008): "Only including randomized evidence in a meta analysis might be a suboptimal approach."

Including Observational Data

a) Naïve Pooling

b) Inclusion as Prior Information

c) 3-level hierarchical Model

Including Observational Data

Naïve Pooling

- Treats all trial designs the same
- Cannot adjust for potential bias.
- Cannot down-weight particular designs.

Inclusion as Prior Information

prior   OBS Data   Likelihood

Posterior

Prior:
$N(\mu,\tau)$

Adjustment for bias:
- Overprecision: $N(\mu, \tau * \xi)$
- Overestimation: $N(\mu + \alpha, \tau)$

3-level hierarchical Model

Study Level   Study-Type Level   Overall Level

A vs. P₁
A vs. P₂
A vs. Pᵣ
B vs. P₁
B vs. P₃
...
B vs. Pₙ

A vs. P
A vs. B
B vs. P

A vs. P
A vs. B
B vs. P

A vs. P₂
A vs. P₃
...
A vs. Pₖ
B vs. Pₙ
B vs. P₃
...
B vs. Pⱼ

A vs. P
A vs. B
B vs. P

→ NMA model including only RCTs.

→ Same Model for OBS data.

3-level hierarchical Model

Study Level   Study-Type Level   Overall Level

→ Combine Evidence from difference designs.

Random Effects Model:

$$\left.\begin{matrix} \mu_{RCT} \\ \mu_{OBS} \end{matrix}\right\} \sim N(\mu, \tau)$$

Model accounts for between trial design heterogeneity.

3-level hierarchical Model

→ Combine Evidence from difference designs.

Adjust for Bias:

$$\mu_{RCT} \sim N(\mu, \tau)$$

$$\mu_{OBS} \sim N(\mu, \tau * \xi)$$

(Overprecision)

3-level hierarchical Model

→ Combine Evidence from difference designs.

Adjust for Bias:

$$\mu_{RCT} \sim N(\mu, \tau)$$

$$\mu_{OBS} \sim N(\mu + \alpha, \tau)$$

(Overestimation)

3-level hierarchical Model

→ Combine Evidence from difference designs.

Model allows to quantify the difference between trial designs.

NMA: Example (II)

RA Example (II)

RA Example (II)

RA Example (II)

Summary

Summary

- <u>Synthesising Evidence</u> is an integral part in assessing the efficacy of an intervention.

- <u>Meta Analysis</u> provides a tool to combine evidence from difference sources.

- <u>NMA</u> is useful for comparing treatments, when head to head evidence is not sufficient.

  ⚠ It is important to **be aware of the assumptions** made.

  ⚠ **Different input data give different results.**

  ⚠ **Choice of methodology impacts the results**.

Thank you!
Questions?

Update on Pharmacoeconomics in the Irish Healthcare Setting

23rd- 24th March 2015

Recent cost containment initiatives and effects on state-funded drug expenditure

Susan Spillane PhD MPharm DipStat MPSI

National Centre for Pharmacoeconomics
NCPE Ireland

Presentation concepts

- Components of state-funded drug expenditure in Ireland
- Cost containment initiatives which have occurred in past and recent years
  - Industry, contractor, legislation, co-payments..
  - Focus on reference pricing
- Recent figures on state-funded drug expenditure
  - Trends in pricing, uptake, generic usage..
- Illustration of effects of reference pricing
  - Case study: statin drugs

STATE FUNDING OF PHARMACEUTICALS
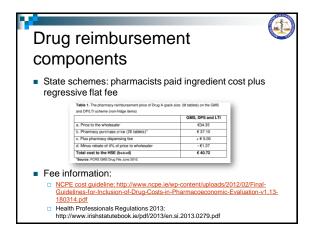
Community sector pharmaceuticals

- Privately funded non-prescription medicines
- Privately funded prescriptions
- State-provided or state-subsidised
  - DP, GMS, LTI, High-tech drugs, Methadone, Hardship scheme medicines…
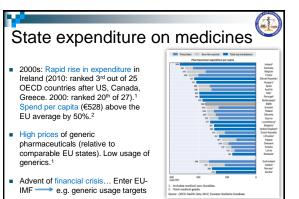
Pharmacy reimbursement schemes

- Four main schemes:
  - General Medical Services (GMS) scheme
    - 'Medical card' patients (means testing)
  - Drugs Payment (DP) scheme
    - Threshold for claims: €144 per individual/family unit per month
  - Long-term illness (LTI) scheme
    - 16 conditions covered: CF, MS, Epilepsy, Diabetes, parkinsonism…
  - High Tech Drugs (HTD) arrangements
    - Hospital-initiated drugs supplied through community pharmacies

- …Data analysis implications
  - 'Dispensing data'   prescribing data, but can make inferences..
  - If examining prescribing trends, DP scheme does not provide the 'full' picture

Drug reimbursement components

- State schemes: pharmacists paid ingredient cost plus regressive flat fee

Table 1. The pharmacy reimbursement price of Drug A (pack size: 28 tablets) on the GMS and DP/LTI scheme (non-fridge items)

	GMS, DPS and LTI
a. Price to the wholesaler	€34.35
b. Pharmacy purchase price (28 tablets)*	€ 37.10
c. Plus pharmacy dispensing fee	+ € 5.00
d. Minus rebate of 4% of price to wholesaler	- €1.37
Total cost to the HSE (b+c+d)	€ 40.72

*Source: PCRS GMS Drug File June 2010.

- Fee information:
  - NCPE cost guideline: http://www.ncpe.ie/wp-content/uploads/2012/02/Final-Guidelines-for-Inclusion-of-Drug-Costs-in-Pharmacoeconomic-Evaluation-v1.13-180314.pdf
  - Health Professionals Regulations 2013: http://www.irishstatutebook.ie/pdf/2013/en.si.2013.0279.pdf

PROMPT FOR ACTION

State expenditure on medicines

- 2000s: Rapid rise in expenditure in Ireland (2010: ranked 3rd out of 25 OECD countries after US, Canada, Greece. 2000: ranked 20th of 27).[1] Spend per capita (€528) above the EU average by 50%.[2]

- High prices of generic pharmaceuticals (relative to comparable EU states). Low usage of generics.[1]

- Advent of financial crisis… Enter EU-IMF ⟶ e.g. generic usage targets

[1] Brick A, Gorecki PK, Nolan A. Ireland: Pharmaceutical Prices, Prescribing Practices and Usage of Generics in a Comparative Context. ESRI Research Series 32. June 2013.
[2] OECD (2012), Health at a Glance: Europe 2012, OECD Publishing. http://dx.doi.org/10.1787/9789264183896-en

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COST CONTAINMENT INTERVENTIONS

Interventions 2006-2010

- IPHA agreements:
  - 2006:
    - New medicines:
      - External ref price basket increased from 5 to 9 countries
      - Formal pharmacoeconomic assessments (NCPE)
      - Ex-factory price reviews in 2008 and 2010
    - Off-patents:
      - Reduction in prices at intervals 2006-2009
  - 2010:
    - February: Additional off-patent reductions
    - December: Further price reductions and rebates for 2011

Interventions 2006-2010

- 2009 pharmacy contractor changes:
  - Dispensing fees set by statute
  - Pharmacy drug item mark-up (DPS and LTI) reduced from 50% to 20%
  - Wholesale mark-up reduced 17.66% to 10% (except controlled drug and fridge)

- 2008-2010: DP scheme threshold increases from €85 to €120

- 2010: GMS 50c Rx charge (up to €10/month)

- 2012: delisting of products (e.g. omega-3, glucosamine)

Interventions 2011-March 2015

- IPHA agreement 2013-2015:
  - June: Interim price reductions
  - Oct 2012:
    - Ex-factory prices aligned to average of 9-country basket where no generic available
    - If generic available: Prices dropped to 50% original price (in stages)

- APMI agreement 2013-2015:
  - Oct 2012
    - Generics to be ≤50% pre-patent originator price

Interventions 2011-March 2015

- 2011-2013 pharmacy contractor changes:
  - 2011: Pharmacy mark-up (DPS and LTI) reduced from 50% to 20% for non-drug items
  - 2013: Pharmacy mark-up on drug items (DPS and LTI) reduced from 20% to 0%
  - Wholesale mark-up reduced 10% to 8% (controlled drug: 17.66% to 8%; fridge: 17.66% to 12%)

- 2011-2013: DP scheme threshold increases from €120 to €144 (remains at €144 to date)

- 2013: GMS Rx charge increase to €1.50, up to €19.50/month (Jan), then €2.50, up to €25/month (Dec)

New initiatives…

- Medicines Management Programme:
  - Preferred Drugs Initiative
  - Inhaler cost guidance

- Health (Pricing and Supply of Medical Goods) Act 2013:
  - Generic Substitution
  - Reference Pricing

HSE MEDICINES MANAGEMENT PROGRAMME
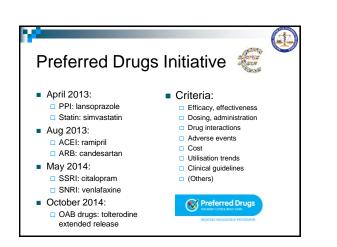
Aims of the MMP

- Enhancing evidence-based prescribing and optimising patient safety through a reduction in medication-related adverse events
- Facilitating cost-effective prescribing through initiatives targeting high cost medicines, e.g. **Preferred Drugs initiative** and Prescribing and Cost Guidance
- Focusing on **cost effectiveness** to ensure value for money in relation to all medicines
- Encouraging **generic prescribing**
- Ensuring that patients have access to essential medicines
- Supporting prescribers to prescribe safely and appropriately in a wide range of therapeutic areas through drug safety initiatives, e.g. Prescribing Tips and Tools.

www.hse.ie/yourmedicines/ *"About" section*

Preferred Drugs Initiative

- April 2013:
  - PPI: lansoprazole
  - Statin: simvastatin
- Aug 2013:
  - ACEI: ramipril
  - ARB: candesartan
- May 2014:
  - SSRI: citalopram
  - SNRI: venlafaxine
- October 2014:
  - OAB drugs: tolterodine extended release

- Criteria:
  - Efficacy, effectiveness
  - Dosing, administration
  - Drug interactions
  - Adverse events
  - Cost
  - Utilisation trends
  - Clinical guidelines
  - (Others)

Preferred Drugs
THE RIGHT CHOICE.RIGHT NOW
MEDICINES MANAGEMENT PROGRAMME

GENERIC SUBSTITUTION AND REFERENCE PRICING

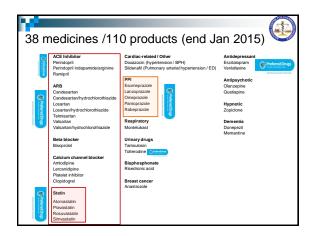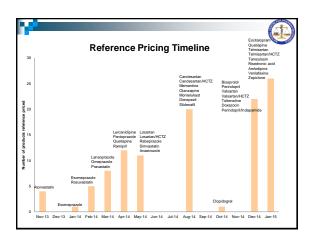## The Health (Pricing and Supply of Medical Goods) Act 2013

- Introduces a system of generic substitution and reference pricing.
  - □ Setting a common reimbursement price, or reference price, for a group of interchangeable medicines.
  - = maximum price that HSE will reimburse to pharmacies for all medicines in the group.

- First drug: atorvastatin:
  - □ Deemed interchangeable August 2013
  - □ Reference price set November 2013

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38 medicines /110 products (end Jan 2015)

ACE Inhibitor
Perindopril
Perindopril indapamide/arginine
Ramipril

ARB
Candesartan
Candesartan/hydrochlorothiazide
Losartan
Losartan/hydrochlorothiazide
Telmisartan
Valsartan
Valsartan/hydrochlorothiazide

Beta blocker
Bisoprolol

Calcium channel blocker
Amlodipine
Lercanidipine

Platelet inhibitor
Clopidogrel

Statin
Atorvastatin
Pravastatin
Rosuvastatin
Simvastatin

Cardiac-related / Other
Doxazocin (hypertension / BPH)
Sildenafil (Pulmonary arterial hypertension / ED)

PPI
Esomeprazole
Lanzoprazole
Omeprazole
Pantoprazole
Rabeprazole

Respiratory
Montelukast

Urinary drugs
Tamsulosin
Tolterodine

Bisphosphonate
Risedronic acid

Breast cancer
Anastrozole

Antidepressant
Escitalopram
Venlafaxine

Antipsychotic
Olanzepine
Quetiapine

Hypnotic
Zopiclone

Dementia
Donepezil
Memantine

Slide 1

Reference Pricing Timeline

Number of products reference priced

Nov-13 — Atorvastatin

Dec-13 — Esomeprazole

Jan-14 — Esomeprazole
Rosuvastatin

Feb-14 — Lansoprazole
Omeprazole
Pravastatin

Mar-14 — Lercanidipine
Pantoprazole
Quetiapine
Ramipril

Apr-14 — Losartan
Losartan/HCTZ
Rabeprazole
Simvastatin
Anastrozole

Aug-14 — Candesartan
Candesartan/HCTZ
Memantine
Olanzapine
Montelukast
Donepezil
Sildenafil

Oct-14 — Clopidogrel

Dec-14 — Bisoprolol
Perindopril
Valsartan
Valsartan/HCTZ
Tolterodine
Doxazocin
Perindopril/Indapamide

Jan-15 — Escitalopram
Quetiapine
Telmisartan
Telmisartan/HCTZ
Tamsulosin
Risedronic acid
Amlodipine
Venlafaxine
Zopiclone

Slide 2

More interchangeable drugs…

Ongoing
- Acetylsalicylic acid
- Metformin
- Salbutamol
- Oxycodone

- (+ ongoing additions to lists established already)

HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Completed
- Tramadol
- Diclofenac

- Capecitabine
- Temozolomide

- Fluoxetine
- Paroxetine
- Citalopram
- Sertraline
- Mirtazapine

- Risperidone

- Clarithromycin
- Co-Amoxiclav

- Alendronic acid

Slide 3

RECENT FIGURES

Recent expenditure:

- GMS, DP, LTI, High-tech. Medicines and appliances, Dec 2013 – Nov 2014:
- €1.92 billion*:
  - Ex-factory price: €1,325 billion
  - Wholesale mark-ups: €107 million
  - Pharmacy fees: €379 million
  - VAT: €115m

HSE Statement to Joint Committee on Health, 12/03/2015

Medical card (GMS scheme) holders 2010 - 2014

Number of patients holding medical cards

32% Irish population

41% Irish population

38% Irish population

80,680 fewer cards in the year 2014
(HSE Dec14 report)

2013-2014 http://www.hse.ie/performanceassurancereports/
2010-2012 PCRS communications

Number of items dispensed under the GMS scheme

Number of items dispensed

2010 2011 2012 2013 2014

GMS Ingredient Cost per Item (*2014 Provisional Data)

DPS Gross Cost per item

LTI Gross Cost per Item (*2014 Provisional Data)

http://www.hse.ie/eng/services/news/media/app.pdf

Generic and off-patent drugs as % of off-patent GMS market

% of off-patent market

Off-patent   Generic (INN/branded generic)

Proprietary, off-patent and generic items dispensed expressed as a proportion of all GMS items dispensed.

Proportion of GMS items (%)

Proprietary   Off-patent   Generic (INN/branded generic)

177

Total GMS expenditure (includes pharmacy fees)

All products
Proprietary
Off-patent
Generic branded
Generic INN

CASE STUDY: STATINS

Total expenditure on statins (GMS +DP/LTI)

All statins
(fitted line)

Overall patient numbers..

Number of patients receiving statins

Total expenditure on statins (GMS +DP/LTI)

Mean expenditure per patient

Number of patients on each PPI (GMS + DPS/LTI) pre/post April 2013

Significant upwards trend in simvastatin April – August 2013: APC= +2.28%, p<0.05
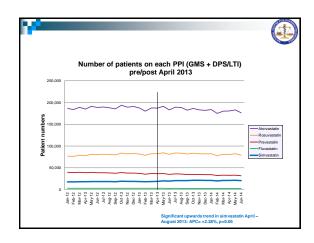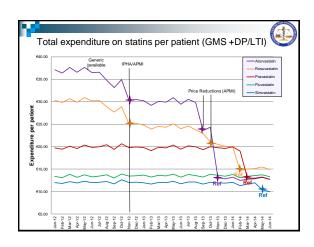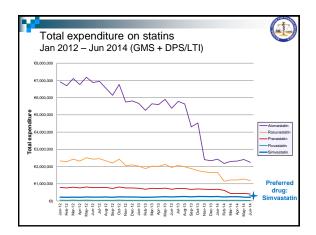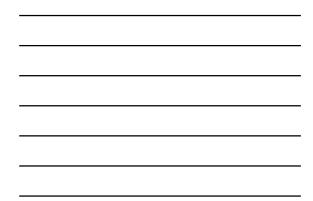
180

Overall summary

- Many multi-faceted cost containment initiatives have been put in place.
  - Aim: manage increasing expenditure within the GMS/DP/LTI schemes while minimising impact on patient care.
  - Types: Industry agreements, legislative changes, changes for contractors, HSE initiatives to promote cost-effective prescribing.

- Analysis of PCRS dispensing claims data, particularly the GMS database, provides information on the success of such initiatives.

- Total expenditure has remained stable, or fallen, against a backdrop of an increasing claimant population.

- Generic substitution has led to a sharp increase in the proportion of the off-patent market held by INN/branded generics.

- Reference pricing has led to significant reductions in total expenditure within high volume drug classes.

Further initiatives?

- Further roll-out of reference pricing in 2015…

- Introduction of prescribing incentives?

- Compulsory INN prescribing, as recommended by the Troika?
  - Medicinal Products (Prescription and Control of Supply) (Amendment No.2) Regulations 2014 : Compulsory INN prescribing as part of cross-border directive

- Next big challenge?: High-tech drugs….

Useful sources of information: products

- List of items evaluated by NCPE:
  - http://www.ncpe.ie/pharmacoeconomic-evaluations/all-drug/
- PCRS monthly product updates 2008-2015: prices, additions, withdrawals..
  - http://www.sspcrs.ie/libr/html/monthlyproductupdate.pdf
- Downloadable list of items reimbursed by the PCRS
  - http://www.sspcrs.ie/druglist/pub
- List of items reference priced (dates, prices)
  - http://www.hse.ie/referenceprice/

Useful sources of information: trends

- HSE monthly Performance Assurance Reports Medical card coverage
  - Numbers of items dispensed on schemes
  - http://www.hse.ie/eng/services/publications/corporate/performanceassurancereports/
- HSE monthly Management Data Reports
  - Scheme expenditure
  - http://www.hse.ie/eng/services/publications/corporate/performanceassurancereports/
- PCRS Financial and Statistical Analyses
  - 2005-2012. 'Top 100' items.
  - http://www.hse.ie/eng/Staff/PCRS/PCRS_Publications/Primary_Care_Reimbursement_Service.html
- NCPE drug utilisation reports
  - Generic usage, overall and for some individual drugs.
  - http://www.ncpe.ie/research/drug-utilisation/generic-drug-utisation/

Useful sources of information: policy changes

- (pre 2012) Paul K. Gorecki, Anne Nolan, Aoife Brick, Sean Lyons. Pharmaceuticals Delivery in Ireland. Getting a Bigger Bang for the Buck. ESRI Research Series Number 24, January 2012. Available at: https://www.esri.ie/publications/

- (2006-2015): HSE Statement to Joint Committee on Health, 12th March 2015
  - Appendix includes summary of interventions
  - http://www.hse.ie/eng/services/news/media/pressrel/statemarch15.html

Additional reading

- Aoife Brick, Paul K. Gorecki, Sean Lyons. Ireland: Pharmaceutical Prices, Prescribing Practices and Usage of Generics in a Comparative Context. ESRI Research Series Number 32, June 2013. Available at: https://www.esri.ie/publications/
- Aoife Brick, Paul K. Gorecki, Anne Nolan. Usage of Generics in Ireland: Recent trends and policy developments. Journal of Generic Medicines, 2013 Vol. 10(2) 72-85.
- Valerie Walshe. Community drug expenditure and recent cost containment measures. Irish Medical Journal, February 2013.
- Statutory Instrument No. 279/2013 - Health Professionals (Reduction of Payments to Community Pharmacy Contractors) Regulations 2013. Available at: http://www.irishstatutebook.ie/2013/en/si/0279.html
- Barry M, Usher C, Tilson L. Public Drug Expenditure in the Republic of Ireland. Expert Review of Pharmacoeconomics & Outcomes Research, June 2010, Vol. 10, No. 3 : Pages 239-245.
- Joint Department of Health and Children/Health Service Executive working group. Proposed Model for Reference Pricing and Generic Substitution, 2010. Available at: http://health.gov.ie/publications-research/publications/2010/
- Barry M et al. Economies in Drug Usage in the Irish Healthcare setting. 2009. Available at: http://health.gov.ie/publications-research/publications/2009/

Thank you!

- *Please feel free to ask a question or to offer comments.*

Patient registries – examples using the CF registry of Ireland and the ICORN HCV treatment registry

Aisling O'Leary and Abaigeal Jackson
24th March 2015

National Centre for
Pharmacoeconomics
NCPE Ireland

Outline

- General overview of patient registries

- Focus on the Cystic Fibrosis Registry of Ireland and outcomes

- Design, operation of and outcomes from the Irish Hepatitis C Outcomes and Research Network - ICORN Treatment Registry

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Patient registry – a definition

- *'a patient registry is an organised system that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and that serves a predetermined scientific, clinical, or policy purpose(s). The registry database is the file (or files) derived from the registry'*
  - *Glicklich AHRQ*

Outcomes from patient registries

- Provide a real-world view of clinical practice

Purposes of patient registries:
- To describe the natural history of disease

- To determine clinical and/or cost-effectiveness

- To assess safety and harm

- To measure or improve quality of care

Effective Health Care Program

Volume 1

Registries for Evaluating Patient Outcomes: A User's Guide

Third Edition
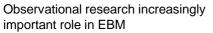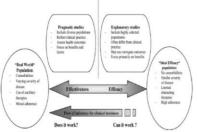
Patient registry outcomes for key stakeholders

- Clinicians
  - Real-world overview of disease, current treatment practices & clinical outcomes
- Institution
  - Degree of adherence to evidence-based practice/guidelines
- Patients
  - Increase understanding of natural history, contribute to development of treatment guidelines and facilitate research
- Payer's perspective
  - Actual use of procedures, devices or treatments in practice & effectiveness in different populations
- Regulatory perspective
  - Post-approval studies e.g. evaluation of safety signals

Observational clinical research and patient registries

- Registries essentially observational cohort studies

- Well-designed observational research is an important component of the evidence pyramid

- Patient registries & observational studies collect, collate & analyse outcome data
  - Generalisability increased, increased representativeness of outcomes as modified outwith the trial setting

- Useful when RCTs not feasible or unethical

- Often lead to additional studies

Observational research increasingly important role in EBM
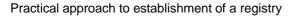
Types of registries & associated outcomes

- Disease or condition registries – profile of patients, treatments, outcomes e.g. post-approval studies

- Product registries – clinical, safety, comparative effectiveness, cost-effectiveness

- Health services registries - evaluation of processes & outcomes of care or quality assessment measurement purposes

- Registries for policy purposes
  - Coverage with evidence development (CED)

Approach to establishment of a registry

- Rooted in good clinical research practice
- Development of research protocol – define purpose
  - Research question(s)
    - Primary & secondary outcomes
  - Choice of study design
  - Size and duration
  - Internal and external validity (sources of bias)
- Ethical issues
  - Ethical approval
- Data management and analysis
  - Issues particularly pertaining to observational research

HANDBOOK FOR GOOD CLINICAL RESEARCH PRACTICE (GCP)
GUIDANCE FOR IMPLEMENTATION

Practical approach to establishment of a registry

- Registry team
  - Governance and oversight plan (SAC)
  - Development of a project plan

- Identification of key stakeholders

- Assessment of feasibility
  - Site support, data collection issues

- Operational considerations
  - Staff resources, financial

Data elements – data, what data?

- Only collect the minimal dataset that will answer research question(s)

- Identification of domains that will fulfil registry purpose

- Selection of data elements

- Must be consensus among key stakeholders

- Leads to development of study tools

- Procedures for data collection and timing of collection

Bayes

Patient registries and ethical issues

- Adherence to ethical principles of:
  - Respect for persons as autonomous agents
    - Patient consent, data confidentiality

  - Beneficence
    - Ensure study is worth while (not futile)

  - Justice
    - Use of ethical analyses

UKRIO UK Research Integrity Office

Data management considerations

- Biostatistical input

- Guidelines for data management - SoPs
  - ☐ Handling missing data
  - ☐ Invalid entries etc.
  - ☐ Quality control and data cleaning
  - ☐ Data tracking
  - ☐ Coding data

- Storing and securing data

Data analysis

- Descriptive

- Analytical

- N.B. Need to address issue of confounding
  - ☐ Stratified analysis
  - ☐ Multivariate analysis
  - ☐ Sensitivity analysis
  - ☐ Use of propensity scoring

The growth of registries and publications

Examples of patient registries

- Broad range across:
  - Acute and chronic illnesses
  - Medical devices
  - Surgical interventions

- Varying study designs

NARC*MS

EU.B.I.R.*D

DREAM

NJR National Joint Registry
www.njrcentre.org.uk
Working for patients, driving forward quality

Patient registries for the evaluation of health outcomes

Abi Jackson, PhD.
CFRI Research Fellow
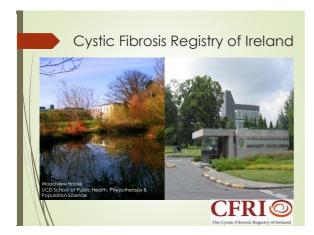
CFRI

Outline

- What is the Cystic Fibrosis Registry of Ireland (CFRI)?
- What is cystic fibrosis?
- CFRI outcome measures
- Outcomes research
  - Survival
  - Lung function
  - Healthcare provider (HSE) direct medical costs
  - Phase IV pharmacovigilance:– the Kalydeco® experience

CFRI

Cystic Fibrosis Registry of Ireland

Woodview House
UCD School of Public Health, Physiotherapy &
Population Science

CFRI
The Cystic Fibrosis Registry of Ireland
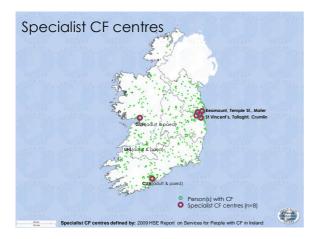
CFRI functions

- Mission statement: "…[the CFRI] will endeavour to collect and analyse information relating to CF in order to improve the quality of care for all of the people with CF in the Republic of Ireland."
- Established 2002
- An independent organisation
- Core funding c/o HSE Service Level Agreement
- Three full-time and one part-time staff member
- Managed by an Executive Committee:
  - Irish paediatric and adult Respiratory Consultants
  - Multi-disciplinary CF care team representatives
  - Patient representatives

CFRI
The Cystic Fibrosis Registry of Ireland

Specialist CF centres

Beamount, Temple St., Mater
St Vincent's, Tallaght, Crumlin

GUH (adult & paed)

UHL (adult & paed)

CUH (adult & paed)

- Person(s) with CF
- Specialist CF centres (n=8)

Specialist CF centres defined by: 2009 HSE Report on Services for People with CF in Ireland
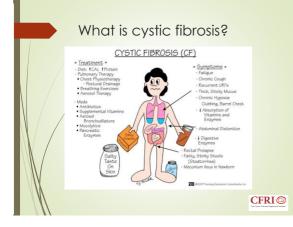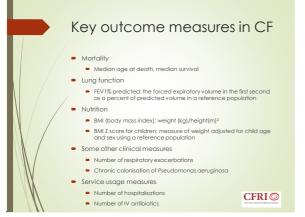
What is cystic fibrosis?

- an inherited, life-limiting condition that affects breathing, digestion and reproduction
- there is no cure
- becomes more severe with age
- symptoms and severity of CF vary from person to person
- life expectancy has increased over the past 20 years
- median survival is now approximately 40 years

CFRI

What is cystic fibrosis?

CFRI

Key outcome measures in CF

- Mortality
  - Median age at death, median survival
- Lung function
  - FEV1% predicted: the forced expiratory volume in the first second as a percent of predicted volume in a reference population
- Nutrition
  - BMI (body mass index): weight (kg)/height(m)²
  - BMI Z score for children: measure of weight adjusted for child age and sex using a reference population
- Some other clinical measures
  - Number of respiratory exacerbations
  - Chronic colonisation of *Pseudomonas aeruginosa*
- Service usage measures
  - Number of hospitalisations
  - Number of IV antibiotics

CFRI

Outcomes research

- Routine data reporting
  - CFRI Annual Reports (2002-2013)
  - European CF Society Patient Registry
- Ad-hoc data reporting
  - Department of Health, HSE
  - Health technology assessment (HTA) process
- Research projects
  - CF survival
  - Health service usage and costs
  - Phase IV pharmacovigilance
    - European Medicines Agency (EMA) requirements

Sources of CF outcome measures

Outcome 1: CF survival

	Predicted median survival (years) for persons with CF surviving their first birthday		
	Republic of Ireland	United States	Difference
Births 1980-84			
Male	32.3 years	37.8 years	-5.5 years
Female	24.7 years	31.5 years	-6.8 years
Births 1985-94			
Male	51.1 years	50.9 years	+0.2 years
Female	39 years	42.4 years	-3.4 years

Source: Jackson et al. Thorax, 2011;66;p674-679.

Outcome 2: Lung function

Source: Cystic Fibrosis Registry of Ireland Annual Report 2013

Outcome 3: Healthcare costs

- Direct costs include:
  - Hospitalisations
  - Maintenance therapies
    - Antibiotics
    - Beta-agonists
    - Mucolytics
    - Pancreatic enzymes

	2011*
Cost (€)	n=854
Mean	23,800
Median	14,600
FEV1% (≥6 yrs)	n=718
Severe (<40%)	62,200
Moderate (40-69%)	33,600
Mild (≥70%)	16,600

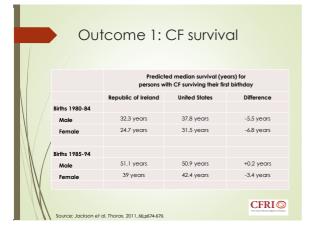*Provisional estimates

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Outcome 4: Kalydeco®

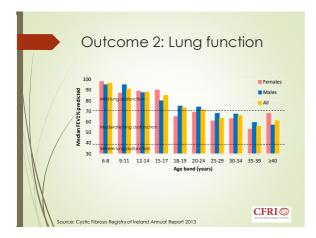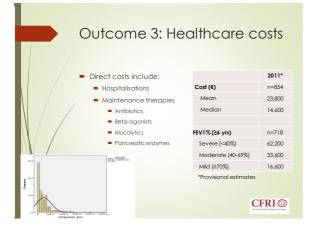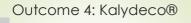- Developed by Vertex Pharmaceuticals Inc in conjunction with the Cystic Fibrosis Foundation
- One of the most expensive drugs (>€200k pa per patient)
- A drug approved for 4-5% of CF patients with the G551D genotype
- G551D is characterized by a dysfunctional CFTR protein on the cell surface
- Improves the transport of chloride through the ion channel
- Treats the underlying cause rather than the symptoms of the disease

Outcome 4: Kalydeco®

- Phase IV pharmacovigilance
  - Evaluate the long-term safety of ivacaftor (Kalydeco®) in the post-authorisation phase (effectiveness)
  - Separate ivacaftor registry would be burdensome to patients and staff at CF care centres
  - Work with the patient registries worldwide
  - Objectives
    - Pulmonary exacerbations: compare incidence in ivacaftor and comparator cohort
    - Adverse drug reactions: compare incidence in ivacaftor and comparator cohort
    - Serious adverse events and adverse events leading to withdrawal of ivacaftor: compare incidence in ivacaftor and comparator cohort

CFRI
The Cystic Fibrosis Registry of Ireland

Summary

- Registries offer an independent, valid source of data
- Capture a range of outcome measures:
  - morbidities, mortality, health service usage
- Registries provide opportunities to:
  - monitor quality of healthcare services
  - monitor the effectiveness of medications post-authorisation
  - inform planning of future health services

CFRI
The Cystic Fibrosis Registry of Ireland

Thank you for your attention

E: abaigeal.jackson@ucd.ie
T: 01 – 716 3177
W: www.cfri.ie
@abaigeal_jackson

CFRI
The Cystic Fibrosis Registry of Ireland

ICORN hepatitis C outcomes registry

- Set up contingent on HTAs conducted by the NCPE in 2012
  - Era of direct-acting antiviral therapies

- Establishment of Irish Hepatitis C Outcomes and Research Network (ICORN)

- Aim to develop a national registry of patients with HCV infection on treatment with DAA triple therapies

- Prospective observational longitudinal outcomes study design
  - Formal research protocol
  - Ethical approval from SJH/Tallaght REC
  - Patients consented for participation

ICORN

Outcomes assessed

- Primary end-points
  - Clinical response/cure (virus eradication - SVR)
  - Stratified according to baseline profile

- Secondary end-points
  - Viral response at different time points
  - On treatment virological failure
  - Relapse rates
  - Adverse events
  - Adherence to complex decision rules
  - Analysis of premature discontinuation

ICORN

Participating centres

Galway University Hospital

Cork University Hospital

Dublin:
1. SVUH
2. BEU
3. SJH - Hepatology & ID
4. MMUH – Hepatology & ID

St. Luke's Hospital, Kilkenny

ICORN

Development of the registry

- Selection of outcome data variables
  - ICORN clinicians

- Hosting and web tool development
  - Dublin Centre for Clinical Research
  - Attempted to embed decision rules

- Site engagement

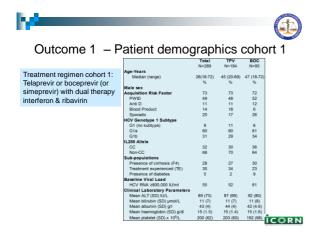- Data collection

- Data collation

- Quality control and analysis

Data sources

- Data variables
  - Baseline & longitudinal

- CRF (paper)
- Chart review – extraction
- Data input to registry
- Validation sources

Operational issues

Outcome 1 – Patient demographics cohort 1

Treatment regimen cohort 1: Telaprevir or boceprevir (or simeprevir) with dual therapy interferon & ribavirin

	Total N=289	TPV N=194	BOC N=95
Age-Years			
Median (range)	26(18-72)	45 (20-69)	47 (18-72)
	%	%	%
Male sex	73	73	72
Acquisition Risk Factor			
PWID	49	48	52
Anti D	11	11	12
Blood Product	14	18	6
Sporadic	20	17	26
HCV Genotype 1 Subtype			
G1 (no subtype)	9	11	6
G1a	60	60	61
G1b	31	29	34
IL288 Allele			
CC	32	30	36
Non-CC	68	70	64
Sub-populations			
Presence of cirrhosis (F4)	28	27	30
Treatment experienced (TE)	30	34	23
Presence of diabetes	5	2	9
Baseline Viral Load			
HCV RNA ≥800,000 IU/ml	55	52	61
Clinical Laboratory Parameters			
Mean ALT (SD) IU/L	89 (73)	87 (69)	92 (80)
Mean bilirubin (SD) µmol/L	11 (7)	11 (7)	11 (8)
Mean albumin (SD) g/l	43 (4)	44 (4)	42 (4.6)
Mean haemoglobin (SD) g/dl	15 (1.5)	15 (1.4)	15 (1.6)
Mean platelet (SD) x 10^9/L	200 (62)	203 (60)	192 (68)

Outcome 2 – Clinical outcomes cohort 1

- Response
  - Rapid viral response (RVR)
  - Early viral response (EVR)
  - Extended viral response (eRVR)
  - SVR

- Relapse rates

- Adverse events

- Analysis of premature discontinuation

ICORN

Outcome 2 – Micro-costing study cohort 1

- Direct costs:
  - OPD attendances
  - Laboratory/diagnostic investigations
  - Patient admissions
  - Management of AEs
  - Drug costs
  - Staff costs

ICORN

Additional studies associated with registry

- Two expanded access programmes facilitated through the ICORN registry (with PCRS)
  - Cohort 2 – Sofosbuvir + ledipasvir + ribavirin in patients with Child-Pugh B/C or decompensated liver disease
  - Cohort 3 – Paritaprevir (boosted with ritonavir), ombitasvir plus dasabuvir ± ribavirin
  - Outcomes: Clinical, safety

- Practical contribution of the registry & ICORN
  - Profiling of patients nationally pre-treatment
  - Development of protocols for sites
  - Facilitating sharing of information – teleconferences, drug queries etc.

ICORN

On-going and proposed research studies

- Collaborative studies with other members of ICORN/international researchers

- Model of care study – Project-ECHO
  - Pilot commencing March 2015

- Addressing pharmacovigilance aspect of registry

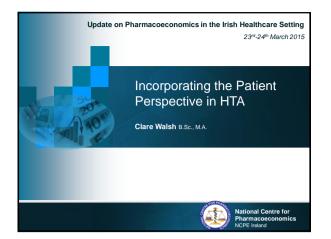- Quality improvement studies

- Qualitative studies

ICORN

Summary

- HCV registry provides important outcome data on expensive treatments

- Key is the multi-site co-operation and support of clinicians, nursing staff, pharmacists and others

- Requires additional resources at a more formal level as workload increases

- Results of research disseminated through national & international conferences and biomedical literature

- Rich and valuable data for clinicians, allied healthcare professionals, pharmacists and policy makers

Thank you. aoleary?@stjames.ie

Update on Pharmacoeconomics in the Irish Healthcare Setting

23rd-24th March 2015

Incorporating the Patient Perspective in HTA

Clare Walsh B.Sc., M.A.

National Centre for
Pharmacoeconomics
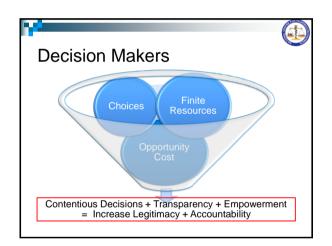NCPE Ireland

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Outline

- Why/Rationale for PI in HTA process
- Definition of 'The Problem'
- Introduction to Current Research
- Key Concepts of PI
    - Three W's (and a H)
    - Evaluation Challenges
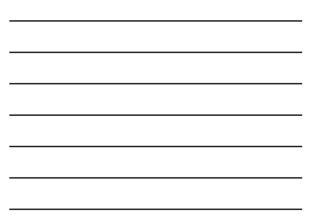- Future Research - Framework

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Why & Rational for PI in HTA

- Broadening of scope
- Defines a role for the patient as an 'expert witness'
- Unique insight to living with an illness
- Rationing Decisions reflect patient/public values

Theorised Goals for PPI in HTA

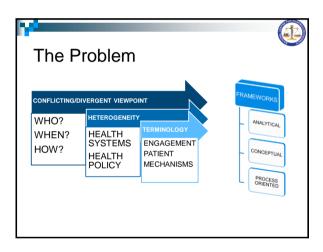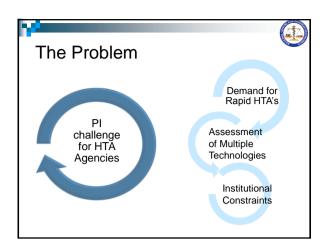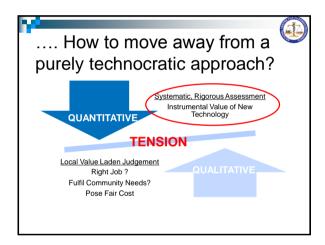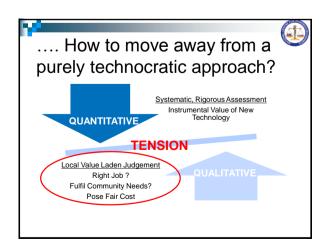|	
Democratic	Informed, Transparent, Accountable, Legitimate Decisions
Scientific	Promoting more comprehensive science of HTA
Instrumental	Making better quality decisions across all stages of HTA
Developmental	Increasing public understanding about health technologies and HTA

Decision Makers

Choices
Finite Resources
Opportunity Cost

Contentious Decisions + Transparency + Empowerment = Increase Legitimacy + Accountability

Opportunity Cost

A NEW LIVER FOR MARC WILL COST THE NHS £73,000

Opportunity Cost

£73,000
IS THE SAME PRICE AS..

A NURSE'S SALARY FOR 2 YEARS

9 HIP REPLACEMENTS

40 HOSPITAL BEDS FOR A WEEK

What would you decide

The Problem

CONFLICTING/DIVERGENT VIEWPOINT

WHO?
WHEN?
HOW?

HETEROGENEITY

HEALTH SYSTEMS

HEALTH POLICY

TERMINOLOGY

ENGAGEMENT
PATIENT
MECHANISMS

FRAMEWORKS

ANALYTICAL

CONCEPTUAL

PROCESS ORIENTED

Move from theory to practice

Available online at www.sciencedirect.com

ScienceDirect

HEALTH POLICY

ELSEVIER

Health Policy 82 (2007) 37–50

www.elsevier.com/locate/healthpol

Bringing 'the public' into health technology assessment and coverage policy decisions: From principles to practice

Julia Abelson [a,*], Mita Giacomini [a,1],
Pascale Lehoux [b,2], Francois-Pierre Gauvin [a,3]

[a] Department of Clinical Epidemiology and Biostatistics, Centre for Health Economics and Policy Analysis,
McMaster University, Health Sciences Centre, Hamilton Ontario, Canada L8N 3Z5
[b] Département d'administration de la santé, Université de Montréal, CP 6128Succ.
Centre-ville, Bureau 6097, Montréal, Que., Canada H3C 3J7

The Problem

- PI challenge for HTA Agencies
- Demand for Rapid HTA's
- Assessment of Multiple Technologies
- Institutional Constraints

…. How to move away from a purely technocratic approach?

QUANTITATIVE

Systematic, Rigorous Assessment
Instrumental Value of New Technology

TENSION

Local Value Laden Judgement
Right Job ?
Fulfil Community Needs?
Pose Fair Cost

QUALITATIVE

…. How to move away from a purely technocratic approach?

QUANTITATIVE

Systematic, Rigorous Assessment
Instrumental Value of New Technology

TENSION

Local Value Laden Judgement
Right Job ?
Fulfil Community Needs?
Pose Fair Cost

QUALITATIVE

Current Research

- Systematic Literature Review
- Inductive & Deductive Content Analysis
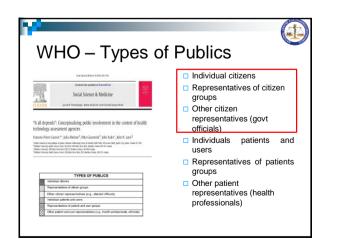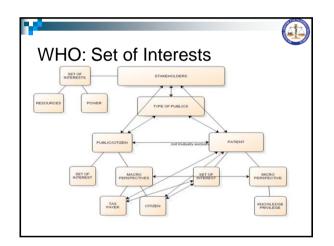- Identification and Clarification of Key Concepts

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Conceptual Flowchart

GOALS AND OBJECTIVES
Define the goals and objectives for PPI

TYPES OF PUBLICS
Define 'who' will be involved

PUBLIC   PATIENT

MACRO PERSPECTIVE   MICRO PERSPECTIVE

PREFERENCES, VALUES , KNOWLEDGE

DOMAINS & PHASES OF INVOLVEMENT
Policy Domain, Organisational Domain, Research Domain

TYPE OF INVOLVEMENT
Information, Consultation, Participation

LEVEL OF INVOLVEMENT
No control   High Control

MECHANISMS OF INVOLVEMENT

IMPACT
Macro Impact, Micro Impact, Influences

Key Concepts-
The three W's (and a H!) of PI

WHY   WHO   WHERE   HOW

Conceptual Flowchart

WHO – Types of Publics

- Individual citizens
- Representatives of citizen groups
- Other citizen representatives (govt officials)
- Individuals patients and users
- Representatives of patients groups
- Other patient representatives (health professionals)

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WHO: Set of Interests

WHO: Set of Interests

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WHO: Set of Interests

WHO – INTERNATIONAL SURVEY

WHO - Equity

- Non members of patient group/organisation
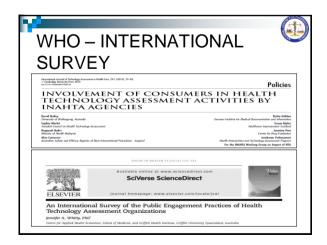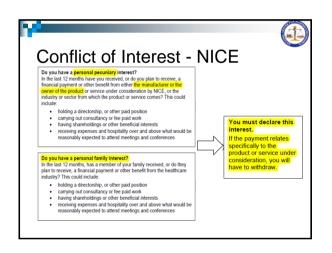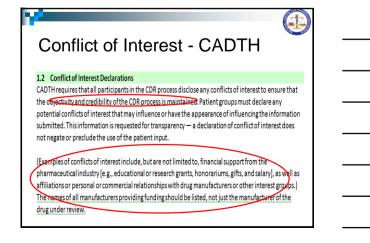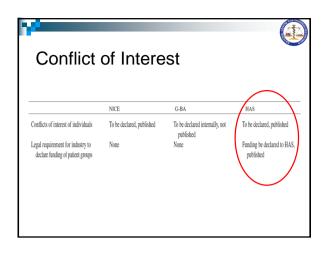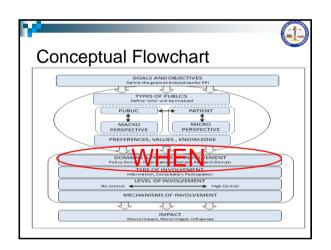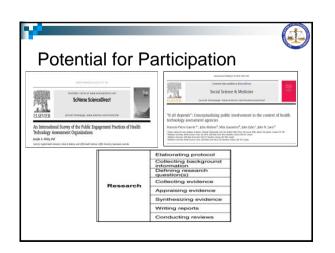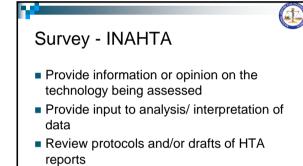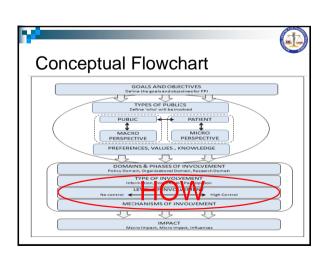- Patients with low level of health literacy

Conflict of Interest - NICE

Do you have a personal pecuniary interest?
In the last 12 months have you received, or do you plan to receive, a financial payment or other benefit from either the manufacturer or the owner of the product or service under consideration by NICE, or the industry or sector from which the product or service comes? This could include:

- holding a directorship, or other paid position
- carrying out consultancy or fee paid work
- having shareholdings or other beneficial interests
- receiving expenses and hospitality over and above what would be reasonably expected to attend meetings and conferences

You must declare this interest.
If the payment relates specifically to the product or service under consideration, you will have to withdraw.

Do you have a personal family interest?
In the last 12 months, has a member of your family received, or do they plan to receive, a financial payment or other benefit from the healthcare industry? This could include:

- holding a directorship, or other paid position
- carrying out consultancy or fee paid work
- having shareholdings or other beneficial interests
- receiving expenses and hospitality over and above what would be reasonably expected to attend meetings and conferences

Conflict of Interest - CADTH

1.2 Conflict of Interest Declarations

CADTH requires that all participants in the CDR process disclose any conflicts of interest to ensure that the objectivity and credibility of the CDR process is maintained. Patient groups must declare any potential conflicts of interest that may influence or have the appearance of influencing the information submitted. This information is requested for transparency — a declaration of conflict of interest does not negate or preclude the use of the patient input.

(Examples of conflicts of interest include, but are not limited to, financial support from the pharmaceutical industry [e.g., educational or research grants, honorariums, gifts, and salary], as well as affiliations or personal or commercial relationships with drug manufacturers or other interest groups.) The names of all manufacturers providing funding should be listed, not just the manufacturer of the drug under review.

Conflict of Interest

	NICE	G-BA	HAS
Conflicts of interest of individuals	To be declared, published	To be declared internally, not published	To be declared, published
Legal requirement for industry to declare funding of patient groups	None	None	Funding be declared to HAS, published

Conceptual Flowchart

Potential for Participation

Survey - INAHTA

Policies

INVOLVEMENT OF CONSUMERS IN HEALTH TECHNOLOGY ASSESSMENT ACTIVITIES BY INAHTA AGENCIES

David Hailey
University of Wollongong, Australia

Sophie Werkö
Swedish Council on Health Technology Assessment

Rugayah Bakri
Ministry of Health Malaysia

Alan Cameron
Australian Safety and Efficacy Register of New Interventional Procedures -Surgical

Britta Göhlen
German Institute for Medical Documentation and Information

Susan Myles
Healthcare Improvement Scotland

Jasmine Pwu
Center for Drug Evaluation

Jomkwan Yothasamut
Health Intervention and Technology Assessment Program

For the INAHTA Working Group on Impact of HTA

Survey - INAHTA

- Provide information or opinion on the technology being assessed
- Provide input to analysis/ interpretation of data
- Review protocols and/or drafts of HTA reports

Conceptual Flowchart

A LADDER OF CITIZEN PARTICIPATION

Sherry R. Arnstein

8	Citizen control	Degrees of citizen power
7	Delegated power	
6	Partnership	
5	Placation	Degrees of tokenism
4	Consultation	
3	Informing	
2	Therapy	Nonparticipation
1	Manipulation	

Tokenism

"I think he's just going through the motions."

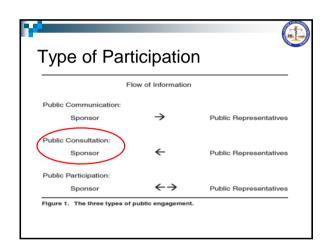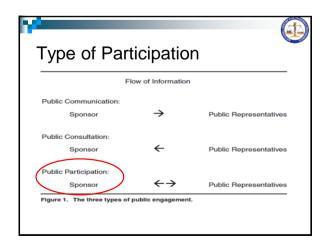Type of Participation

Flow of Information

Public Communication:
  Sponsor → Public Representatives

Public Consultation:
  Sponsor ← Public Representatives

Public Participation:
  Sponsor ←→ Public Representatives

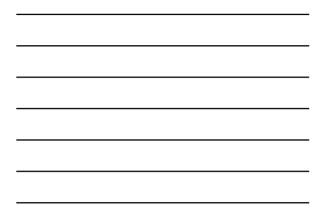Figure 1. The three types of public engagement.

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DOMAINS & PHASES OF INVOLVEMENT
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Information, Consultation, Participation

LEVEL OF INVOLVEMENT
No control ← → High Control

MECHANISMS OF INVOLVEMENT

IMPACT

Evaluation of PPI

Product of Involvement	Quality of Process
	Quality of Decisions
Process of Involvement	Was rationale & purpose achieved?
	Is the process fair? Is the process transparent?
Mechanism of Involvement	Other Methods?
	No Involvement

FUTURE RESEARCH

Comprehensive and Flexible Framework

Element 1

- Identifying clear goals for each stage of the HTA process

Comprehensive and Flexible Framework

Element 2

- Ensuring conceptual clarity and consistency in the use of public (and patient) engagement terminology

Comprehensive and Flexible Framework

Element 3

- Identifying promising public- and patient-engagement models that could be adapted to the HTA process

Comprehensive and Flexible Framework

Element 4

- Identifying strategies to support evaluation of approaches to public and patient engagement

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Summary

Summary

Summary

Summary

- Complexity Exists
- Timelines Uncertain
- Research continues

THANK YOU!