Clinical and economic consequences of non-adherence

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Background

Poor adherence is common in chronic conditions

“Drugs don't work in patients who don't take them”
— C. Everett Koop

Poor adherence

↓ clinical benefit of therapy

▪ has an impact on cost

⇒ May therefore compromise the clinical and economic effects of drug therapies
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Step 1
Clinical effects

Step 2
Societal effects

Step 3
Economic effects

Step 4
Economic value of improving adherence

Poor adherence
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Why should we assess the economic value?

- Rising demand of health care
- Budget constraints
- Rapid development of medical technological possibilities

⇒ Choices have to be made
⇒ Efficiently allocate health care resources
Health economic evaluation - Background

- Annual rise in the number of published studies
- Increased use of economic data in decisions about the reimbursement or use of health technologies
- Formal use of economic evaluations in health care decision-making (e.g. drug reimbursement)
- The fourth hurdle: efficacy, safety, quality and cost-effectiveness
Full economic evaluation

« Comparative analysis between two or more health technologies in terms of costs and effects »

Cost A → Intervention A → Outcome A
Cost B → Intervention B → Outcome B

Differences in costs ?
Relationship ?
Differences in outcome ?
Incremental cost-effectiveness ratio

\[ \text{ICER} = \frac{(C_A - C_B)}{(E_A - E_B)} = \frac{\Delta C}{\Delta E} \]

= The additional cost per Quality-Adjusted Life-Years (QALY) gained from the comparator treatment

Intervention adopted if ICER < \( \lambda \) (willingness to pay per effectiveness unit)

Commonly accepted thresholds varied between €20,000 and €80,000 per QALY gained
Cost-effectiveness plane

Cost difference

ICER = slope of the line between the estimate and the origin

Effect difference

Cost-effectiveness threshold value

REJECT

ADOPTION

Plan de coût - efficacité

B

Rejection

Adoption

Cost difference

Effect difference
The burden of osteoporosis in Europe

- 1 in 3 women and 1 in 5 men aged 50 years will have an osteoporotic fracture
- 22 millions of women and 5.6 millions of men have osteoporosis
- 3.5 millions new fractures every year (10,000 per day)
- Costs of osteoporosis: €37 billions
- 43,000 men and women death as a consequence of fractures

IOF-EFPIA, Kanis, IOF-ECCEO Congress 2012
Poor adherence with osteoporosis medications

Proportion of patients with adequate adherence (MPR≥80%) at 12 months for oral bisphosphonates

Poor adherence

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Impact of non-adherence on osteoporotic fracture risk

Ross et al. Value Health 2011;14:571-81

+28% (18%-38%)

Meta-analysis
113,376 patients

Increased risk of osteoporotic fractures

Adherent (MPR>80%) Non-adherent (MPR<80%)

Imaz et al. Osteoporos Int 2010;21:1943-51

+46% (34%-60%)

Meta-analysis
171,063 patients

Increased risk of osteoporotic fractures

Adherent (MPR>80%) Non-adherent (MPR<80%)
Impact of non-adherence on hip fracture risk

Belgian Social Security Database
Osteoporotic women ≥45
Case-control study: 901 Hip Fx - 4505 controls
Adjusted for age and duration of follow-up
Daily or Weekly ALD

Impact of non-persistence on osteoporotic fracture risk

Ross et al. Value Health 2011;14:571-81

Rabenda et al. OI 2008;19:811-18
Healthy adherer effect

= Adherence to drug treatment may be a surrogate marker for overall healthy behavior

- High adherence to placebo ↓ fracture risk by 50% (33%-78%)
  
  *Curtis et al. Med Care 2011;49:427-35*

- No evidence of healthy adherer bias in a frail cohort of seniors
  
  *Cadarette et al. Osteoporos Int 2011;22:943-54*

- Observational study → limited role of healthy adherer effect
  
  *Curtis et al. Arthritis Care Res 2012 [Epub Ahead of Print]*
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Efficacy → clinical effectiveness

SIMULATION MODEL (e.g. Markov model)

- To estimate outcomes (fractures, Quality-Adjusted Life-Years)
- Scenarios:
  1. No treatment
  2. Real-world adherence
  3. Full adherence
Incorporating adherence in modeling

**PERSISTENCE**
- At risk of discontinuation within 3 years (6, 12, 18, 24, 30 and 36 months)
- Refill gap period

**IMPLEMENTATION**
- In the subgroup of persistent patients
- High implementation (MPR≥0.8) – Low (MPR < 0.8)
- Lower efficacy for the ‘low’ group
- Drug costs adjusted by mean MPR in the group

**RE-INITIATION RATES**
- One year after stopping therapy
The societal burden of poor adherence in Ireland

Hiligsmann et al. Value Health 2012;15:604-12
The societal burden of poor adherence

- Adherence / persistence
- Refill gap period
- Treatment re-initiation

<table>
<thead>
<tr>
<th>Belgium (1)</th>
<th>Sweden (2)</th>
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<td>-61%</td>
<td>-69%</td>
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(1) Hiligsmann et al. Health Policy 2010;96:170-77
(2) Landfeldt et al. Bone 2011;48:380-88
Poor adherence

Step 1  Clinical effects

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Impact of non-adherence on cost-effectiveness

Non-adherence

↓ Clinical effectiveness

Impact on effectiveness

Impact on costs

Non-adherence

↓ Therapy cost
↑ Fracture-related costs
? Total healthcare costs

Impact on cost-effectiveness
**Impact of poor adherence on effectiveness and costs**

Hiligsmann et al. Value Health 2012;15:604-12
Impact of poor adherence on cost-effectiveness

Cost-effectiveness plane. The incremental cost-effectiveness ratio is represented by the slope of the line from the origin.

IRELAND

Budget of €20,000

Real-World: 1.68 QALYs
Full Ad: 3.15 QALYs

Hiligsmann et al. Value Health 2012;15:604-12
Impact of poor adherence on cost-effectiveness

Hiligsmann et al. Health Policy 2010;96:170-77
Impact of medication adherence on the cost-effectiveness of bisphosphonates vs. no treatment

Hiligsmann et al. Calcif Tissue Int 2010;86:202-210
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Poor adherence
Adherence intervention and cost-effectiveness

Adherence intervention

- Improved adherence
  - More doses taken
    - Fewer fractures
    - More side effects
      - More QALYs
      - Reduced fracture costs
        - Less QALYs

Cost of adherence intervention

- Increased drug & medical costs
  - Cost-Effectiveness
ICERs for adherence interventions vs usual care

No specific interventions

No studies have examined the feasibility and acceptability of a specific adherence-enhancing intervention

Hypothetical interventions

ICERs for a variety of hypothetical interventions

- **Costs**: marginal (e.g. monitoring) and one-time costs (e.g. education program)

- **Effectiveness**: improvements between 10% and 50% (adherence and/or persistence)
The economic value of improving medication adherence

WTP = €50,000 per QALY

Cost (in €) per QALY gained of hypothetical adherence-enhancing interventions according to their cost and effect on adherence

Hiligsmann et al. Value Health 2012;15:604-12
The economic value of improving medication adherence

**United States**
A hypothetical intervention with a one-time cost of $250 reducing discontinuation by 30%
ICER of $29,571 per QALY gained

**Sweden**
ICER threshold of €60,000
10% improvement → €225
30% improvement → €676
50% improvement → €1130

**Belgium**
ICER threshold of €45,000
10% improvement → €73
25% improvement → €149
50% improvement → €239

Sensitivity analyses on the effects of an intervention to improve economic outcomes

Patrick et al. JCEM 2011;96:2762-70
Discussion – Key findings

- Approximately 50% of the benefits of osteoporosis medications are lost due to poor adherence and persistence

- Poor adherence with osteoporosis medications results in a doubling of the cost per QALY gained from these medications

- Programs to improve adherence have the potential to be an attractive approach to improve the allocation of resources
Discussion – Economic

- Adherence = important determinant of cost-effectiveness analyses

⇒ Persistence and adherence should be an integral part of pharmacoeconomic analyses (1,2)

- Lack of inclusion could bias the results and lead to suboptimal allocation of resources (3)

- Importance of estimating the economic value of adherence-enhancing interventions

(1) Hughes et al. Value in Health 2007:10:498-509
(3) Hiligsmann et al. Pharmacoeconomics 2011;29:895-911
Conclusion

Non-adherence with medications

↓ clinical benefits of drugs

↓ economic value of drugs

= critical hurdle to disease management

⇒ Improving adherence is urgently needed but is a complex task

The development of effective and cost-effective interventions to support adherence should be a priority for patients, healthcare providers and the pharmaceutical company
Thank you for your attention

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