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How do we evaluate cost-effectiveness in transfusion and haemovigilance?

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Eur J Vasc Endovasc Surg (2008) **36**, 258–264

ELSEVIER

Carotid Stenting versus Carotid Endarterectomy: Evidence Basis and Cost Implications

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WHY SHOULD WE *evaluate cost-effectiveness in transfusion and haemovigilance?*

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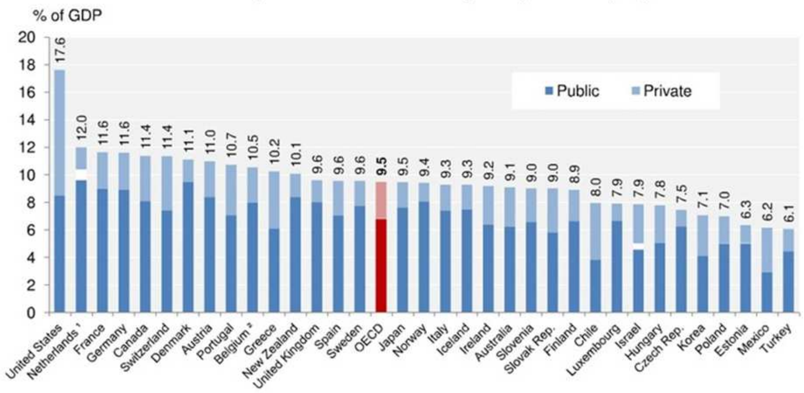
Health care expenditure

At 17.6% of GDP in 2010, US health spending is one and a half as much as any other country, and nearly twice the OECD average

Total health expenditure as a share of GDP, 2010 (or nearest year)



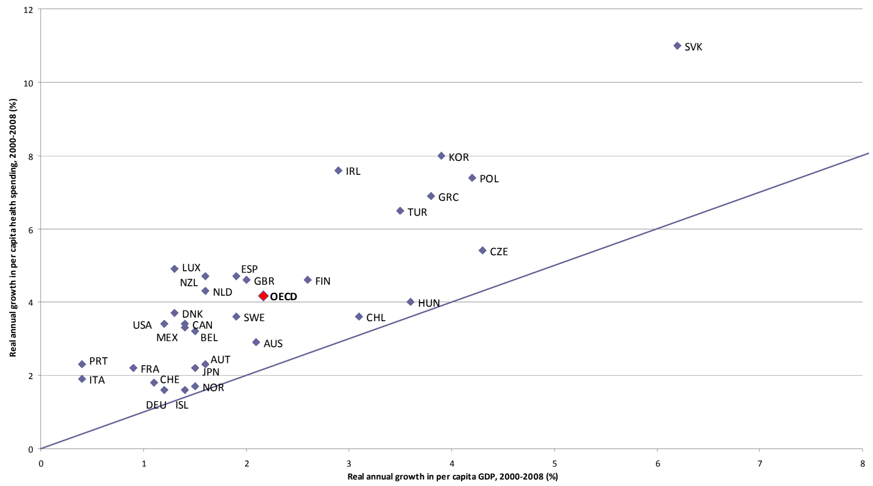
1. In the Netherlands, it is not possible to clearly distinguish the public and private share related to investments.
2. Total expenditure excluding investments.
Information on data for Israel: http://dx.doi.org/10.1787/888932315602.

Source: OECD Health Data 2012.

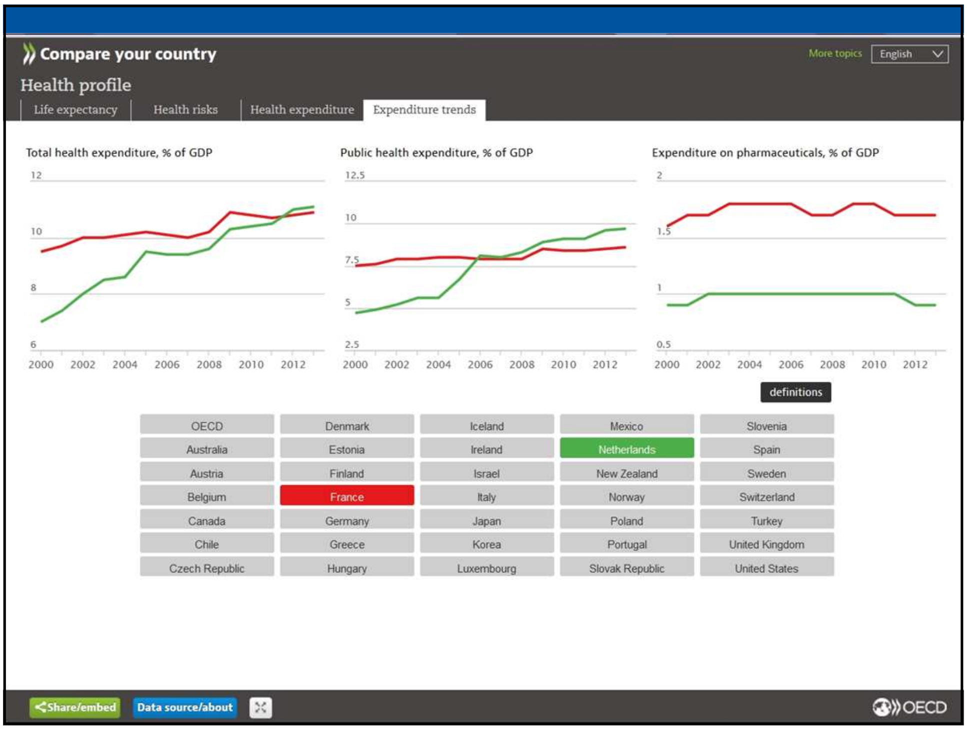
4

Disproportional growth

Figure 1. Annual growth in health expenditure and GDP, 2000-2008

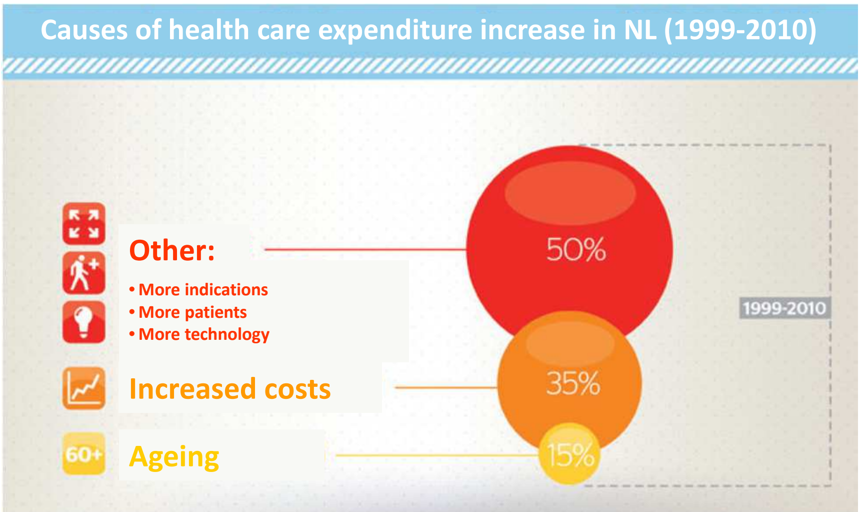


Notes: 2000-2006: Luxembourg and Portugal. 2000-2007: Australia, Denmark, Greece, Japan and Turkey. 2000-2009: Iceland.
Source: *OECD Health Data 2010*.



Causes of health care expenditure increase

Causes of health care expenditure increase



Cost-effectiveness assessment

Cost-effectiveness assessment involves an evaluation of:

1) Costs
   - Perspective (e.g. health care, societal)
   - Direct costs / Indirect costs
   - Costs inside / outside health care

2) Effects
   - Health Effects: Quality Adjusted Life Years (QALYs)

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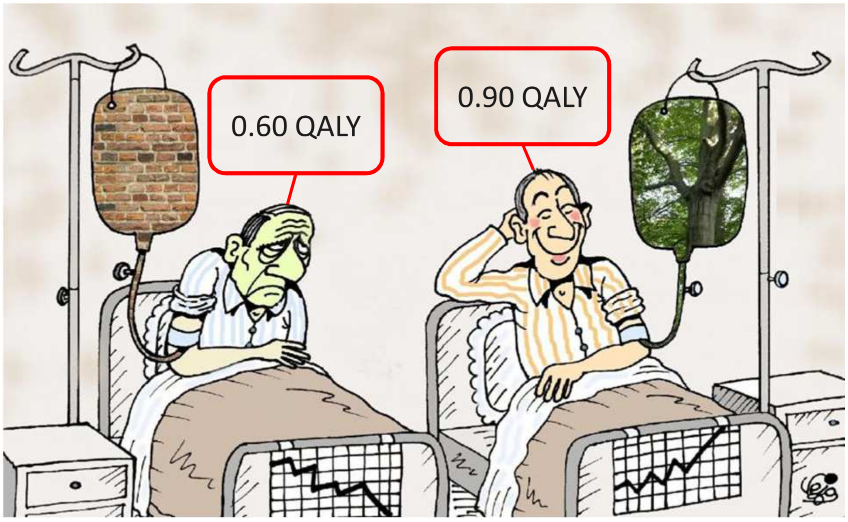
QALY assessment



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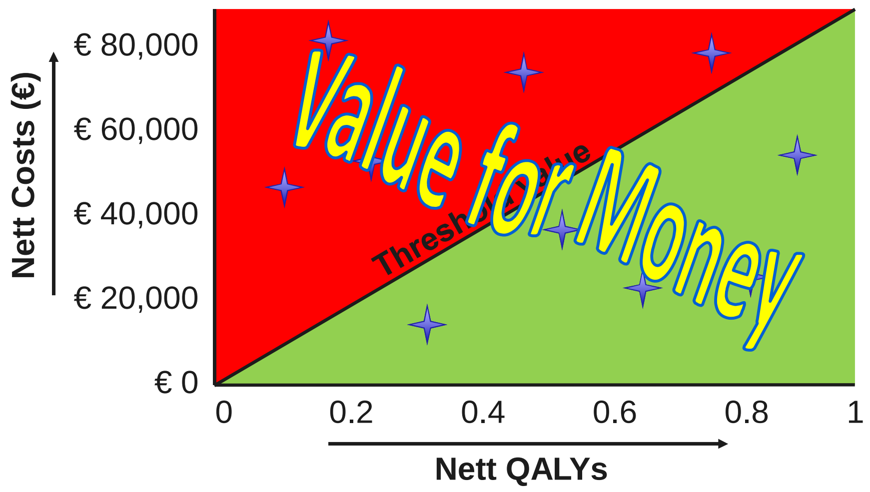
Presenting costs and effects

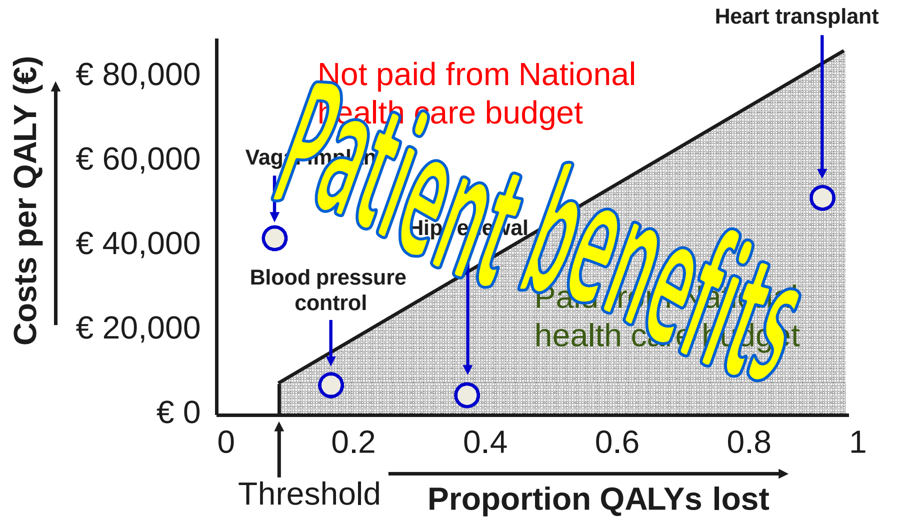


International comparison of Cost per QALY thresholds

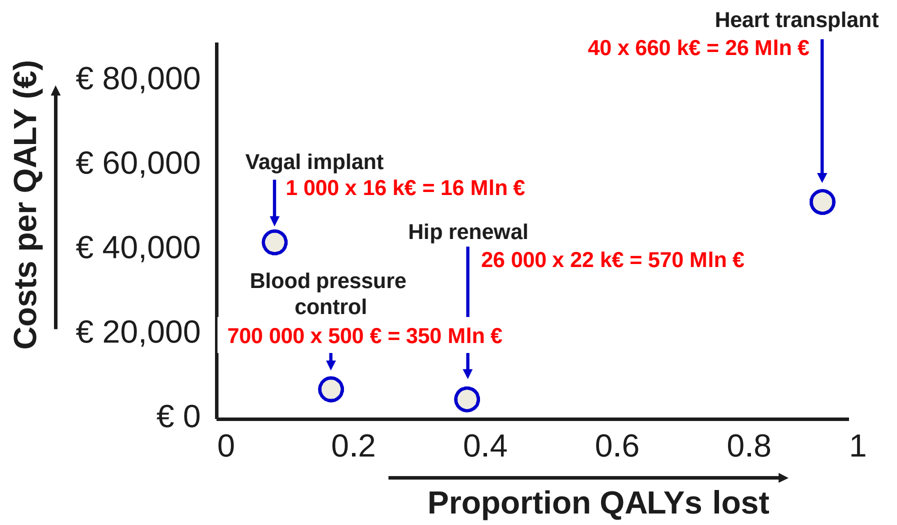
Country	Currency	Threshold local currency	Threshold in € per QALY
US	USD	50 000-100 000	36 600-73 200
Sweden	SEK	500 000	54 000
UK	GBP	30 000	44 500
Australia	AUSD	42 000-76 000	26 200-47 400
Canada	CND	20 000-100 000	13 700-68 700
The Netherlands	EURO	20 000-80 000	20 000-80 000
New Zealand	NZD	20 000	11 200

§ World Bank proposes that a QALY may cost up to 3 times the GDP, independent of prosperity of the country considered

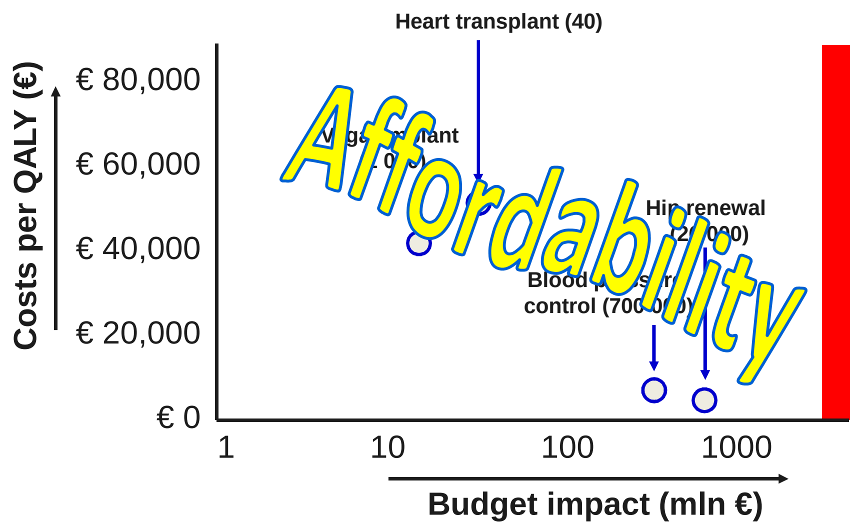
Health impact and cost per QALY



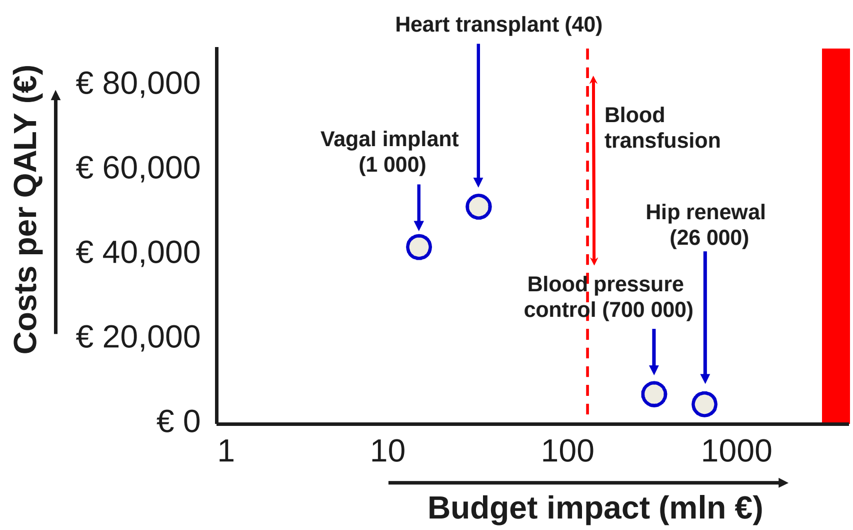
What is the financial impact



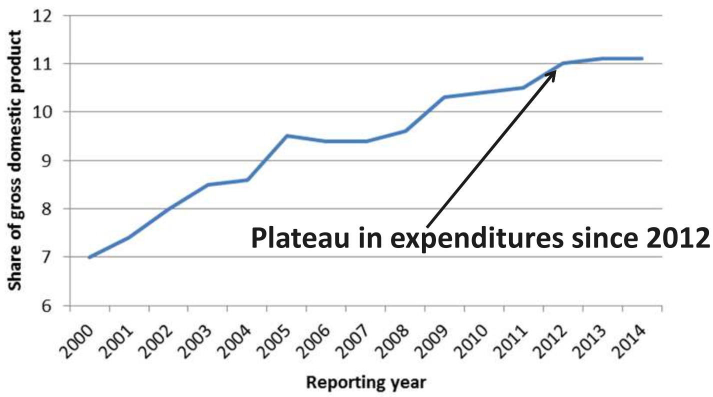
Cost-effectiveness and financial impact



Cost-effectiveness and financial impact



Halt to the increase in expenditure in NL



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Why evaluate cost-effectiveness ?

- Health economic assessment provides rational guidance for the selection of 'optimal' health care interventions, taking into account:
  - Cost-effectiveness (value for money)
  - Health impact (patient benefit)
  - Budget impact (affordability)
  - ....
- Essential for maintaining an affordable health care system
- Blood for transfusion is (perceived) a very expensive product (in the Netherlands it covers 0.5% of the total hospital health care budget)

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Cost-effectiveness assessment

Generic elements of any CE assessment:

1) Specification of the goal/setting/perspective
2) Selection of data sources
3) Outcome assessment (Costs & Effects)
4) Modelling (e.g. disease progression)
5) Time horizon
6) Discounting
7) Uncertainty / sensitivity analysis
8) Validity assessment

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Cost-effectiveness assessment

Cost-effectiveness assessment involves an evaluation of:

1) Costs
   - Perspective (e.g. health care, societal)
   - Direct costs / Indirect costs
   - Costs inside / outside health care

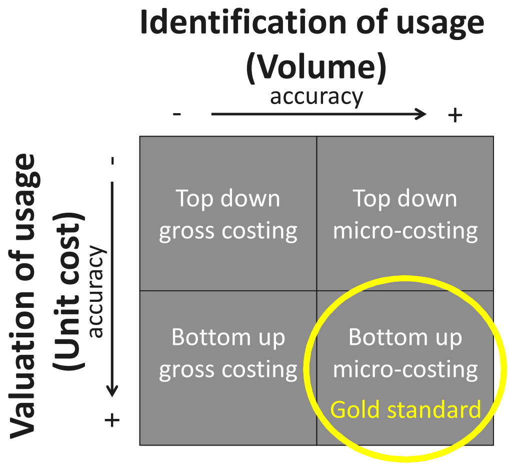
2) Effects
   - Health Effects: Quality Adjusted Life Years (QALYs)

Which cost categories to include?

Character

Domain	Direct related to treatment /disease	Indirect related to treatment /disease
Inside health care (i.e. medical costs)	Direct costs inside healthcare (i.e. direct healthcare cost)	Indirect cost inside healthcare (i.e. indirect healthcare costs)
Outside health care (i.e. non medical costs)	Direct costs outside healthcare (i.e. direct non-healthcare costs)	Indirect costs outside healthcare (i.e. indirect non-healthcare costs)

Assessment of costs



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Cost-effectiveness versus Cost-utility?

- One can define *any* outcome to express the efficiency of an intervention:
  - Cost per infection prevented (effect=infections)
  - Cost per millimetre of mercury in blood pressure reduction (effect=blood pressure)
  - Cost per death prevented (effect=mortality)

  - Cost per QALY (effect=healthy life years)

➡ Normalised health value which allows a meaningful comparison of outcomes: ***Utility***

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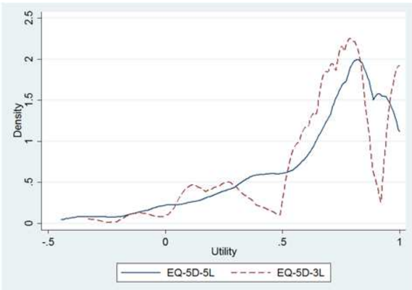
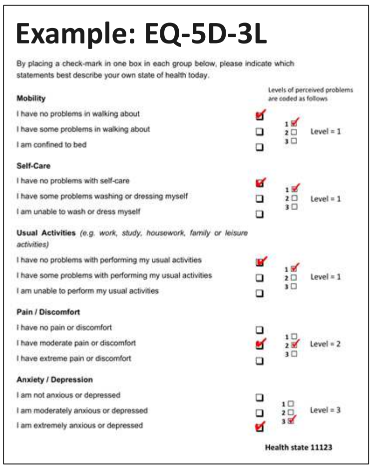
How to measure health

- Health questionnaires
  - Generic (EQ-5D, HUI, SF-6D)
  - Disease specific





Example: EQ-5D-3L

By placing a check-mark in one box in each group below, please indicate which statements best describe your own state of health today.

Levels of perceived problems are coded as follows

Mobility
I have no problems in walking about
I have some problems in walking about
I am confined to bed
Level = 1

Self-Care
I have no problems with self-care
I have some problems washing or dressing myself
I am unable to wash or dress myself
Level = 1

Usual Activities *(e.g. work, study, housework, family or leisure activities)*
I have no problems with performing my usual activities
I have some problems with performing my usual activities
I am unable to perform my usual activities
Level = 1

Pain / Discomfort
I have no pain or discomfort
I have moderate pain or discomfort
I have extreme pain or discomfort
Level = 2

Anxiety / Depression
I am not anxious or depressed
I am moderately anxious or depressed
I am extremely anxious or depressed
Level = 3

Health state 11123

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Quality of outcome data

Various data sources may be available:

- Systematic reviews
- Randomized controlled trials
- Non-randomized studies
- Health care administration data

GRADE handbook: a common, sensible and transparent approach to grading quality of evidence and strength of recommendations developed by the GRADE Working Group

GRADE

http://www.gradeworkinggroup.org/

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Impact of study design

Study design:

1) Randomized controlled trials
   – No bias (exposure is randomly distributed)
   – Limited applicability (conditioned setting)
2) Non-randomized studies / data
   – Potentially biased results (requires bias correction)
   – Broad applicability

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Assessing transfusion (complication) effects

…..is complex because:

- Transfusion is (mostly) an adjuvant therapy
  – outcomes (costs and effects) *are confounded* with the outcome of the primary intervention
  – outcomes (primary and complications) *have to be separated* from the primary intervention
- The effects of a transfusion are dependent on the primary intervention
- Transfusion exposure is variable

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Cost-effectiveness studies

- Quite some studies on the *cost* of transfusion
- Few studies on the cost-effectiveness of blood transfusion
- Few studies on the cost-effectiveness of blood transfusion complications
- Debate on the findings

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Some examples

- Age of RBCs, PLTs and FFPs in relation to transfusion complications
- Use of autologous blood transfusion
- Pre-operative transfusions for Sickle-cell patients
- Liberal vs restrictive RBC usage (cardiac / hip surgery)
- CE of screening/treatment for pathogens

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Assessment of cost of TACO

ClinicoEconomics and Outcomes Research — Dovepress
open access to scientific and medical research
Open Access Full Text Article — ORIGINAL RESEARCH

Fluid overload is associated with increases in length of stay and hospital costs: pooled analysis of data from more than 600 US hospitals

This article was published in the following Dove Press journal:
ClinicoEconomics and Outcomes Research
25 June 2013
Number of times this article has been viewed

Glenn Magee[1]
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[1]Premier Research Services, Charlotte, NC, USA; [2]CSL Behring, King of Prussia, PA, USA

Background: Fluid overload, including transfusion-associated circulatory overload (TACO), is a serious complication of fresh frozen plasma (FFP) transfusion. The incidence of fluid overload is underreported and its economic impact is unknown. An evaluation of fluid overload cases in US hospitals was performed to assess the impact of fluid overload on length and cost of hospital stay.
Study design and methods: Retrospective analysis was performed using a clinical and economic database covering >600 US hospitals. Data were collected for all inpatients discharged during 2010 who received ≥1 unit FFP during hospitalization. Incidence of fluid overload was determined through International Classification of Diagnosis (ICD-9) codes. Multivariate regression analysis was performed for primary outcome measures: hospital length of stay (LOS) and total hospital costs.
Results: Data were analyzed for 129,839 FFP-transfused patients, of whom 4,138 (3.2%) experienced fluid overload (including TACO). Multivariate analysis, adjusting for baseline characteristics, found that increased LOS and hospital costs were independently associated with fluid overload. Patients diagnosed with fluid overload had longer mean LOS (12.9 days

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Assessment of cost of TACO

Table 1 Patient characteristics

Characteristic	Fluid overload (n = 4138)	No fluid overload (n = 125,701)	P-value
Age			
Mean (SD), years	64 (17.5)	65 (19.7)	0.002[a]
<18, n (%)	99 (2.4%)	4415 (3.5%)	<0.001[b]
18 to 39, n (%)	255 (6.2%)	8209 (6.5%)	
40 to 64, n (%)	1547 (37.4%)	40,398 (32.1%)	
65 to 79, n (%)	1536 (37.1%)	42,825 (34.1%)	
≥80, n (%)	701 (16.9%)	29,854 (23.8%)	
Admission type, n (%)			<0.001[b]
Surgical	2606 (63.0%)	57,145 (45.5%)	
Medical	1532 (37.0%)	68,556 (54.5%)	
Emergency department admit, n (%)			<0.001[b]
No	3086 (74.6%)	79,728 (63.4%)	
Yes	1052 (25.4%)	45,973 (36.6%)	
Bleed status,[c] n (%)			<0.001[b]
No	3075 (74.3%)	77,729 (61.8%)	
Yes	1063 (25.7%)	47,972 (38.2%)	

Table 1 Patient characteristics

Characteristic	Fluid overload (n = 4138)	No fluid overload (n = 125,701)	P-value
Major diagnostic categories,[d,e] n (%)			<0.001[b]
Circulatory system	1650 (39.9%)	28,649 (22.8%)	
Digestive system	526 (12.7%)	22,964 (18.3%)	
Infectious and parasitic DDs	381 (9.2%)	11,171 (8.9%)	
Hepatobiliary system and pancreas	368 (8.9%)	10,419 (8.3%)	
Respiratory system	224 (5.4%)	8426 (6.7%)	
Musculoskeletal system and connective tissue	213 (5.1%)	9953 (7.9%)	
Kidney and urinary tract	169 (4.1%)	4631 (3.7%)	
Nervous system	142 (3.4%)	10,165 (8.1%)	
Diuretic use (≥1 days),[c] n (%)			<0.001[b]
No	15.0%	39.3%	
Yes	85.0%	60.7%	

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Assessment of cost of TACO

Table 3 Mean (standard deviation) length of stay and hospital costs per visit*

Outcome	Fluid overload (n = 4138)	No fluid overload (n = 125,701)	% increase	P-value
Univariate analysis				
Hospital LOS (days)	15.3 (15.1)	11.9 (18.2)	28.6%	<0.001
ICU LOS (days)	4.4 (7.9)	3.0 (7.2)	46.7%	<0.001
Total hospital cost ($)	$56,817 ($59,195)	$37,168 ($53,795)	52.9%	<0.001
Multivariate analysis				
Hospital LOS* (days)	12.9 (0.9)	10.0 (0.7)	[illegible].0%	<0.001
ICU LOS (days)	6.0 (0.8)	5.2 (0.7)	[illegible].7%	<0.001
Total hospital cost† ($)	$46,644 ($3433)	$32,582 ($2354)	[illegible].2%	<0.001

Notes: *Significant factors in the multivariate model (all significant $P < 0.001$, unless otherwise indicated): fluid overload, diuretic use; admission through ER ($P = 0.01$); two or more units of FFP; hospital bed size smaller less than 100 ($P = 0.0032$); female ($P = 0.0031$); black ($P = 0.002$), Hispanic, or other ($P = 0.003$) group than white; any region relative to West South Central except New England, West North Central, and Pacific (Mountain $P = 0.0167$); urban versus rural; bleed status; †significant factors in the multivariate model (all significant $P < 0.001$, unless otherwise indicated): fluid overload, diuretic use; admission through ER; two or more units of FFP; hospital bed size smaller than 500; black, Hispanic, or other ($P = 0.003$) group than white; any region relative to West South Central except East North Central or West North Central; bleed status.

2.9 days

14 062 UD$

Shortcomings:

- Black box
- "One size fits all" approach
- Only considering cost (duration of stay)
- Correction for clinical irrelevant variables
- No stratification for nr of transfusions

Impact → ?

Bottom-up expert elicitation approach

Transfusion-associated Circulatory overload complications	Severity grade 2, 3 or 4	Severity grade 0-1	Costs (€)
Exclusion of administrative errors (%)			
Haemolysis Investigation (%)			
Blood group serology investigation (%)			
Bacteriology (%)			
Chest X-ray (%)			
HLA investigation (%)			
Longer hospital stay (in days)			
Admission to ICU (in days)			
Extra nurse time (minutes)			
Hemovigilance co-worker time (minutes)			
Extra doctor time (minutes)			
Administration of diuretics			
Other			

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Bottom-up expert elicitation approach

Transfusion-associated Circulatory overload complications	Severity grade 2, 3 or 4	Severity grade 0-1	Costs (€)
Exclusion of administrative errors (%)	83	75	
Haemolysis Investigation (%)	27	28	
Blood group serology investigation (%)	27	28	
Bacteriology (%)	15	15	
Chest X-ray (%)	78	48	
HLA investigation (%)	6	6	
Longer hospital stay (in days)	1.0	0.0	
Admission to ICU (in days)	1.2	0.0	
Extra nurse time (minutes)	62	28	
Hemovigilance co-worker time (minutes)	57	41	
Extra doctor time (minutes)	41	17	
Administration of diuretics	100%	100%	
Other	-	-	

Bottom-up expert elicitation approach

Transfusion-associated Circulatory overlo	Severity grade 2, 3 or 4	Severity grade 0-1	Costs (€)
Exclusio	83	75	20.41
Haemol	27	28	7.64
Blood g	27	28	11.27
Bacteriology (%)	15	15	10.01
Chest X-ray (%)	78		
HLA investigation (%)	6		
Longer hospital stay (in days)	1.0		
Admission to ICU (in days)	1.2		
Extra nurse time (minutes)	62	28	32.35
Hemovigilance co-worker time (minutes)	57	41	29.50
Extra doctor time (minutes)	41	17	100.84
Administration of diuretics	100%	100%	6.78
Other	-	-	-
TOTAL Cost:	3,754.75	134.38	

Factor 1.5 less extended stay

Factor 3.4 less cost

Differences (and potential causes)

No extreme differences

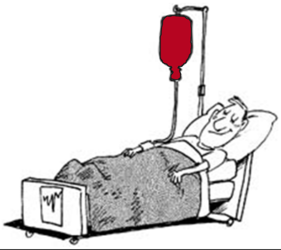
Data analysis	Expert elicitation
Unit cost for UK setting	Unit cost for Dutch setting
Overestimation LOS because limited correction 1 vs 2 or more for number of transfusions (exposure)	Underestimate because of cautious judgements by experts
	Only foreseen consequences accounted for
	Narrow coverage: view of experts of their own hospital experience only
	Highly transparent (and data are accessible)

Cost-effectiveness assessments of transfusion (complications)

- Many supporting guidelines available (even for blood transfusion: *ABO RBDM framework*)
- Take a practical approach: integrate all data available
- Perfection is the enemy of the good
- If databases are used: obtain expert (epidemiological) advice for analysis
- GRADE handbook: focus on what is critical for decision making

Take home messages

- Economic evaluations support optimizing health care expenditure
- Evaluation of adjuvant therapies -like blood transfusion- is complex
- Care comes first



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