Cost-effective treatment of breast cancer
Paris, 5/2/2016

Didier Verhoeven

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AZ Klina
voluit voor zorg

AZ Sint-Jozef Malle

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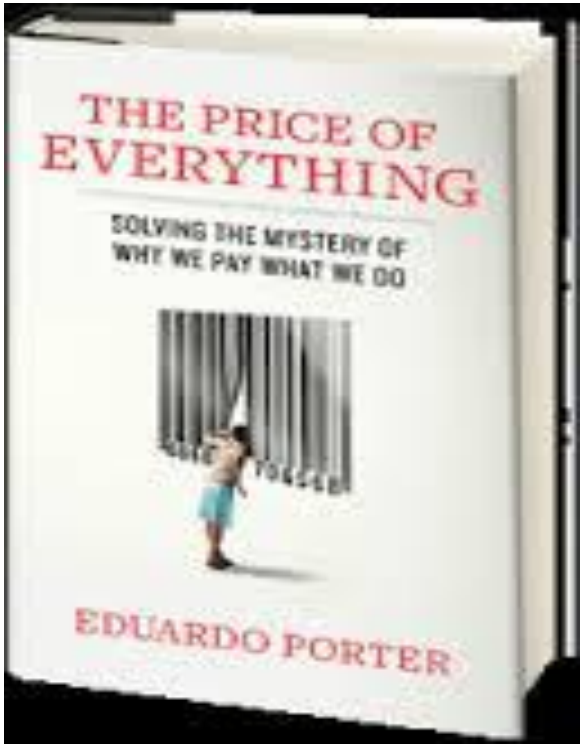
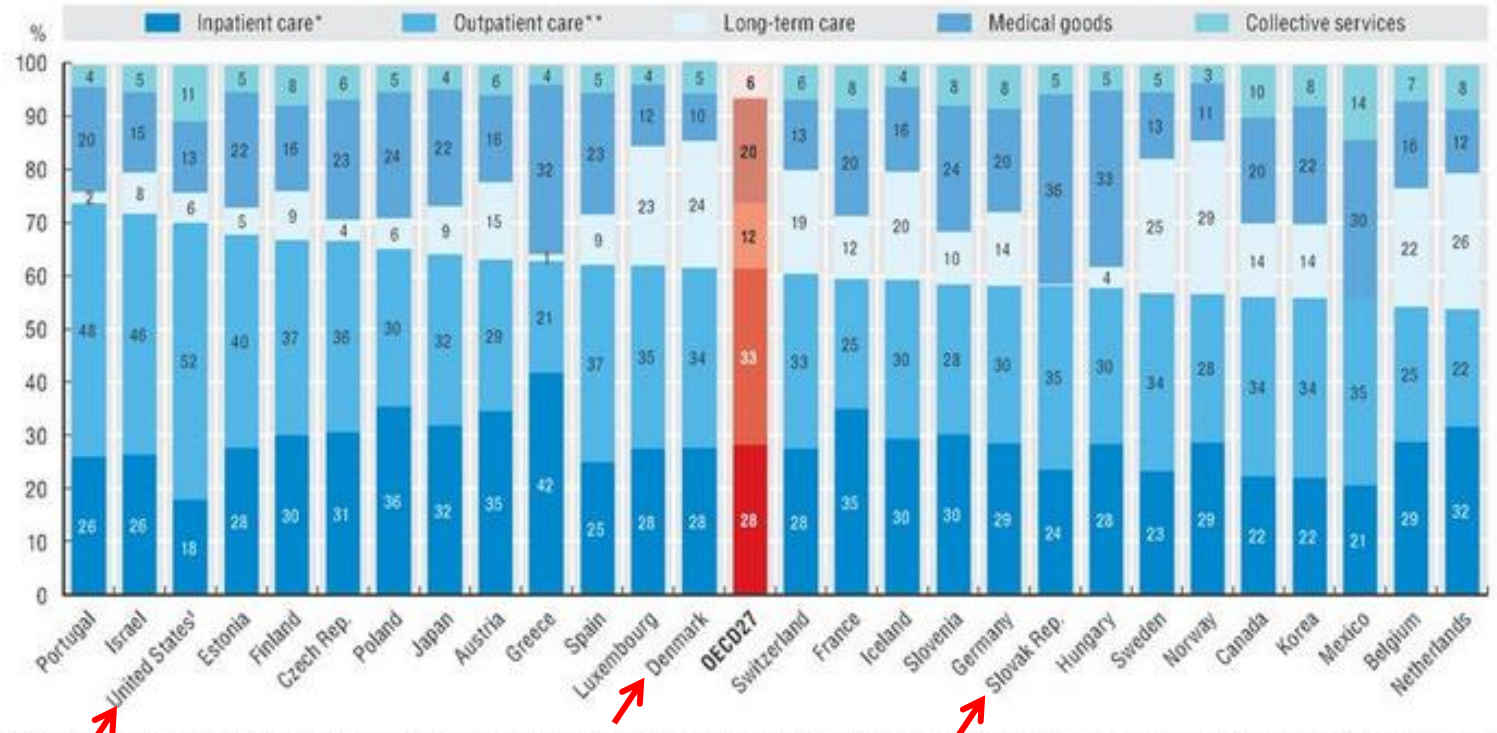
- **Price: A changing vision with an ethical dimension**
- Price and value are difficult to determine
- Medical need influences the willingness to pay
- A debate between society, authorities and pharma
- Much more than medication matters !



- The health system creates conditions for the economy to recover; spending on health is an investment
- The high cost of personalized medicine poses a serious challenge to the principle of equal access
- Effective action on prevention/early diagnosis will free up resources to improve access to high-quality care

Current health expenditure by function of health care (2013)

9.6. Current health expenditure by function of health care, 2013 (or nearest year)



Note: Countries are ranked by curative-rehabilitative care as a share of current expenditure on health. * Refers to curative-rehabilitative care in inpatient and day care settings. ** Includes home-care and ancillary services.

1. Inpatient services provided by independent billing physicians are included in outpatient care for the United States.

Source: OECD Health Statistics 2015, *http://dx.doi.org/10.1787/health-data-en.*

StatLink http://dx.doi.org/10.1787/888933281277

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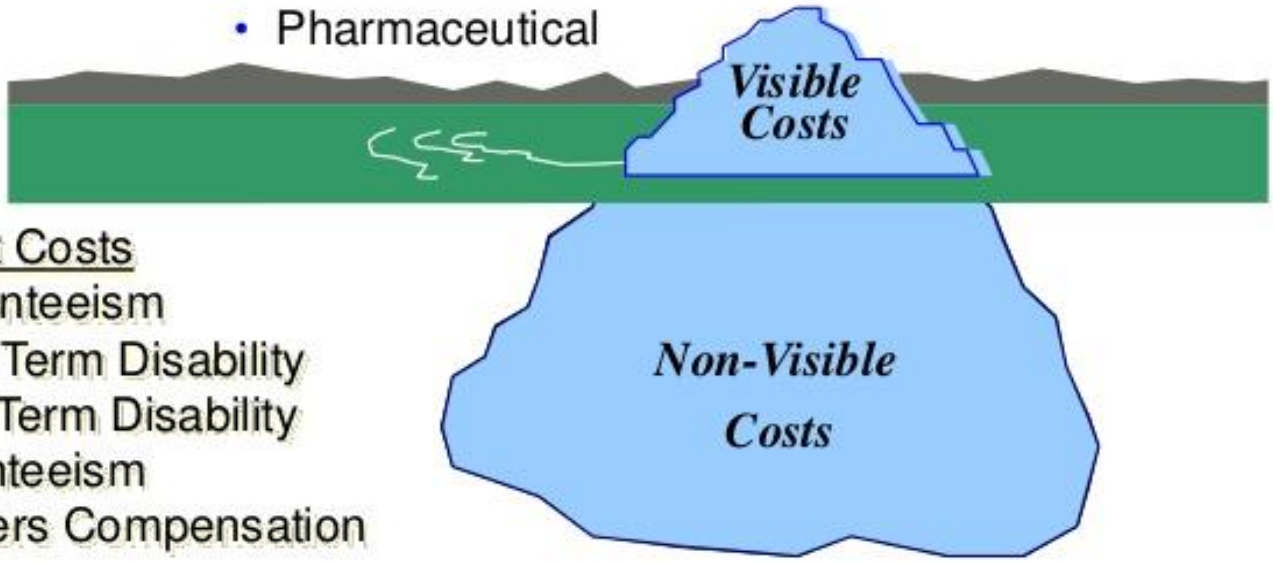
Iceberg Phenomenon
Direct vs. Indirect Costs

Direct Medical Costs
- Medical
- Pharmaceutical



Indirect Costs
- Presenteeism
- Short Term Disability
- Long Term Disability
- Absenteeism
- Workers Compensation

Indirect Costs represents 2-3 times Direct Medical Costs

Burden and cost of Breast Cancer

- 10% (The Netherlands) to 20% of total cancer cost (US-2012)
  - Direct (1/3: prevention, treatment)
  - Indirect costs (2/3: inability to work, relevant for disease as breast cancer striking before retirement)
  - Medical cost of breast and prostatic cancer are nearly half the cost of bowel, lung or leukemia (first year of diagnosis , Belgian data : 2008-2009)
- Cancer rises more in developing countries

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Reasons of rising cost

- High income countries
  - Ageing population
  - Increasing incidence
  - Increasing cost of cancer care
  - Increasing cost of developing drugs
  - Intensity of treatment (lines of chemo, …)
  - Cost of “more” technologies
- Low income countries
  - Growing BC burden, because of growing and ageing population with changing lifestyle habits

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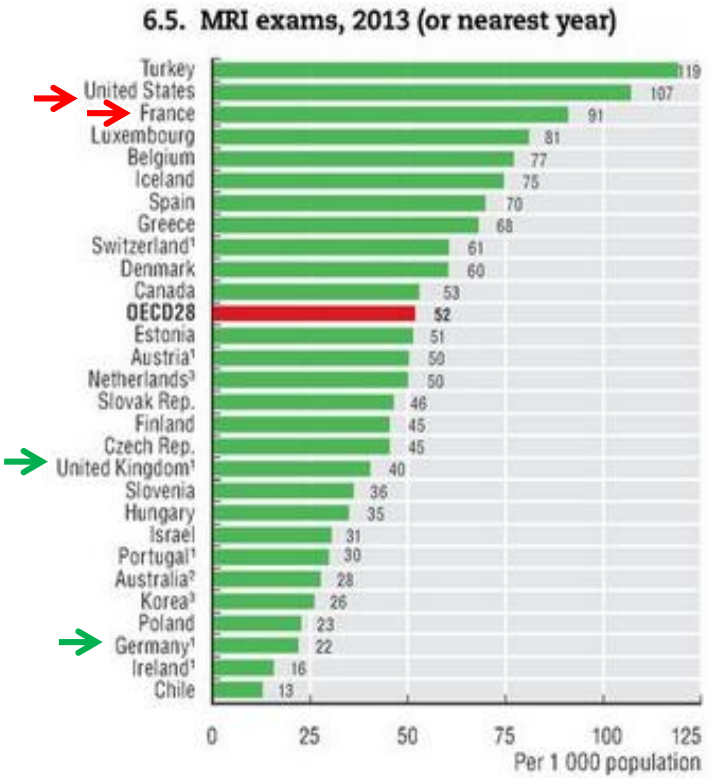
More technologies : CT-NMR (OECD,2013)

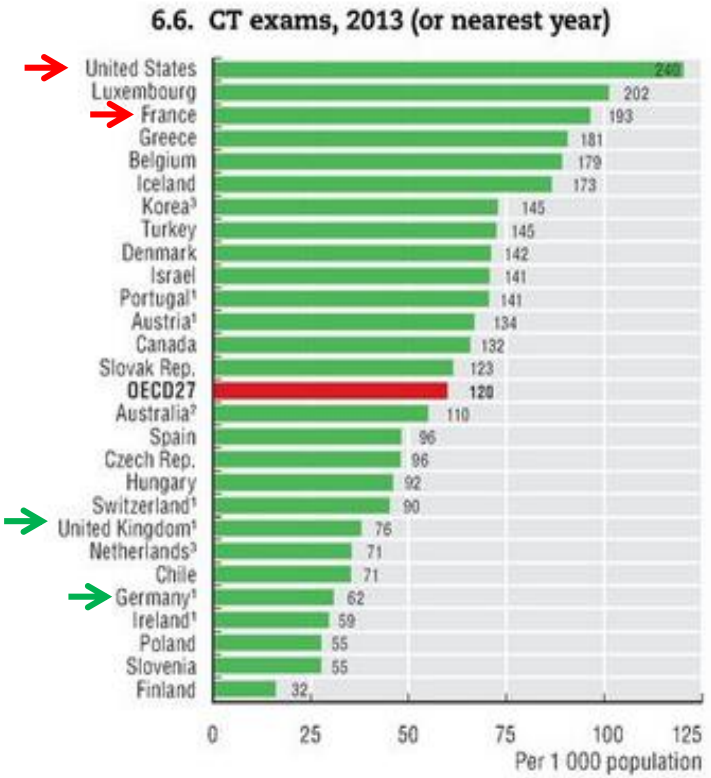


1. Exams outside hospital not included (in Ireland, exams in private hospital also not included).
2. Exams on public patients not included.
3. Exams privately-funded not included.

Source: OECD Health Statistics 2015, http://dx.doi.org/10.1787/health-data-en.

StatLink http://dx.doi.org/10.1787/888933280972

Information on data for Israel: http://oe.cd/israel-disclaimer



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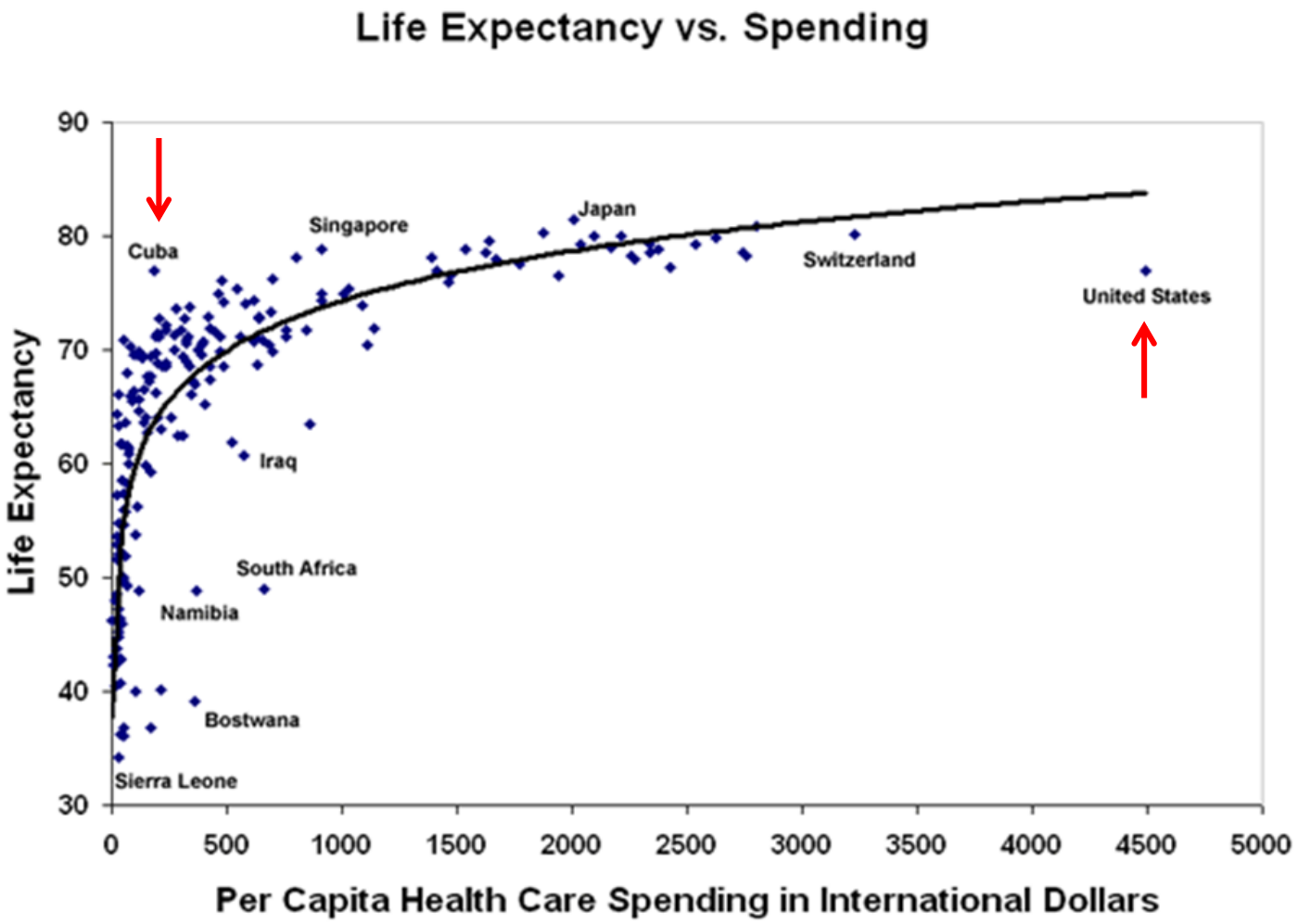
Does higher expenditure lead to better health outcome ?



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Total budget of breast cancer care

- **Breast cancer budget** represent 0,2% of GDP (France, 2004)
  - Direct cost : 1,5 miljard euro
  - Prevention and research : 0,1 miljard euro
  - Indirect cost, loss of productivity : 2 miljard euro
- **Attributable cost** decreasing with age (German data)
  - 30 -45y : 10.000 euro, 90% of all health cost
  - 70 y : 5.000 euro
  - 80-90 y: 50 % of all health cost
  - 90 y : 3.000 euro
- Budget depending on the **stage of the tumor** (Belgian data),
  - Primary, metastases
- Depending on the **treatment** (US data)
  - Surgery, radiation, chemotherapy

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Mean cost of BC treatment (€)

(Belgium - Cocquyt et al.2003) (in function of stage and treatment)

Treatment	Node negative	Node popospositive	RELAPS	Metastases
Surgery	*489*	*603*	*332*	*412*
Radiotherapy	*935*	*1198*	*789*	*658*
Chemotherapy	*933*	*3300*	*6087*	*5030*
Hormono	*286*	*272*	*299*	*291*
Other treatment	*38*	*318*	*192*	*229*
Other medication	*83*	*1084*	*293*	*2013*
Imaging	*481*	*738*	*577*	*1521*
Pathology	*208*	*231*	*103*	*90*
Markers	*23*	*37*	*41*	*77*
Other tests	*110*	*250*	*320*	*369*
Visits	*332*	*605*	*451*	*725*
Day Clinic	*471*	*693*	*816*	*975*
Hospitalisation	*2504*	*4354*	*2534*	*4161*
TOTAL	*6893*	*13684*	*12834*	*16551*

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Rough estimation cost treatment BC (US)

US data, Warren et al. 2008 - www.health.costhelper.com 2014

Modality	% patients	% cost	Estimation cost ($)
SURGERY	*90,9*	*24,64*	
**mastectomy*			*15.000-50.000*
**breast conserving + RT*			*17.000-35.000*
**reconstruction (prothesis)*			*5.000-15.000*
**reconstruction (flap)*			*25.000-50.000*
RADIOTHERAPY	*51,2*	*11,04*	
CHEMOTHERAPY	*24,2*	*14,8*	*10.000-100.000*
HOSPITALISATION	*23*	*18,34*	
OTHER COST		*31,17*	
TOTAL (LOCAL BC)		*100 %*	*100.000*
ADVANCED-METASTATIC BC			*300.000*

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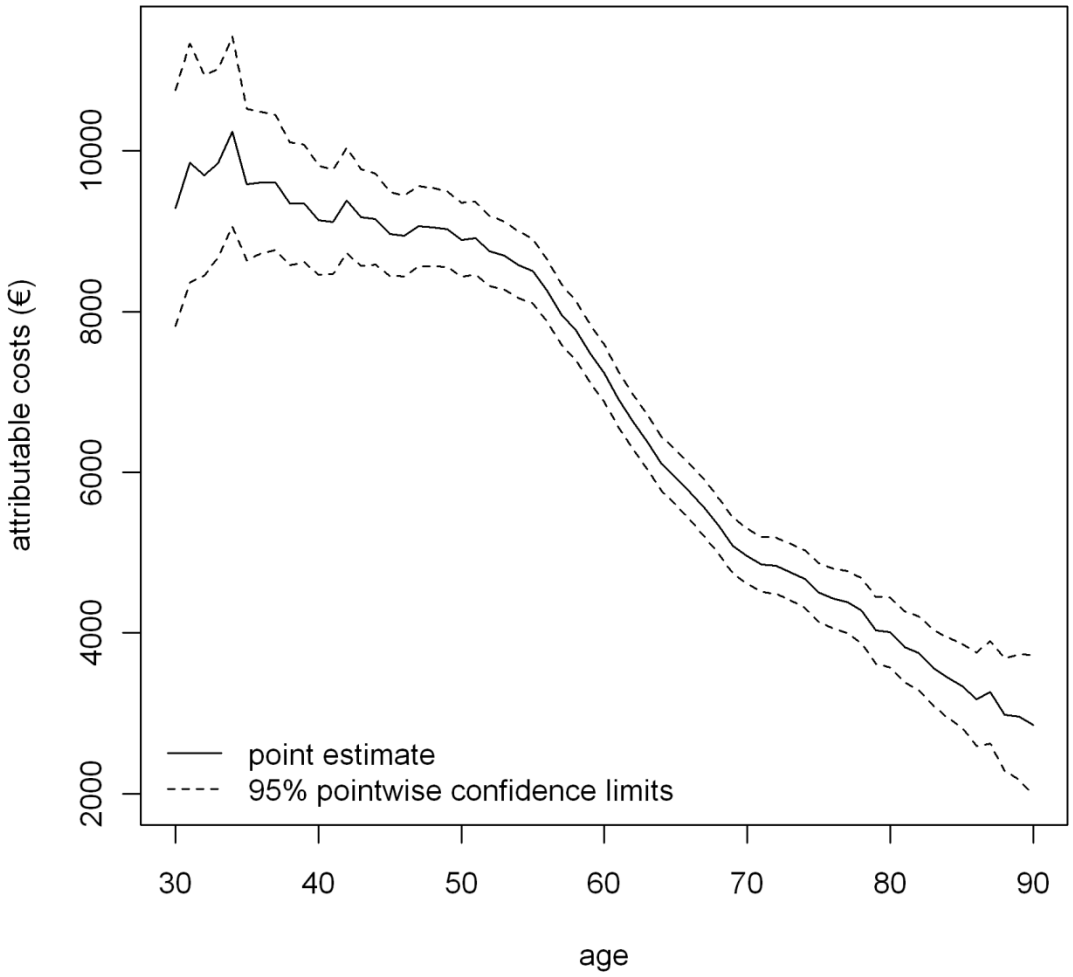
Breast cancer attributable cost in Germany (2012)



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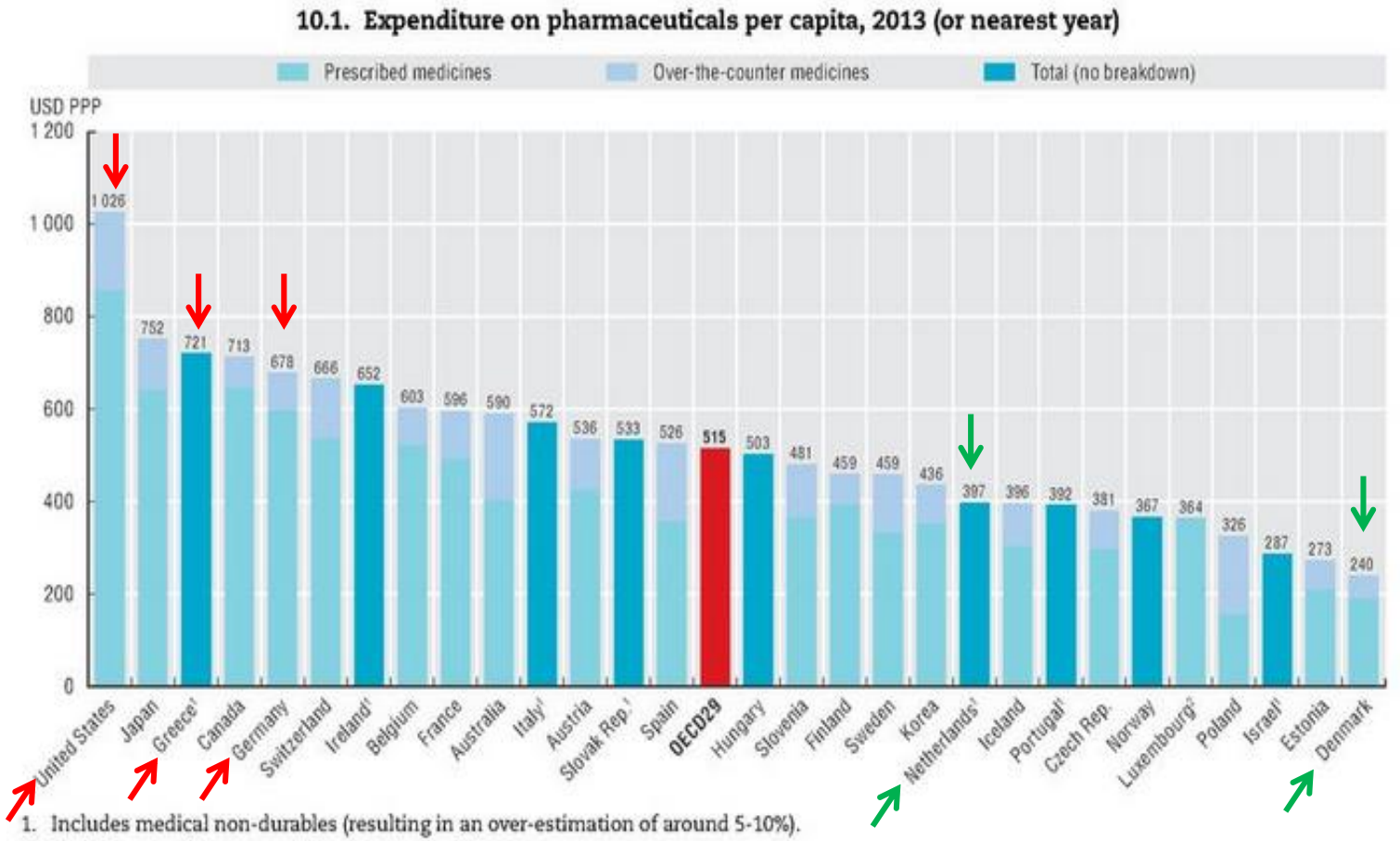
Expenditure on pharma per capita and as share of GDP, 2012



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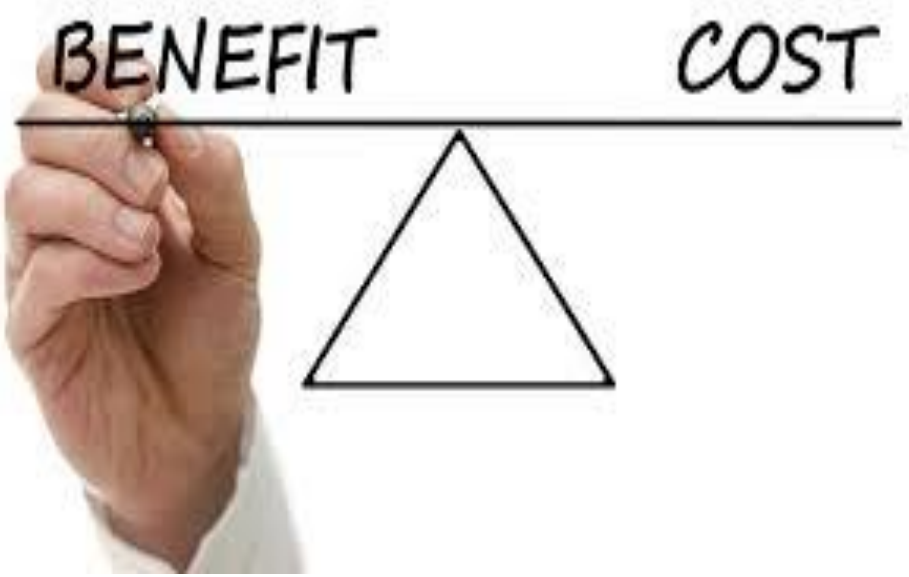
Budget constraints

$$\text{Value} = \frac{\text{Benefit}}{\text{Cost + Toxicity}}$$



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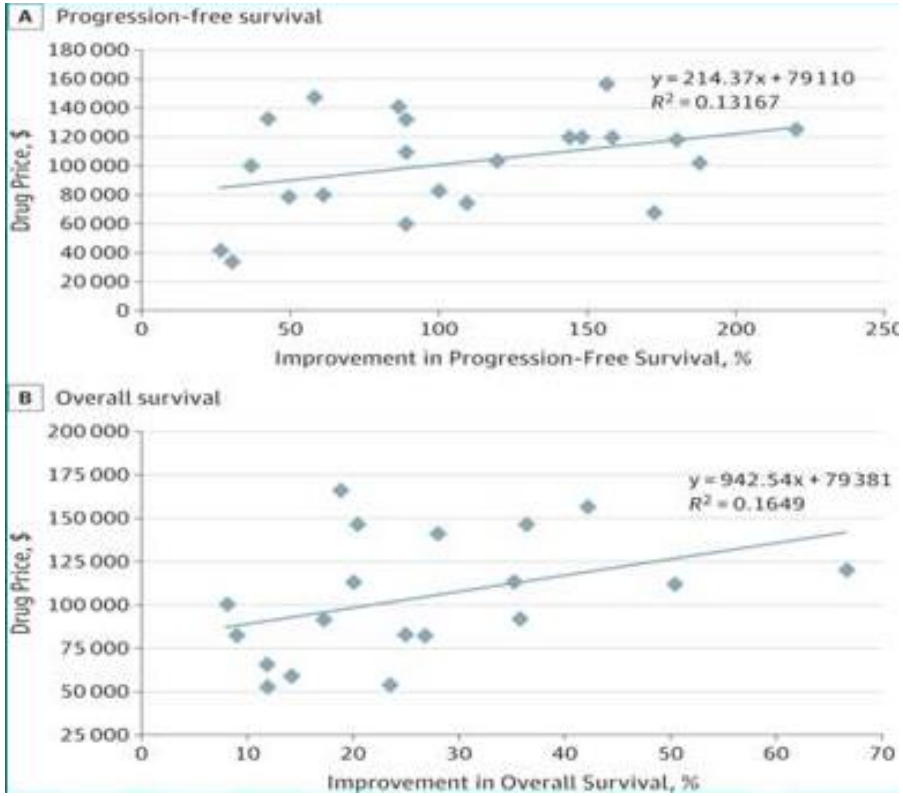
Pricing reflects the market

- No clinical relationship between cost and the % improvement in PFS or OS



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Ex-factory price of cancer drugs in European countries,New Zealand and Australia – Lancet oncology, 2015

	BE	DE	EL	FR	NL	NZ	SE	UK
Bevacizumab	1214	1326	**992**	1088	1209	NA	**1336**	1085
Denosumab	188	238	**176**	NA	214	NA	**242**	187
Eribulin	NA	400	NA	**320**	374	NA	**410**	370
Everolimus	117	126	**97**	126	106	NA	**139**	116
Gemcitabine	NA	120	NA	**102**	124	**209**	106	167
Lapatinib	NA	17	12	16	15	16	**18**	**11**
Paclitaxel	NA	320	**223**	NA	309	NA	**396**	252
Trastuzumab	623	676	**458**	536	579	**809**	**695**	478
Zoledronic acid	214	282	**128**	215	NA	**329**	**305**	204

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Hidden deals

- Between companies :Roche-Novartis :430 million euro

- Between government and companies
  - Discounts are confidential
  - Higher price transparancy needed
  - Public payers risk overpayment !

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ASCO Statement: A conceptual framework to assess the value of cancer treatment options

JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

American Society of Clinical Oncology Statement: A Conceptual Framework to Assess the Value of Cancer Treatment Options

Lowell E. Schnipper, Nancy E. Davidson, Dana S. Wollins, Courtney Tyne, Douglas W. Blayney, Diane Blum, Adam P. Dicker, Patricia A. Ganz, J. Russell Haverman, Robert Langdon, Gary H. Lyman, Neal J. Meropol, Therese Mulvey, Lee Newcomer, Jeffrey Peppercorn, Blase Polite, Derek Raghavan, Gregory Rossi, Leonard Saltz, Deborah Schrag, Thomas J. Smith, Peter P. Yu, Clifford A. Hudis, and Richard L. Schilsky

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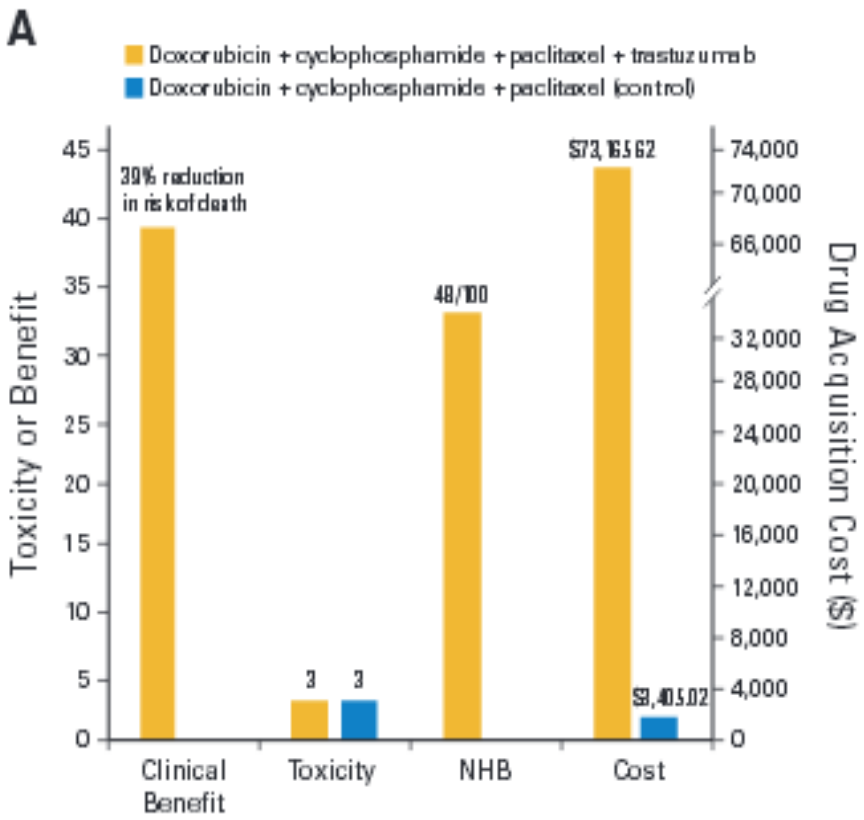
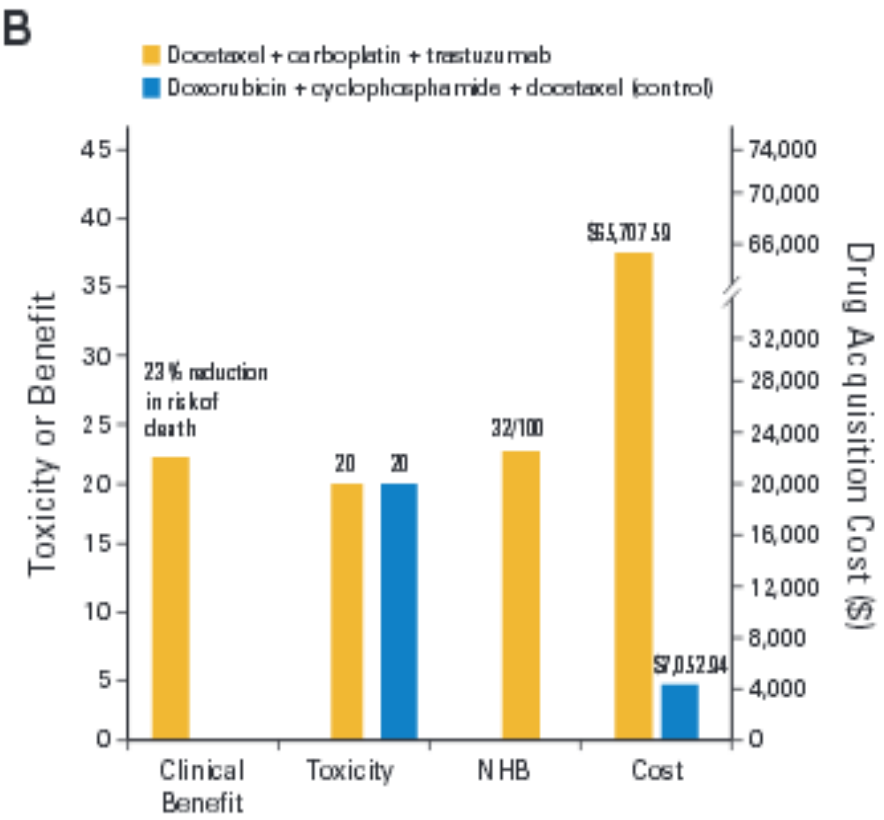
Clinical benefit, toxicity, net health benefit (NHB) and cost of two regimens when compared with standard-of-care regimen in Her-2 + BC





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The ESMO Magnitude of Clinical Benefit Scale (ESMO-MCBS), Annals 2015

- Evidence of clinical benefit is derived mainly from phase III randomized trials
- Magnitude of clinical benefit
  - range from small to substantial
  - recommendations need grading
- ESMO developed a tool to stratify clinical benefit

Background

Table 2. Maximal preliminary scores

Treatments with curative intent (form 1)

>5% improvement of survival at ≥3-year follow-up

Improvements in DFS alone HR <0.60 (primary end point) in studies without mature survival data

Treatments with non-curative intent (form 2)

Primary outcome OS (form 2a)

Control ≤12 months

HR ≤0.65 *AND* gain ≥3 months *OR*

Increase *in* 2-year survival alone ≥10%

Control >12 months

HR ≤0.70 *AND* gain ≥5 months *OR*

Increase *in* 3-year survival alone ≥10%

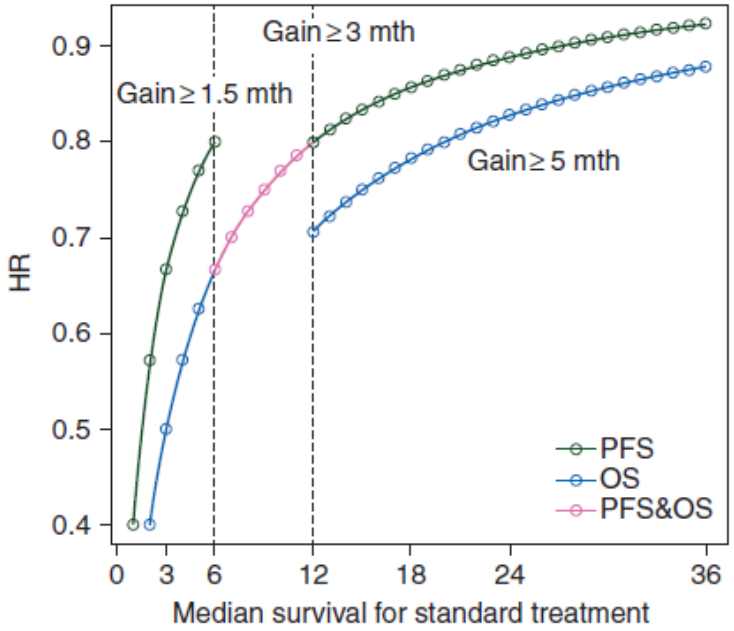
Primary outcome PFS (form 2b)

Control ≤6 months

HR ≤0.65 *AND* gain ≥1.5 months

Control >6 months

HR ≤0.65 *AND* gain ≥3 months



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ESMO-MCBS: Breast Cancer

Table 4. Field testing ESMO-MCBS v1.0: breast cancer

Breast cancer												
Medication	Trial name	Setting	Primary outcome	PFS control	PFS gain	PFS HR	OS control	OS gain	OS HR	QoL Toxicity	ESMO-MCBS	Ref.
Chemotherapy ± trastuzumab	HERA	(Neo)adjuvant HER-2-positive tumours	DFS	2-year DFS 77.4%	8.40%	0.54 (0.43–0.67)					A	[56]
T-DM1 versus lapatinib + capecitabine	EMILIA	Second-line metastatic after trastuzumab failure	PFS and OS	6.4 months	3.2 months	0.65 (0.55–0.77)	25 months	6.8 months	0.68 (0.55–0.85)	Delayed deterioration	5	[57, 58]
Trastuzumab + chemotherapy ± pertuzumab	CLEOPATRA	First-line metastatic	PFS	12.4 months	6 months	0.62 (0.52–0.84)	40.8 months	15.7 months	0.68 (0.56–0.84)	No improvement	4	[59–62]
Lapatinib ± trastuzumab	EGF104900	Third-line metastatic	PFS	2 months	1 months	0.73 (0.57–0.93)	9.5 months	4.5 months	0.74 (0.57–0.97)		4	[63, 64]
Capecitabine ± lapatinib		Second-line metastatic after trastuzumab failure	PFS	4.4 months	4 months	0.49 (0.34–0.71)			NS		3	[65]
Eribulin versus other chemotherapy	EMBRACE	Third-line metastatic after anthracycline and taxane	OS				10.6 months	2.5 months	0.81 (0.66–0.99)		2	[66]
Paclitaxel ± bevacizumab		First-line metastatic	PFS	5.9 months	5.8 months	0.60 (0.51–0.70)			NS	No improvement	2	[24]
Exemestane ± everolimus	BOLERO-2	Metastatic after failure of aromatase inhibitor (with PFS >6 months)	PFS	4.1 months	6.5 months	0.43 (0.35–0.54)			NS	No improvement	2	[67]

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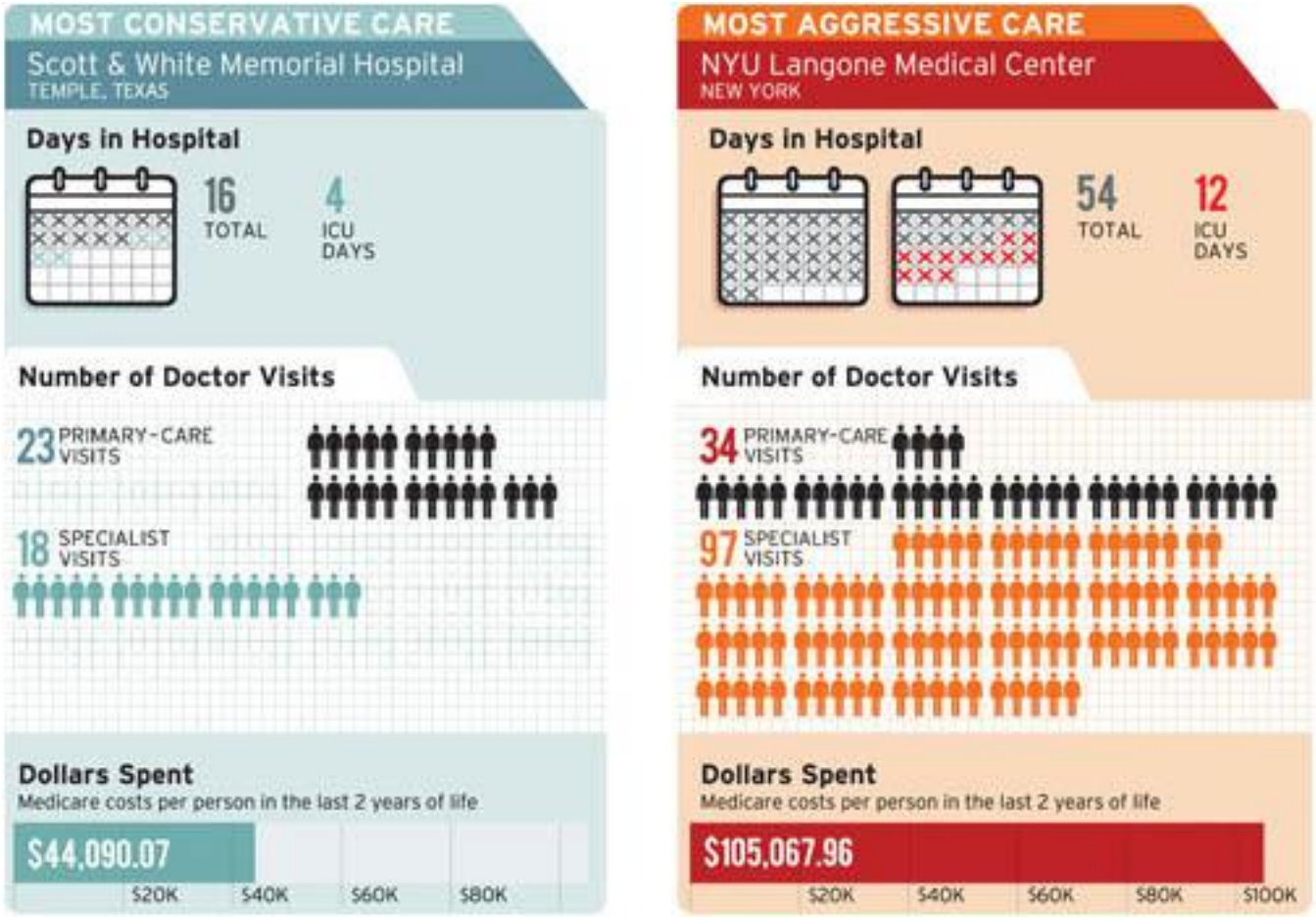
Some remarks

- Minimal required products !
- Negative studies ?
- Head to head comparisons ?
- Pace of conversion to generics is slowing (their price is rising)
- Hope for every patient ?

Too much treatment ? More pain,without gain ?
Medicare costs per person in the last 2 years of life



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Future perspectives

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Could health economics/policy play a role in modifying clinical variability?

- Reimbursement systems are part of the story, but the culture of the hospital matters
  - clinical leadership
  - defining cut-off's
  - combining quality data with reimbursement promoting high value care
    - Ratio : diagnostic work-up and treatment in function of treated pathology and outcome
- "Difference between population data and individual clinical criteria"
- Develop resource-stratified guidelines to maximize the outcome in developing countries

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Concluding: How can we save money ?

- Avoid overtreatment and overdiagnosis
- Early diagnosis lowers the cost
- Evidence based medicine and quality management
- Networking and breast centers
- Shortens treatments (hypofractionation,…)
- Ambulatory care (surgery, systemic treatment)
- Introduce precision medicine
- Transparency in price-setting
- Cutting in the administrative burden

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Ideal situation

- Adopting an integrated oncological care pathway:
  - General Practitioner
  - Screening/awareness
  - Diagnostic unit
  - Multidisciplinary discussion with good leadership
  - Evidence based therapy
  - Follow-up / shared care
  - Quality control and discussion of results

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Thank for your attention !

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