

Dure geneesmiddelen

Perspectief van de ziekenhuisfarmacie

Jos Kosterink



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Jos Kosterink, hospital pharmacist, professor in hospital and clinical pharmacy,

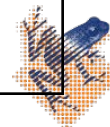
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Groningen Research Institute of Pharmacy, Pharmaco-Therapy,- Epidemiology and -Economics,
RUG

Disclosures

<ul style="list-style-type: none">• Research grants• Honorarium advisory board	<ul style="list-style-type: none">• Amgen, Genentech, Pfizer, MSD• Amgen Europe, MSD



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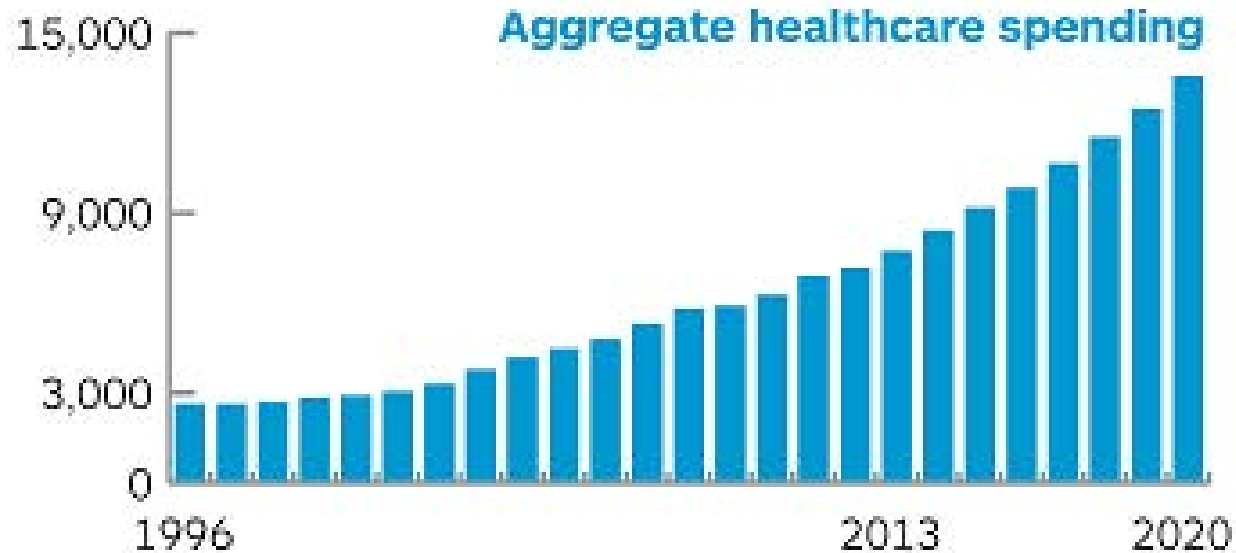
Dure geneesmiddelen in perspectief

ziekenhuis (professional) perspectief

- Uitgaven gezondheidszorg
- Geneesmiddel uitgaven
- Innovation/new drugs/trends
- Toegankelijkheid voor de patiënt
- Betaalbaarheid/duurzaamheid
- Initiatieven ziekenhuis (professionals)

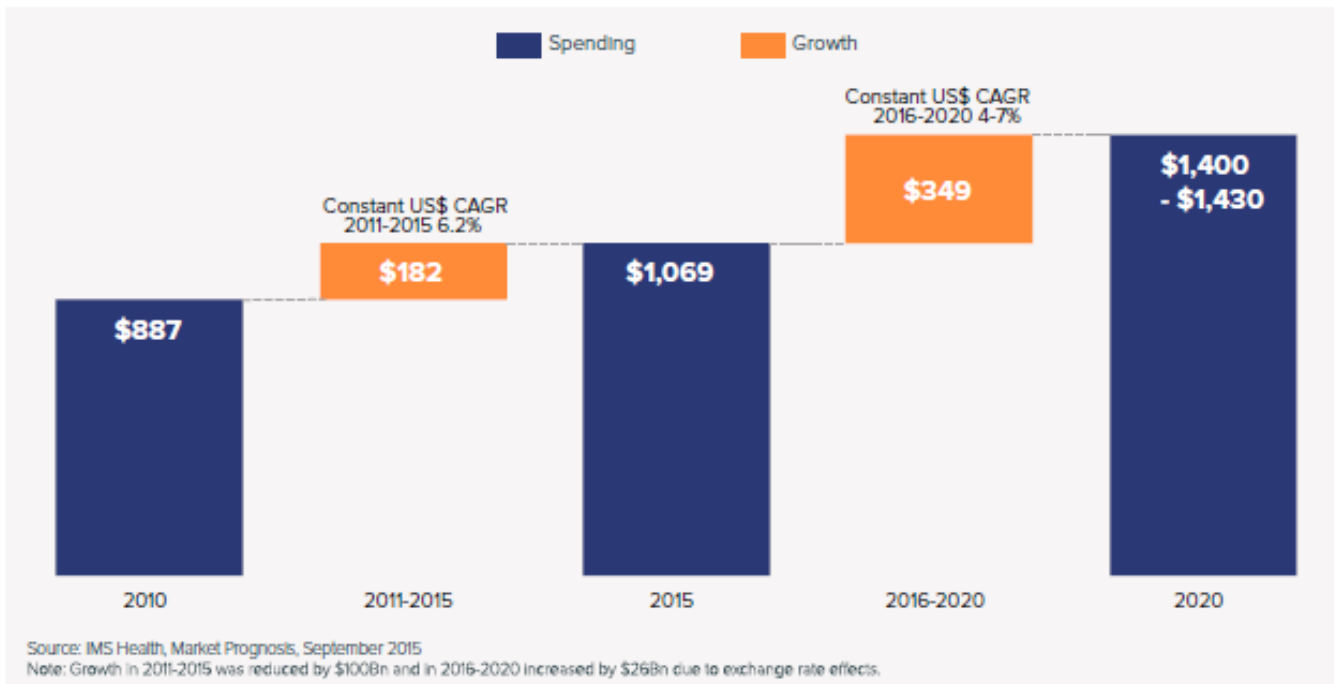
Healthcare spending

The world is on a health kick (US\$ billions)



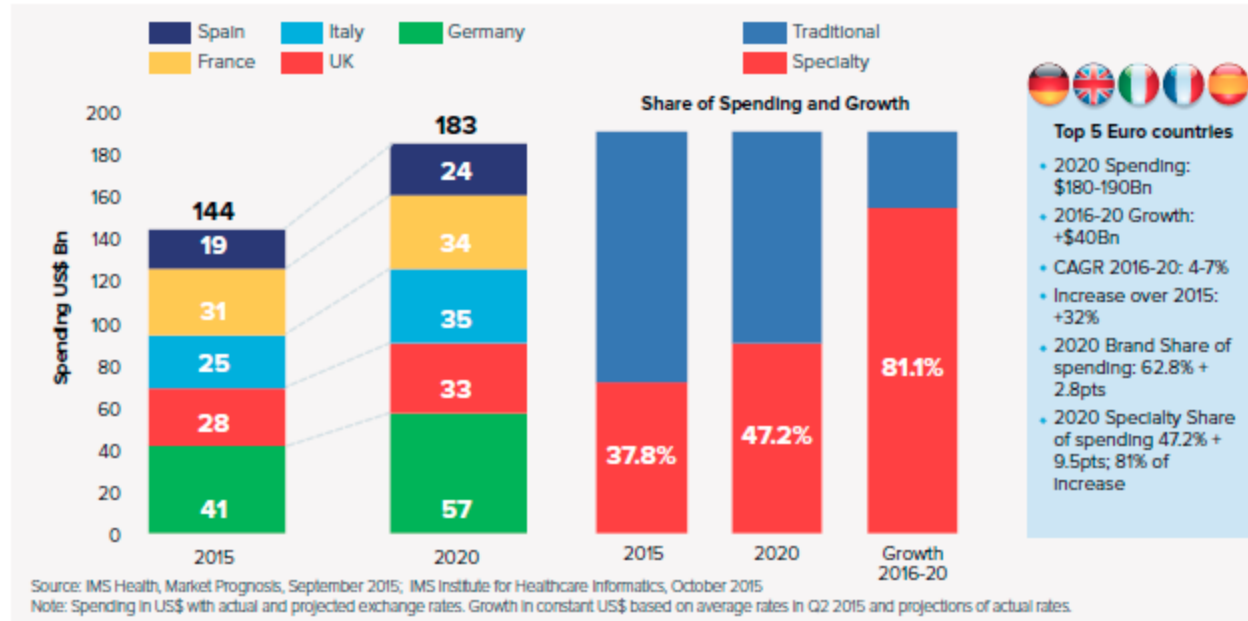
Global Spending Pharmaceuticals (2010-2020) US\$ billions

Exhibit 7: Global Spending and Growth, 2010-2020



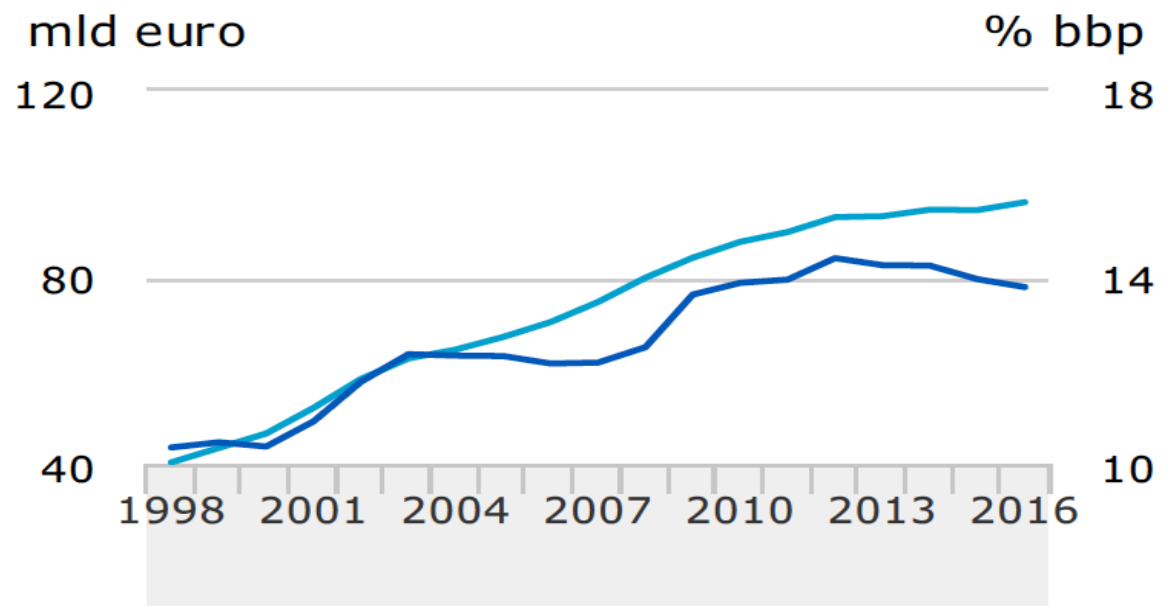
EU Spending Pharmaceuticals (2015-2020)

Exhibit 14: Top 5 European Countries Spending US\$Bn, 2015 and 2020



Total expenditures/costs health care The Netherlands (source CBS)

- 96.1 billion
- 13.8% GDP
- Hospital care:
€27 billion

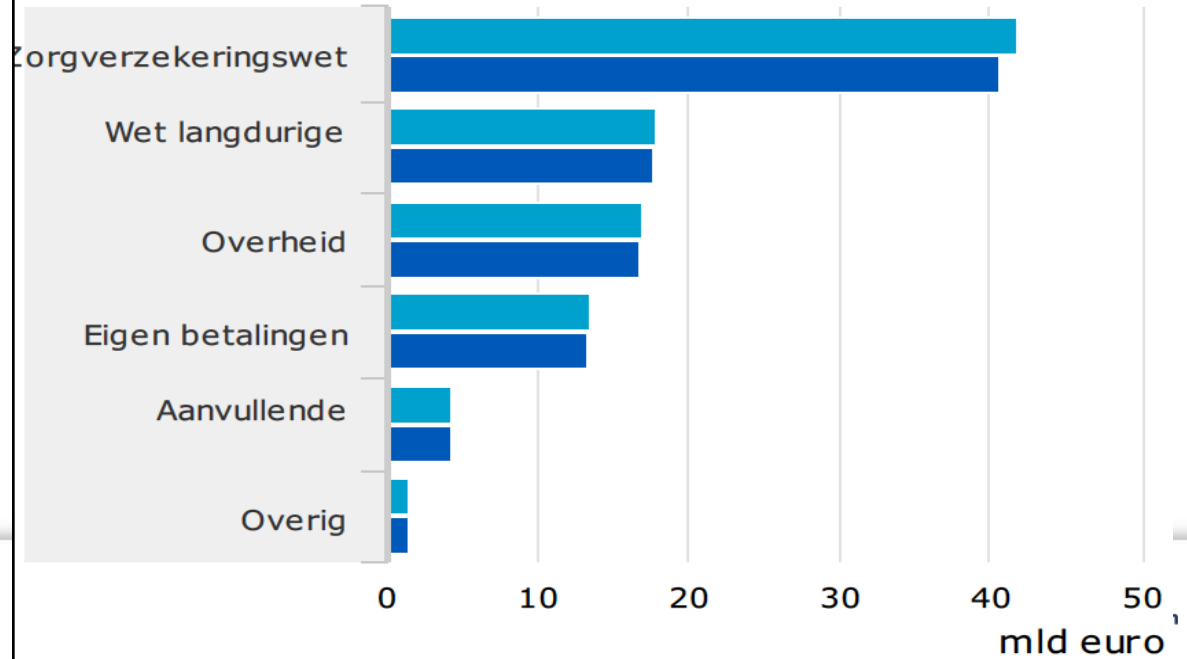


— mld euro
— % bbp (rechteras)

Total expenditures/costs health care The Netherlands (source CBS)

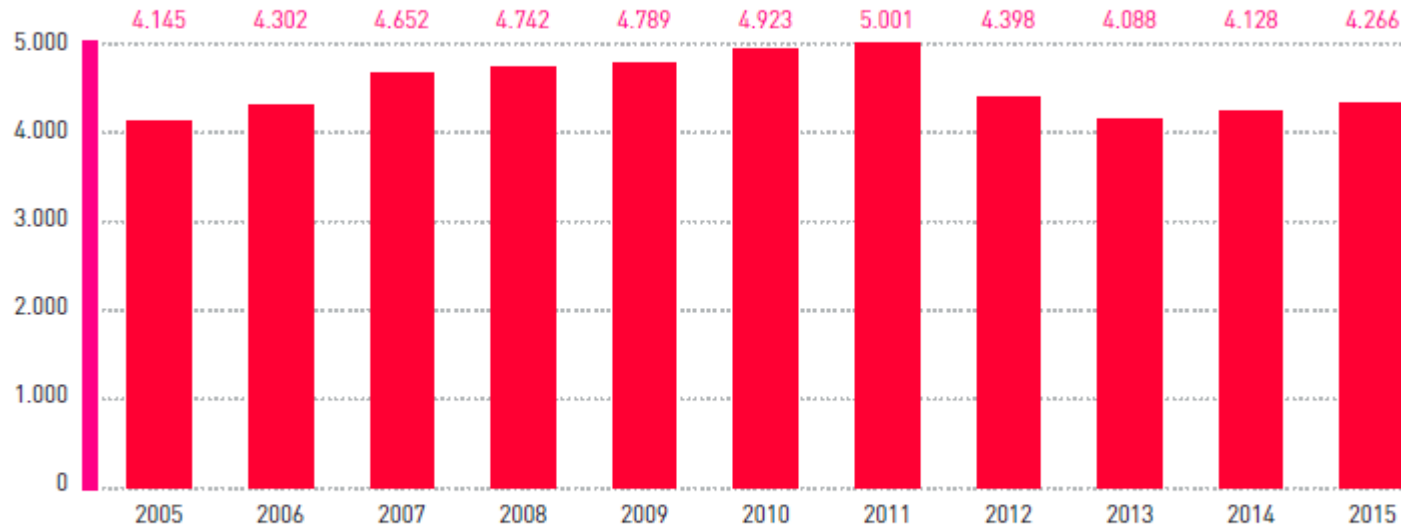
- 96.1 billion
- 13.8% GDP
- Hospital care:
€27 billion

Financiering van de zorguitgaven



Total spending pharmaceuticals The Netherlands (in Bn €)

Total spending pharmaceuticals local pharmacies/
first line care



Total 2015:
€6.5 billion

**Including
Hospitals:**
€2.2 billion

Expensive drugs:
€1.7 billion

Uitgavenstijging van 3,3% in 2015 is meevaller voor overheid.

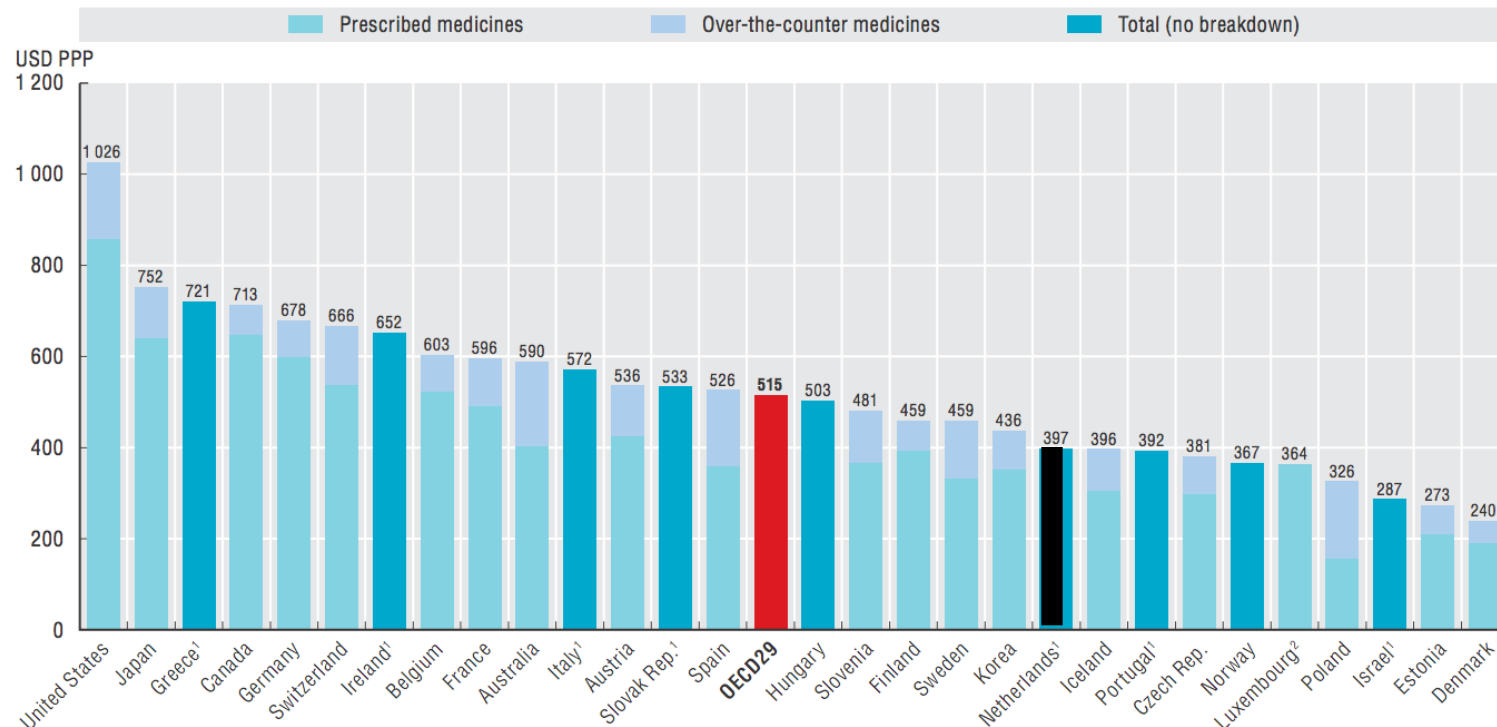
Bron: Stichting Farmaceutische Kengetallen



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Expenditure on pharmaceuticals per capita

10.1. Expenditure on pharmaceuticals per capita, 2013 (or nearest year)



1. Includes medical non-durables (resulting in an over-estimation of around 5-10%).

2. Excludes spending on over-the-counter medicines.

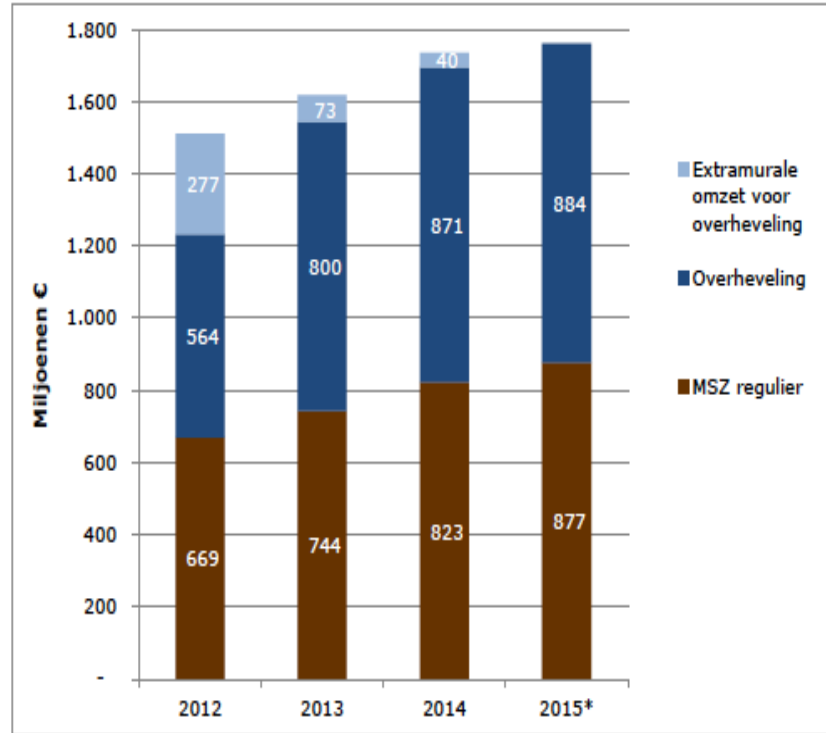
Source: OECD Health Statistics 2015, <http://dx.doi.org/10.1787/health-data-en>.



MSZ geneesmiddelen

2.1.1 Totale omzet msz-geneesmiddelen

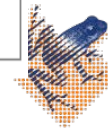
Figuur 1. Totale omzet msz-geneesmiddelen 2012 - 2015



Source: NZa



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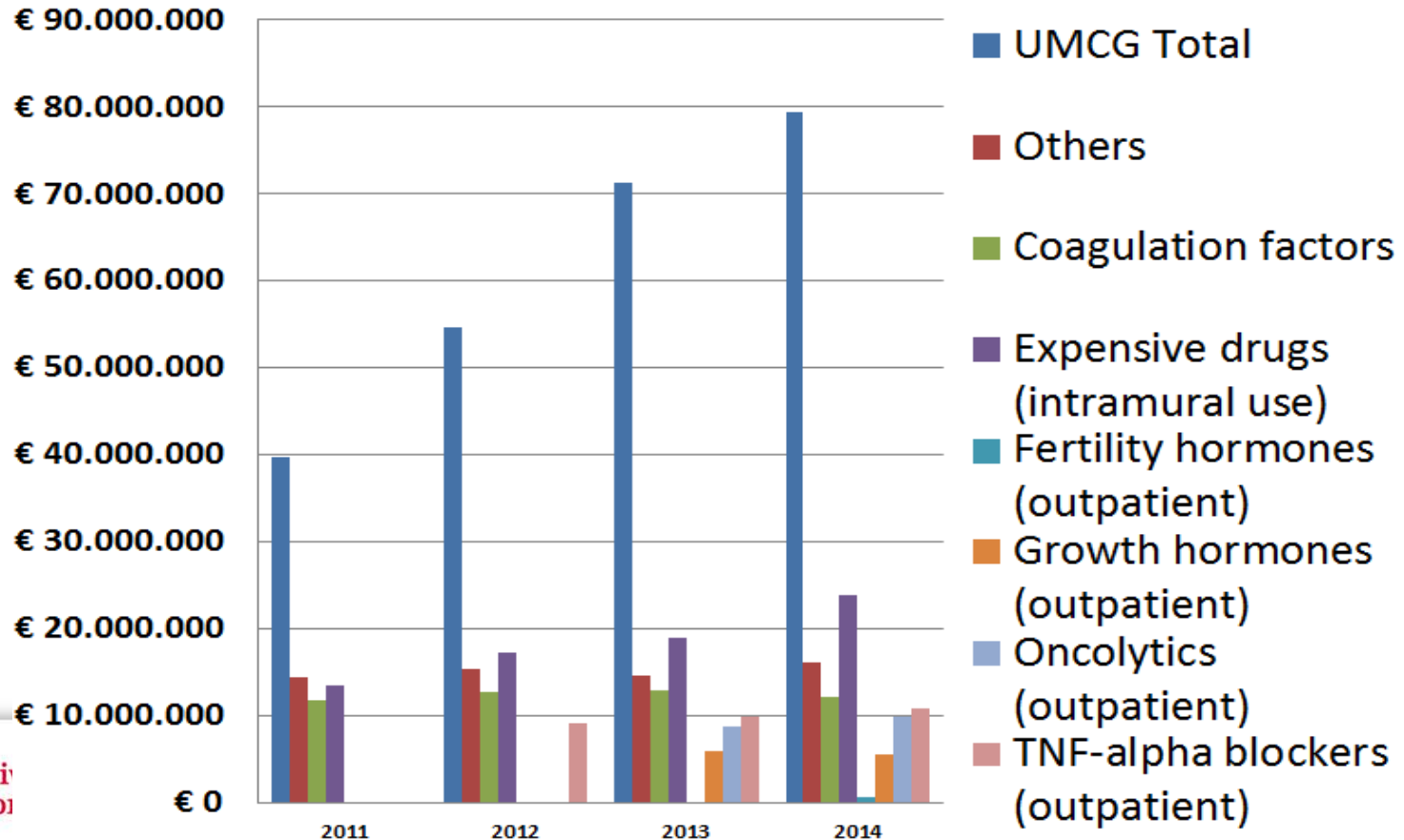
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Expensive Drugs Top 25

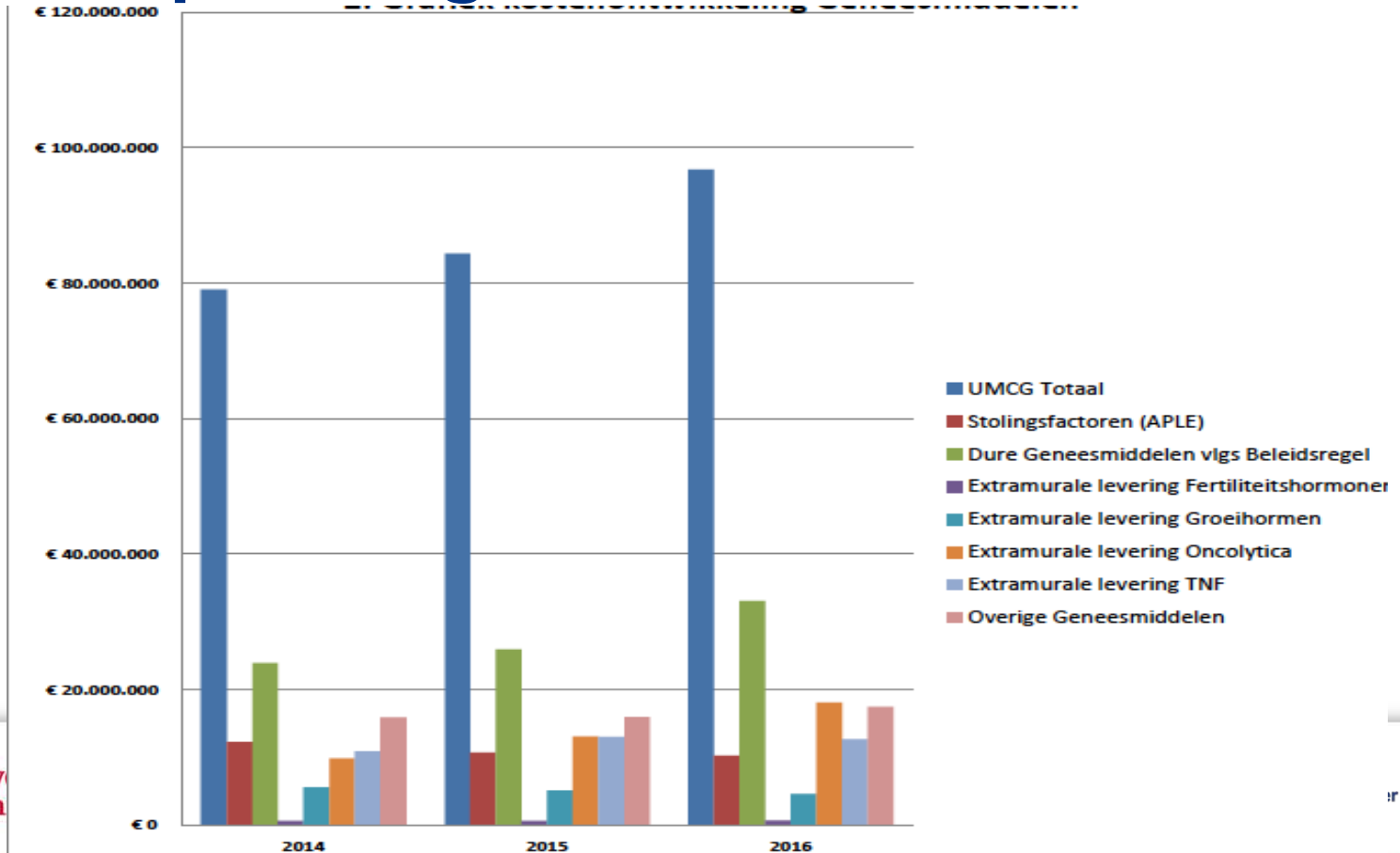
Rang 2014 (2013)	Stofnaam	Groep	Totale omzet (x €1.000)
1 (1)	Adalimumab	TNF-alfaremmers (anti-reumatica)	223.053
2 (2)	Etanercept	TNF-alfaremmers (anti-reumatica)	155.197
3 (3)	Infliximab	TNF-alfaremmers (anti-reumatica)	154.007
4 (4)	Trastuzumab	Oncolytica	79.530
5 (5)	Rituximab	Oncolytica	62.021
6 (6)	Alglucosidase alfa	Stofwisselingsziekten	53.796
7 (9)	Bevacizumab	Oncolytica	49.541
8 (10)	Lenalidomide	Oncolytica	47.080
9 (8)	Immunoglobuline i.v.	Immunoglobuline	46.936
10 (7)	Somatropine	Groeihormonen	43.165
11 (12)	Advate	Stollingsfactoren	37.872
12 (11)	Imatinib	Oncolytica	36.702
13 (15)	Pemetrexed	Oncolytica	34.013
14 (16)	Bortezomib	Oncolytica	33.495
15 (13)	Kogenate Bayer	Stollingsfactoren	30.248
16 (17)	Abirateronacetaat	Oncolytica	29.442
17 (19)	Ustekinumab	Overig anti-reumatica	29.221
18 (-)	Ipilimumab	Oncolytica	26.339
19 (20)	Eculizumab	Overig	24.856
20 (24)	Golimumab	TNF-alfaremmers (anti-reumatica)	23.369
21 (18)	Everolimus	Oncolytica	22.659
22 (14)	Docetaxel	Oncolytica	20.827
23 (23)	Paclitaxel	Oncolytica	20.428
24 (25)	Tocilizumab	Overig anti-reumatica	19.328
25 (21)	Natalizumab	MS middelen	16.749

Source: NZa

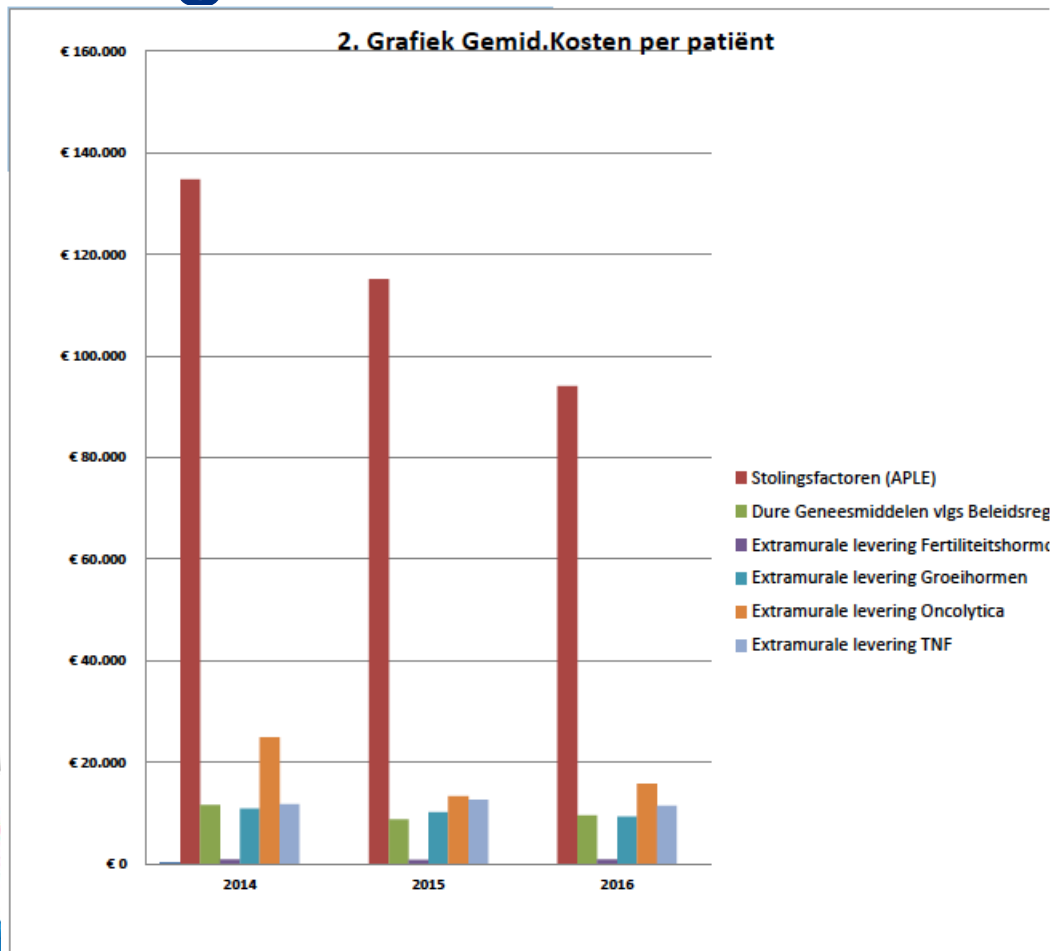
Total spending Pharmaceuticals UMCG



Total spending Pharmaceuticals UMCG



Spending Pharmaceuticals UMCG (€)



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Healthwise Dure



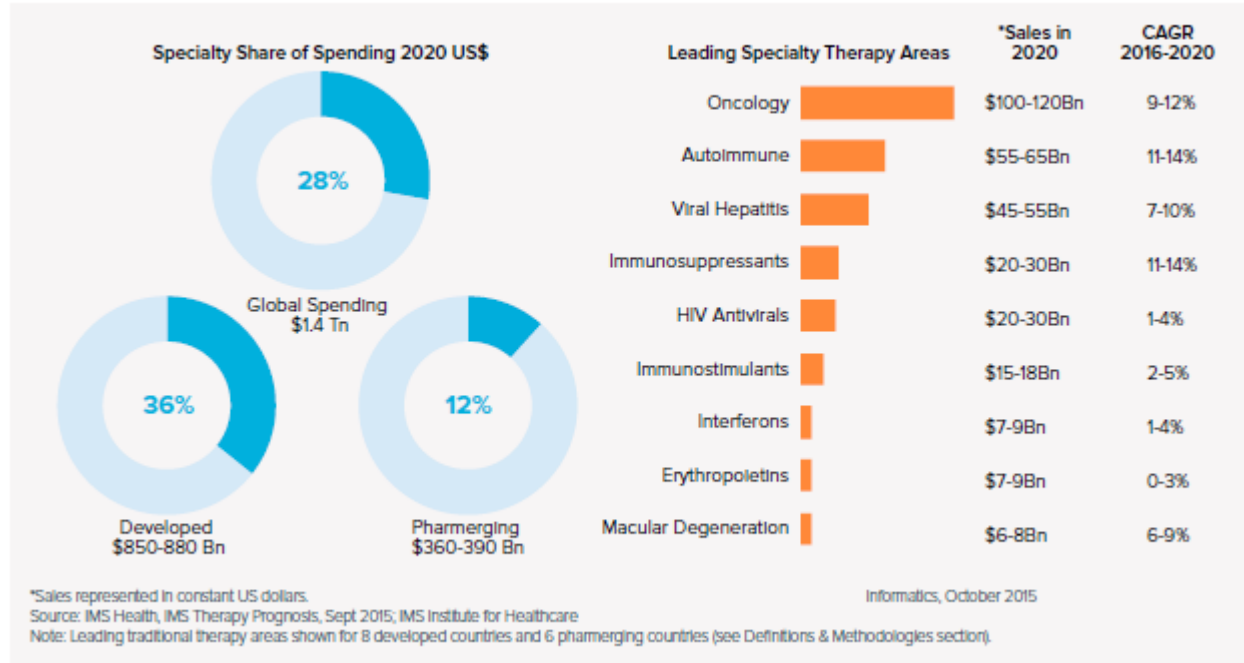
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Innovation

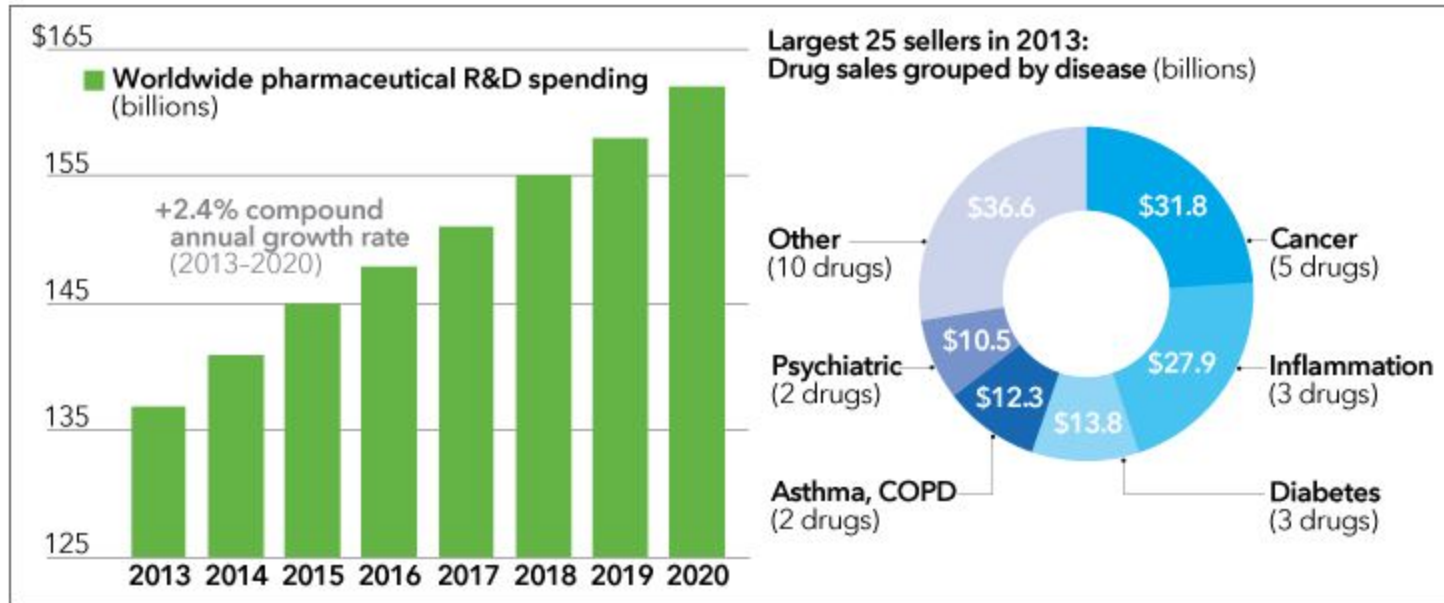
- Academia
- Pharma
- For the benefit of the patient?

Specialty Medicines and leading therapy areas (Global)

Exhibit 8: Specialty Medicines and Leading Therapy Areas in 2020

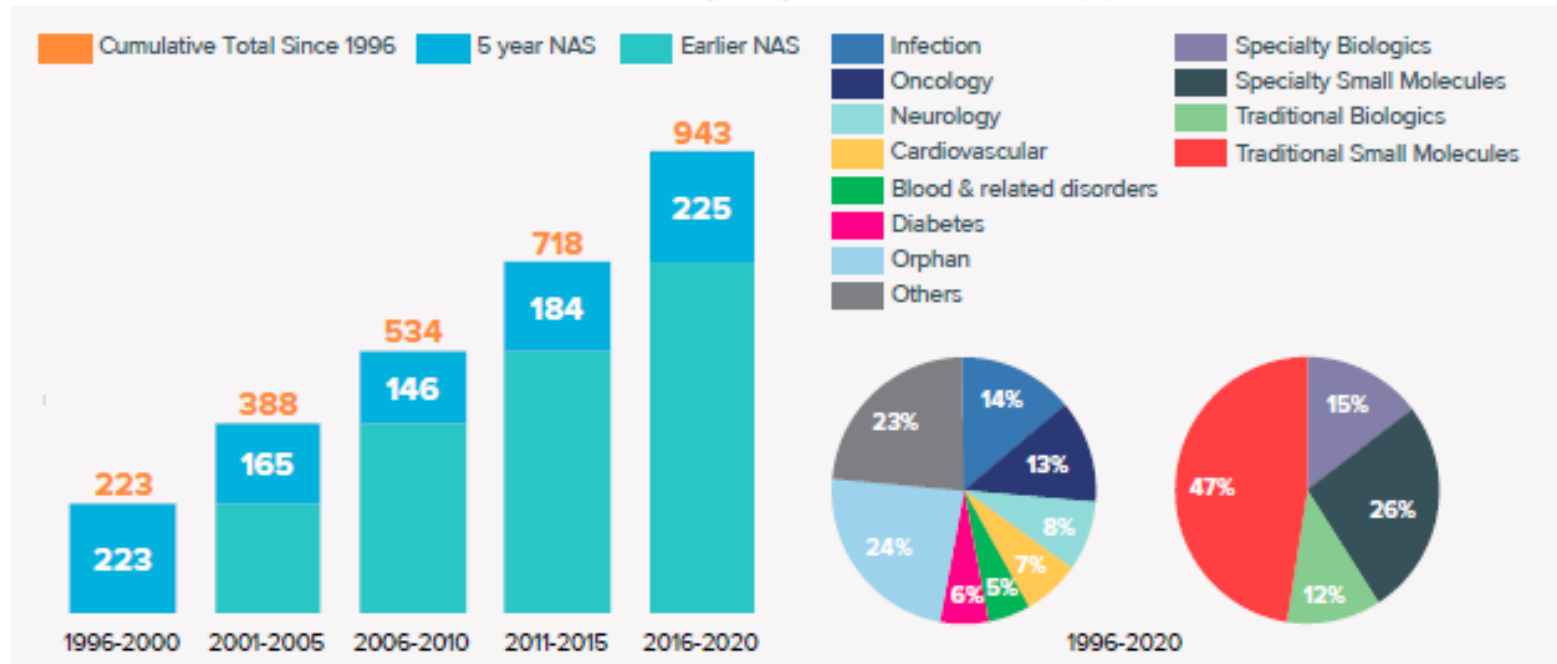


Worldwide pharmaceutical R&D spending



Global New Active Substances

Exhibit 18: Global New Active Substances (NAS) Available Since 1996



Source: IMS Health, IMS Institute for Healthcare Informatics, October 2015

Note: Disease categories based on therapy areas and expected launches 2016-20. Orphan drugs are those to treat small populations with rare diseases, and are defined separately by U.S. FDA and the European Medicines Agency (EMA). Any medicine with an orphan designation for an approved use within the first year after global launch are categorized as Orphan. Half of designated orphan indications are granted more than a year after original approval.



Echte innovaties?

- Veel me-too
- Echte doorbraken komen zelden voor

NATIONAL CANCER INSTITUTE PRECISION MEDICINE IN CANCER TREATMENT

Discovering unique therapies that treat an individual's cancer based on the specific genetic abnormalities of that person's tumor.



Precision medicine

Definition:

"An emerging approach for therapy and prevention, taking into account individual variability in genes, environment, and lifestyle for each person."



Use and effectiveness of drugs

- **Facts and Figures**

- \$800-1000 billion
- 90% drugs are only effective in 40% of population
- \$350 billion ineffective prescription

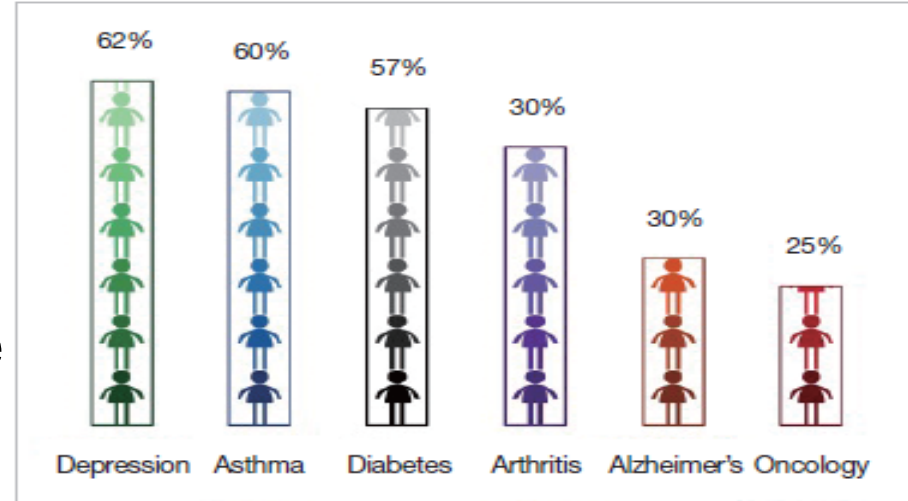


Figure 1. Inefficacy of the one-dose-fits-all approach. This figure depicts the percentage of patients for whom a major drug is effective on average. With the high variability across diseases, 38% to 75% of patients fail to respond to a treatment. The average response rate of a cancer drug is the lowest at 25%, suggesting that 75% of patients with cancer are over-dosed and will potentially suffer from an adverse drug reaction. From Spear BB, et al. Trends Mol Med 2001;7:201-4 [1].

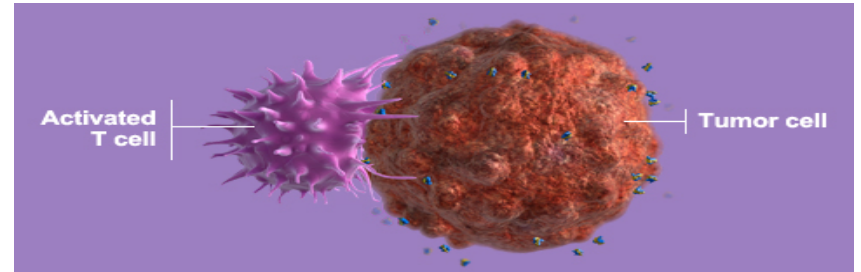


New classes of drugs

Targeted therapy



Immunotherapy



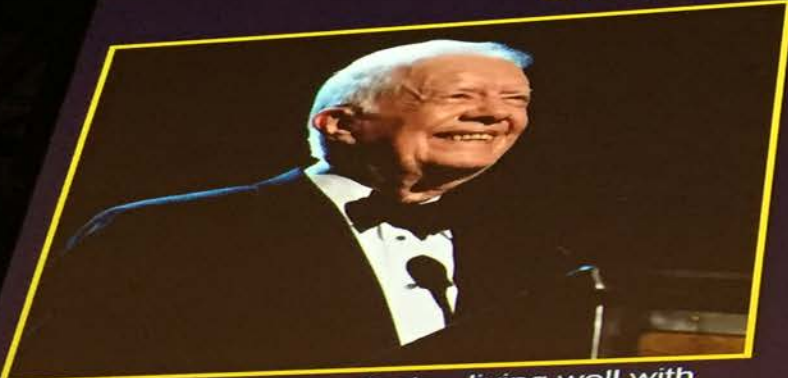
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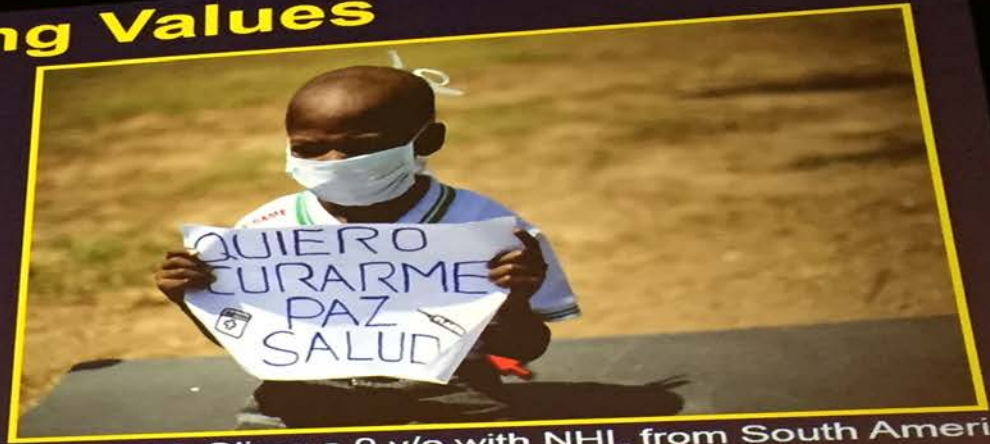
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Patient access

Conflicting Values



Former president Jimmy Carter, living well with metastatic melanoma and chemo costs estimated to exceed \$100,000/year



Deceased: Oliver a 9 y/o with NHL from South America potentially curative chemo was unaffordable

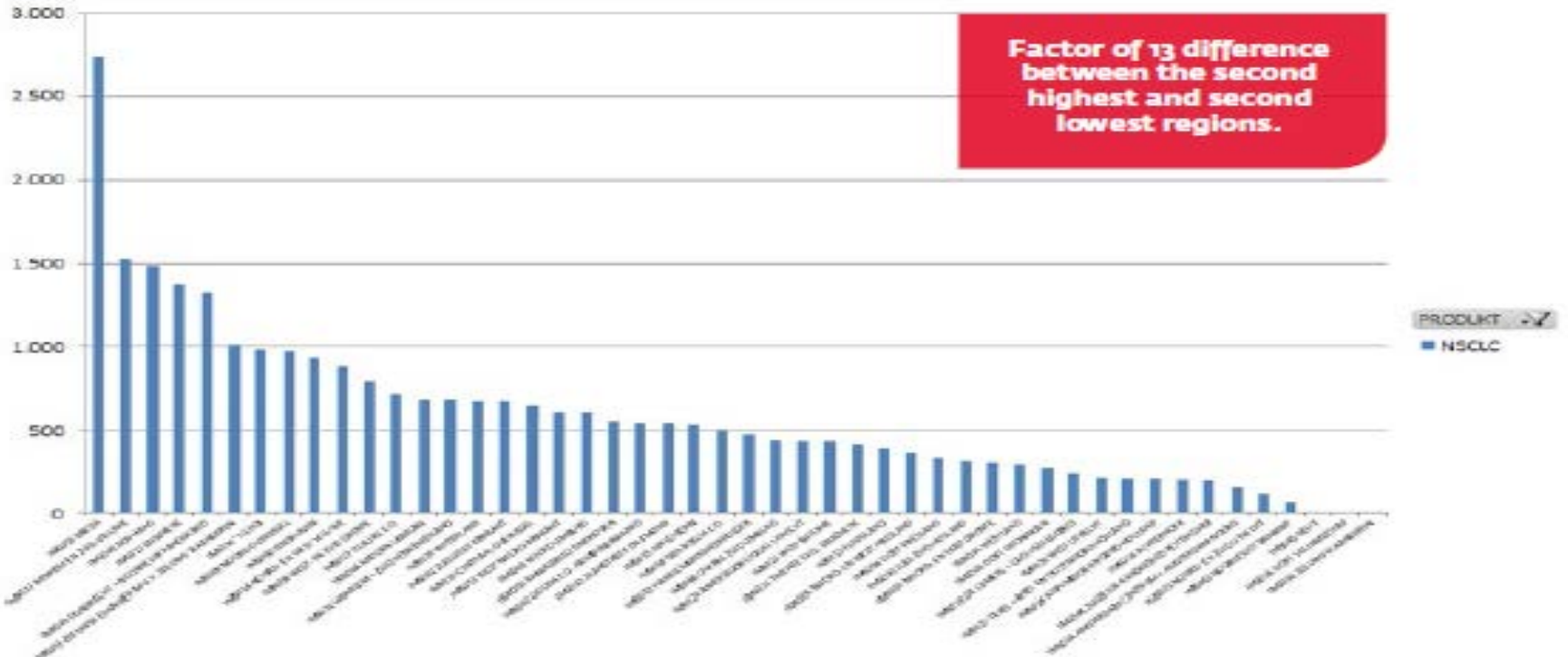
PRESENTED AT ASCO ANNUAL MEETING '16

Differences in access to relevant new anticancer drugs in Europe

- Differences between countries in:
 - drug related health care expenditures
 - drug prices
 - access time to drugs after approval by EMA
- Sometimes lack of drug supply in “countries with cheaper drugs” due to parallel import to “countries where the drug is more expensive”
- Unequal access within some countries:
 - sometimes (co)-payment of the drug costs by patients required



Regional differences in use of EGFR inhibitors for lung cancer in NL



Betaalbaarheid/duurzaamheid

Spending expensive anti-cancer drugs The Netherlands

Table 1: Total cost of inpatient use of expensive anti-cancer drugs based on data from the GIP Drug Information System, dated June 2015 (drugs from the Dutch Healthcare Authority's add-on list)

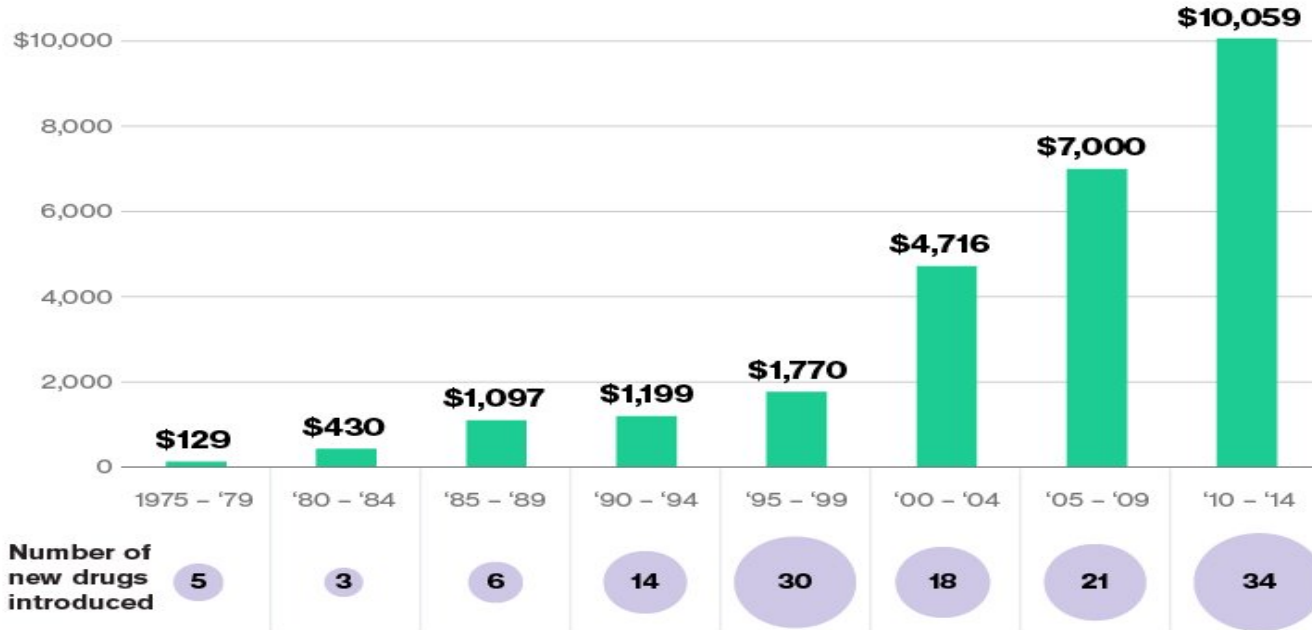
Total costs (in € million)	376	455	554	675
Increase compared to 2011		+ 21%	+ 47%	+ 80%

*The 2014 figure was derived from sales data, based on the pharmaceutical industry's list price (exclusive of VAT).

Source: Farminform

Cancer Drugs Hit Market at Ever-Higher Prices

The median monthly cost for new cancer drugs in the U.S. has soared since the 1970s despite an increasing number of available brands.

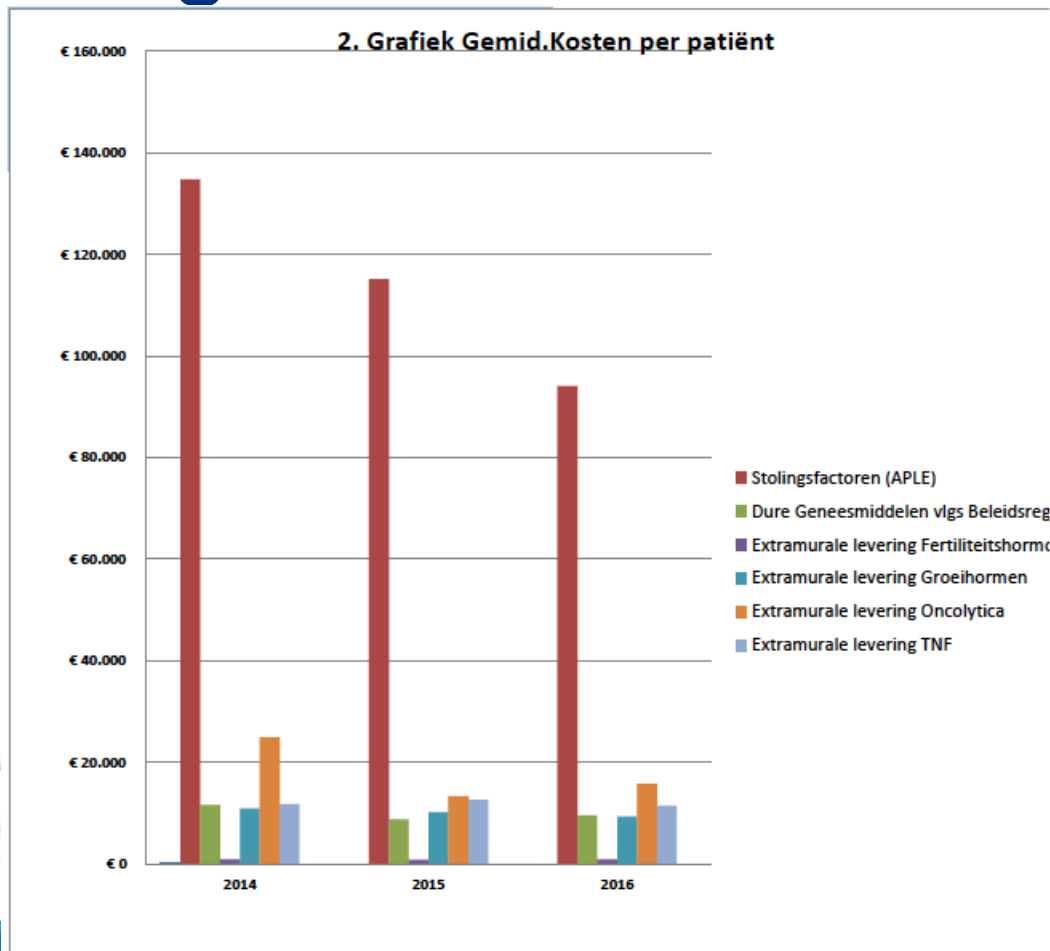


Note: Costs are monthly Medicare prices for each drug the year it was introduced, adjusted for inflation; drugs approved through early December 2014 are included.
Source: Peter Bach and Geoffrey Schnorr at Memorial Sloan Kettering Cancer Center



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Spending Pharmaceuticals UMCG (€)



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Effective new anti-cancer drugs, But the funding system is creaking at the seams

Obstacles to, and solutions for, the use of
expensive anti-cancer drugs

1 July 2015, Dutch Cancer Society



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KWF
KANKER
BESTRIJDING



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© Dutch Cancer Society 2015

Uitdagingen

- Meer en complexere ziektes cq patiënten
- Meer geneesmiddelen
- Toename van de kosten

Veel stakeholders

en de interactie met de zorgprofessional

- Pharma (en andere shareholders)
- Min. VWS / Zorginstituut NL
- Wetenschappelijke verenigingen
- Zorgverzekeraars
- Ziekenhuisbestuur
- Dokters (geneesmiddelkeuze en voorschrijven)
- Apothekers: geneesmiddelkeuze en inkoop
- Patiënten / patiënten belangen verenigingen



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National level

- Specifiek budget voor dure geneesmiddelen
- ZINI
- Horizon scans toekomstig dure geneesmiddelen
- Sluis; Prijsonderhandelingen door de minister/EU
- No cure no pay
- Value Bases Pricing

- Nationale coördinator



PERTUZUMAB

MAAR VOOR HET
ALGEMEEN BELANG,
ADVISEREN WIJ
EUTHANASIE!



Sluis nivolumab en pembrolizumab niet-kleincellig longcarcinoom

- ZINI boordeling: farmacotherapeutisch rapport, kosten-effectiviteit, budget impact
- Niet kosten-effectief: circa €140.000,- per QALY
- Onderhandeling Min. VWS met Pharma
- Prijsafspraken: prijs??

Rapport FMS

INHOUD

INLEIDING	6
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Visiedocument Dure Geneesmiddelen



NVMO Cie BOM

PASKWIL 2016 superioriteit

Palliatief, effectiviteit

- winst totale overleving > 12 weken of HR < 0,7 +
- winst progressievrije overleving > 12 weken of HR < 0,7 +

Gradering volgens ESMO-MCBS (inclusief bijdrage door QoL-analyse)

Bijwerkingen (verschil tussen de behandelarmen)

- lethaal (absoluut) < 5% +
- acuut, ernstig < 25% +
- chronisch beperkend +

Kwaliteit van leven

- QoL-analyse gevalideerde test(s) verricht +

Impact van behandeling

- acceptabele behandellast +

Medicijnkosten

mediane behandelduur
per 28 dagen
prijsverschil in vergelijking met standaardbehandeling

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HOVON

- Pomalidomide bij Multipel Myeloom
- Strikte toepassing conform richtlijn; pay for benefit
- Consultatie centra
- Afspraak zorgverzekeraar, pharma en behandelaren

Biosimilars FMS/NVZA

NVZA Toolbox Biosimilars

Een praktische handleiding voor succesvolle implementatie van biosimilars in de medisch specialistische zorg

april 2017



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Ziekenhuisbestuur /zorgverzekeraar

- Transparantie financiële arrangementen dure geneesmiddelen
- Formularium; preferentiebeleid; richtlijnen
- Incentives/shared saving

Zorgprofessionals

- De spreekkamer is niet de plek om over geld te spreken. Daar **geldt** het **belang** van de **patient**.
- Zinnig en doelmatig gebruik van (dure) geneesmiddelen wordt besproken tussen patiënt en dokter/andere zorgprofessionals
- Maatschappelijke verantwoordelijkheid: advies overheid, WV, ziekenhuisbestuur, werkgroepen nationaal en lokaal

Doelmatige inkoop

- **Bundelen van inkoopkracht
NFU/iZAAZ/Zorgverzekeraars**
- **UMCG initiatieven:**
 - stollingsfactoren; biosimilars; TNF-alfa remmer
 - preferent rec factor VIII: €2,5 milj
 - infliximab biosimilar: €1-2,5milj
 - preferent TNF-alfa remmer bij RA: etanercept oplopend naar € 2 milj

Doelmatig gebruik en toepassen vb Reumatologie en MDL

- De Poeet-studie(ZonMw): reumatoïde artritis(RA) in remissie; de TNF-blokker wordt gestopt.
- Binnen het GLAS- cohort: groot cohort patiënten met spondylarthropathie(M.Bechterew) in UMCG en MCL, : Patient-Tailored Dose Reduction Of Tumor Necrosis Factor-Alpha Blocking Agents.
- Astep studie, waarbij bij patiënten met RA en Bechterew spiegels van biologicals worden bepaald. Afhankelijk van de spiegels, wordt dan de dosis aangepast (verlaagd en soms misschien verhoogd)
- MDL: TNF care project bij ziekte Crohn en colitis ulcerosa
- Protocollair voorschrijven/landelijke richtlijnen



Barrières en hobbels

- Maken van keuzes over disciplines of instituten heen inclusief het wegen van de belangen van de individuele patiënt
- Vemenging van “(onderzoek) belangen” tussen professionals/instituten en pharma
- Wisselende afspraken tussen ziekenhuizen en zorgverzekeraars
- Onduidelijke governance
- Onvoldoende incentives; whats in it for me???

Conclusies en Aanbevelingen (1)

- Inkoopafspraken zo veel mogelijk scheiden van andere relaties met firma's
- Speelveld voor doelmatige inkoop en toepassing creëren. Rol voor ziekenhuizen/professionals/zorgverzekeraars

Initiatief NFU en ZN

- Doelmatigheidsprojecten continueren en uitbouwen ook in afstemming met zorgverzekeraars
- Gaan voor eigen Preferentiebeleid
- Intensievere monitoring/uitkomstenonderzoek (registries).
- Declaratie op basis van nacalculatie en netto " inkoopprijs"; nader afspraken met zorgverzekeraars over daadwerkelijke kosten en innovatiegelden (incentives/shared savings)

Conclusies en Aanbevelingen (2)

- Shared savings inzetten voor zorginnovatie
- Protocollair gebruik/conform landelijke richtlijnen
- Pay for benefit en No cure no pay afspraken (industrie en zorgverzekeraar)
- Goede anticipatie op nieuwe ontwikkelingen: Blijven monitoren van de ontwikkelingen in het gebruik en het op de markt komen van nieuwe (dure) geneesmiddelen
- Relatie met Pharma primair mbt nieuwe ontwikkelingen/onderzoek
- Multidisciplinaire samenwerking/werkgroepen en patiënt participatie
- Heldere governance





www.umcg.nl

**DANK VOOR UW AANDACHT
VRAGEN??**



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Stelling

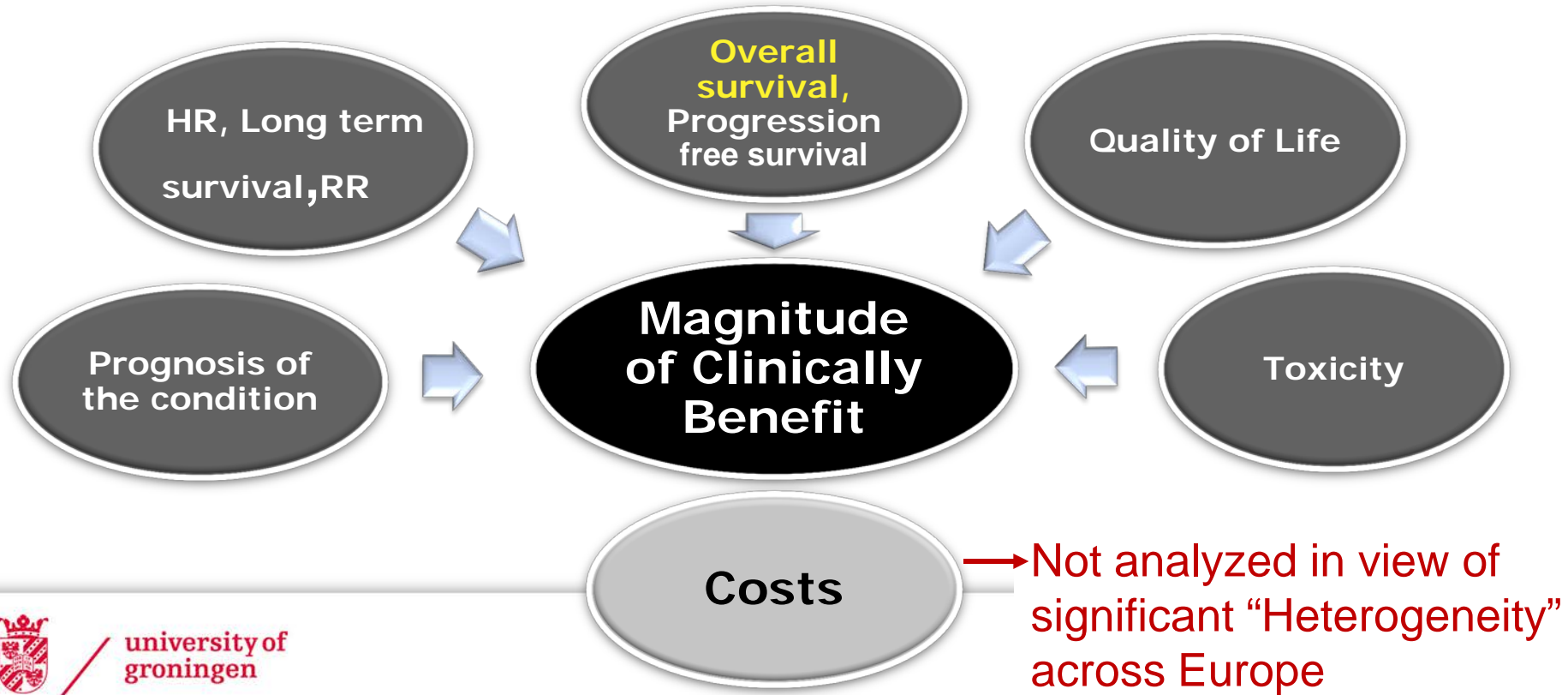
- A lot of expensive drugs are really too expensive while others are relatively cheap
- A lot of so called innovative (expensive) drugs are not innovative at all

Therefore development of an ESMO Magnitude of Clinical Benefit Scale (ESMO-MCBS)

ESMO

- **Committed**
 - to promote high-quality, rational, responsible & affordable cancer care
- **Wants to**
 - highlight treatments which bring substantial improvements to the duration of survival and/or the QoL of cancer patients
 - use the scale for accelerated reimbursement evaluation

Factors taken into account for ESMO-MCBS



Field testing Breast Cancer



Medication	Trial	Setting	Primary outcome	PFS control	PFS gain	PFS HR	OS control	OS gain	OS HR	QoL	ESMO-MCBS
Chemo +/- trastuzumab	HERA	(Neo)Adjuvant HER-2 positive tumors	DFS	2 y DFS 77.4%	8.4%	0.54 (0.43-0.67)					A
T-DM1 vs capecitabine + lapatinib	EMILIA	2 nd line metastatic after trastuzumab failure	PFS & OS	6.4 m	3.2 m	0.65 (0.55-0.77)	25 m	6.8 m	0.68 (0.55-0.85)	Later deterioration	5
Trastuzumab + chemo +/- pertuzumab	CLEOPATRA	1 st line metastatic	PFS	12.4 m	6 m	0.62 (0.52-0.84)	40.8 m	15.7 m	0.68 (0.56-0.84)	~	4
Lapatinib +/- trastuzumab	EGF 104900	3 rd line metastatic	PFS	2 m	1 m	0.73 (0.57-0.93)	9.5 m	4.5 m	0.74 (0.57-0.97)		4
Capecitabine +/- lapatinib	Geyer, 2006	2 nd line metastatic after trastuzumab failure	PFS	4.4 m	4 m	0.49 (0.34-0.71)			NS		3
Eribulin vs other chemo	EMBRACE	3 rd line metastatic after anthracycline & taxane	OS				10.6 m	2.5 m	0.81 (0.66-0.99)		2
Paclitaxel +/- health	Miller, 2007	1 st line metastatic	PFS	5.9 m	5.8 m	0.6			NS	~	2

Underlying Premises ESMO-MCBS

1. Cure takes precedence over deferral of death
2. Direct endpoints such as survival and QoL take precedence over surrogates such as PFS or RR
3. DFS in curative disease is a more valid surrogate than PFS or RR in non-curative disease
4. Interpretation of the evidence for benefit derived from surrogate outcomes (such as PFS) may be influenced by secondary outcome data





3 Rules, one of them

Check for:

- indicators of severe toxicity or reduced grade 3-4 toxicity that bothers patients
- Quality of life advantage validated scale



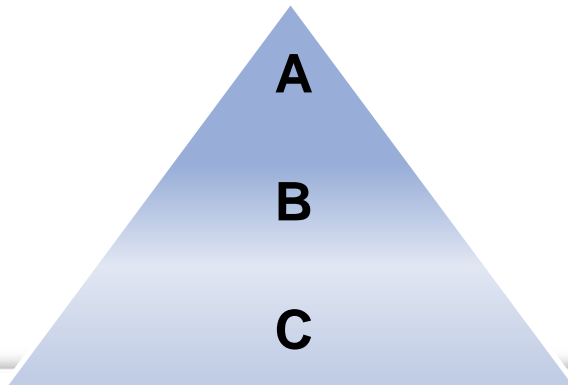
- Report final adjusted grade taken into account toxicity and quality of life



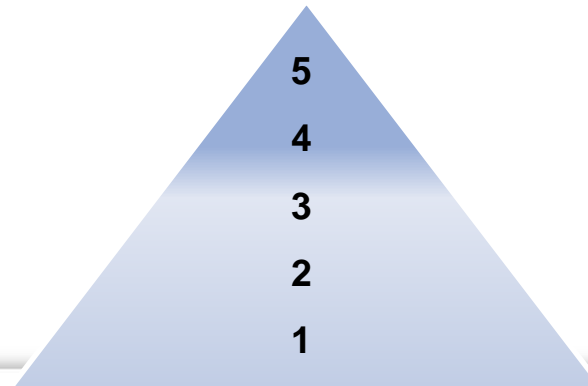
ESMO-MCBS substantial improvements

- Curative setting A & B or non-curative setting 5 & 4

Curative



Non-curative



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