Forecast Special Care Drugs

Development of the market of special care drugs

IGES Institut

Berlin, April 6th 2010

IGES Institut GmbH · www.iges.de
Friedrichstraße 180 · 10117 Berlin · Germany
☎ +49 30 230 80 90 · 🖷 +49 30 230 80 911

Content

- **Data and Methods**
- **Results and Discussion**
  - Special Care
  - Solitary Drugs

Methods

Data and influencing factors

- **Data**
  - Data base *Nationale Verordnungsinformation (NVI)* from Insight Health for the time period January 2003 to December 2009
- **Influencing factors**
  - Patent expiry
  - Expected introduction of generics / biosimilars
  - Expected adjustments of references prices (RP)
  - Where necessary, further influencing factors depending on the specific active ingredient (AIP) or therapeutic group (e.g. expected number of treatable patients after market access; competing products etc.)

Methods (1): modeling of consumption and sales

- **Approach**
  - Modeling of the expected consumption (DDD) for the years 2010 to 2013
  - Estimation of price development (sales price per DDD, weighted by number of receipts) for the years 2010 to 2013
  - Calculation of the expected sales for 2010 to 2013:
    - DDD X sales price
- **Application to the top-selling active ingredient groups***
  - Single AIP (top-selling AIP → about 90% of sales 2009 of the active ingredient group → n = 149 single AIPs)
  - Remaining AIPs of the respecitve group are summarized

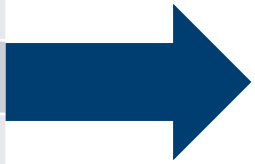
*** For the AIP groups of allergenic drugs. infusion solusions. mistletoe extracts and narcotics a simpliefied approach was used.**

Methods (2): modeling the expected pipeline

- **Data basis**
  - Pipeline list of the VfA
  - Own research and analysis
- **Assumptions**
  - How much new AIPs within a group till 2013?
  - Year of expected market launch?
- **Modeling per group with the help of known new entries since seit 2003**
  - Average annual usage from year 1 to 4 after market entry
  - Average annual sales from year 1 to 4 after market entry

Sub-groups of special care

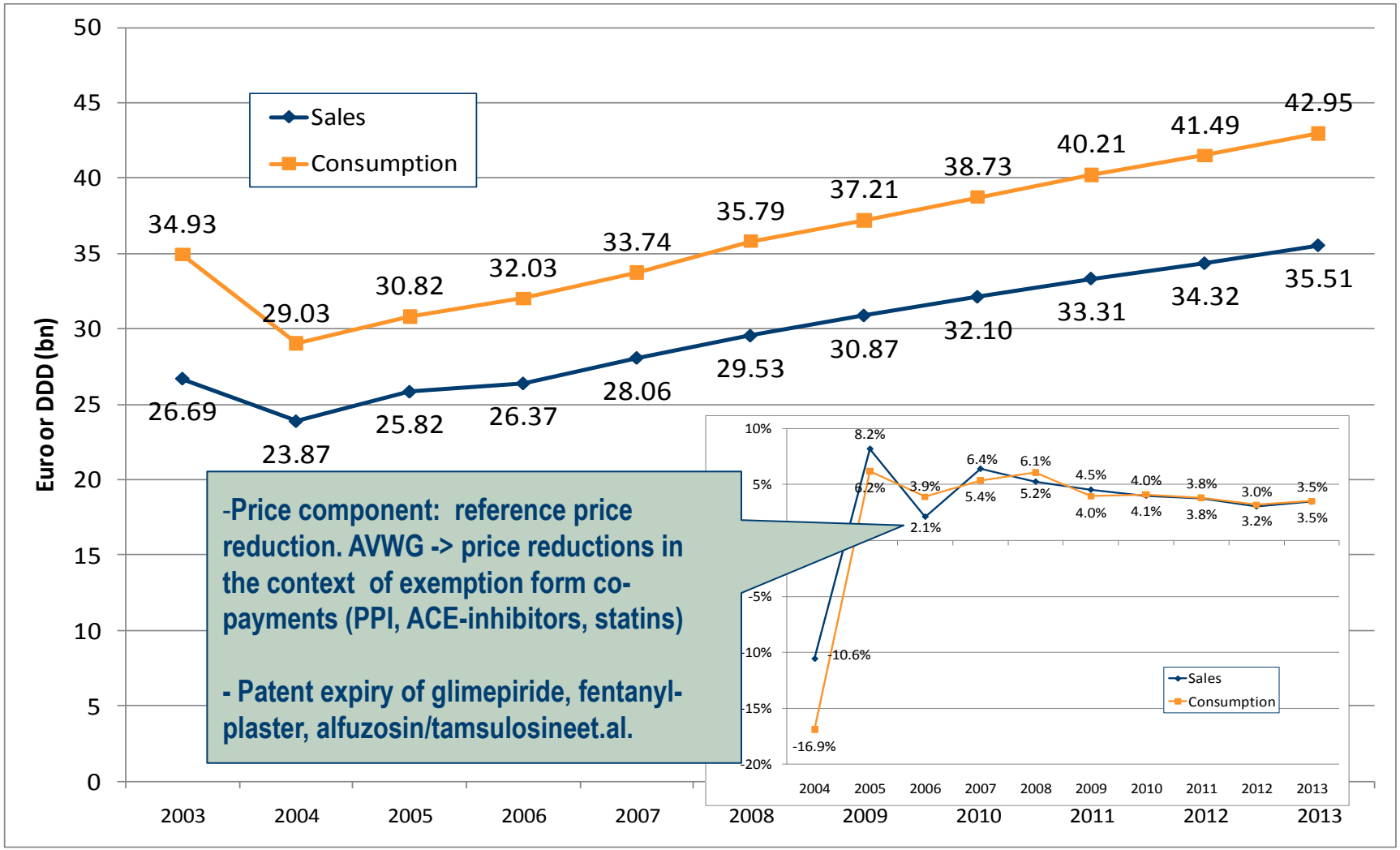
Group of Ingredient
Neurology (N03, N04, N07)
L04 Immunosuppressants
Cancer
L03 Immunostimulants
Miscellaneous (antidote. tests et.al.)
HIV
Infections (J02, J04, J05, J06, P01)
V01 Allergens
B03 Epo
B05 Infusions
Metabolism products (A16)
Coagulation (hemophilia, fibrinolysis)
Immune system (DMARDS M01)
Anesthetics. surgery (N01, N03)



Sub-Group Cancer
Cancer - new mode of action
Cancer - endocrine therapy (L02)
Cancer - conventional cytostatic drugs
Cancer - viscum

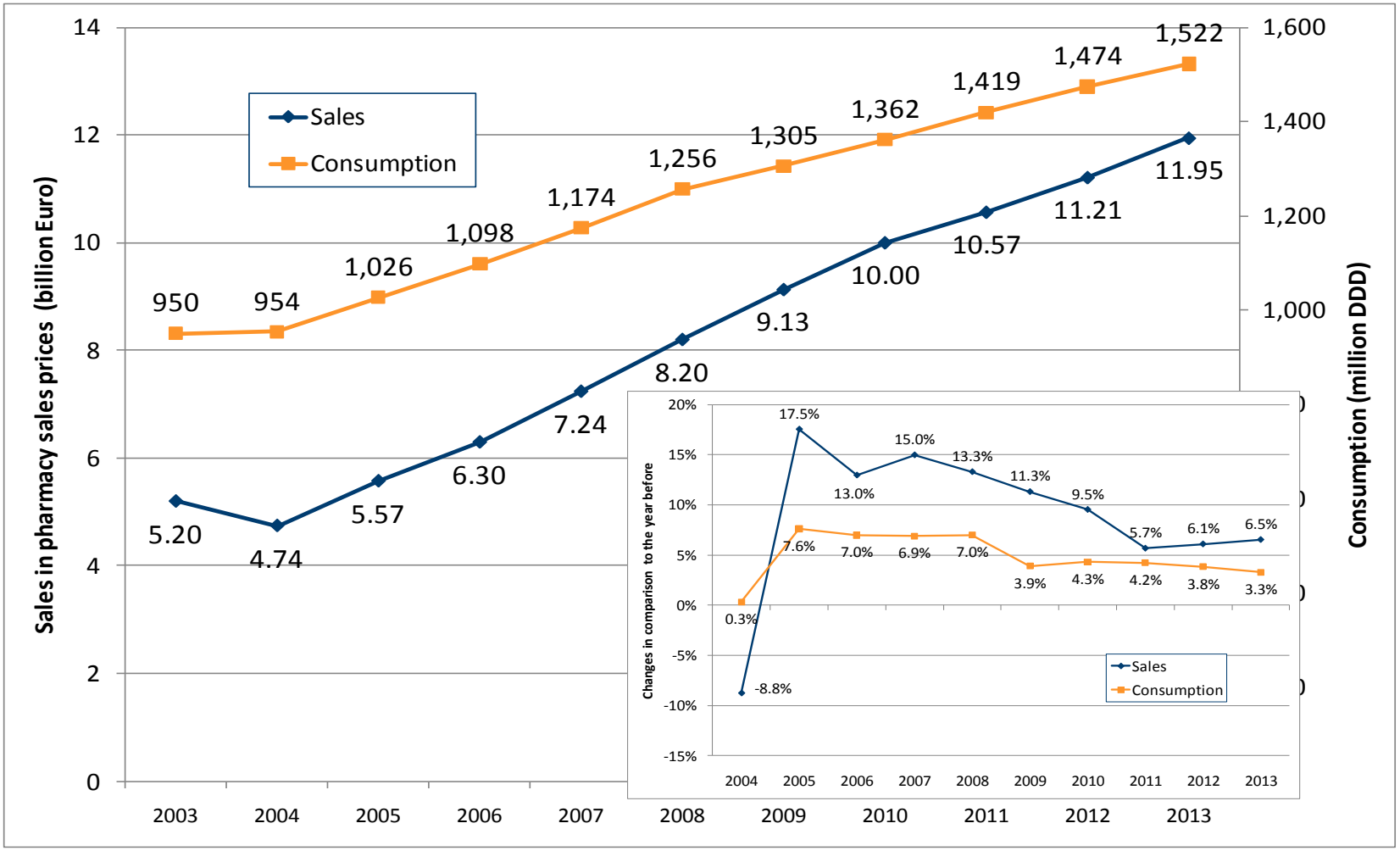
Results

Development of sales and consumption for the whole drug market in Germany (SHI)



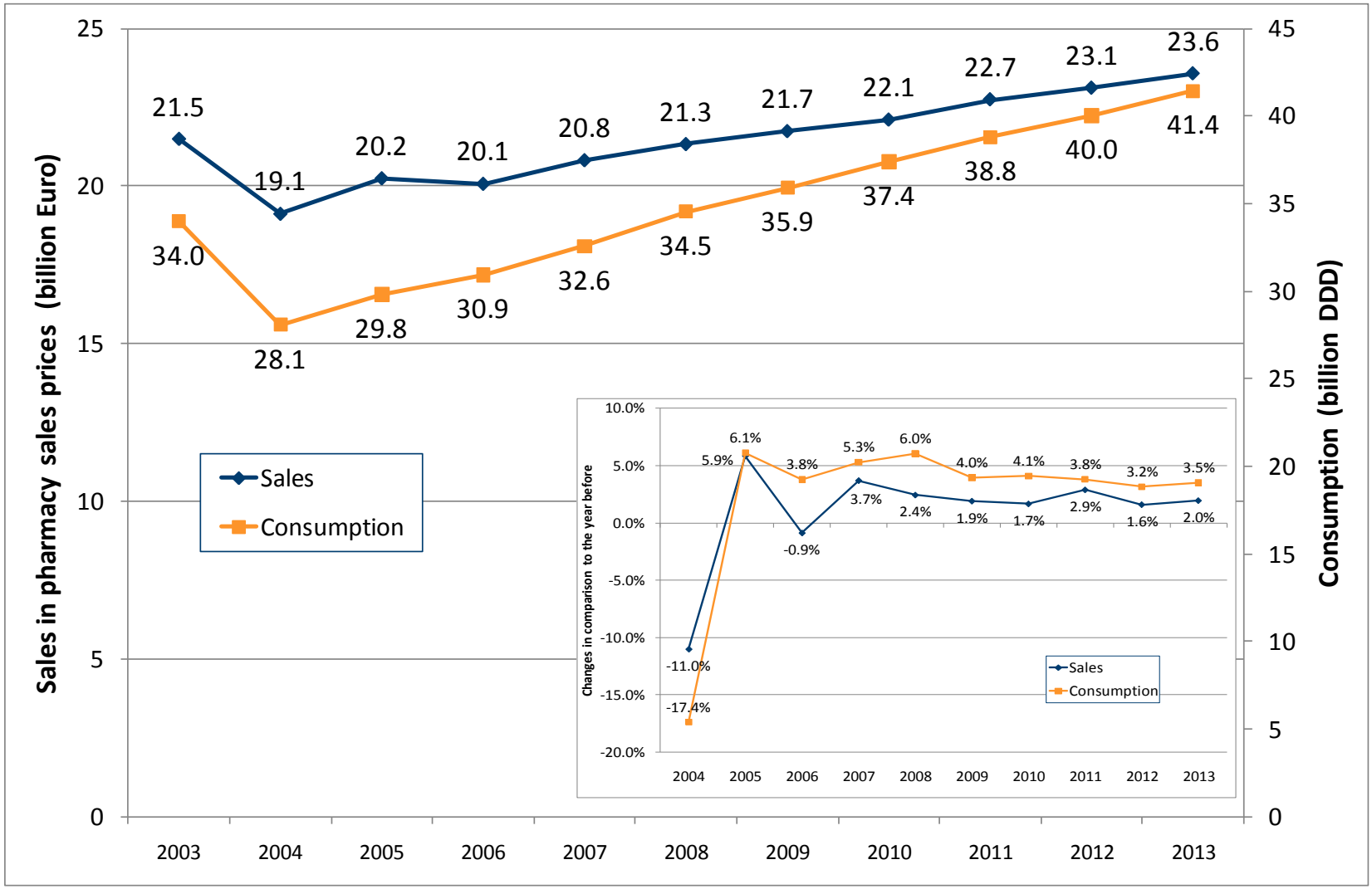
Calculations by IGES based on NVI (Insight Health)

Development of sales and consumption: Special Care



Calculations by IGES based on NVI (Insight Health)

Development of sales and consumption: Basic Care



Calculations by IGES based on NVI (Insight Health)

Overview of sales 2003-2009-2013 (m €)

Drug group	No. of compounds analyzed separately	2003	2009	2013
Immunosuppressants (L04)	20	507.1	1 602.2	2 762.5
Cancer (L01, L02)	40	798.2	1 536.6	1 947.2
Nervous system (N03, N04, N07)	19	976.1	1 753.1	1 879.8
Immunostimulants (L03)	5	775.1	1 245.3	1 436.3
Others (somatropin, bosentan, and others)	19	594.7	789.6	1 047.0
HIV / AIDS (J05)	11	366.4	641.7	960.1
Allergens (V01)	aggregated	192.0	345.0	503.3
Infectious diseases (J02, J04, J05, J06, P01)	11	281.9	379.5	458.7
Blood substitutes and perfusion solutions (B05)	aggregated	117.4	204.0	270.6
Erythropoetins (B03)	2	369.8	266.7	224.8
Metabolic disorders (A16)	10	66.9	156.2	212.0
Antihemorrhagics (B02)	10	70.5	94.1	112.2
Immune system (DMARDS M01)	2	47.7	78.4	99.7
Anesthetics, surgery (N01, M03)	aggregated	32.8	37.3	43.1
Total		5 196.8	9 129.8	11 957.3

Calculations by IGES based on NVI (Insight Health)

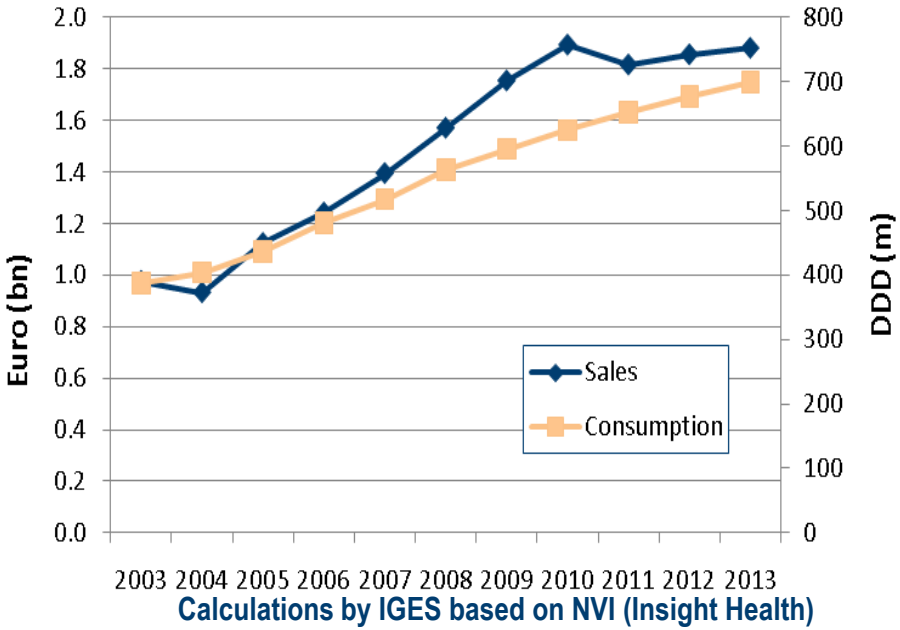
Overview of sales 2003-2009-2013 (m €) in the sub-groups of cancer

Group of Ingredient	No. of AIP analyzed separately	2003	2009	2013 (01/21/2010)	2013
Cancer - new mode of action	20	121.6	699.8	1,177.0	1,129.2
Cancer - endocrine therapy (L02)	10	459.2	601.9	778.0	589.3
Cancer - conventional cytostatic drugs	10	177.0	207.2	281.9	203.8
Cancer - viscum	aggregated	40.4	27.7	42.6	24.9
Total		798.2	1,536.6	2,279.4	1,947.2

Calculations by IGES based on NVI (Insight Health)

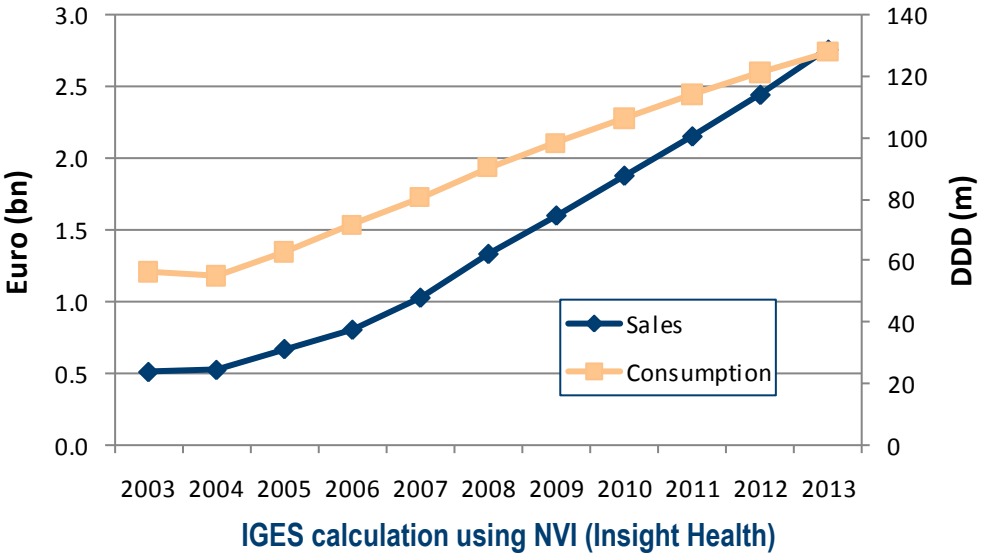
Neurvous system

- Further growth of consumption (aging of population), although with decreasing slope
- Patent expiries:
  - topiramat (late 2009);
  - future: rivastigmin, levetiracetam, pramipexol
- Pregabalin
  - Dominant compound is pregabalin (2009 about 13% of sales, 2013 about 23%).
  - Presumptions: saturation of consumption; moderate price increase (2,9% per year).

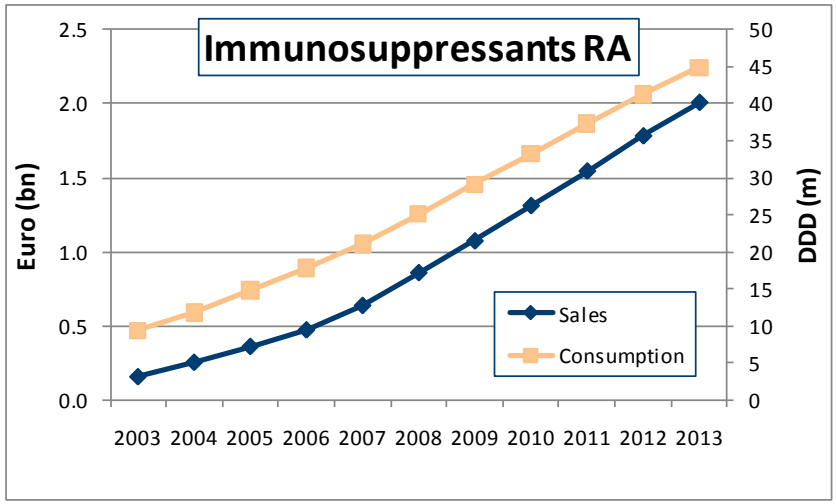


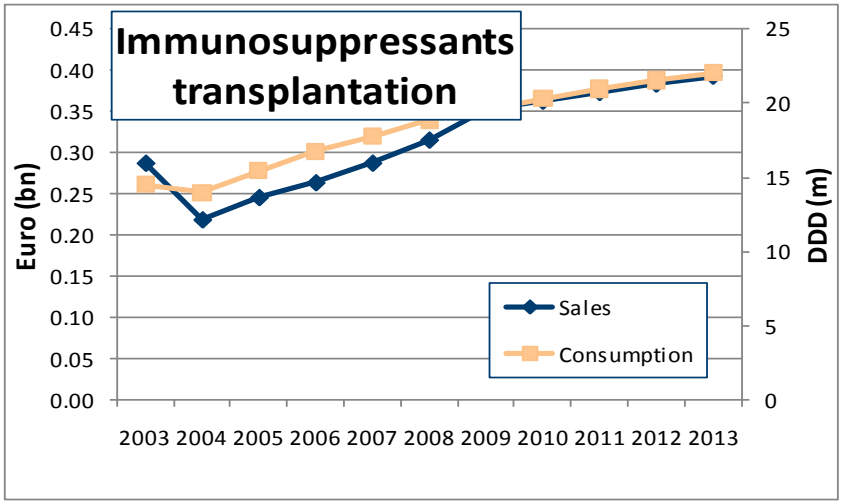
Immunosuppressants

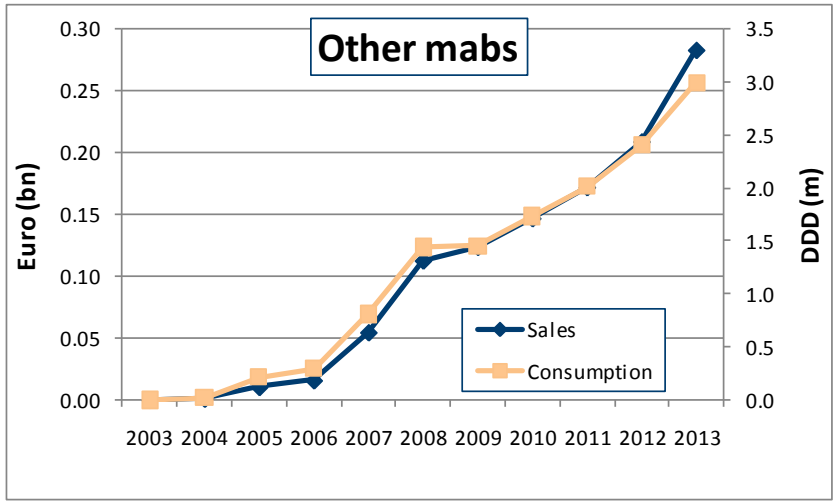
- TNF inhibitors show highest growth. Presumption: price stability due to increasing number of compounds (competition)
- Patent expiries:
  - Tacrolimus 2010
  - No further important expiries (Adalimumab 2016, Etanercept not before 2012)
- Sales increase more than consumption: Effect of structural shifts (share of low-price compounds like azathioprine or methotrexate is decreasing)

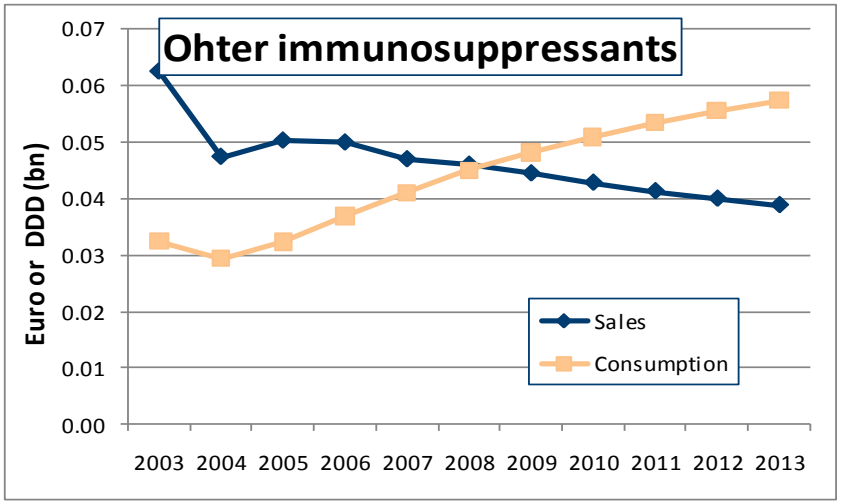


Development for subsegments of immunosuppressants





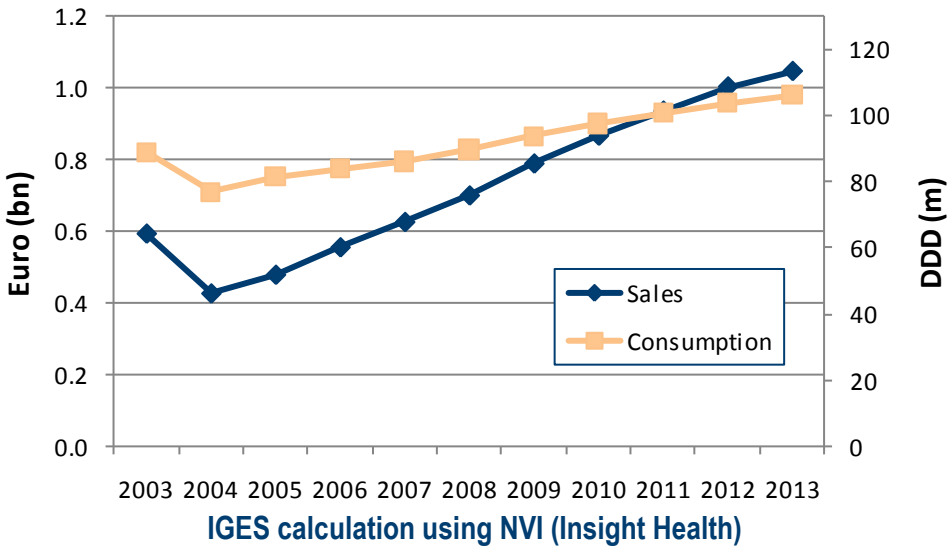




Calculations by IGES based on NVI (Insight Health)

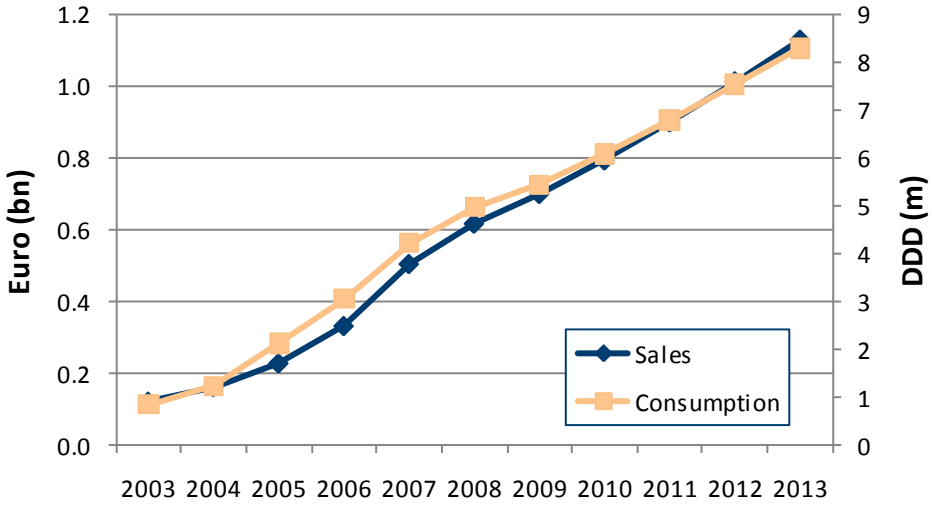
Others (somatropin, bosentan, other hypothalamic and pituitary hormones, antipsoriatics, antidotes, and others)

- Somatropin and bosentan show highest sales (38% of the group). Consumption still increasing, but there will be saturation, because the number of patients is limited.
- There will be a damped increase of somatropin sales, because there are specifications (association of SHI physicians and SHI), that the share of biosimilars should reach 7.5% in 2010. Presumption: 5% for 2010 and further increase for the following years.



Cancer drugs – mabs and protein kinase inhibitors

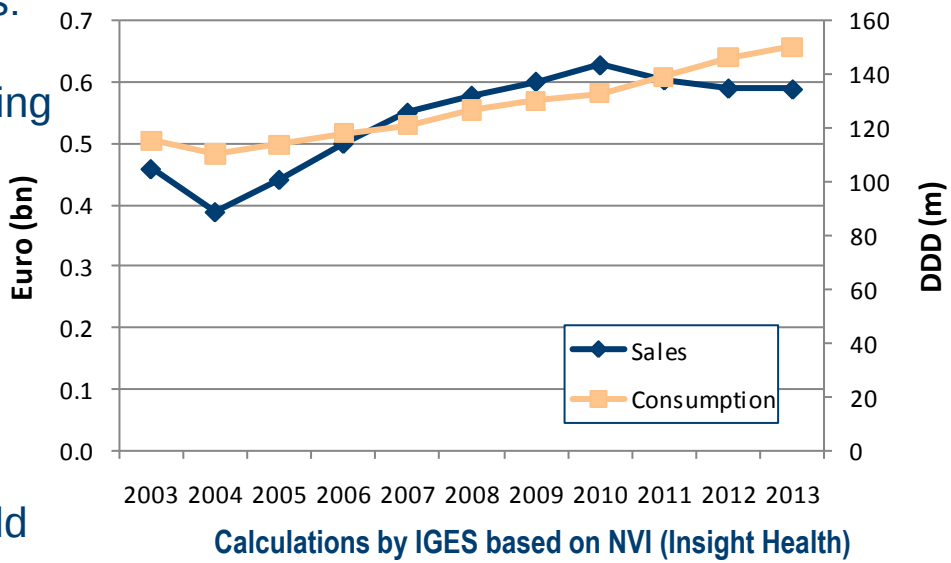
- Imatinib is dominant: 37% sales share in 2009, 33% in 2013. Consumption will increase further (surviving patients need futher treatment, new patients need new treatment). Patent expiry not before 2015.
- Development of consumption is different in most other compounds: Saturation can be assumed soon, because i) number of patients is lower, ii) suvival is shorter than in imatinib-treated patients.
- Prices will increase moderately (compared to other groups); however, the level of prices is high.



IGES calculation using NVI (Insight Health)

Cancer drugs – endocrine therapy

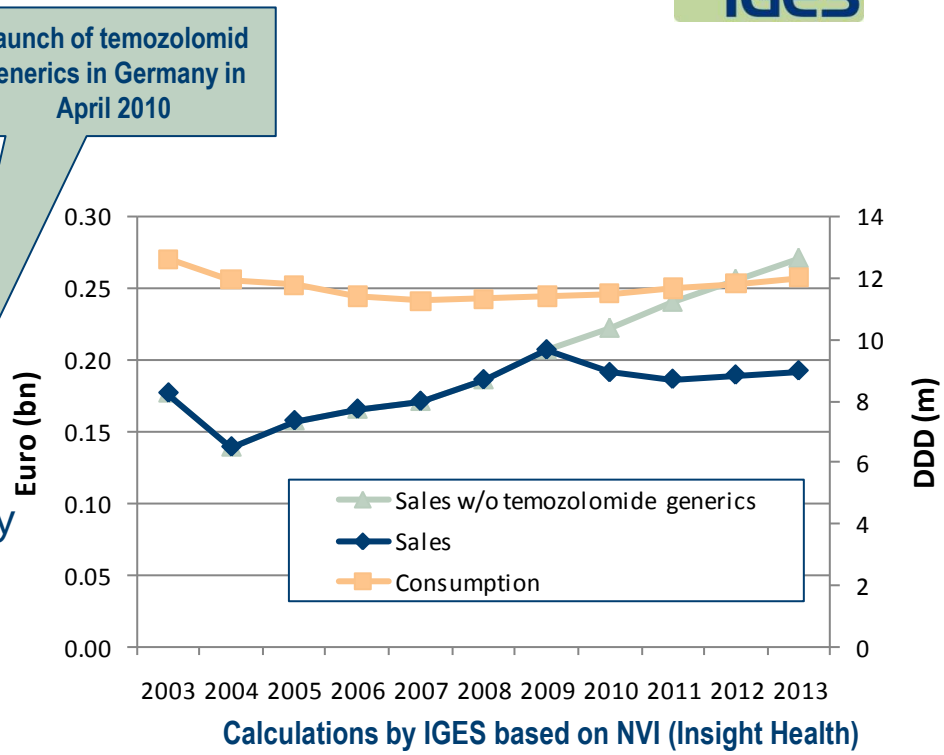
- Patent expiries of aromatase inhibitors (anastrozole end of 2010; presumptions: exemestan early 2011, letrozole 2012)
  → in 2011 sales decline despite increasing consumption
- Consumption of low cost tamoxifen declining. The prices of aromatase inhibitor generics will be higher than for tamoxifen. Hence, higher savings than modeled here are not very likely.
- Patents of buserelin and goserelin should have already expired. In total the consumption of theses two drugs is decreasing
- Development of abarelix / degarelix is uncertain; mechanism of action shows an advantage compared to buserelin / goserelin. Presumption: linear growth, better development of degarelix.



Calculations by IGES based on NVI (Insight Health)

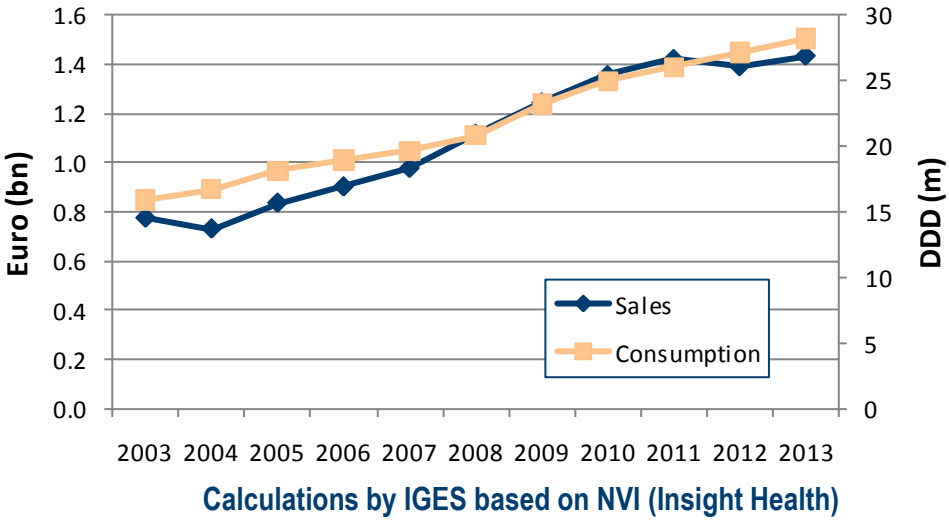
Cancer drugs – conventional antineoplastic agents

- Temozolomid ist the most important drug (41% of sales in 2009).
  - Teva has EU-approval since end of January 2010.
  - Merck lost patent litigation in USA (Patent until 2014)
  - Teva wants to wait for the decision of the Federal Circuit. Market entry possibly not before August 2013.
- Drug with the second highest sales (Capecitabin; indicated in advanced mamma-ca, colon-ca): sales decline since the end of 2008. In May 2009 study results came up that the survival of older patients with breast cancer is shortened.



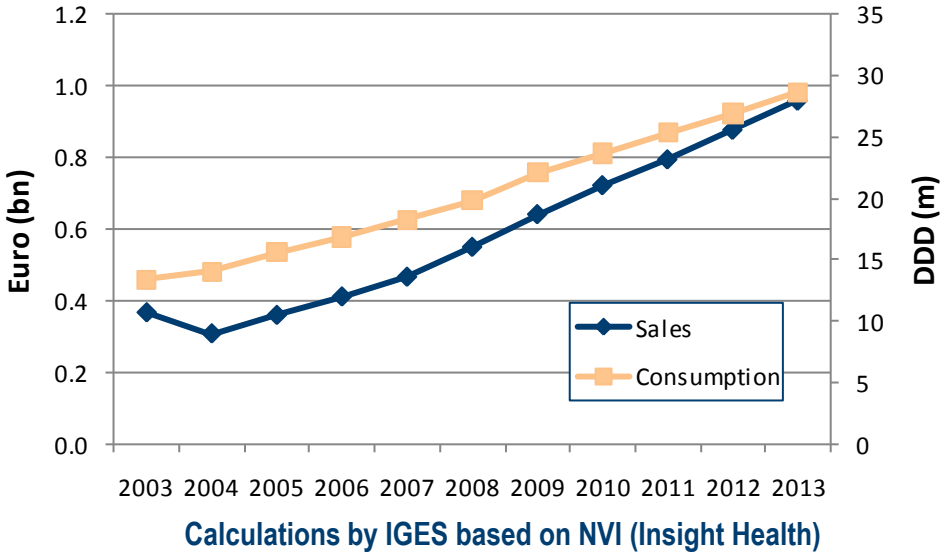
Immunostimulants

- Interferon beta-1b: since 2009 „bioidentical“ (Extavia) with lower price
  - causes price cut for original
  - increase in consumption
  - presumptions
    - reference price in 2011
    - biosimilars in 2012
    - price stability
- Glatiramer acetate
  - Further increase of consumption
  - Unclear: Development of price. Until now price similar to interferon beta. If price increase would be lower in the future, sales would be lower than predicted.



HIV / AIDS

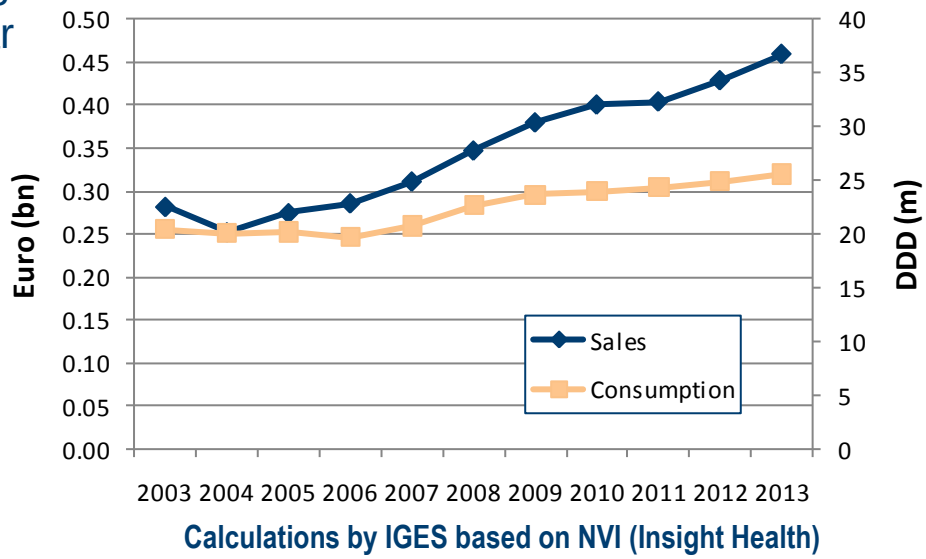
- Further increase of consumption, because the number of chronical ill patients is still rising.
- Several patent expiries expected in 2010: abacavir, lamivudin, nevirapin, saquinavir. Corresponding assumptions were considered. Drugs which patents expire have a comparatively small market share (max 5% of sales), so no large savings expected.
- Further market entries expected, some with new mode of action.
- Sales rise stronger than consumption: Partly an artifact because the proportion of fixed combinations increases and calculated DDDs are not comparable to mono drugs (for corresponding fixed combinations the calculated amount of DDDs is much lower).



Calculations by IGES based on NVI (Insight Health)

Infectious diseases

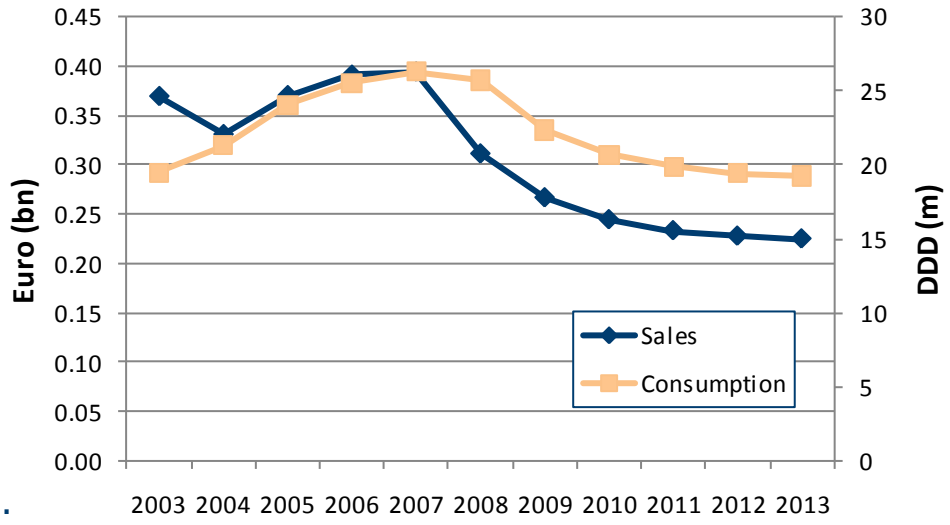
- Sales growing faster than consumption: Caused mainly by the highest selling drug (human immunoglobulins for intravascular administration) which shows high price increases – there are no evidence for lower price increases in the next years.
- Interesting: “sales driver“ is not an innovative product,but a blood product.
- Fluconazole and itraconazole under reference price scheme. Reference price reduction assumed in 2011.
- Patent expiry of ribavirin. Generics assumed at the beginning of 2011.
- Growth of sales in 2012 because of assumed effects about new entries.



Calculations by IGES based on NVI (Insight Health)

Erythropoetins

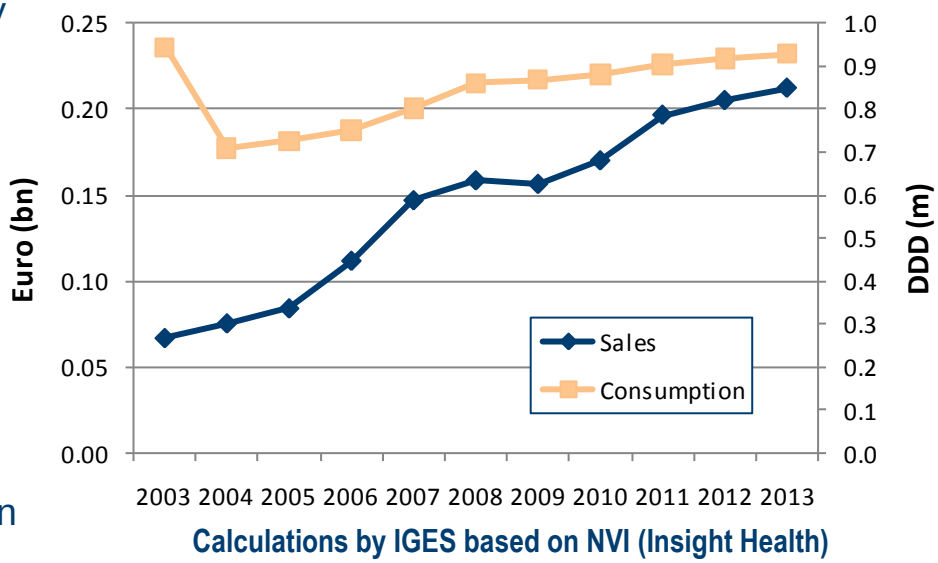
- Consumption is declining because of restrictions in oncological indications. However, relative constant (but unknown) demand by dialysis patients → evening-up to a steady level.
- Reference price adjustment was assumed and modeled
- Stronger decline of sales possible if other ways of distribution (other than retail pharmacy) become more common.



Calculations by IGES based on NVI (Insight Health)

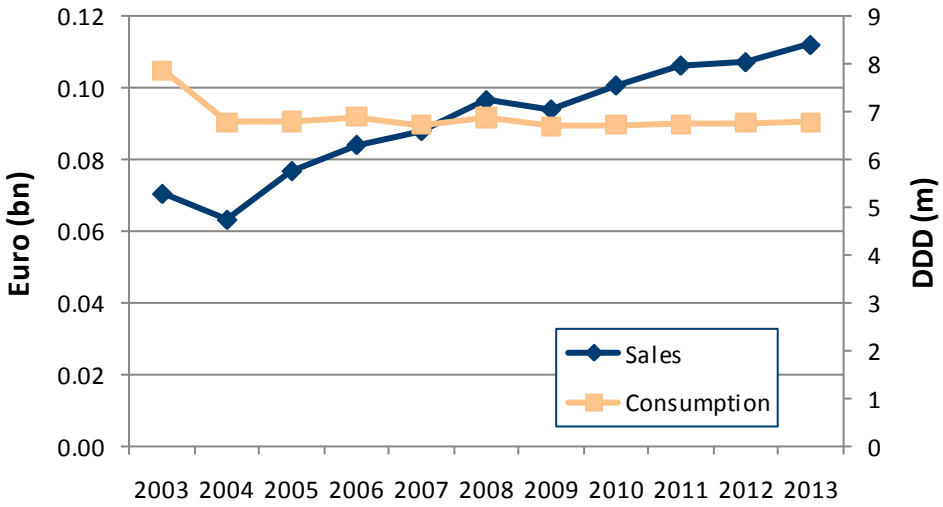
Metabolic disorders

- Under present circumstances: the group faces a satiation of demand; moderate price growth.
- A significant increase of sales till 2013 is hardly expected under the given assumptions:
  - Only two follow-on drugs of imiglucerase (Morbus Gaucher) announced
  - Number of patients is limited
- Drop of sales in 2009: delivery bottleneck for imiglucerase (since summer 09) leads to dramatic decline of consumption. (about one third). Genzyme announced capability of full delivery for the mid of April 2010.
- Further development depends fundamentally on the number of additional new drugs (besides the two drugs already considered) and their indications.



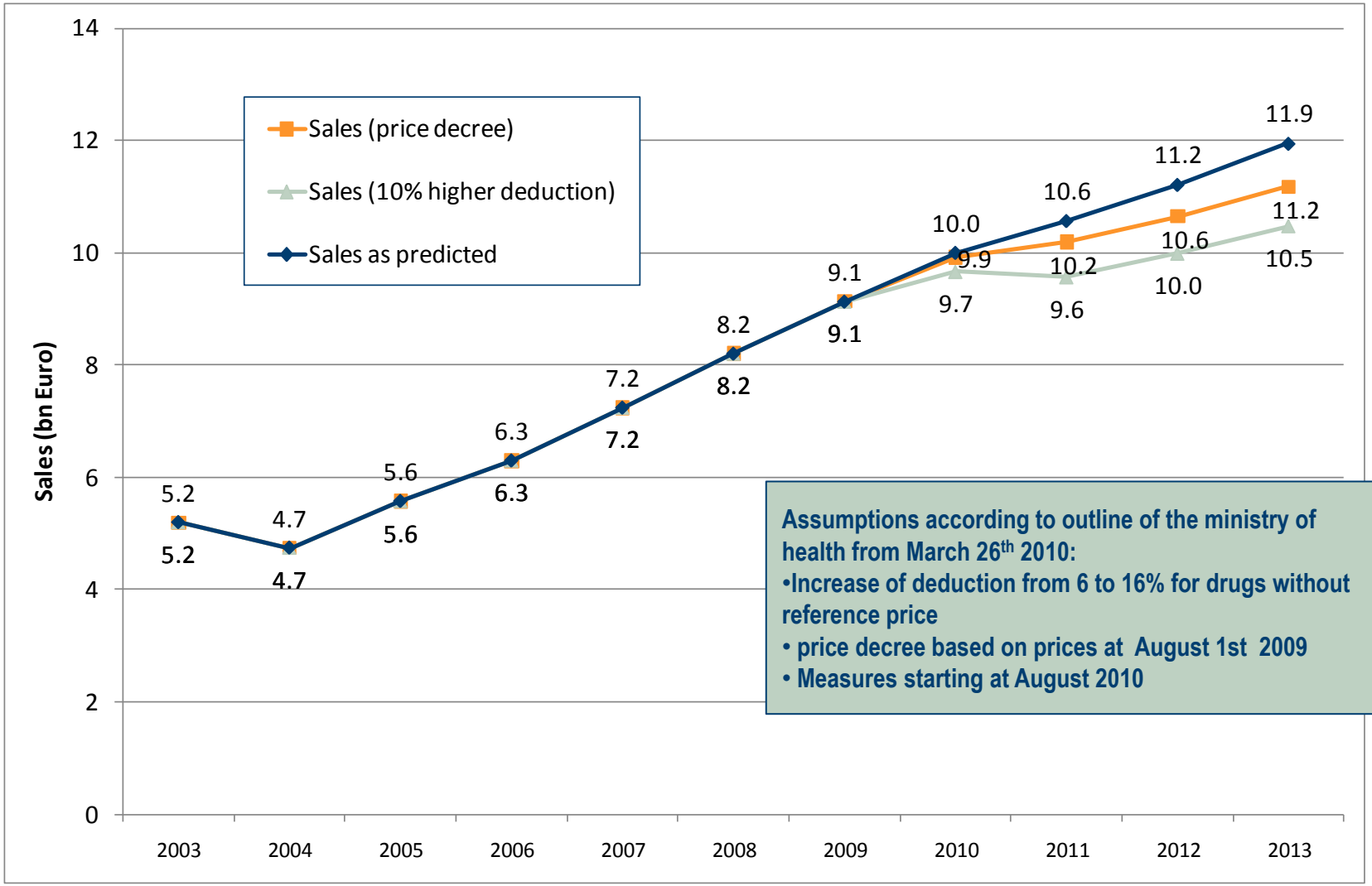
Antihemorrhagics

- Consumption nearly constant
  - number of patients with coagulopathy is stable
  - only one new therapeutic option (drug for Morbus Werlhof)
- Reasons of growth in sales:
  - price increases
  - structural shifs (low cost products still declining, high cost drugs growing)
- Assumptions for patent expiry:
  - octocog-alfa 2010 → biosimilars as of 2012
  - moroctocog patent probably also expires: very small market (€1.2m), approval of biosimilar may not be profitable.



Calculations by IGES based on NVI (Insight Health)

Influence of measures currently discussed by the coalition



Calculations by IGES based on NVI (Insight Health)

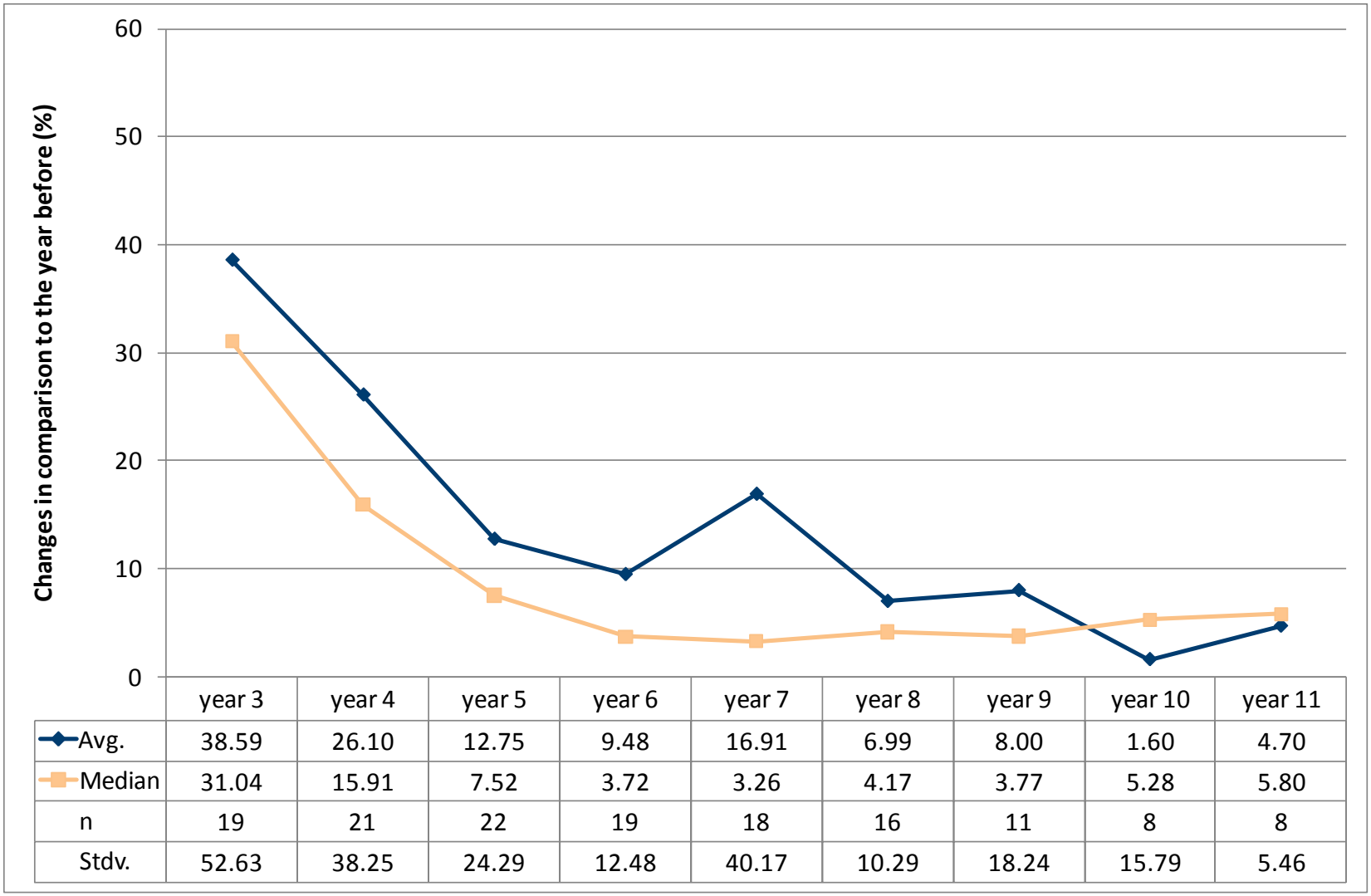
Solitaires

Overview of the development of solitaires
(Entry since 2001 in the areas A16, L01 and L04)

Drug	Indication	2003	2009	2013
Imatinib	CML	86,90	260,63	380,49
Sunitinib	renal cell carcinoma		99,72	120,48
Erlotinib	NSCLC		65,58	90,01
Sorafenib	renal cell carcinoma, lung cancer		59,13	67,26
Trastuzumab	breast cancer, HER2-positive	18,79	43,99	40,46
Imiglucerase	Gaucher disease I	48,61	41,28	56,45
Agalsidase alfa	Fabry disease	8,26	30,04	42,87
Bevacizumab	colon cancer, lung cancer		29,48	30,80
Alglucosidase	Pompe disease		23,10	26,58
Lapatinib	second line following therapy with trastuzumab		21,15	39,50
Agalsidase beta	Fabry disease	4,42	21,12	19,04
Dasatinib	resistence against imatinib		19,07	29,02
Nilotinib	resistence against imatinib		16,31	37,14
Idursulfase	mucopolysaccharidosis II		13,62	15,84
Eculuzimab	paroxysmal nocturnal hemoglobinuria (PNH)		12,74	12,74
Galsulfase	mucopolysaccharidosis VI		6,55	7,72
Laronidase	mucopolysaccharidosis I	0,09	5,16	5,80
Bexaroten	cutaneous T-cell lymphoma	1,36	4,27	6,89
Nitisinon	tyrosinemia I		3,53	4,62
Miglustat	Gaucher disease I	0,11	3,12	4,39
Gefitinib	lung cancer with mutation of EGFR		1,37	6,30
Betain	homocystinuria		0,65	0,00
Canakinumab	cryopyrin-associated periodic syndromes (CAPS)		0,11	3,97
Catumaxomab	malignant ascites		0,04	0,16
Alitretinoin	Kaposi sarcoma (cutaneous lesions)	0,00	0,00	0,00
Total		**168,54**	**781,75**	**1048,53**

Calculations by IGES based on NVI (Insight Health)

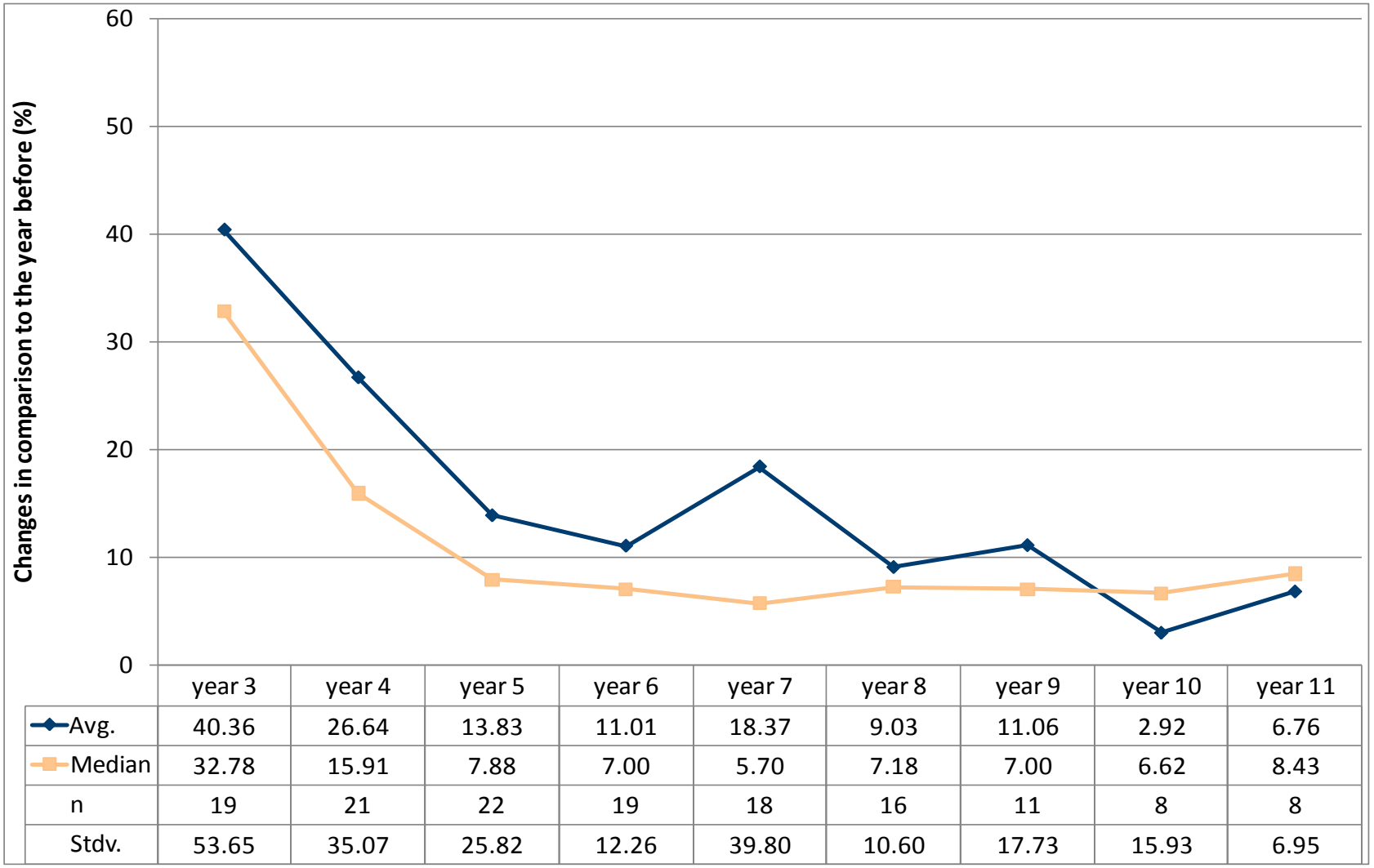
Development of the changes in consumption in case of solitaires (in years after entry)



	year 3	year 4	year 5	year 6	year 7	year 8	year 9	year 10	year 11
Avg.	38.59	26.10	12.75	9.48	16.91	6.99	8.00	1.60	4.70
Median	31.04	15.91	7.52	3.72	3.26	4.17	3.77	5.28	5.80
n	19	21	22	19	18	16	11	8	8
Stdv.	52.63	38.25	24.29	12.48	40.17	10.29	18.24	15.79	5.46

Calculations by IGES based on NVI (Insight Health)

Development of the changes in sales in case of solitaires (in years after entry)



	year 3	year 4	year 5	year 6	year 7	year 8	year 9	year 10	year 11
Avg.	40.36	26.64	13.83	11.01	18.37	9.03	11.06	2.92	6.76
Median	32.78	15.91	7.88	7.00	5.70	7.18	7.00	6.62	8.43
n	19	21	22	19	18	16	11	8	8
Stdv.	53.65	35.07	25.82	12.26	39.80	10.60	17.73	15.93	6.95

Calculations by IGES based on NVI (Insight Health)

www.iges.de