Introduction of cancer drugs - a focus on the Nordic countries

Comparator Report on Patient Access to Cancer Medicines in Europe Revisited
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My background

- 1977  MD Karolinska Institutet (KI), Stockholm, Sweden.
- 1981  Specialist in surgical oncology.
- 1982  PhD “Tamoxifen in breast cancer”.
- 1984-85 Post doc Roswell Park Cancer Institute, Buffalo, NY, USA.
- 1987  Specialist in oncology.
- 1987  Associate professor (KI).
- 1998-2003 Medical lead/director oncology Lilly and BMS.
- 2003-  KI research projects (www.comparatorreports.se)
- 2010-2012 Strategic advisor cancer Southern health care region, Sweden.
- 2012-2016 Head, dept of Oncology, Skåne University hospital, Lund, Sweden.
- 2016- Strategic advisor cancer Southern health care region and consultant in oncology at dept of Surgery, Hallands hosp, Halland, Sweden.
Cancer, an old-age disease. This has implications on access

Number of new cancer cases by age group and gender in Europe, 2012
Source: Ferlay et al (2013)
Cancer incidence is increasing

Cancer incidence cases per 100,000 inhabitants (crude rates, both sexes)

Notes: Hatched bars indicate that national estimates are based on regional data or based on neighboring countries.
Several factors can explain the increased incidence

Increase from 2.6 to 3.4 million cases between 1995–2012 in Europe*

Equals a 31% increase

Possible reasons

- Population growth: Total population grew by 5%
- Population aging: Share of 65+ in the total population up from 15 to 18%
- Risk factors: smoking, obesity, physical activity
- Screening
- Epidemiological development in other major diseases

* Europe includes here even the remaining Balkan states, Belarus, Moldova, Ukraine, and Russia.
Survival is improving

5-year age-adjusted relative survival rates for all cancers in patients aged ≥15 years, 1990–2007

Notes: Hatched bars indicate that national estimates are based on regional data.
Source:EUROCARE-3 to EUROCARE-5
Multiple factors contribute to increased survival

• Stronger increase in cancer incidence ($\approx 30\%$) than in mortality ($11\%$) between 1995 and 2012
• Reflected by simultaneous improvements in survival rates

Explanation: “major advances in cancer management” (De Angelis et al, 2014)

• Primary prevention: affected incidence, but cannot explain differential trends between incidence and mortality
• Screening: roll-out of mass screening programs since the 2000s; but large improvements in survival happened even before
• Diagnostics: enhanced possibilities of accurate treatment (Lichtenberg, 2014)
• Treatment: advances in medical treatment (e.g. novel cancer drugs) (Lichtenberg, 2014; Uyl-de Groot et al, 2010)
Large variations in cost of cancer per capita

Health spending on cancer: €169 in Europe 2014, but large country variations

Notes: Hatched bars indicate that the direct cost is estimated based on data from similar countries.
From drug discovery to patient access

- Drug development by pharma or academia
- Clinical trials
- Drug approval
  - Quality, efficacy and safety
- EMA in EU and FDA in the US
- After EMA approval it takes 2-3 months before EU ”approval”

- Value is then evaluated by different Health Technology Assessment (HTA) units in different countries.
- Focus on overall survival (OS) and quality of life (QoL).
- Cost per quality adjusted life years (QALY) is usually determined.
- A national agreement on price/costs is reached.
  - HTA vs drug company
  - May take up to 2 years or more but usually within 1 year.
Trend towards more targeted therapies, with immunotherapies also entering the market in later years. Too many drugs approved? PFS vs OS??

Source. EMA (2016)
Spending on cancer drugs doubled from €19 to €38 (in 2014 prices) in Europe
But large country variations

Notes: Data for EE, LV, LU, and EL only comprise retail sales. * The value for 2005 for IE is from 2006 and for PT from 2010.
Source: IMS Health MIDAS database
Direct costs are stabilizing while indirect costs are decreasing.

Notes:
- “direct” = direct health cost of cancer
- “m-loss” = productivity loss due to premature mortality from cancer. 2014 prices.

Cancer is defined as ICD-10 C00-D48 for direct health costs, and C00-C97,B21 for productivity loss.
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Health economics

Utility

1.0
0.5

1 year
2 year
Life expectancy

1 QALY

1 QALY
HTA process in different countries

- **Denmark**
  - Danish Medical Agency
- **Finland**
  - Pharmaceutical Pricing Board (PPB), Social Insurance Institute of Finland
- **Norway**
  - Norwegian Medicines Agency; Norwegian Institute of Public Health
- **Sweden**
  - TLV/NT
The value of new drugs

• A number of initiatives have been launched to assist in determining the value of new cancer medicines.
• Value as defined by ESMO-MCBS and actual uptake is connected, although not statistically significant. ESMO-MCBS also correlates with HTA assessments in France and Germany, but does not correlate well with assessments in Sweden. In particular, there is large variation for drugs receiving a MCBS of 4.
• Assessment of value and cost-effectiveness needs to become more integrated and iterative to take into account new data over time.
The Swedish process for introduction of oncology drugs

- Post EMA/EU approval.
- TLV (Tandvårds och Läkemedelsförmånsverket) for prescription drugs.
- NAC/NT/SKL (Nationella gruppen för cancerläkemedel/Nya Terapier/Sveriges Kommuner och Landsting) + TLV for hospital drugs.
- National recommendation by the NT group and a level 1, 2 or 3 for introduction.
- The post EMA/EU process may take 6-24 months.
- No budget is linked to the recommendation.
- The process may change 2019-20.
How has access to new cancer drugs been in selected countries?
Spending (SEK) on cancer drugs per incident case in different health care regions in Sweden.
New drugs for prostate cancer.

![Diagram showing sales per case (thousand €) for abiraterone acetate and enzalutamide in Denmark, Norway, Sweden, and EU Total in 2014.](image-url)
Immune therapy in metastatic melanoma (Ipilimumab)

Sales (thousand €) per case

- Denmark
- Norway
- Sweden
- EU

Years: 2009 to 2014
Access in Sweden to new drugs for melanoma and prostate cancer in relation to patients in need.

Percentage of patients in need having access 2011-2015
Pertuzumab use (SEK/ mortality in breast cancer) in different health care regions in Sweden.
HER2 drug (trastuzumab, pertuzumab, lapatinib and TDM-1) use (SEK/mortality in breast cancer) in different health care regions in Sweden.
Palbociclib use (SEK/ mortality in breast cancer) in different health care regions in Sweden.
Access in Norway and Denmark 4-5x Sweden (Medical need in 2017 was ~150 000 SEK/mortality)
Konsekvenser för individuella patienter i Region Skåne

- Herceptin (HER2+ bröstcancer) 2000-2005
  - ~100 pat fick inte behandling och gick miste om ca 1 års överlevnad.

- Yervoy (metastatiskt melanom) 2011-2012
  - ~50 pat fick inte behandling och 12-14 gick miste om långtidsöverlevnad (>5 år) och sannolik bot.

- Ibrance (hormonkänslig spridd bröstcancer)
  - Enbart 10-12 av 250 pat (prognos våren 2017) fick behandling 2017. Övriga gick miste om 10-12 mån förlängd sjukdomskontroll.
Införande av SoS nationella riktlinjer för behandling av kolorektalcancer- ett misslyckat projekt

Nils Wilking
Leg läk, Docent, Kl.

Anna Forsberg
Leg ssk, Professor, LU.
Förskrivning av CRC LM i Region Skåne efter projekt 04-12 2016
Användning från 2015-01 tom 2017-12 i tSEK/månad.
OBS Det som händer när det blir mediauppmärksamhet i oktober 2017.

Avastin® alt. Zaltrap® (Avastinkonkurent)- prio 8-9 enligt SoS riktlinjer
Vectibix® ska bara ges om allergi mot Erbitux®
A ten-digit-PIN is maintained by the National Tax Board for all individuals that have resided in Sweden since 1947.

According to Swedish law, the birth of the newborn child must be reported within 1 month after birth.

It is estimated that 90% of all births and 93% of all deaths are reported to Statistics Sweden within 10 days, and 98 and 100% respectively within 30 days.

Denmark, Finland and Norway have very similar PIN systems.
Take home messages

• High quality registries, especially in cancer, enables unique research opportunities and follow up.

• The key to success is the PIN.

• The PIN provides Sweden with a unique opportunity to collect Real World Data/Evidence (RWD/RWE).

• Sweden can provide RWD/RWE data, not only for cancer, but for all areas in health care.
Förslag till Värdebaserad BudgetProcess (VBP) för cancerläkemedel i Region Skåne

Nils Wilking

Jan 2017
Vad innebär VBP?

• Värdet av enskilt LM vid enskild diagnos/ linje i terapin bestäms baserat på TLV alt andra HTA källor.
  – Regional lista; uppdateras årligen alt vid behov.

• Värde sätts baserat på Life Year Gained (LYG)/QALY (Quality Adjusted Life Years) vinst med tak på (LYG 5-700 tSEK; QALY 700-1000 tSEK).
  – Ex LM X ger vid diagnos A (behandlingslinje 2) en förbättrad överlevnad med 3 månader (QALY + 2 mo) dvs får kosta max 150 tSEK/Pat

• Antal pat i RS beräknas och budget allokeras till resp enhet.
  – I RS beräknas det finnas ca 100 pat med diagnos A (behandlingslinje 2) dvs totalt anslås 100x 150 tSEK=15 000 tSEK/år i RS. Fördelas efter betalande klinik.

• Uppföljning sker kvartalsvis.

• Viss ”buffertbudget” till resp vc samt möjlihet till regional ”förstärkning” baserat på ev nya evidens.
VBP möjliggör följande:

• Att bästa möjliga överlevnad och livskvalitet för regionens cancerpatienter inom givna ekonomiska ramar uppfylls.

• Ramarna för cancerläkemedelsbehandling bestäms regionalt baserat på evidens- och budgetläge.  
  – Man undviker lokala, förskrivarstyrda, variationer i användning.

• En jämlig vård inom regionen.

• Budgetkontroll baserat på en förbättrad uppföljning.
The future

• Allocate budget based on value.
• Value is based on clinical studies.
  – PFS, OS, QoL.
• Collect real world data including PREMs and PROMs to define definite value.
Conclusions

- Cancer is a disease of old age. Present HTA evaluations do not take that into account.
- The HTA process slows down access in many countries including Sweden.
- Even after a positive HTA evaluation access to important cancer drugs may be very slow, especially in countries with regionalized health care.
  - Local budget considerations>> national/ international recommendations and guidelines.
- EMA has been criticized for approving too many drugs on surrogate endpoints like PFS/ progression free survival.
- **BUT!** It is up to the medical community to sort out the drugs that are of value, i.e. fulfill both PFS and OS and QoL criteria.
If any questions after this presentation please contact:

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