Cancer registries in support of planning and assessing population-based oncology outcomes in Europe

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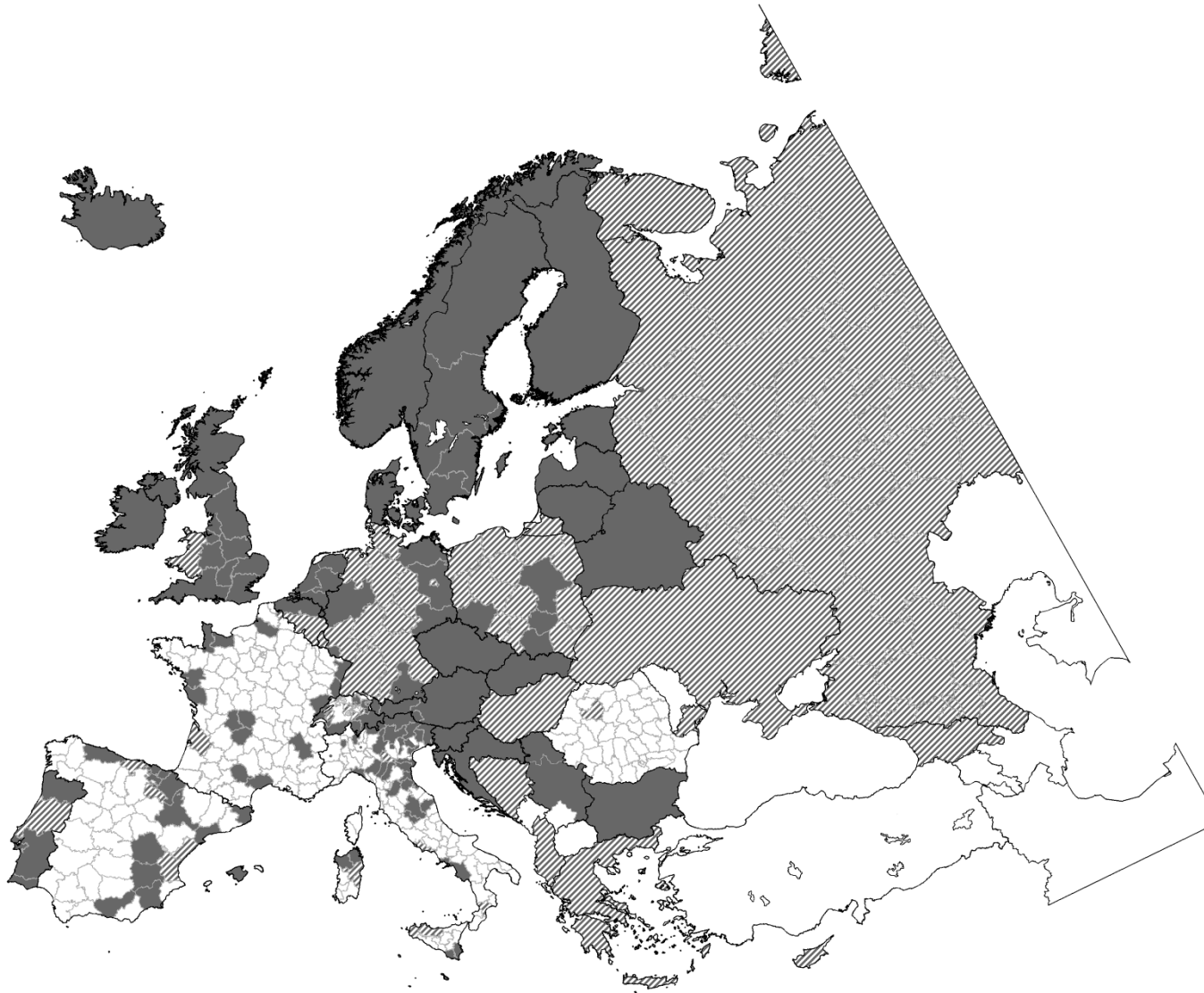Professor of Cancer Surveillance at Erasmus MC Rotterdam NL

Disclosure of interest

- Funded as coordinator by EU DG Research & Innovation
  - Within 6th and 7th Framework

- At Erasmus University MC Rotterdam, Dept of Public Health:
  - for translational epidemiology within EORTC Melanoma Group

- At Comprehensive Cancer Centre South (IKZ) & Eindhoven Cancer Registry
  - Also serving industry
  - Especially in phase 4 studies of utilization of targeted drugs
    - Haematological malignancies (Pharos project)
    - Kidney cancer

- Funded by DG Research & Innovation in FP 7
- Aims to strengthen infrastructure etc. for population-based cancer registries in the EU
  - Looking at good practices and stakeholders
    - Increasingly patients
  - Defining & Attacking the bottlenecks
    - Fantasy
    - Funding
    - Privacy

European Cancer registry coverage 2002

- Dark = High quality CR & i[...]
- Dashed = CR but not yet i[...]

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Critical importance/relevance of cancer in Europe in 2012 and beyond

- **Most frequent cause of death at age 25-75 yrs**
  - At middle age (35-69 yrs): about 50% of all deaths
    - NB lowering cardiovascular mortality

- **Lifetime risks**: up to 30-40%
  - Affected by failing prevention, mass screening and second cancers

- **Increasing in old age and with higher expectations → greater complexities with co-morbidities**
  - Dilemma's of over under- and overtreatment, especially at age 75+

- **Prevalence rising** from 1 to 5% → awareness

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Major ongoing changes: increasing interest & impact for cancer registries

- **Individualization (**more subgroups, new classifications)
  - **Molecular medicine**: diagnosis & treatment
    - Patterns of care, also palliative , 2nd , 3rd , 4th line etc.
      - Study questions *please* on utilization & nasty side effects
  - **Geriatric oncology**
    - Co-morbidities + their treatment: patterns of care etc
    - Study questions on over- and undertreatment
- **Increasing prevalence → Survivorship**
  - Disease + individual + long term side effects
  - Follow-up , surveillance: more or less active

A population-based cancer registry could provide objective information

- **On Incidence of all, including rare /multiple cancers**
  - Variation in time and place
  - Conduct or Support studies of etiology and screening
- ***On Detection & Survival of all cancers***
  - *Variation in time and place*
  - *Conduct or support prognostic studies: short/long term*
- ***On Process and outcome of oncological care***
  - *Variation in time and place*
  - *penetration & impact of new treatment approaches including survivorship*
  - *Contribute to planning and cost-effectiveness*

Position of cancer registries as of 2012

- A rather strong position for the cancer registries within cancer control (50+% of EU)
  - Public health and just survival

- **A rather small & heterogeneous position in the domain of quality of care (<25%)**
- Same for Quality of Life
  - Stronger in the northwest
  - Weaker to none in the south → east

Badly needed: actual picture of oncological realities on the ground

- Despite extensive guideline circus
- Usually large geographic variation in:
  - Processes and outcome (albeit less)
  - Of onco-care delivery
  - (and structure as well: subspecialization !!)
- **Even more in case of:**
  - new treatments (expensive or not)
  - Follow-up regimes
  - older patients and by SES

How to make these roles clear for the program owners & stakeholders of CR's

- **Structure the research activities**
  - Through designating research domains
  - From input (data collection) to output
  - Describe the capabilities & training needed
- **Show the anatomy and physiology of the CR as a program**
  - Because it is so multiple and heterogenous
- **Use metafors which also give perspective**
  - From milk to butter and cheese
  - The tree

Cancer registries are part of Public Health & clinical Research programmes
(often set up by 'others')

Cancer risk

- **Public Health + Prevention**
  - Monitoring: variation of incidence in time and place
    - Planning: scenario's etc .
  - Etiology & prevention
    - Linking to cohort studies: EPIC
    - Multiple primaries
    - Determinants of inequality
      - SES, Migrants

- **Public Health + Clinical**
  - Evaluation of mass screening
    - Linking to screening cohorts
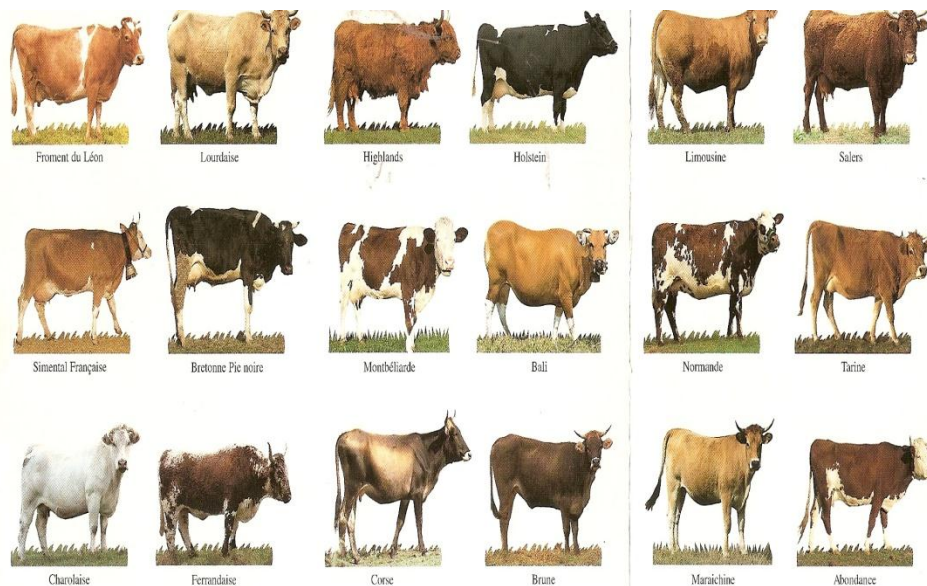   - Assessment of aggressiveness

Cancer outcome

- **Quality of Care**
  - Process
  - Outcome
    - Recurrence/death
  - Survivorship
  - Cost-effectiveness

- **Prognosis**
  - Biological determinants
  - Co-morbidity: elderly
  - Rare/uncommon tumours

Major role of registry: lay the basis for

- Understanding change by describing variation in time and/or place
- Discussions on medical aspects are brought at a higher level
    - Within the registry but also outside

- From retrospective to prospective evaluation also based on scenario developments

- Rather reality testing than truth finding

Romantic picture of the cancer registry:
from (uniform?) milk to multi-taste cheese?

ESMO, 2012

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The new registration tree input from roots & fertilizer. Output through leaves & fruits for stakeholders

Showing 4 major research domains

Public health
- primary prevention
- Evaluation mass screening

Quality of care
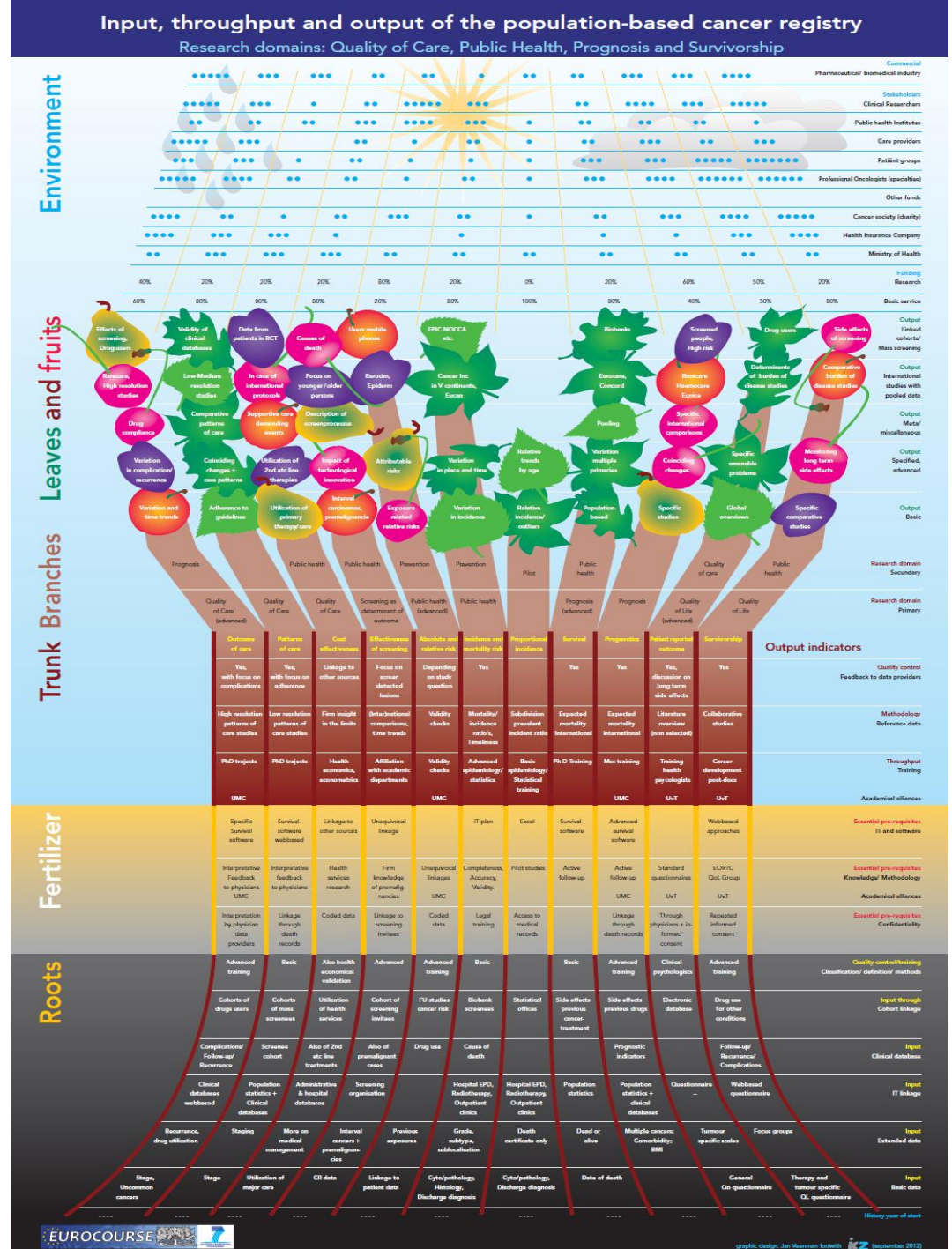- *process*
- *outcomes*
- *cost-effectiveness*

Prognosis
- *Determinants of Survival*
- *translational/clinical epidemiology*

Quality of life
- *patient reported oucome*
- *Aspects of survivorship*

Input, throughput and output of the population-based cancer registry — Research domains: Quality of Care, Public Health, Prognosis and Survivorship

Major strengths of cancer registries (real & potential)

- **Population-based**: all patients (almost)
  - As good as oncological care offered
- **Neutral**
- **Operational already since 1950's**
  - Many standards developed & problems solved
  - Linked with many cohorts
- **Part of international oncological network (IARC)**
  - Public health
    - Etiology & prevention
    - Mass screening
  - Cancer Research

Examples of population-based clinical studies using the cancer registry

- Patterns of care in the elderly
  - Staging e.g. colon cancer
  - Adjuvant treatments
  - Utilization of targeted drugs
  - Referral patterns to Radiotherapy
- Favourable Impact on survival of regionalization
- Rare cancers
- Survivorship: long term side effects
- Changing to sentinel node procedure in BC

Cancer registries and medical oncology: curative & palliative

- **Patterns of (primary) care studies of all patients**
  - **Variation of penetration** of primary treatments
    - Also of radiotherapy , immunotherapy etc
  - changes in survival related to systemic therapy
    - by stage , grade and age and co-morbidity
    - Penetration of molecular diagnosis
    - Then linked to biobanking → **translational research**
  - Occurrence of long term side effects (multiple cancer)
    - A.o. through survivorship studies /care plans
    - Input for scenario's of cost effectiveness

http://eco.iarc.fr/EUCAN/Default.aspx

[WWW.EUROCOURSE](http://www.eurocourse.org) .ORG

Change = Raison d'être of chronic disease registration: → watch out & adapt

- **Changes to be expected in:**
  - Underlying causes (tobacco, UV, viruses etc.) →
  - Detection, staging & treatment
  - Migration: regional and global (often SES-related)
  - Also in new /same (un)expected long term **(side) effects**: For better or for worse

- → Scenario based planning/allocation of (wo)manpower & **resources → 10-20 years**

Trees need to grow and bear fruits: through roots of clinical practice

a major statement

- Reality check serves to raise the level of _professional discussion_ in a multi-disciplinary setting
- through neutral feedback

- to check clinical
  – Validity
  – relevance

- However primarily intended to protect patients against
- _over- or undertreatment_
  – in regions/countries **without** functioning registries
- **And detect harmful**
  – **long term side effects**
- **So what matters is:**
  – Speed
  – Lightfootedness
  – Interaction with clinicians

So, what happened in WP 6

- Inventory of major clinical challenges related to unique, position of cancer registry
  - Population-based
  - Independent , neutral, external validity

- Any weakness: being (too) slow

- NB internal validity determined by
  - Oncological care as it is (the swamp)
  - Interaction through a.o. Feed back
  - Your registry personnel and access to data

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3 meetings with about 100 participants

- Making an overview of best practices
- Focussing then on
  - Geriatric oncology: cancer management in old (M Janssen)
  - Patient reported outcome: Melissa Thong, Lonneke vd Pol
  - Methodology of studying effects of regionalization & concentration
  - Linkage to & synergy with clinical databases
    - Pharmaco-epidemiology (van Herk-Sukel): systemic treatments
    - Tumor-specific specialty focussed clinical databases (A Green, M Lambe. M Wouters)
    - General clinical oncological databases (Germany)
    - Radiotherapy databases : referral primary & subsequent therapy

clinical evaluation

- With cancer registries as they
  - **Are:** thus with or without access to clinical records (50%)
  - **Can/may/should develop (with extra funding)**
    - Also staging/treatment(s) of recurrence/progression
    - Survivorship studies

- **Cancer registries as sampling frames for a.o. audits**
  - Opportunities (funding)
  - Limitations (privacy?)

- **Professional initiatives of clinical databases (population-based?)**
  - using the cancer registries for expertise, linking
  - Asking PopulationBased cancer registries to collect and analyse more data

Via Survivorship studies to patient registries (vd Poll et al. EJC 2011)

Patients view

- 20 year prevalence
- From 1 to now 3-4%
- From 5-25% in older people
- Suffer from variety of signs & symptoms

Eurocourse wp 6 inventory

- Literature overview
- About 150-200 studies
- More or less population-based
- 60% breast cancer

- Agreement on methods of approach and motives
  - Long term side effects
  - Interventions to improve QL
  - Obstacles

Challenges and pitfalls of clinical registries

- **Proliferation of databases**
  - Quality purposes (professional objectives: hurry ?)
    - To avoid dependency of others
    - provide cloud, power etc.

- **Strengthening but also (potentially) weakening traditional cancer registries → fragmentation**
  - **Only more than just data Infrastructure or -provider**
  - Methodologically and procedurally potentially unsound
    - Input valid?, neutral
    - Information can have legal impact (closure of hospitals)

Assume that cancer patients are in danger in the absence of any transparency or presence of cancer registries

- **Issues are**
  - How to inform doctors, patients & authorities in their absence after peer review
    - discussions needed → begin with population-based registries
  - thus needed: Rapid publication of variation in care delivery, soundly assessed
  - Shun details: expeditionary observational fishing studies with large amounts of data
    - Costing more than 200 € per patient
- Thus: study questions & clinical involvement are essential
    - Stratified by age

However: adress inequalities in care delivery among &within Member States

- If 50% of the EU population is covered at all
  - and 50% of this 50 % can do such clinical work
  - But fortunately rapidly growing

- (local) funding essential (= in your own interest)

- According to inventory:
  - Unfavourable in SE Europe
  - Favourable situation develops in:
    - UK, Holland, Belgium, Norway, Sweden, Denmark
    - Following in Finland Italy, Spain, Germany, France ??

more roads leading to Rome

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High/medium/low resolution studies of detection, staging and 1st treatment (Eurocare)

Very good idea but:

Sloppy performance (too few €)

- > 10 years after diagnosis
- small numbers
- arbitrary selections of relatively well performing :
- length bias in case of screening

- Also badly funded but by whom? Whose interest??
  - At home or EU?

Better Solution??

Stronger Responsibility at country/regional level

- Noblesse oblige
- perspectivise performance

- Rigorous study questions
  - Leading to discussion rather than fighting for truth

- Imagine reporting for non-participants to the study
  - And to patient groups

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Content & methodology

- **Geriatric oncology:**
  - expanding data sets with co-morbidity by good practices
- **Survivorship:** idem
  - (see Lonneke's presentation)
- **Regionalization etc:** idem
  - macro
- **Clinical registries:** chaotic
  - Pharmaco-epidemiology
  - Surgical: popping up
  - Systemic therapy assessment
    - Definite form to be found

Strategically: collaborate

- **With each other**
  - following the best practices
- **With loco-regional & clinical doctors through PhD students**
- European level: representatives from clinical oncological societies
- **Seek synergy with EORTC** through phase 4 studies (also ordered by EMA)
  - W Groups like QL, melanoma
  - EORTC is broadening interest to effectiveness after estimating efficacy

Implications for us: to intensify

- → Learning from each other
  - **Paradox : good data are often result from good work**
  - Rapid communication for when there are no data
  - How to come from nowhere to somewhere and then to 'heaven'
    - = More than publishing
    - …motivation comes from transparency through literature

Points of interest

- Do not try to be or become perfect
  - Multi-causality anyhow
  - Don't be perfect and slow
  - Follow the 20-80% rule and become perfect later
- Realize that it is only/primarily quality of care that matters (done in a scientific way)
  - Provoking discussion rather than truth

- Databases & registries are not an aim in itself

WP6: Interesting domains for population-based clinical cancer research

Tumour/Content driven

- **Cancer in the elderly**
  - < 70-80 yrs: yes ,but …..
  - > 75-80 yrs: no, unless
  - Co-morbidity → complexity
- **Treatment oriented**
  - New: ággressive multimodal /specific targeted therapies
  - Variation in utilization

- **Effects of regionalisation/ centralisation**
  - More roads lead to Rome
  - Micro versus macro

Methodology driven

- **Survivorship**
  - Amenable conditions
  - Spot over- or undertreatment
- **Clinical databases**
  - Short term: audit
    - Complications/recurrence
  - Long term:
    - side effects (incl vascular)
- **Cost effectiveness**
  - Input for modelling
  - Broader scope of change

Example of translational epidemiology: male-female difference in melanoma prognosis (Joosse et al., Esther de Vries etc)

- Known from cancer registries with information on stage/Breslowthickness , subsite &type
- Also needed:
  - data on ulceration and Mitotic activity
- Lit review of determinants & mechanisms:
  - behaviour, embryological, ROS
- Proposal to study this to melanoma experts
  - In: Munich cancer registry (data on progression)
  - With extensive surveillance data in EORTC-trials

Message from the platform: patients expect 'us' to collaborate & be valid + relevant + timely

- **Thus Important aspects**
  - data protection and safety + integrity
  - Benefits and dangers of modern IT
    - especially webbased data bases are vulnerable)

  - Attention for research process from begin to end
    - Methodology of population-based work
    - Be quick (also to serve uncovered areas)

    - ENCR can do a lot if adequately supported
      - Also from its own constituents (= good governance)
      - From the various stakeholders

Example of emerging challenge in 2013: impact of new treatments of advanced/metastatic/hormone refractory prostate cancer

- About 4-8 new targeted drugs approved vy FDA/EMA (soon?)
  - Each adding 4-6 months
  - with substantial side effects
- Huge international consortia of medical oncologists (de Bono et al., Sternberg)
  - Randomized trial etc etc
- Role of cancer registries ???
  - Variation in utilization at population level
  - Monitor 'çostly' side effectsincl QL

Challenges and paradoxes

- → Learning from each other
  - **Paradox : good data are often result from good work**
  - Rapid communication for when there are no data
  - How to come from nowhere to somewhere and then to 'heaven'
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Another example of Translational epi: peritoneal carcinomatosis with colorectal cancer

- < 10% of patients , with bad & less bad prognosis
- Few cancer registry studies being made (Klaver et al., Lemmens , de Hingst)
- Role of grade, subsite
- Explore role of heating
- Animal tests
- RCT

Essential type of study questions: simplicity = validity

Role of age, gender, SES /stage
- In various phases of the disease
- Specific biological quastions in case of biobanks
  - Existing pathology labs
  - De novo? Still rather rare

- Utilization of the various therapies
  - yes/no if yes: fully/partly
  - In case of drugs: dosages/schemes ?
  - In case of radiotherapy: access to their databases
  - In case of surgery: support of surgical audits so that they are independent

European dimension: why spend EU money and how?

- Quality of care is responsibility of the care system in each memberstate
- Learn form others
- If not happening now

Most needed : reinforcement of infra structure

But realise

- Most cancer registries are collecting data on
  - All : 50-150 cancers
  - At all ages
  - Newly diagnosed cancers + follow-up

- Doing active datacollection & quality control
  - Much standardization needed
- Involved in 4+ research domains with their specific knowledge and study questions

Beneficiaries

16 out of 17

from regions (6)

or countries <12 million

Executive Board from

-Finland, Sweden, Denmark

- Holland (2), Ireland

- Italy (2)

-Subcontractors from:

- France (IARC)

- Holland (MedLawconsult;)

- Belgium: ECCO