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

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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 & in CI 5 (VII–IX)
- Dashed = CR but not yet in CI 5 (VII–IX)

ESMO, 2012
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
Major ongoing changes: increasing interest & impact for cancer registries

• **Individualization** (more subgroups, new classifications)
  – Molecular medicine: diagnosis & treatment
    • Patterns of care, also palliative, 2\textsuperscript{nd}, 3\textsuperscript{rd}, 4\textsuperscript{th} 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 \rightarrow 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 metaphors 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

ESMO, 2012
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?
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 outcome
- Aspects of 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 \(\rightarrow\) translational research
  - Occurrence of long term side effects (multiple cancer)
    - A.o. through survivorship studies /care plans
    - Input for scenario’s of cost effectiveness

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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. Feedback
  - Your registry personnel and access to data
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
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: address 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
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
Conclusions wp 6
clinical evaluation is already booming

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: aggressive 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/Breslow thickness, 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 web-based 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 ‘costly’ side effects incl QL

ESMO, 2012
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’
    • = More than publishing
    • ...motivation comes from transparency through literature
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 questions 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 infrastructure
But realise

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

• Doing active data collection & 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

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