Cancer and pharmacoepidemiology in Finland

Information sources and research possibilities
What I will talk about

- Register-based data sources available in Finland
- Register linkage method
- Available background data for health research
- The Finnish Cancer Registry
- Other, most commonly used health registers for pharmacoepidemiological research
- Examples of studies related to cancer and pharmacoepi conducted in Finland
- Pros & cons of register-based approach
History of main mandatory data sources in health research

- **Finnish Cancer Registry**
  - Cancer incidence (1953)
  - Cancer screenings (1963)

- **Statistics Finland**
  - Causes of death (1971)

- **Population Register Center**
  - PID’s for all residents alive (1967)

- **Social Insurance Institution**
  - Reimbursable diseases (1967)
  - Reimbursable medicines (1994)

- **National Institute for Health and Welfare**
  - Hospital discharges
  - Malformation register (1963)
  - Medical birth register (1986)
  - Abortions and sterilisations (1977)

Miia Artama Dublin 23.9.2013
Finnish health registers

- Cancers 1953
- Health care personnel 1955
- Tuberculosis and STI 1958
- Malformations 1963
- Occupational diseases 1964
- Special medications 1964
- Adverse drug reactions 1966
- Hospital discharges 1967
- Mass screenings 1968
- Causes-of-death 1969
- Abortions and sterilisations 1977
- Exposure to cancer-hazardous material 1979
- Endoprostheses 1980
- Visual impairments 1983
- Births 1986
- Infectious diseases 1989
- Dental implants 1994
- Prescribed drugs 1994
- Outpatient visits in public hospitals 1998
  in health care centres 2011
Main information sources

Statistics Finland
- Complete ID
- Occupation, education, SES, place of residence, causes of death

Population Register Center
- Complete ID
- Place of birth
- Residential history
- Living coordinates
- Living conditions
- Parent-child –links
- Siblings
- Emigration/immigration date
- Date of death

Social Insurance Institution
- Complete ID
- Reimbursable diseases
- Prescribed drugs
- Disability pensions

Hospital labs
- Complete ID
- Details on cancer treatment etc.

Finnish Cancer Registry
- Complete ID
- Cancer incidence
- Cancer screenings

Finnish Institute for Occupational Health
- Complete ID
- Register of persons exposed to carcinogens

National Institute for Health and Welfare
- Complete ID
- Hospital discharges
- Births
- Malformations
- Abortions and sterilisations
- Hospital discharges
- Outpatient visits
- Blood sera (maternity cohort etc.)
- Survey data: life habits (smoking, alcohol, diet, BMI, physical exercise)
Register linkage method

- Based on unique ID entitled to all Finnish citizens
  - Improves the completeness of information
  - Relatively cheap to conduct
  - Recall bias and low participation rates can be avoided
- Population-level information is possible
  - Large study populations
  - Provides also results on population-level 😊
Register linkage method

- Administrative register data are available for research purposes
  - With separate permissions from the maintaining institutions
  - Informed consent is not needed, if the registered persons are not contacted
  - If information on medical records is used, a statement from ethical board(s) of the hospital area(s) is needed
Background data from Population Register Centre

- Updated continuously by Population Register Centre
- Frequently used as a reference / control group source
- Complete ID
- Country of birth
- Residencial history
- Living coordinates
- Emigration / immigration
- Link between parents and children / siblings
- Date of death
Background data from Statistics Finland

- Updated continuously by Statistics Finland
- Complete ID
- Education
- Income
- Socioeconomic status
- Country of birth
- Residence
- Marriages / divorces
- Link between parents and children / siblings
- Causes of death
Finnish Cancer Registry

- Register is established 1953
- Information on all cancer cases diagnosed in Finland
- Notification is a standard format set by the Finnish Cancer Registry
- Statistics Finland sends information of all death certificates where cancer is mentioned
### Notification to the Finnish Cancer Registry

<table>
<thead>
<tr>
<th>Personal identifier</th>
<th>Full name</th>
<th>1 [ ] Male</th>
<th>2 [ ] Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postal code</td>
<td>Municipality of residence</td>
<td></td>
<td></td>
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<tr>
<td>Previous cancer (if any):</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Primary site</td>
<td>Date of diagnosis</td>
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</tbody>
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#### CURRENT NEOPLASM

| Primary site | Date of diagnosis |

**Basis of diagnosis (one or more choices):**

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### FINNISH CANCER REGISTRY, laboratory notification

<table>
<thead>
<tr>
<th>Name</th>
<th>Personal identifier</th>
<th>Sex</th>
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<tr>
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</tbody>
</table>

| Sender of specimen (hospital and/or physician) |

| Primary site |

| Other sites |

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Included information of the Finnish Cancer Registry

- Includes i.a.:
- name and ID
- municipality of residence
- primary site and date of diagnosis
- basis of diagnosis
- stage: localised, regional metastases, distant metastases
- malignancy
- Histology / cell type
- treatment
- follow-up: date of death or emigration, cause of death
Data quality of the Finnish Cancer Registry

- Good historical files of **exposed persons**; no selection bias, no recall bias
- Plenty of registered data on **confounding factors**
- Complete population registration systems (follow-up for **death and emigration**); no losses to follow-up
- Virtually **complete nationwide**, population-based information on cancers
- Unique **personal identity codes**; no linking errors
- **Legislation** that allows record linkages
Finnish National Health Insurance

- All the Finnish citizens are entitled to Finland’s national health insurance
  - Maintained by the state
  - Financed through tax revenues
  - Includes pharmaceutical reimbursement system
    - Covers totally or partly the costs of prescribed drugs
    - Three reimbursement categories: basic (35%), lower (65%), total (100%) of the costs
  - All the reimbursed chronic diseases and related drugs are registered in the Social Insurance Institution (SII) database
SII databases

- Information on drug purchases and chronic diseases
- Register on Reimbursement Drugs: all medicines prescribed by a doctor and reimbursed by SII
- Special Reimbursement Register: specially reimbursed chronic diseases and related drug purchases
Register on drug purchases

- **Includes:**
  - Personal ID
  - ATC-code
  - Dose
  - Number of purchases
  - Date of purchase
  - Patient’s possible special reimbursement due to chronic disease
Register on reimbursement due to chronic diseases

- Includes information on
  - ID
  - Disease(s) with diagnosis
  - Type of reimbursement (basic, lower, upper)
  - Date of start of the reimbursement
Active research within the Finnish Cancer Registry

- Own research activity
- Own interests to use the data on research
- Apprx. half of the personnel (20) are researchers
- 100 scientific papers and 5 academic dissertations per year
- Impact factor is high (medical sciences 2000-2004 10.2 vs. Univ. Tampere 5.5, Univ. Helsinki 6.3)
Prostate cancer and PSA among statin users in the Finnish prostate cancer screening trial

Teemu J. Murtola¹², Teuvo L.J. Tammela³⁴, Liisa Määttänen⁵, Heini Huhtala¹, Elizabeth A. Platz⁶, Martti Ala-Opas⁷, Ulf-Håkan Stenman⁸ and Anssi Auvinen¹

- Relative risk of prostate cancer between statin or other cholesterol-lowering medication users and non-users was compared.
- Information on medication use was obtained from the national prescription database.
- The overall cancer incidence was decreased among statin-users (HR 0.75, 95% CI 0.63-0.89).
- Cholesterol-lowering with statins seems beneficial for prostate cancer prevention.
A nationwide cohort study on the incidence of meningioma in women using postmenopausal hormone therapy in Finland.

Korhonen K, Auvinen A, Lyytinen H, Yiikorkala O, Pukkala E.

- All women who had used hormone therapy at least for 6 months at the age of 50 years or older during 1994 and 2009 were included.
- Identified from the medical reimbursement register
- Total number of users n=131,500
- Information on meningioma diagnosis was obtained from the Finnish Cancer Registry
- Ever use of estradiol therapy was associated with an increased risk of meningioma (SIR 1.29, 95% CI 1.15-1.44)
- Among women who had used estradiol more than 3 years, the incidence for meningioma was 1.40-fold higher (95% CI 1.18-1.64) than in the background population.
Effect of various forms of postmenopausal hormone therapy on the risk of ovarian cancer--a population-based case control study from Finland.

Koskela-Niska V. Pukkala E. Lyytinen H. Ylikorkala O. Dvba T.

- Evaluation of the effect of various types of hormone therapy on the risk of epithelial ovarian cancer by histological subtype.
- Females with ovarian cancer aged \( \leq 50 \) 1995-2007 from the Finnish Cancer Registry
- Total number of cases was approximately 4000 patients.
- For each case, three controls matched for age and residence were obtained from the Finnish Population Register
- Information on parity, age at delivery, and hysterectomy was included in the analyses.
- The researchers found that estradiol-only therapy use for 5 years or more was associated with an increased risk for overall ovarian cancer (OR 1.35)
Circulating estrogens and progesterone during primiparous pregnancies and risk of maternal breast cancer.


Division of Cancer Epidemiology, German Cancer Research Center, Heidelberg, Germany. a.lukanova@dkfz.de

- A nested case-control study within the Finnish maternity cohort
- Cases: primiparous women with delivered a singleton offspring before the age of 40
- Two individually matched controls by age and time of sampling were selected for each case.
- Hormone levels were measured from the first trimester serum.
- An overall connection between hormone level and breast cancer in the study population was not found
- Estradiol concentrations were positively associated with risk of breast cancer before age 40.
Limitations of the register based data

• No information on use of drugs outside the reimbursement system
  • Over the counter medicines
  • Drugs given for institutionalised persons or in hospitals => possible observation gaps during treatments in hospitals
  • Random use of medicines
Limitations of the register based data (II)

• No certain information on use of the drug, or timing of drug use (based on purchases)
• Administrative health registers are maintained for other purposes than research => probably do not provide all the needed information
Strengths of register-based approach

- Information on
  - Co-morbidity, other diseases
  - drug interactions
  - later adverse effects after cancer
  - Time window for different exposures and outcomes: effects of other diseases/medication before and after cancer, changes in medical and other treatments
Strengths of register-based approach (II)

Excellent possibilities for research and follow-up:

• Detailed and large information on background factors of probably heterogenous patient groups
• Possibilities for long-term follow-up of exposed or cancer cases
• Possibilities for both cohort and case-control settings
Needed collaboration

• Rare exposures / outcomes
  => few cases from individual Register
• New medications on market
  => short follow-up, few cases
• Overall knowledge of each other and available datasources
  => Experience of multi-national studies
  => Keys for larger successful drug safety studies in the future
More information available on

- Finnish Cancer Registry
- SII of Finland
  http://www.kela.fi/web/en
- National Institute for Health and Welfare
- Statistics Finland
  https://www.tilastokeskus.fi/index_en.html
- Population Register Centre
Additional information from

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00130 Helsinki, Finland
E-mail to: miia.artama@cancer.fi