NIVA course:
Nordic Occupational Cancer (NOCCA) Studies
29 - 31 August 2011, Mariehamn, Åland

- **Course Leader:** Eero Pukkala, Finnish Cancer Registry

- **Main topics**
  - demonstration of estimation method and recent findings of the occupational cancer risk of the NOCCA project
  - construction of Nordic Job Exposure Matrix; trends of occupational exposures in the Nordic countries
  - occupation as a determinant of health habits
  - statistical methodologies related to use of partly ecological measurement of work exposures and confounders
  - NOCCA as a source of *IARC Monographs* programme
  - importance of new findings to the occupational health promotion

- **Information:** zsuzsanna.renko@ttl.fi
Unique potential of register-based epidemiology in the Nordic countries

Especially in the studies on occupation and cancer

Eero Pukkala
Finnish Cancer Registry
"Paradise of epidemiology"

- Good historical files of exposed persons
- Much 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 outcome registries (e.g., Cancer Registry)
- Unique personal identity codes; no linking errors
- Legislation that allows record linkages

=> Results are technically true

… but what about the interpretation?
Main data sources
(computerised and linkable)

Population Register Center (VRK) 1967+
- complete ID
- place of birth
- residential history
- living coordinates
- living conditions
- parent-child links
- PID's of children
- immigration/emigration date
- date of death

Social Insurance Institution
- reimbursable diseases 1967+
- reimbursable medicines 1994+

Statistics Finland
- Longitudinal data (1950–1985)
- occupations
- SES, place of residence
- causes of death

Finnish Cancer Registry
- cancer incidence 1953+
- cancer screenings 1963+

National Research and Development Centre for Welfare and Health (STAKES)
- hospital discharges
- birth parameters
- malformations
- Finnish Information Centre for Register Research (RETKI)
- 2009: THL

Public Health Institute (KTL)
- Survey data (Mini Finland 1967, FinRisk 1972+, Adult Population Health Survey 1978+): life habits (smoking, alcohol, diet, BMI, physical exercise etc)
- Blood sera (maternity cohort etc.)

Finnish Institute for Occupational Health (FiOH)
- register of persons exposed to carcinogens (ASA)
- numerous cohorts of exposed persons

Whole population
Population sample

Usually not true: “This cannot be done.”
KEY ISSUE: REGISTER DATA QUALITY
Percentage of cancers registered to Finnish Cancer Registry (2001)

After 3 months

After 12 months
Failures in record linkage between Finnish Cancer Registry and death certificate data.
Effect of errors in linkage key:
Cancer risk among asbestos mine workers (old cohort)

EXCESS risk (SIR 1.35; 1.17-1.55) turns to a significantly DECREASED risk if there are 15% or more linkage failures.
Effect of errors in linkage key:
Cancer risk among asbestos mine workers (old cohort)

If the error is 1%, the expected number is still 31% too high!

Obs: −20%
Exp: + 625%
Can we trust on results based on linked routine registers?
OR from a case-referent study [1]:

Pancreatic cancer in Finland

<table>
<thead>
<tr>
<th>Occupational branch</th>
<th>Case-referent</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>OR(^1)</td>
<td>95% CI</td>
</tr>
<tr>
<td>Agriculture, forestry, fishing</td>
<td>169</td>
<td>0.8</td>
<td>0.7-1.0</td>
</tr>
<tr>
<td>Mining and quarrying</td>
<td>6</td>
<td>1.5</td>
<td>0.6-4.2</td>
</tr>
<tr>
<td>Transport and communication</td>
<td>54</td>
<td>1.0</td>
<td>0.7-1.5</td>
</tr>
<tr>
<td>Textiles and clothes</td>
<td>12</td>
<td>0.7</td>
<td>0.4-1.4</td>
</tr>
<tr>
<td>Sawmilling</td>
<td>10</td>
<td>1.3</td>
<td>0.6-2.9</td>
</tr>
<tr>
<td>Paper and board</td>
<td>17</td>
<td>1.4</td>
<td>0.8-2.5</td>
</tr>
<tr>
<td>Restaurants, cafés, snack bars</td>
<td>7</td>
<td>1.8</td>
<td>0.3-1.9</td>
</tr>
<tr>
<td>Hairdressing, manicure</td>
<td>4</td>
<td>1.8</td>
<td>0.5-6.4</td>
</tr>
</tbody>
</table>

\(^1\) Odds ratios adjusted for age, gender, smoking, alcohol consumption and diabetes.

OR from a case-referent study [1] vs. SIR of census-based calculation [2]:

Pancreatic cancer in Finland

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\(^1\) Odds ratios adjusted for age, gender, smoking, alcohol consumption and diabetes.

\(^2\) Adjusted for social class.


Nordic biological specimen banks as basis for studies of cancer causes and control – more than 2 million sample donors, 25 million person-years and 100,000 prospective cancers

Acta Oncol. 2007; 46: 286-307
# Cervical cancer, top/bottom occupations

(SIR adjusted for social class, ages 35-64 years, Finland)

<table>
<thead>
<tr>
<th>Occupation</th>
<th>SIR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hotel/restaurant manageresses</td>
<td>4.57</td>
<td>1.48-10.7</td>
</tr>
<tr>
<td>Road transport</td>
<td>3.83</td>
<td>1.24-8.93</td>
</tr>
<tr>
<td>Woodworkers NOS</td>
<td>3.35</td>
<td>1.09-7.81</td>
</tr>
<tr>
<td>Waiters in restaurants</td>
<td>2.24</td>
<td>1.44-3.34</td>
</tr>
<tr>
<td>Greasers</td>
<td>2.20</td>
<td>0.89-4.54</td>
</tr>
<tr>
<td>Dressmakers</td>
<td>1.96</td>
<td>1.09-3.23</td>
</tr>
<tr>
<td>Plywood makers</td>
<td>1.89</td>
<td>1.06-3.10</td>
</tr>
<tr>
<td>Waiters in cafés etc.</td>
<td>1.52</td>
<td>0.61-3.71</td>
</tr>
<tr>
<td>Private secretaries</td>
<td>1.48</td>
<td>0.61-3.71</td>
</tr>
<tr>
<td>Hygiene and beauty services</td>
<td>1.38</td>
<td>0.75-2.31</td>
</tr>
<tr>
<td>Agricultural workers</td>
<td>0.31</td>
<td>0.11-0.67</td>
</tr>
</tbody>
</table>

(Pukkala 1995)
If biobank records are linked with the same registers as cancer records in NOCCA, model-based estimates of HPV prevalence (and any factor that can be measured from old serum) can be made for each occupational category.
Biases related to the indication of serum donation

Years since donation

SIR

Sick attendee effect
Healthy screenee effect
"Wild screening" (PSA)
Prostate cancer
Age adjusted (W) mortality 1971-2003

Mortality/100,000

- 41.9
- 38.1
- 34.6
- 31.5
- 28.6
- 26.0
- 23.6
- 21.5
- 19.5
- 17.8
- 16.1
- 14.7
- 13.3
- 12.1
- 11.0
- 10.0
- 9.11
- 8.28

START PAUSE PLAY


Finnish Cancer Registry 09.09.2008
EELIS 14 mo
Occupational cancer: historical view

- **Specific reports** - case reports and publications of analytical studies - on the association between certain occupational exposures and cancer have been published in mass quantity since 1775 when Percival Pott observed that among chimney sweeps in London there were exceptionally many cases of cancer of the scrotum

  Pott P. Chirurgical Observations Relative to the Cataract, the Polypos of the nose, the Cancer of the Scrotum, the Different Kinds of Ruptures, and the Mortification of the Mortification of the Toes and Feet. London, Hawse, Clark and Collins, 1775, pp 63-68.

- **Routine statistics** on the general mortality in different occupational categories have been published in England from the middle of the 19th century


- Since the late 1970s **surveillance systems** of occupational cancer risk have been created in several other countries, including all the Nordic countries.
Table 1. Examples of surveillance systems of occupational cancer (modified from [10])

<table>
<thead>
<tr>
<th>Study</th>
<th>Period</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unlinked death certificate and census data</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Death certificate data</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Massachusetts, U.S.A. [15]</td>
<td>1971-73</td>
<td>17,000</td>
</tr>
<tr>
<td><strong>Cancer registry mortality data</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Los Angeles County Cancer Surveillance Program, U.S.A. [16]</td>
<td>1972-74</td>
<td>60,000</td>
</tr>
<tr>
<td>New Zealand Cancer Registry [17]</td>
<td>1979-83</td>
<td>2,700&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Linked cancer registry incidence and pension scheme data</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pension scheme data for cancer patients, Denmark [18]</td>
<td>1970-79</td>
<td>94,000</td>
</tr>
<tr>
<td><strong>Interview incidence data</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Roswell Park Memorial Institute, U.S.A. [19]</td>
<td>1956-65</td>
<td>14,000</td>
</tr>
<tr>
<td>Case-referent study in Montreal, Canada [21]</td>
<td>1979-85</td>
<td>4,600</td>
</tr>
<tr>
<td><strong>Linked death certificate and census data</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occupational mortality, Norvay [22]</td>
<td>1970-80</td>
<td>27,000</td>
</tr>
<tr>
<td>Occupational mortality, Sweden [23]</td>
<td>1961-70</td>
<td>120,000</td>
</tr>
<tr>
<td>Occupational mortality, Finland [24]</td>
<td>1971-80</td>
<td>20,000</td>
</tr>
<tr>
<td>Occupational mortality, Denmark [25]</td>
<td>1970-80</td>
<td>60,000</td>
</tr>
<tr>
<td>Occupational mortality, Nordic countries [26]</td>
<td>1971-80</td>
<td>141,100</td>
</tr>
<tr>
<td>Ten percent sample of labor force, Canada [27]</td>
<td>1965-73</td>
<td>4,200</td>
</tr>
<tr>
<td>Longitudinal mortality study, U.K. [28]</td>
<td>1971-75</td>
<td>?</td>
</tr>
<tr>
<td><strong>Linked cancer registry incidence and census data</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer incidence by occupation, Norway [29]</td>
<td>1961-84</td>
<td>163,000</td>
</tr>
<tr>
<td>Cancer environment register, Sweden [30]</td>
<td>1961-79</td>
<td>605,000</td>
</tr>
<tr>
<td>Cancer incidence by occupation, Finland [31]</td>
<td>1971-80</td>
<td>39,000</td>
</tr>
<tr>
<td>Occupational cancer study, Denmark [32]</td>
<td>1970-80</td>
<td>115,000</td>
</tr>
<tr>
<td>Longitudinal cancer study, U.K. [33]</td>
<td>1971-75</td>
<td>8,000</td>
</tr>
<tr>
<td><strong>Linked hospital discharge registry incidence and census data</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occupational hospital discharge, Denmark [34]</td>
<td>1981-84</td>
<td>?</td>
</tr>
</tbody>
</table>

<sup>1</sup> Number of cancer cases or deaths.
<sup>2</sup> Only leukemia and controls.
Historical view

• Occupation and **social class** variables are closely intercorrelated.

• Even the most exact occupational classifications include such a burden of general life-style associated factors that the separation of real occupational hazards is problematic, if not impossible.

• It has been estimated from British data that 88% of the occupational variation was due to social class, ethnicity and smoking, and only 12% due to directly occupational exposures.

E. Pukkala

Cancer Risk by Social Class and Occupation

A Survey of 109,000 Cancer Cases among Finns of Working Age
Proportion of incident cancers attributable to occupation
(Finland, ages 35-69, 1971-85)

Men: 0.8-5.5%
Women: 0.7-4.8%

Out of NOCCA cancers: 30,000 – 200,000

Pukkala E. Cancer risk by social class and occupation... Karger 1995
Proportion of incident cancers attributable to social position
(Finland, ages 35-69, 1971-85)

Males: 35%
Females: 16%

Pukkala E. Cancer risk by social class and occupation... Karger 1995
### Social classes

<table>
<thead>
<tr>
<th></th>
<th>Social Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Managers, higher administrative</td>
</tr>
<tr>
<td>II</td>
<td>Lower administrative/clerical</td>
</tr>
<tr>
<td>III</td>
<td>Skilled/specialised blue-collar</td>
</tr>
<tr>
<td>IV</td>
<td>Labourers</td>
</tr>
</tbody>
</table>
Cancers of HIGH social class, men
Finland 1991-1995

SIR

I
II
III
IV

Testis
Small intestine
Skin melanoma
Colon
Prostate
Kidney
Cancers of LOW social class, men

![Graph showing SIR values for different organs](image)
Lung cancer by social class, males
Lung cancer by social class, females
Register-based research in occupational cancer
Elsebeth Lynge
University of Copenhagen
HISTORICAL COHORT STUDY

Linkage between company records, death, emigration, and cancer incidence data
WHEN THE ENTIRE NATION IS THE COHORT
When 4 countries are the cohort:

"Aage 1"

10 million people
1 million cancers

1999
Slik er din KREFT-RISIKO

53 yrker undersøkt:

VERDENS STORSTE UNDERSØKELSE: Yrket ditt kan avgjøre hvilken kreftare du utsettes for. Det viser en ny undersøkelse av ti millioner personer i hele Norden. VG presenterer den fullstendige oversikten over hvilke krefttyper som rammer de ulike yrkene.

HUSK 1000-TIPSET! Ring 22000000
Disse yrkene GIR DEREG KREFT

I undersøkelsen, som har offentliggjøres for første gang, er kreftavisk crent til over 3 millioner personer i Norge, Sverige og Danmark. Dette er en avgjørende inndeling av Kreftavisk crent som rammer de ulike yrkene.

Finn ut hvilke krefttyper du er utsatt for:

- Akademiske yrker
- Helsetjenester
- Hardt
- Bygg og anlegg

- militær
- Jord, skog, grønne

Kilde: VG
KELNERE LEVER FARLIGST

VI du bruge kogte, bør du dogg ørste kelnerforbud. Du har heller ikke tråni
etter et journalisters eller et kinesisk bi. Inder hande.

Så far og rans

Ingen oversekses

Med stof for

Industri:

Handel og bygnings

Jernbanefor og koncert

Transport og kommunikation

Garde og Ibrahim

Indhold, når banedele

Med stof for

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Indhold, når banedele

Med stof for
When 5 countries are the cohort:

”Aage 2”

385 million person-years

3 million cancers

…. front page still to be decided…
From Aage I to Aage II

Occupational history
Job Exposure Matrix

Occupation

Rare cancers
morphology

Sex, Age

Reproductive history, Tobacco smoking,
obesity, alcohol (proxy liver cirrhosis)

Cancer
• February 2005
  Hafjell, Norway

• The acronym
  NOCCA decided for
  the Nordic Occupational
  Cancer Study

• Protocol for the study
NOCCA start meeting (2005): publication plan

- "Aage II": **SIRs by site and occupation**. Monograph, similar as "Aage I" plus the extension of follow-up years, censuses, cancer sites and some new analysis methods.

- How to treat the problem of **multiple comparisons**?
  - calculate an estimate on whether there is a true variation by occupation for each site, or
  - use an empirical Bayesian approach (Steenland et al CEBP 2000)

- Publish SIRs based on **socioeconomic positions**.
  - classify the occupational categories into SES classes, or
  - use extra variable to be collected from census files, most likely education.

- **NOCCA-JEM**-publication by Kauppinen-group
  - presentation of methodology, magnitude of exposures, trends in exposures, with comparison of countries

- Monograph with RRs by sites and agents/exposures, giving **dose-response estimates**, presenting possible gender interactions and adjusting for available cofactors

- **Specific papers** on exposures/occupations/sites.
Individual records of individuals aged 20-64 at any census 1960+

Some of those variables will only be used in specific studies and not all of them can be achieved from all countries. The absolutely necessary variables underlined.

Date of birth; Gender
Date of immigration; Country of birth
Date of first emigration
  Follow-up will end at first emigration even if a person is coming back to country later.
Date of death
Cause of death (in estimating cofactor exposures from index mortality: e.g. liver cirrhosis ≈ alcohol)
Education; Income
Years of birth of all children (for women)

Cancer registry data on primary site for all malignancies:
* date of diagnosis
* topography (site); morphology (histology); behaviour (malignancy)
* stage (localised, regional, distant)

Census information from each census 1960, 1970 and 1980/81, as specific as possible
* occupation; industrial code
* whether self-employed or not; full time employment or not
• **Smoking**: current/former/never smokers by birth cohort, calendar time, ~400 occupational codes
  – Finland: Survey 1978, ok for males
  – Norway: proportion of current and former smokers plus average tobacco consumption by occupation, time and cohort specific, 1965-1999, based on 120,000 persons.
  – Denmark: smoking habits for 5 occupational groups, 5 age groups, 2 genders, different geographic regions, from 1970 and regularly.
  – Sweden: Survey every year from 1963, then 1970 and onwards, 15000 each year, always information on occupation, frequently of smoking.
  – Iceland: Surveys from 1980, with occupation and smoking habits, population samples.

• **Alcohol**: Less data available. Frequency of drinking? Quantity?
  – Denmark: sample of 9000 from 1973
  – Finland: data from 1978+, maybe data also from about 1970
  – Norway: Frequency of drinking from population sample from 1964, men only.
  – Sweden, Iceland: ?

• **Obesity**: % with BMI>30
  – Finland: data from 1978+,
  – Iceland: data from screening (Women’s heart study)
  – Sweden / Norway: will check data availability
  – Denmark: ?

• **Physical activity**:
  – Leisure time activity, for instance defined as % of people who exercise >3x/week. Variable is difficult to define, unsure of what is available. Decision made to **drop** this for the time being.
  – Physical activity at work is included in JEM.
Main data sources
(computerised and linkable)

Population Register Center (VRK) 1967+
- complete ID
- place of birth
- parent-child links
- PIDs of children
- residential history
- living coordinates
- living conditions
- immigration/emigration date
- date of death

Social Insurance Institute
- reimbursable diseases 1967+
- reimbursable medicines 1994+
- disability pensions

Finnish Cancer Registry
- cancer incidence 1953+
- cancer screenings 1963+

Finnish Institute for Occupational Health (FiOH)
- register of persons exposed to carcinogens (ASA)
- FINJEM

Finnish Information Centre for Register Research (RETKI)

National Research and Development Centre for Welfare and Health (Stakes)
- hospital discharges
- birth parameters
- malformations
- Finnish Information Centre for Register Research (RETKI)

Public Health Institute (KTL)
- Survey data (Mini Finland 1967, FinRisk 1972+, Adult Population Health Survey 1978+): life habits (smoking, alcohol, diet, BMI, physical exercise etc)
- Blood sera (maternity cohort etc.)

Statistics Finland
- Longitudinal Census files
  SFS, place of residence
- causes of death 1971+

Whole population
Population sample
Creativeness
NOCCA start: permissions

Tietojen käyttölupa

Dnro: TK-53-909-05
Hakija: Eero Pukkala
Suomen Syöpärekisteri
Liisankatu 21 B
00170 Helsinki

Tietojen käsittelyyn osallistuu myös Pentti Kyyrönen, Suomen Syöpärekisteri

Tilastoaineisto:

Tilastokeskuksen yhteyshenkilö:
Marianne Johnson, Tutkimuspalvelut, Henkilötilastot. puh. 1734 3627

Päätös:

X) Hyväksytään
O) Hylätään
(x) Maksullinen
() Maksuton
ORIGINAL ARTICLE

Occupation and cancer – follow-up of 15 million people in five Nordic countries

EERO PUUKALA¹,², JAN IVAR MARTINSEN³, ELSEBETH LYNGE⁴, HOLMFRIDUR KOLBRUN GUNNARSDOTTIR⁵, PÄR SPARÉN⁶, LAUFÉY TRYGGVADOTTIR⁷, ELISABETE WEIDERPASS³,⁶,⁸,⁹ & KRISTINA KJAERHEIM³

¹Finnish Cancer Registry, Institute for Statistical and Epidemiological Cancer Research, Pieni Roobertinkatu 9, FI-00130 Helsinki, Finland, ²School of Public Health, University of Tampere, Tampere, Finland, ³Cancer Registry of Norway, Oslo, Norway, ⁴University of Copenhagen, Denmark, ⁵Research Center for Occupational Health & Working Life, Reykjavik, Iceland, ⁶Karolinska Institute, Stockholm, Sweden, ⁷Icelandic Cancer Registry, Reykjavik, Iceland, ⁸Samfundet Folkhalsan, Helsinki, Finland and ⁹University of Tromsø, Norway
Study population, follow-up

✓ Cohort of all persons born 1896-1960 (15 million persons)
✓ Occupation defined at age 30+ in first available census (1960,... 1990) = beginning of follow-up
✓ Follow-up for cancer incidence up to death, emigration or 31 Dec 2005
✓ Almost 3 million invasive cancer cases
Kiitos
(Thank you)