IMM Institute of Environmental Medicine
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Register-based research on cancer

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Aim of the research

- To increase our knowledge on causes of cancer
  - → Ultimate goal is to prevent disease
  - → Increase our understanding of the etiology and mechanisms of cancer development
- To increase our knowledge on factors that affect survival after cancer diagnosis
- To follow trends in cancer occurrence
  - → Changes in incidence may give clues on risk factors

Registers important in all analytical cancer epidemiologic studies

- Allow careful definition of the study base, i.e. the study population during the follow-up period
  → Essential for both cohort and case-control studies

- Allow complete follow-up of cancer outcomes
  → Essential for both cohort and case-control studies

- Allow collection of information on important potential confounding factors independent of disease
  → Important for evaluation of potential loss to follow-up or non-participation
  → May reduce number of questions in interviews or questionnaires

Some words of caution

- Need to avoid ”fishing expeditions” – i.e. when combining everything with everything and cherry pick ”significant” findings
- Important knowledge may be lost when analyses are not hypothesis driven – only scratching the surface
- Risk of false positives
- Negative findings less likely to be published – publication bias

- Need to pay attention to potential limitations associated with registration of the specific outcome, exposure and covariates studied

Examples of studies: Melatonin – cancer

- Experimental evidence on cells and animals suggests that melatonin protects against breast cancer development
- Melatonin is produced primarily by the pineal gland during the night
- Melatonin production is suppressed by light
  - → Melatonin production unaffected by light in the majority of completely blind people
  - → Blind people is therefore assumed to on average have a higher exposure to melatonin than the general population
  - → Melatonin production in severely visually impaired persons is suppressed by light

Cancer incidence in blind

- Two cohorts were identified through a registry kept by the Swedish Federation of the Visually Handicapped and from the Hospital Discharge Registry:
  - → 1,567 completely blind
  - → 13,292 severely visually impaired
- Cancer occurrence was observed through the Cancer registry from 1960 or from one year after first registration as blind or visually impaired
- Observed number of cases was compared to expected based on person-years in the cohorts and national age, sex, calendar year specific incidence rates
- SIR for all cancer combined:
  - → 0.69 (95% CI 0.59-0.82) for blind
  - → 0.95 (95% CI 0.91-1.00) for severely visually impaired

Feychting et al. 1998

Cancer in shift workers

- A cohort of 3,250,787 persons gainfully employed in both 1960 and 1970 were followed for cancer incidence from 1971 through 1989
- Information on occupation, industry, socioeconomic status from the 1960 and 1970 censuses
- Job-exposure matrix created based on information on work schedules from the annual Survey of Living Conditions (ULF)
  → Aim was to identify shift work with working hours during the night

- Results for all cancer combined, shift work at both censuses:
  → Men: SIR = 1.01 (95% CI 0.98-1.05)
  → Women: SIR = 1.00 (95% CI 0.82-1.21)
  → Breast cancer: 0.97 (95% CI 0.67-1.40)

Schwartzbaum et al. 2007

Examples from brain tumor research

- Paternal occupational exposure to pesticides associated with increased risk of brain tumor in offspring
- Diabetes associated with a reduced risk of glioma
- Higher prevalence of epilepsy among persons who subsequently were diagnosed with a high grade glioma – as early as >8 years prior to glioma diagnosis
- Allergic conditions associated with a reduced risk of glioma

  → Strongest effects from case-control studies – bias?
- By linkage of the Janus Serum Bank cohort to the Norwegian cancer registry in a nested case-control design we could show that total IgE, a biomarker for allergy, measured at least 20 years before diagnosis, was associated with a reduced risk of glioma

Other examples

- Studies have shown an increased risk of leukemia and brain tumors in children associated with of indicators of fetal growth and neonatal stress
- Survival after cancer diagnosis is associated with socioeconomic status also in Sweden –
  → Much more can be studied within this area
- It will be possible to investigate the effect of the HPV vaccination program on cervical cancer occurrence
  → Registers allow identification of groups with low vaccianation uptake for targeted information
  → Registers make it possible to investigate whether vaccination will discourage women from screening

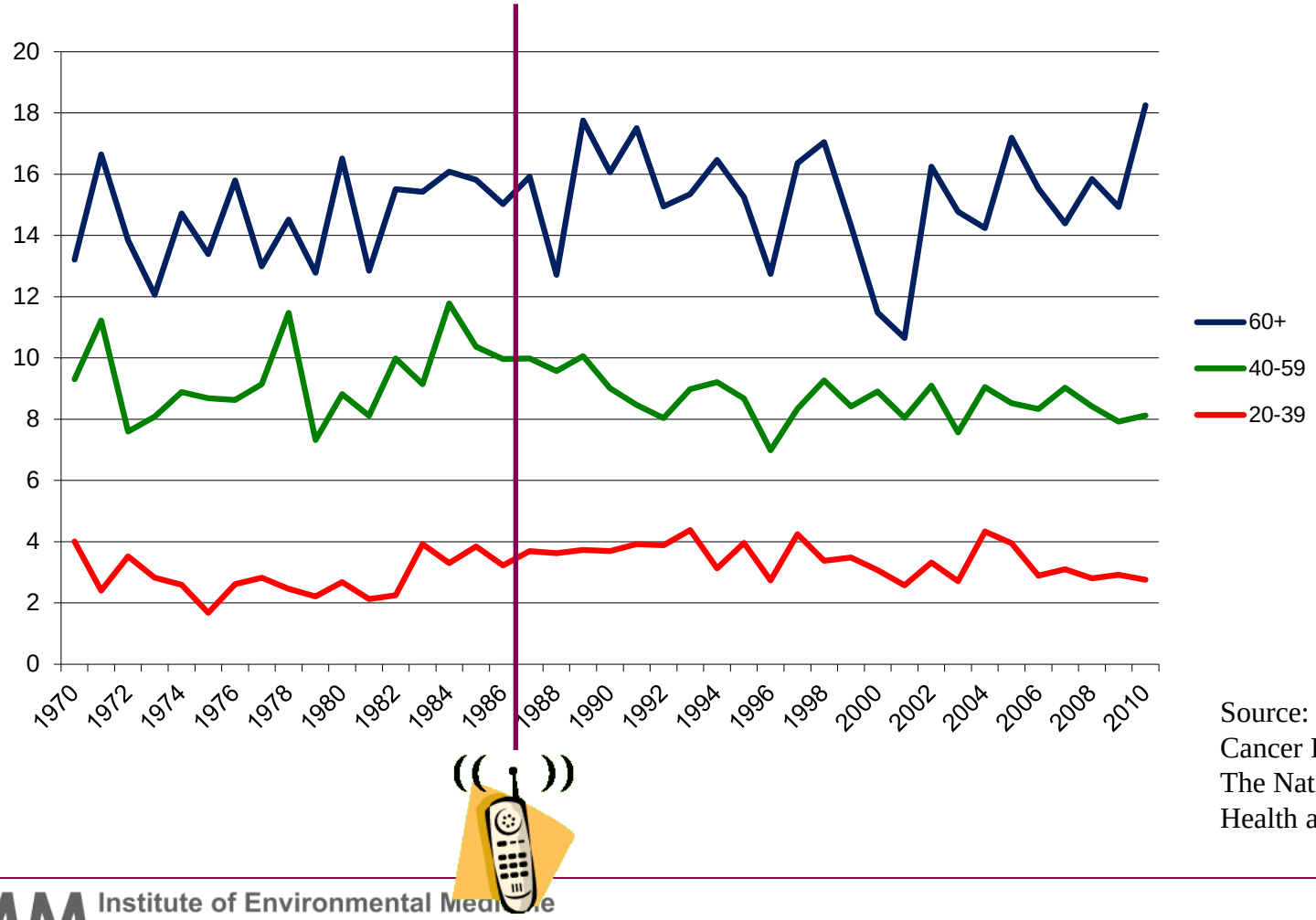
Glioma and mobile phone use

- Research is driven by public concern – exposure prevalence has gone from close to zero up to almost 100% in 25 years
- **Most studies found no increased risk, but there are some exceptions:**
- Hardell et al. 2006
  - → Short term use, 1-5 years: OR=1.6 (1.1-2.4)
  - → Medium term use, 6-10 years: OR=2.2 (1.4-3.4)
  - → Long term use, >10 years: OR=3.6 (1.7-7.5)
- Hardell & Carlberg 2009
  - → Ever use, starting <20 years old: OR=5.2 (2.2-12)
- Interphone cumulative hours of mobile phone use (2010):
  - → OR=1.40 (1.03-1.89) in 10th decile (≥1640 h)
- **What can we learn from registers?**

Glioma incidence, Sweden 1970-2010, Men

per/100 000
age standardized

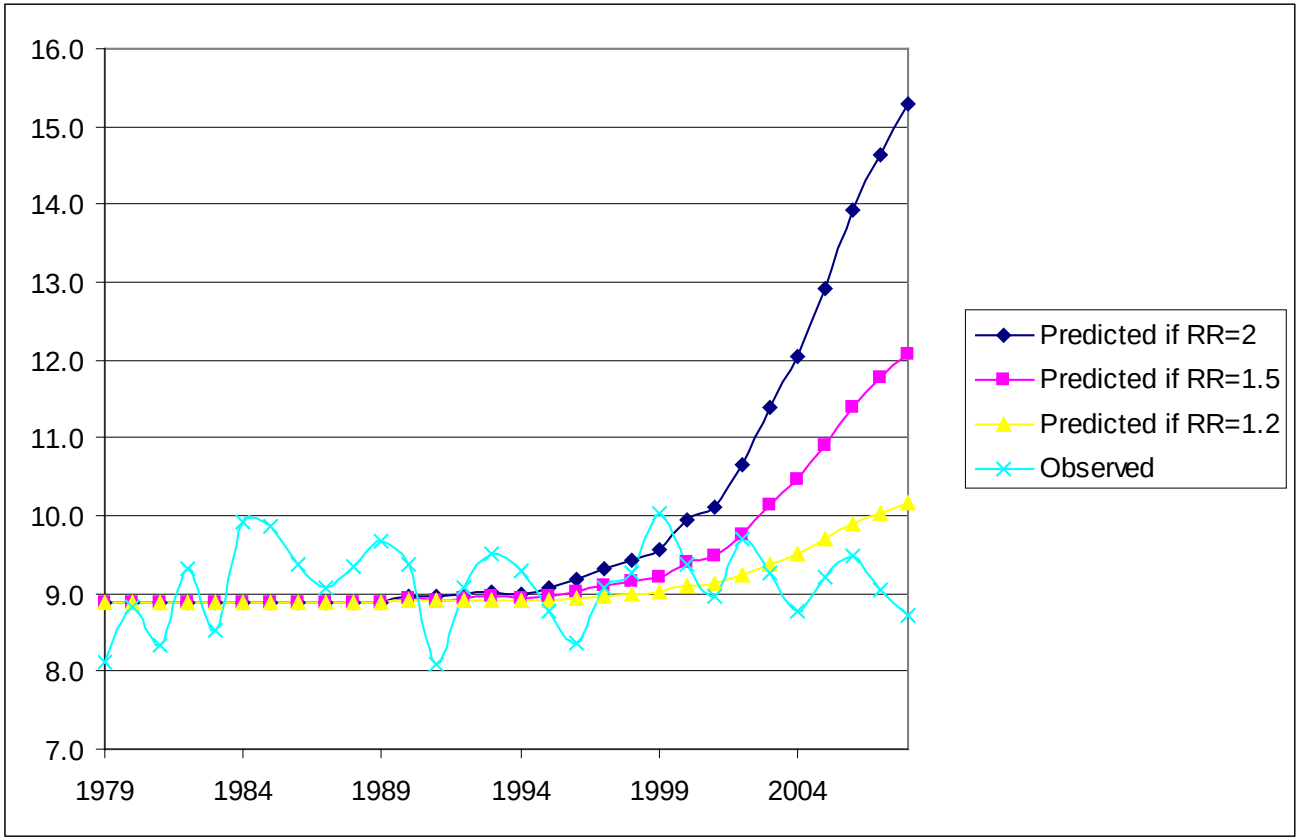
Introduction of handheld
mobile phones



Source:
Cancer Register,
The National Board of
Health and Welfare

Observed and predicted glioma incidence rates under scenarios of risk, Nordic countries, men 40-59 years, 1979-2008

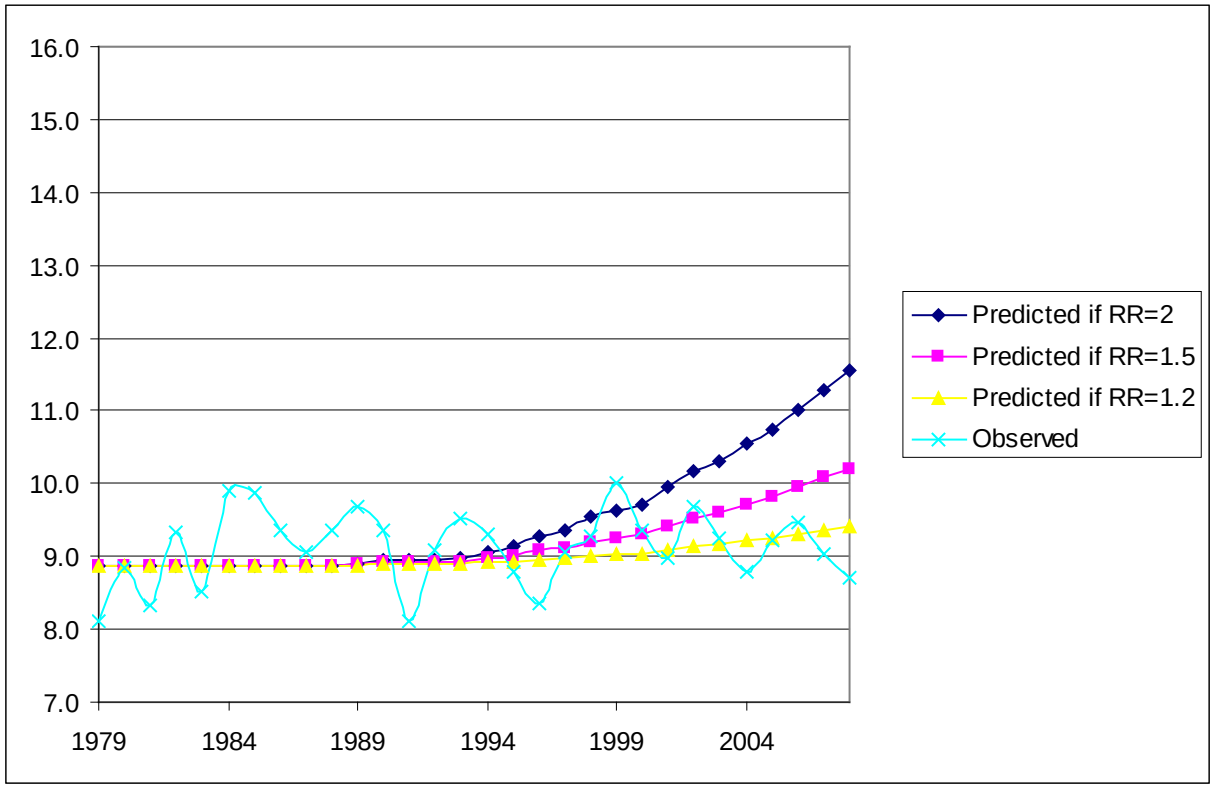
Under the assumption that all users at increased risk after 10 years:



Deltour et al. 2012

Observed and predicted glioma incidence rates under scenarios of risk, Nordic countries, men 40-59 years, 1979-2008

Under the assumption of risk for heavy users (>1640 hours)



Deltour et al. 2012

Nordic registers and other data sources

- Each individual Nordic country too small for studies of rare outcomes
  - → Need to work more towards collaborative studies based on Nordic data
  - → Need to make it easier to share data between Nordic countries – with preserved consideration of ethics and integrity issues

- Combination of national registers with other data bases and biobanks makes science even stronger – many large locally initiated cohorts are available
  - → Encourage collaborations to enable combination of several cohorts with detailed exposure information

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Thank you!

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