Overview of epidemiology of thyroid cancer in the context of the Fukushima accident

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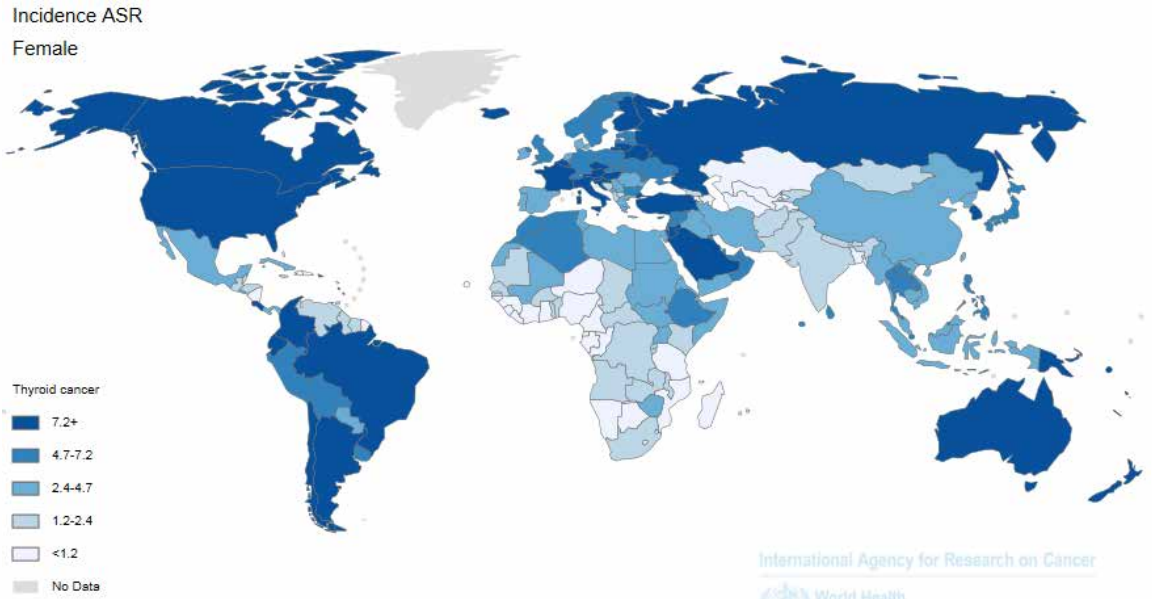
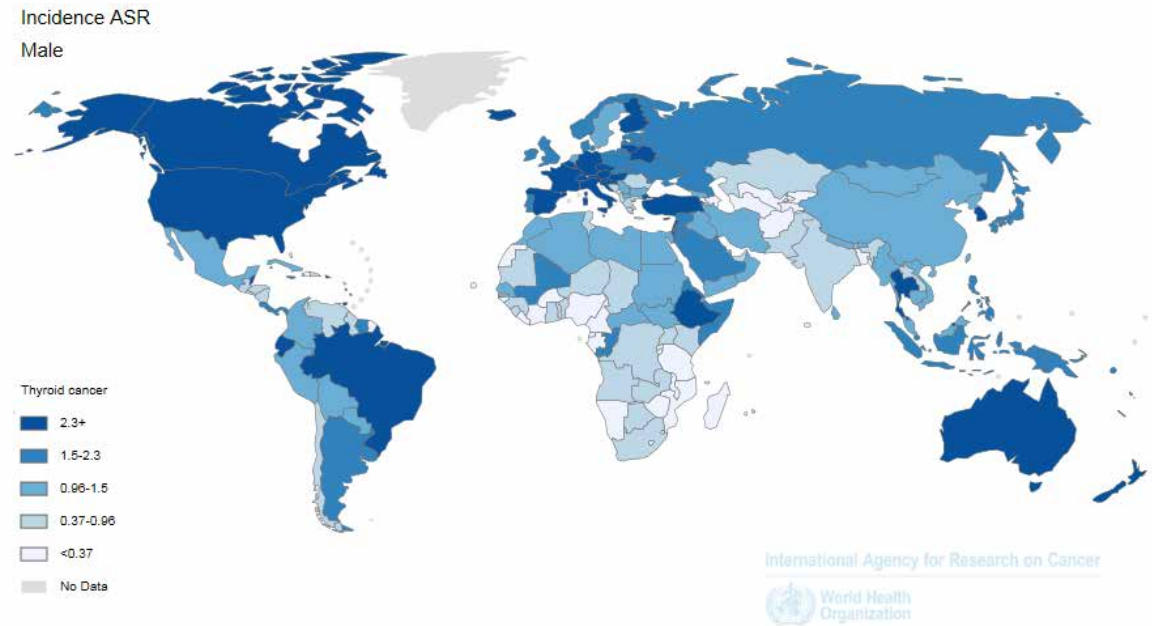
Thyroid cancer incidence





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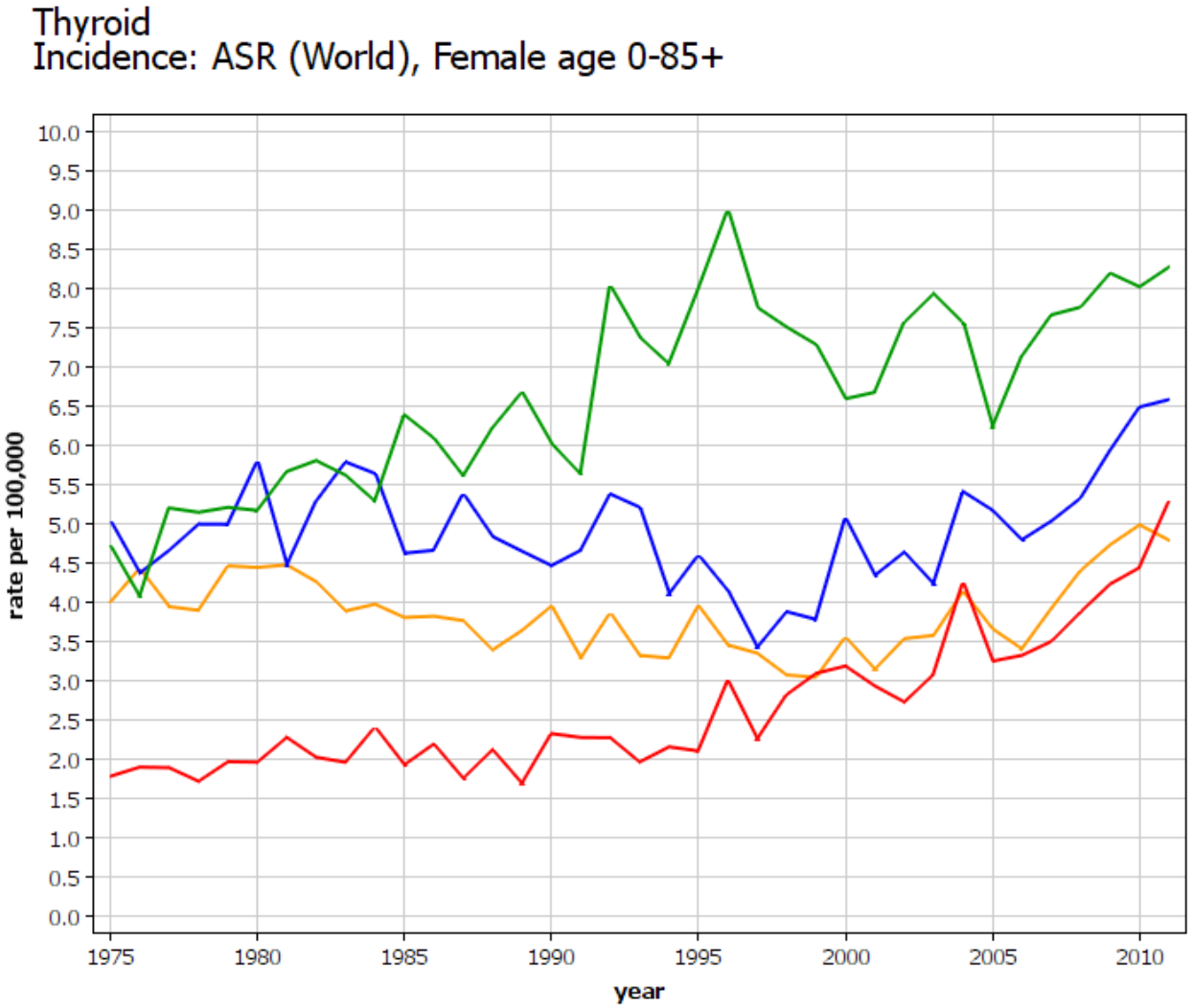
GLOBOCAN 2012

Thyroid cancer incidence

Thyroid cancer in women (Nordic countries separately)



From NORDCAN

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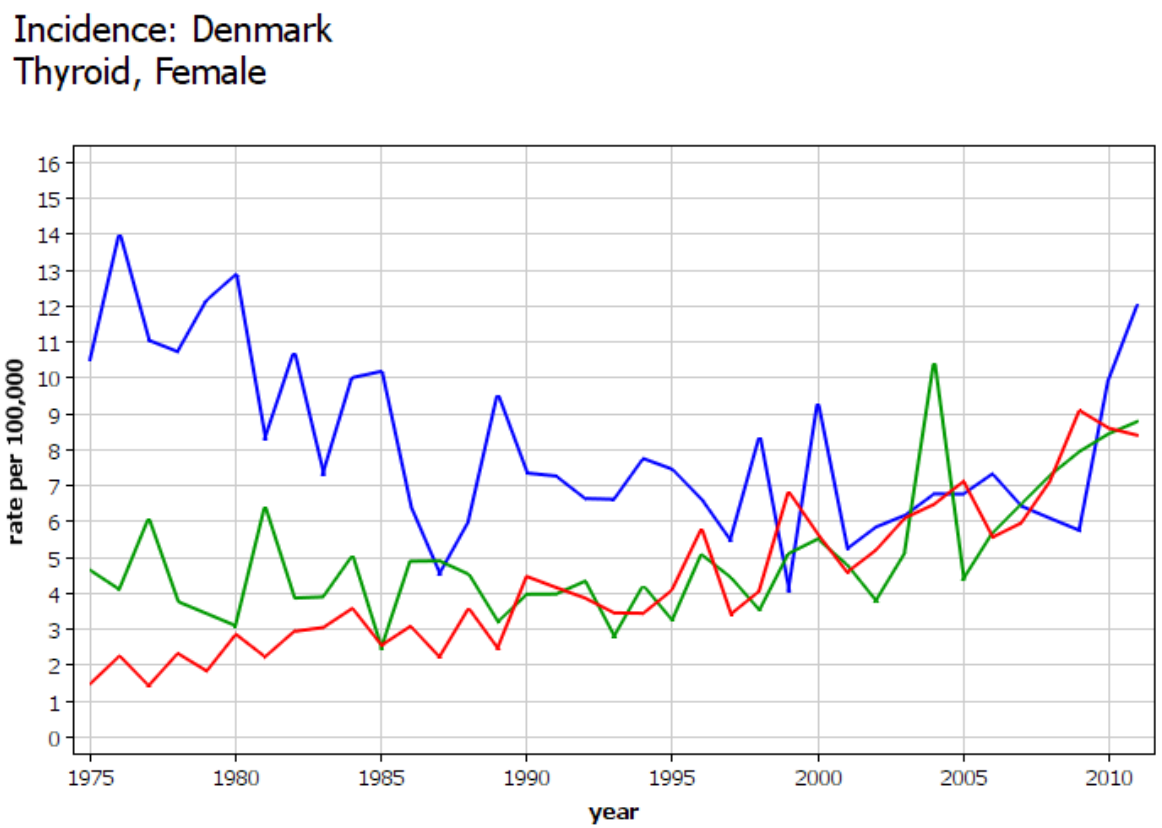
Thyroid cancer incidence

Thyroid cancer in women (Denmark, by age)



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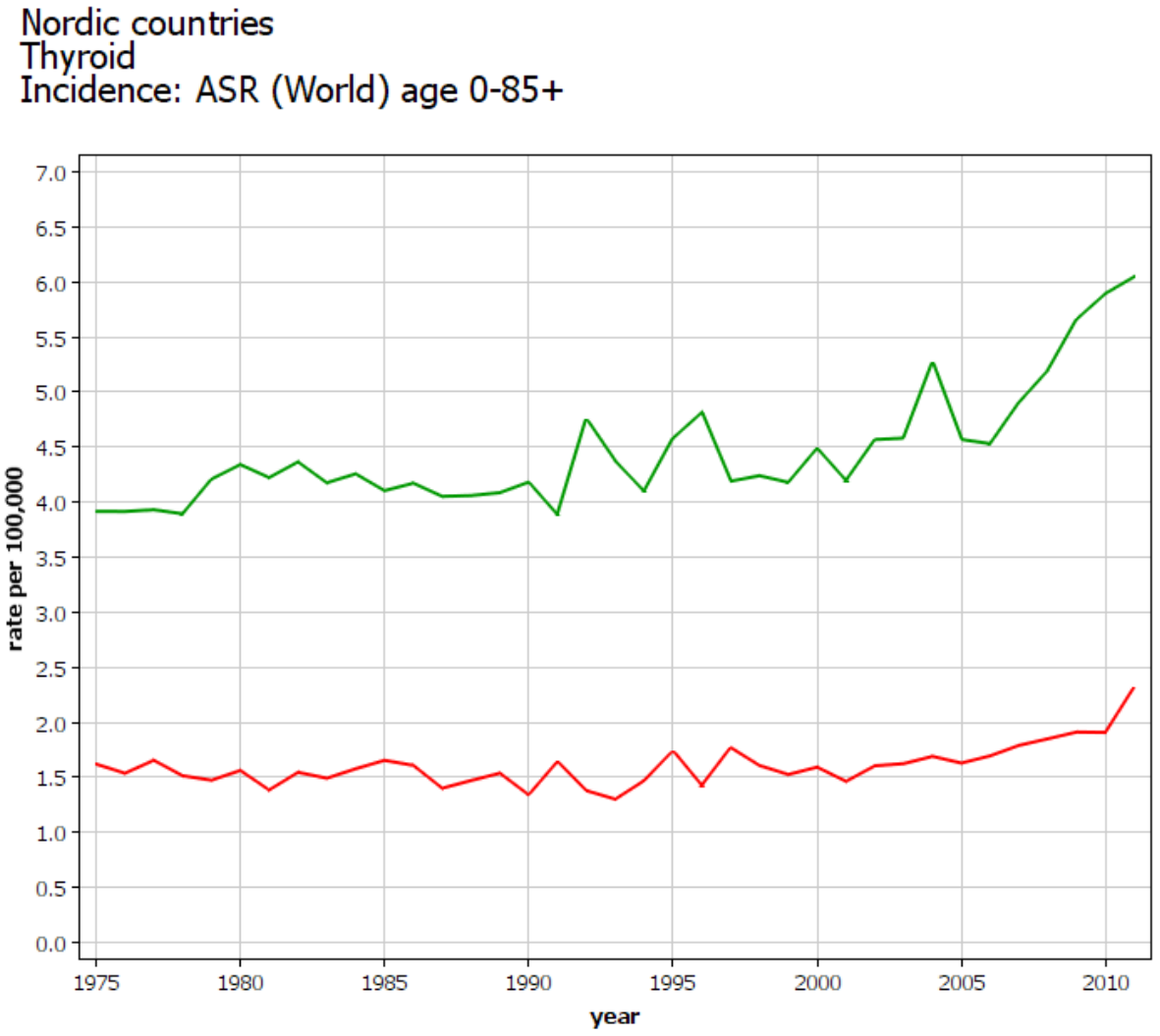
Thyroid cancer incidence

Thyroid cancer in men and women (Nordic countries combined)



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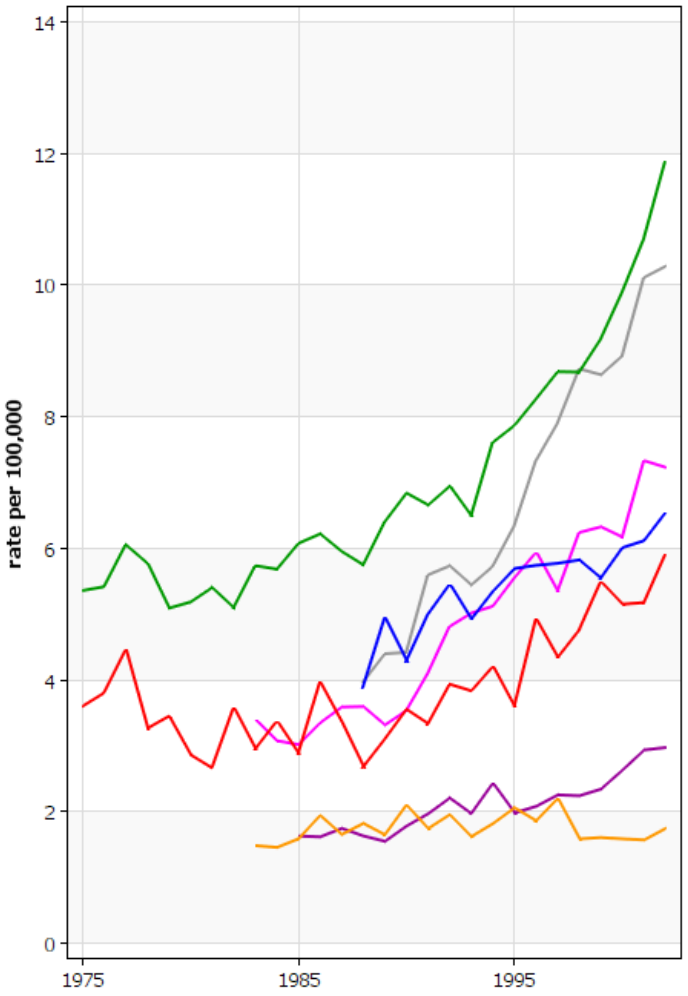
Men

Women

Thyroid cancer incidence



USA Whites

France

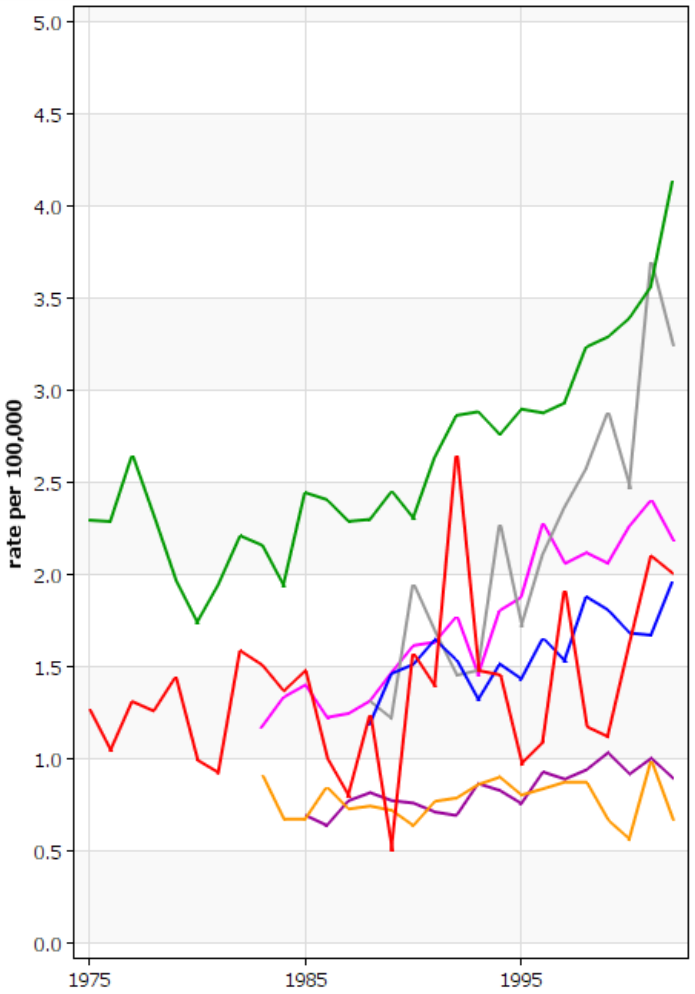
Australia

China

USA Blacks

UK, England

India



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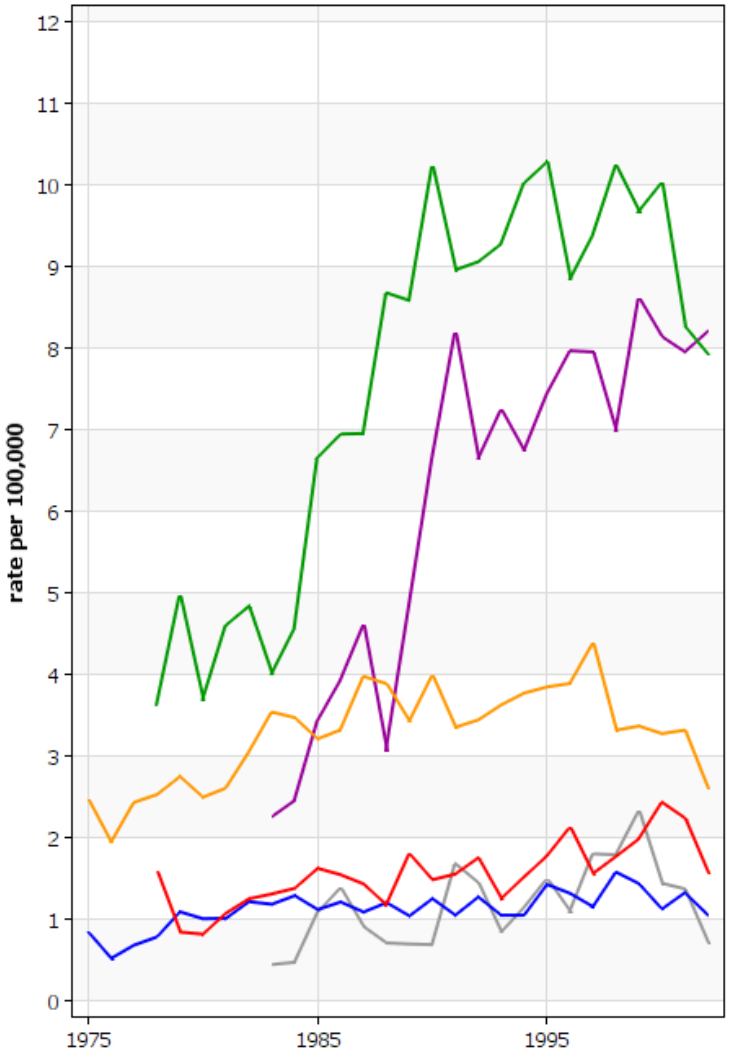
Women

Men

Thyroid cancer incidence

Thyroid cancer in men and women (Japan)



Miyagi, Women

Yamagata, Women

Osaka, Women

Miyagi, Men

Osaka, Men

Yamagata, Men

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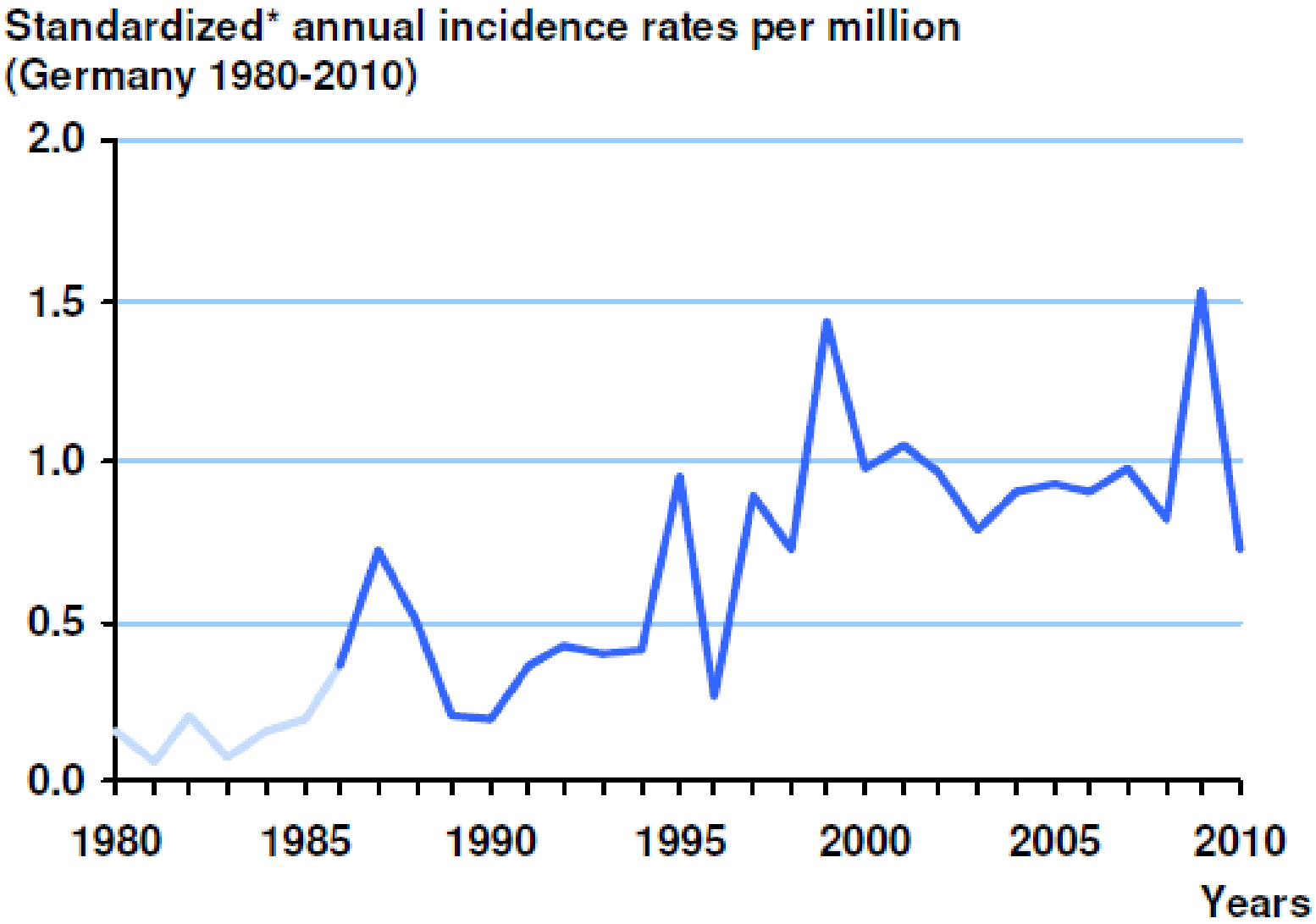
Thyroid cancer in children



Annual report 2011 – German Childhood Cancer Registry

Thyroid cancer occurrence

By age and sex:

- Worldwide, about 3 of 4 cases are in women
- Increase with age in women and men

By time and geography:

- Worldwide, strong increase in incidence
- No increase in mortality (fatality very low)
- Significant variation (including across neighbouring countries)
- Incidence increase differs by country

Factors influencing changes over time

Changes in risk factors:

- Are changes in risk factors compatible with changes in incidence (by time, magnitude, demographics?)

Changes in diagnosis and detection:

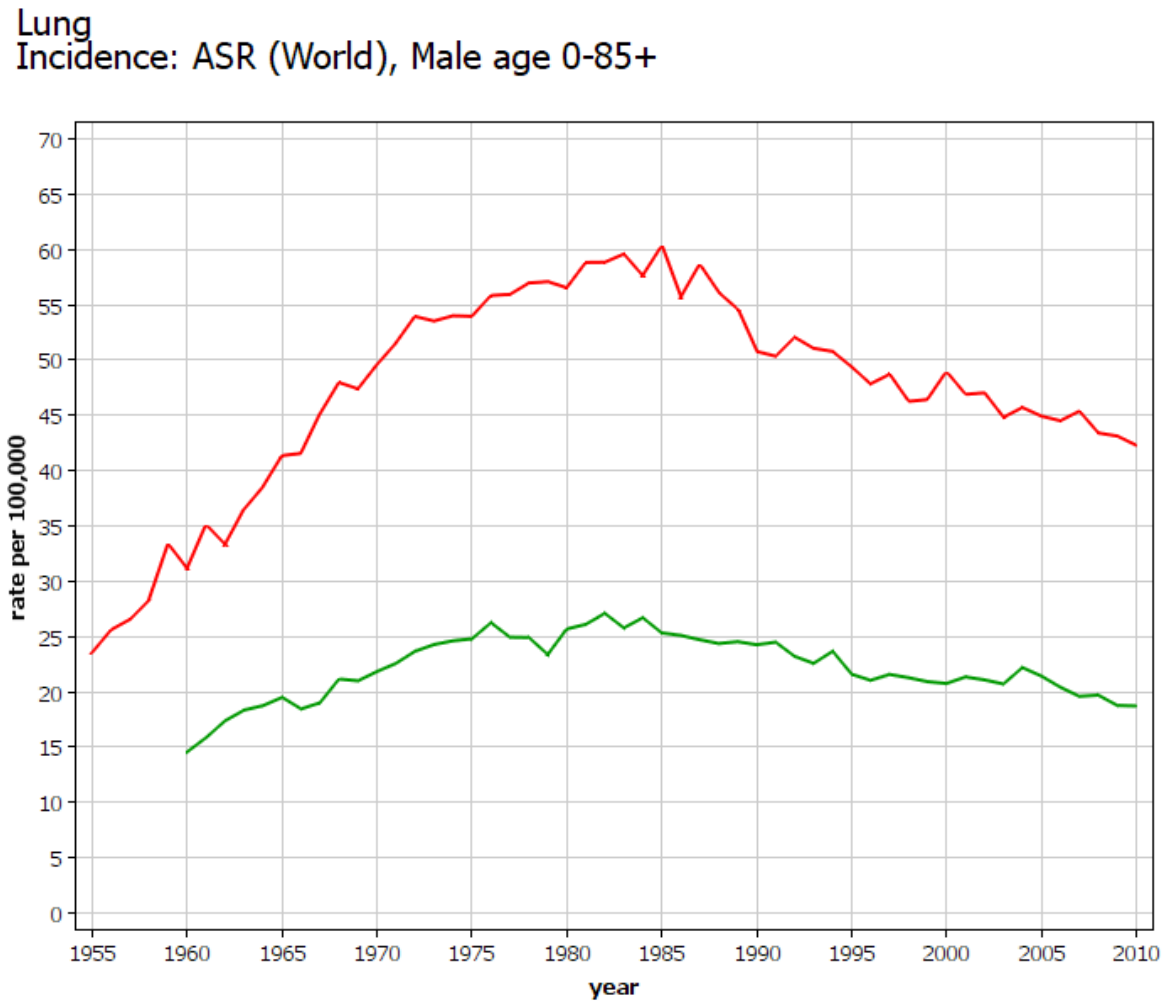
- Improved diagnostics?
- Earlier detection? Over-diagnosis?

Methodological considerations:

- Under-reporting or –registration, change in classification?

Changes in underlying risks: Lung cancer example

Lung cancer risk in Danish and Swedish males over time, influenced by changing smoking behaviour in the underlying populations



Denmark

Sweden

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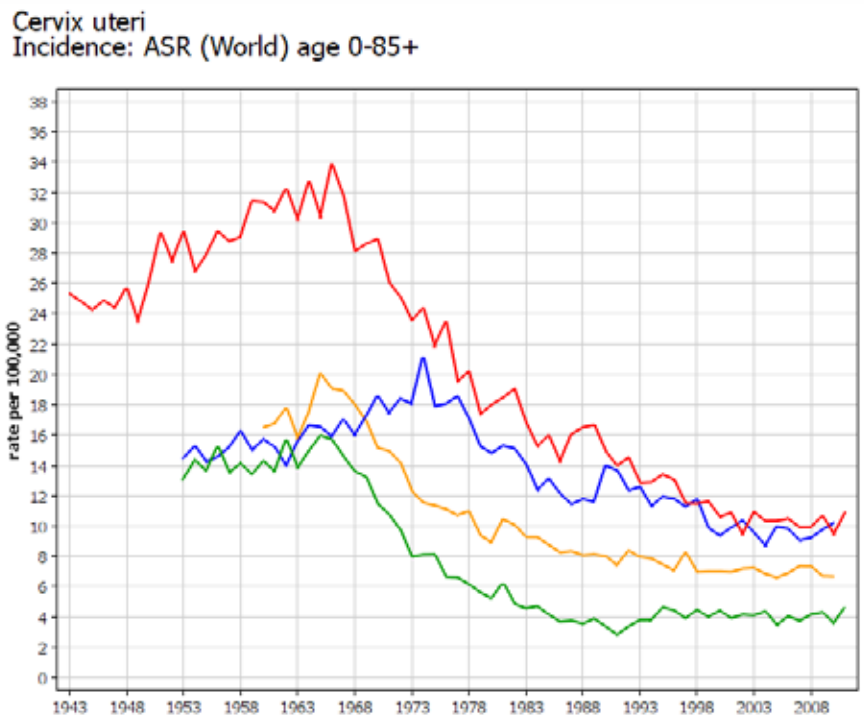
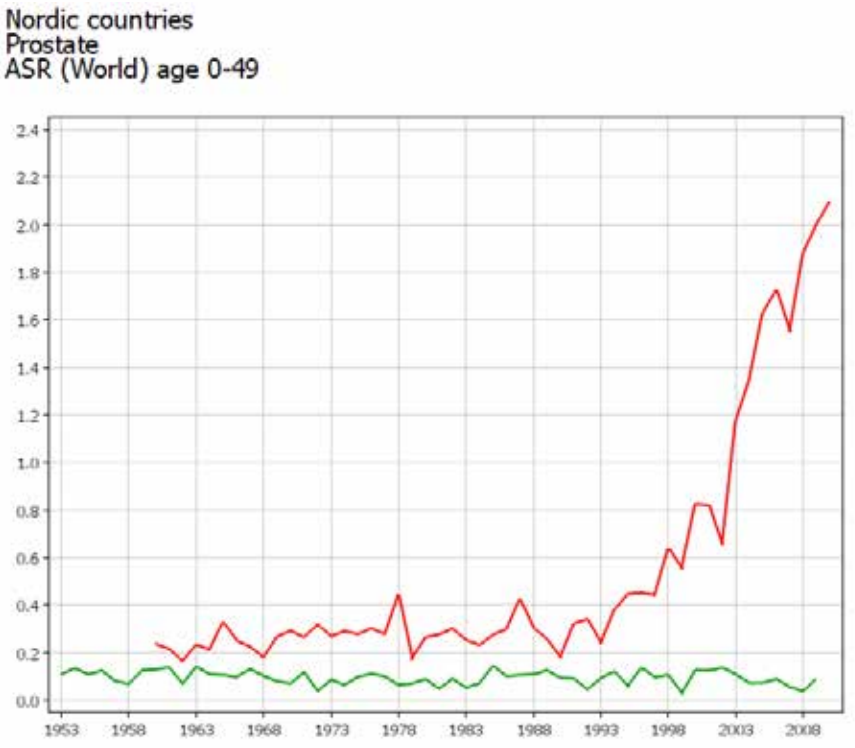
Changes in detection: Examples from screening

Systematic cervix screening



Opportunistic PSA screening



Denmark | Sweden | Norway | Finland | Incidence | Mortality

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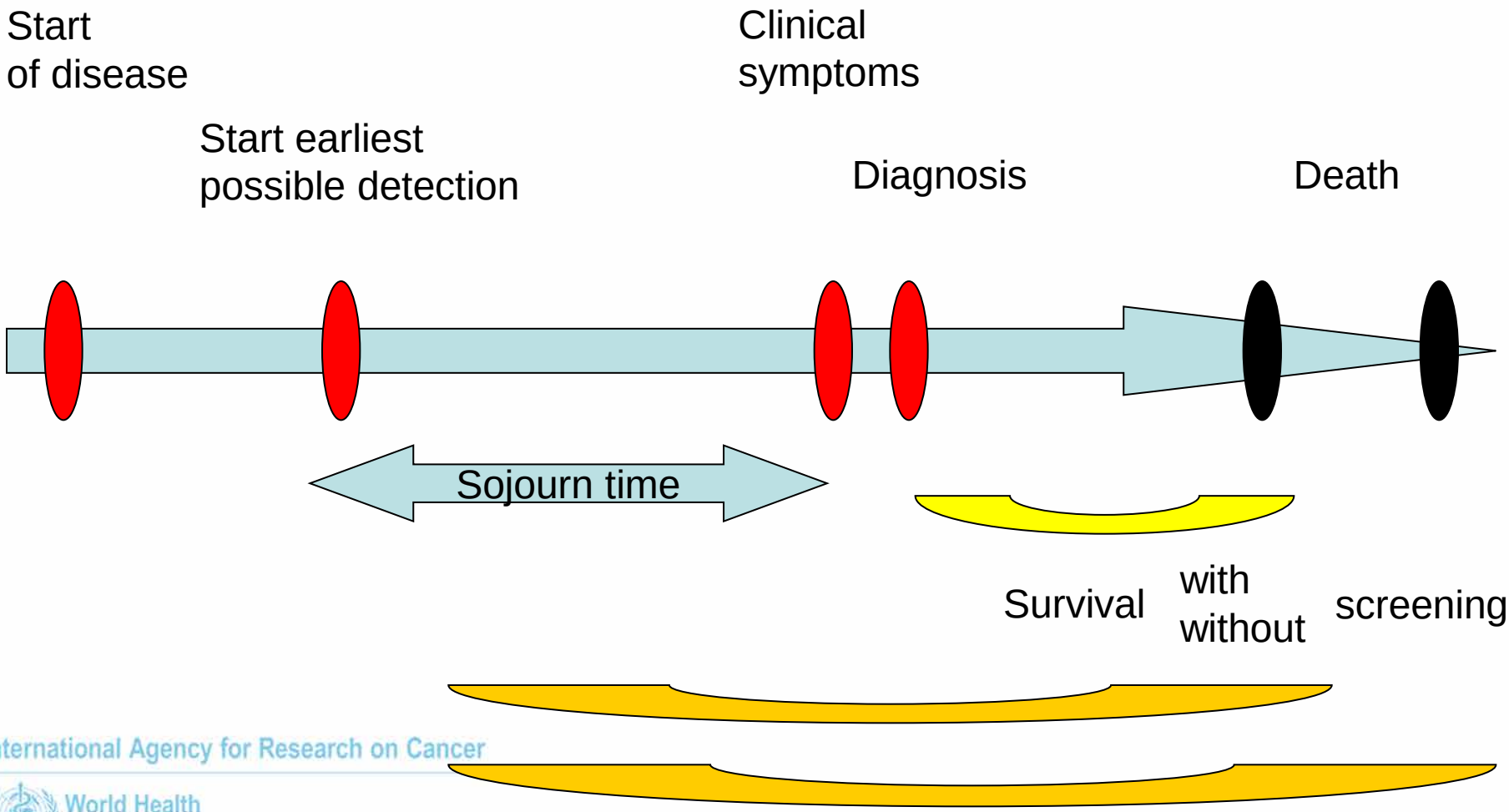
Screening and early detection



Screening and early detection

Effects of screening/early detection:

- Immediate increase in incidence of cancerous pre-lesions and early stage cancers; overall incidence increase
- Longer observed survival (even if no benefit for patients)
- Shift in stage distribution (downstaging)

Questions:

- Mortality reduction
- Long term incidence reduction
- Overlaying other factors influencing time trends

Early detection potential for thyroid cancer

Early detection potential:

- Detection of smaller tumours using ultrasonography
- Detection of smaller tumours in CT and MRI
- Steep increase in small papillary tumours < 20 mm
- Evidence for long sojourn time
- Detection of tumours not needing any treatment
- Small tumours may never progress to cause symptoms or cause death
- Detection rate of small tumours in autopsies

Brito JP et al, BMJ 2013

Re-labelling of early detected small papillary tumours?

Features of thyroid cancer:

- Survival of anaplastic cancers: ~10% survived after 5 years
- Survival of papillary cancers: ~99% survived after 20 years
- Overtreatment and unnecessary harms to patients

Features of thyroid cancer:

- Low risk lesions (<20 mm) with no family history of thyroid cancer, no radiation exposure and no ultrasound evidence of extraglandular invasion
  => micropapillary lesions of indolent course (microPLICs)

Brito JP et al, BMJ 2013

Risk factors of thyroid cancer

- Few established risk factors
  - Ionizing radiation
  - Benign thyroid conditions (e.g., nodules)
  - Family history of thyroid cancer
  - Obesity (height and weight)
  - Iodine deficiency
  - Reproductive factors / hormones ?

Dal Maso et al. Cancer Causes Control. 2009 Feb;20(1):75-86
Kitahara et al. Cancer Epidemiol Biomarkers Prev. 2011 Mar;20(3):464-72

Radiation and thyroid cancer – Lessons learnt from Chernobyl

Reference	Ascertainment period	Number of cases	Number of controls/ size of study population	ERR at 1 Gy (95% CI)
Case-control studies				
Astakhova *et al*, 1998	1988-1992	107	214	OR >=1 Gy vs. <0.3Gy: 5.0 (1.5-16.7) to 5.8 (2.0-17.3)
Kopecky *et al*, 2006	1986-1998	66	132	48.7 (4.8-1,151)
Cardis, Kesminiene *et al*, 2005	1992-1998	276	1,300	4.5 (2.1-8.5) to 7.4 (3.1-16.3)
Screened cohort study				
Tronko *et al*, 2006	1998-2000	45	13,127	5.25 (1.7-25.5)
Zablotska *et al*, 2010	1996-2004	87	11,611	2.15 (0.81-5.47)
External exposures - *Pooled analyses of 7 studies*				
Ron *et al*, 1995		436	119,387	**7.7 (2.1-28.7)**

- *Adapted from Cardis et al, 2006*
- *Studies on thyroid cancer after exposure in childhood related to Chernobyl accident*

Radiation and thyroid cancer – Lessons learnt from Chernobyl

Radiation type	OR at 1 Gy (95% CI)
Total dose	5.5 (2.2 to 8.8)
^{131}I	5.2 (2.2 to 8.2)
All iodine isotopes	5.2 (2.2 to 8.3)
All iodine isotopes, adjusting for external and long-lived nuclides	5.9 (1.6 to 10.2)

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**Cardis et al, 2005*

Exposure in childhood related to the Chernobyl accident

Radiation and thyroid cancer – Lessons learnt from Chernobyl

- Causal relationship between exposure to radioactive isotopes of iodine during childhood and adolescence and increased thyroid cancer risk has been proven
- Excess risks are higher with decreasing age at exposure
- Excess risks appear to be long term (increase is observed at least 25 years after exposure)
- Iodine deficiency and iodine supplementation appear to modify the risk
- Risk increases in thyroid cancers were observed already after 5+ years after the nuclear accidenct
  (Kazakov et al, Nature 1992; Stsjazhko et al, BMJ 1995)

Conclusions

Thyroid screening leads to significant increase in incidence of thyroid cancers

Radiation is an established risk factor for thyroid cancer

At present, increase in thyroid cancer incidence in Fukushima prefecture is very likely to be attributable to thyroid screening

Avoid using oecological data for radiation-related interpretation of thyroid cancer risks

But this in the process of changing…

Future challenges

Disentangling the effect of early detection and possible increase due to radiation exposure in the upcoming years

Surveillance of other cancers than thyroid cancer known to be related to radiation exposure

Address behavioural changes that could lead to a future cancer excess related to indirect effects of the accident

Need for cancer registration

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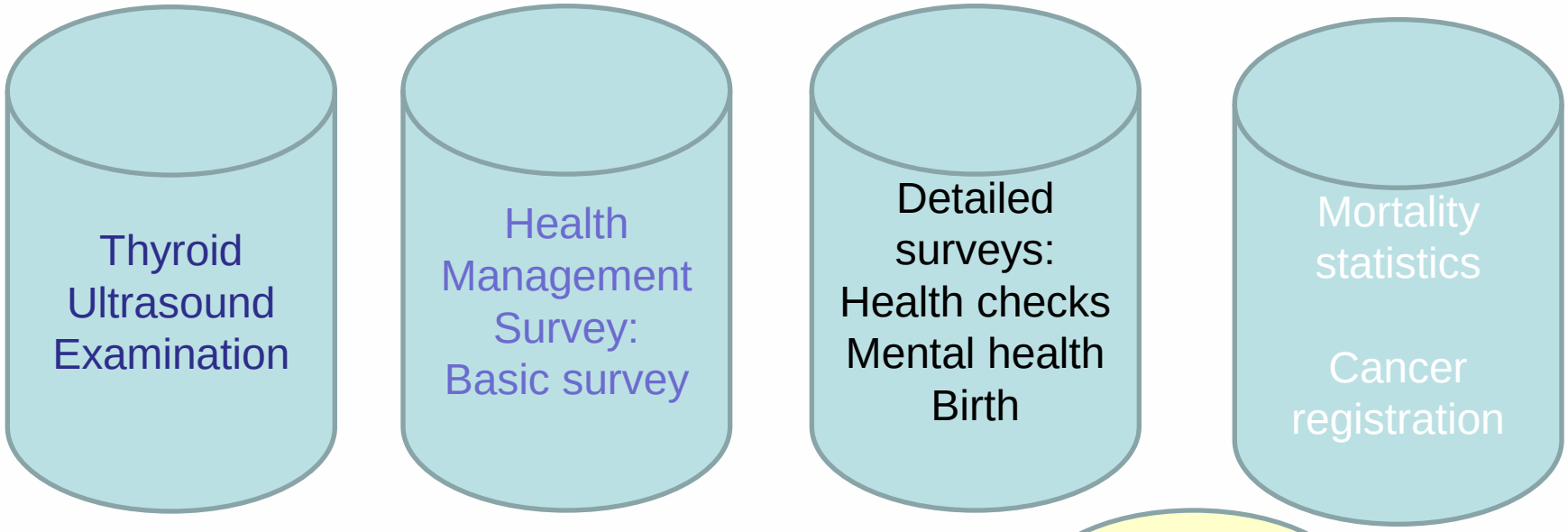
Key messages

Population-based cancer registries play a central role in cancer control programmes because they provide the means to plan, monitor and evaluate the impact of specific interventions in targeted populations.

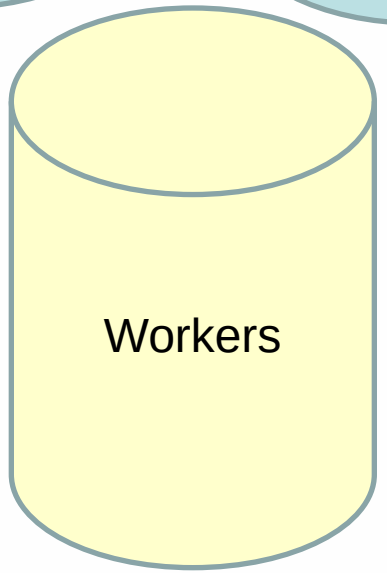
Need for follow up studies



Enabling linkage of information

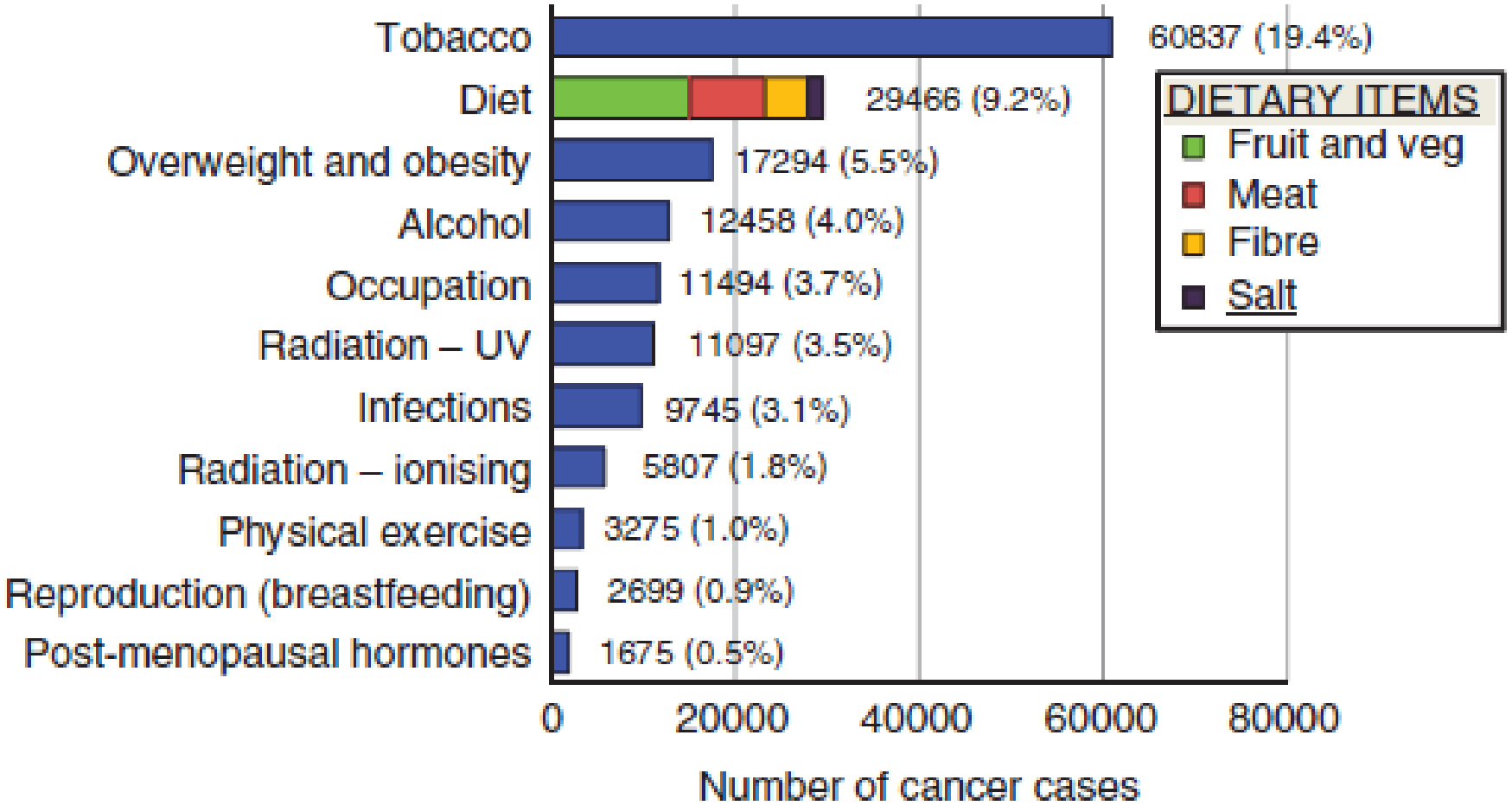
Repeated exposure assessment

Follow up



Known causes of cancer

Example: Attributable cancer risks in the UK



Parkin et al., Br J Cancer, 2011

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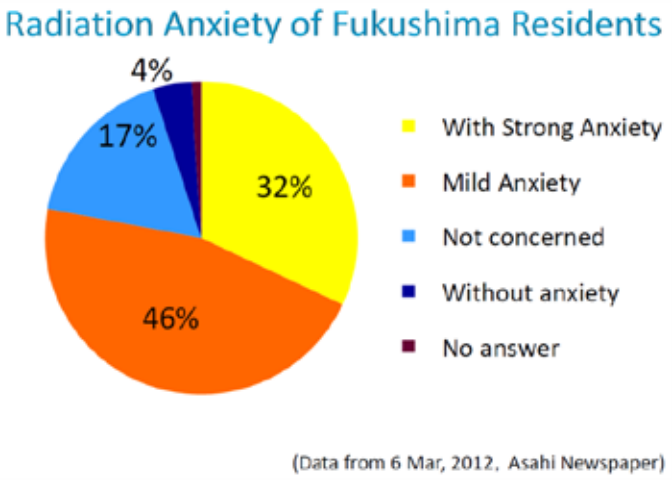
Note: Fruit & vegetables, fibres, physical exercise, breastfeeeding are inveserse relationships; hence, it is their lack associated with cancer

Need for primary prevention



Prevent cancer epidemic due to behavioural changes related to the accident

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<u>Primary prevention:</u>

Possible reactions to anxiety, fear and social and economic stress:

Less physical activity

Increase in tobacco & alcohol use

Replacing local food with processed or « fast » food

Drinking sugary drinks instead of water

Eating unhealthy and gain weight

Final Recommendations

Ensure population-based cancer registration

Ensure linkage of data collected in present activities and enable future individual follow up for cancer and other endpoints

Develop targeted primary prevention programme for the affected population to address possible cancer epidemic resulting from behavioural changes:
- anxiety and stress and related behavioural changes
- changes in diet and physical activity
- social and financial disadvantages