

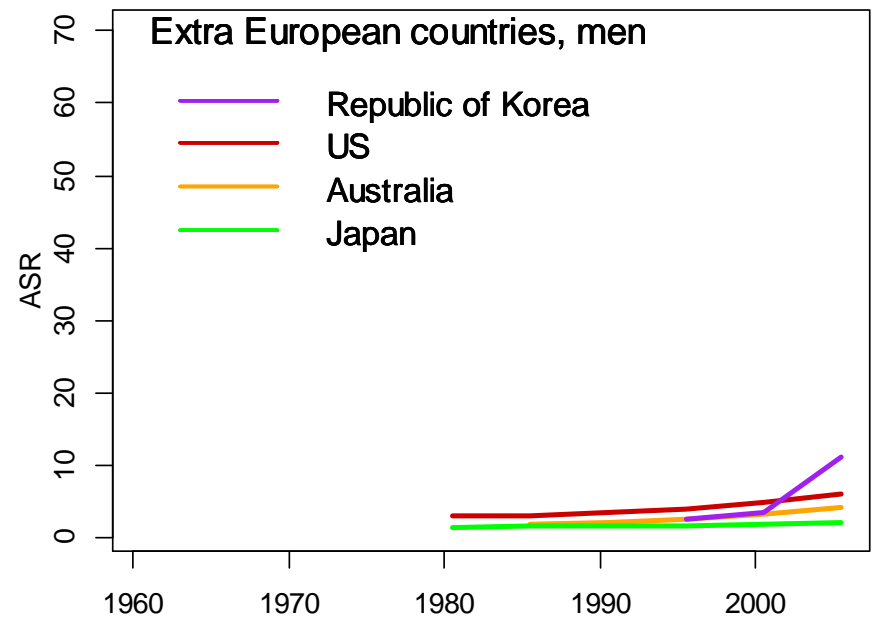
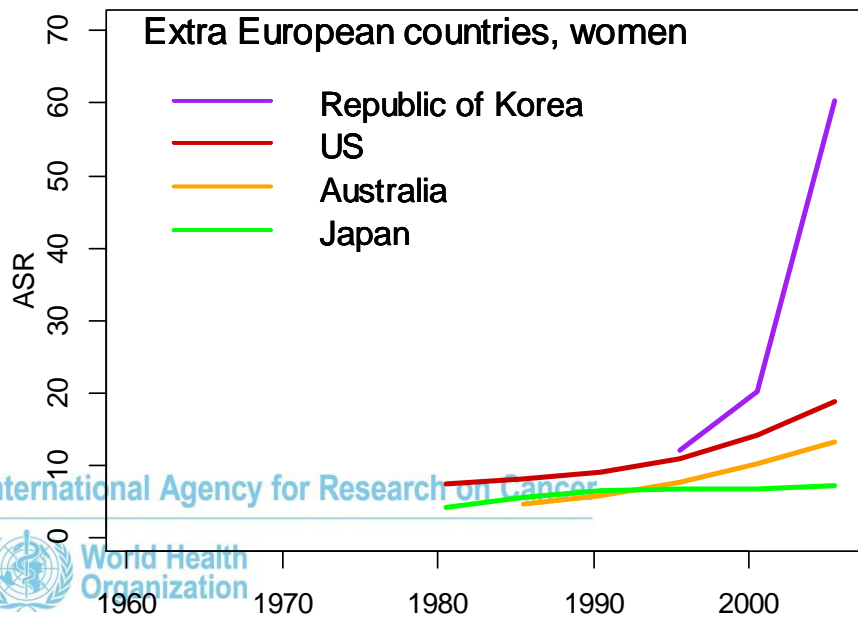
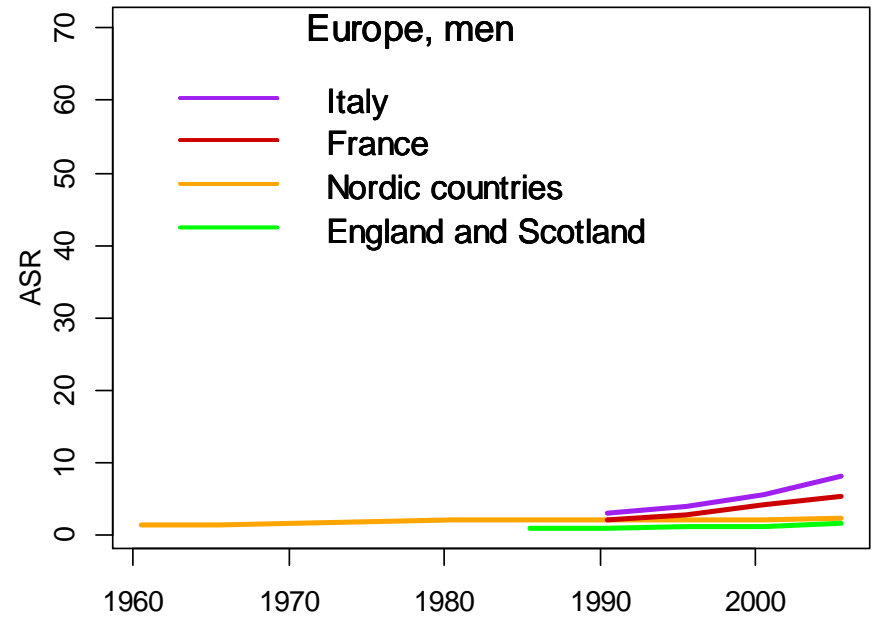
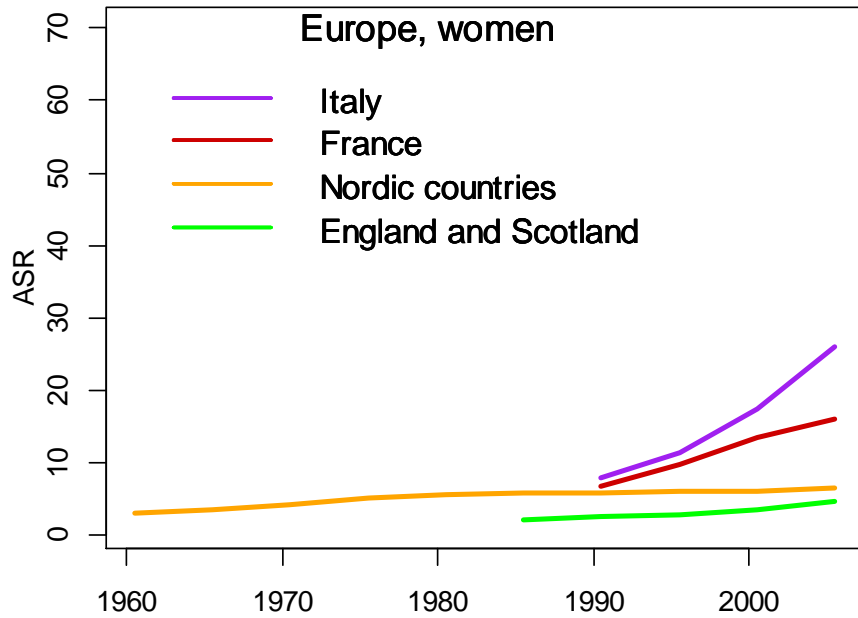


THE IMPACT OF DIAGNOSTIC CHANGES ON THE RISE IN THYROID CANCER INCIDENCE

S Vaccarella, S Franceschi, F Bray, C Wild, M Plummer, L Dal Maso
International Agency for Research on Cancer
Lyon, France

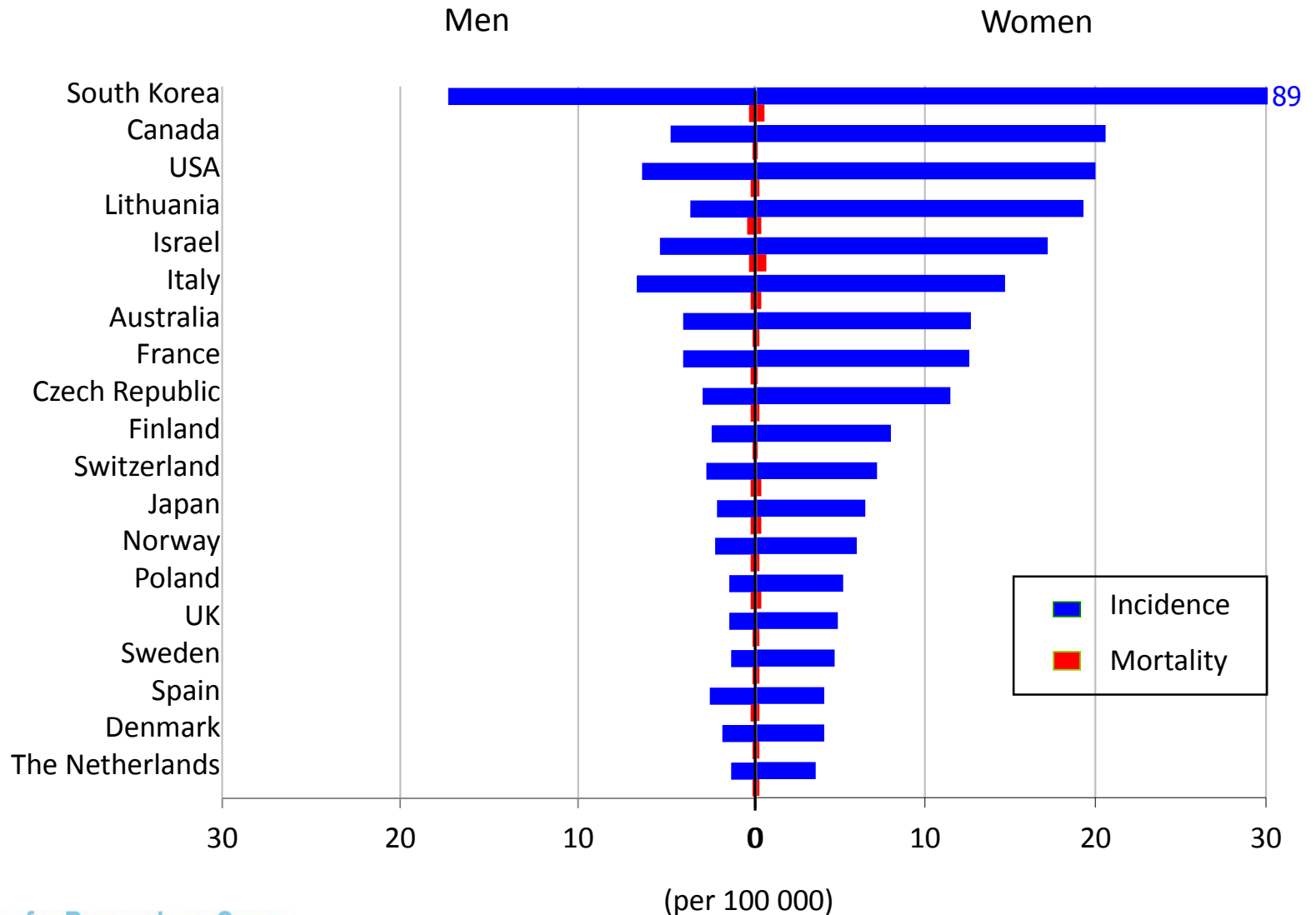
IARC 50th Anniversary Conference

ASR incidence rates of thyroid cancer, 15-79 years



Thyroid cancer in high-income countries (GLOBOCAN, 2012)

Mortality (in red) is nearly invisible and is not increasing anywhere



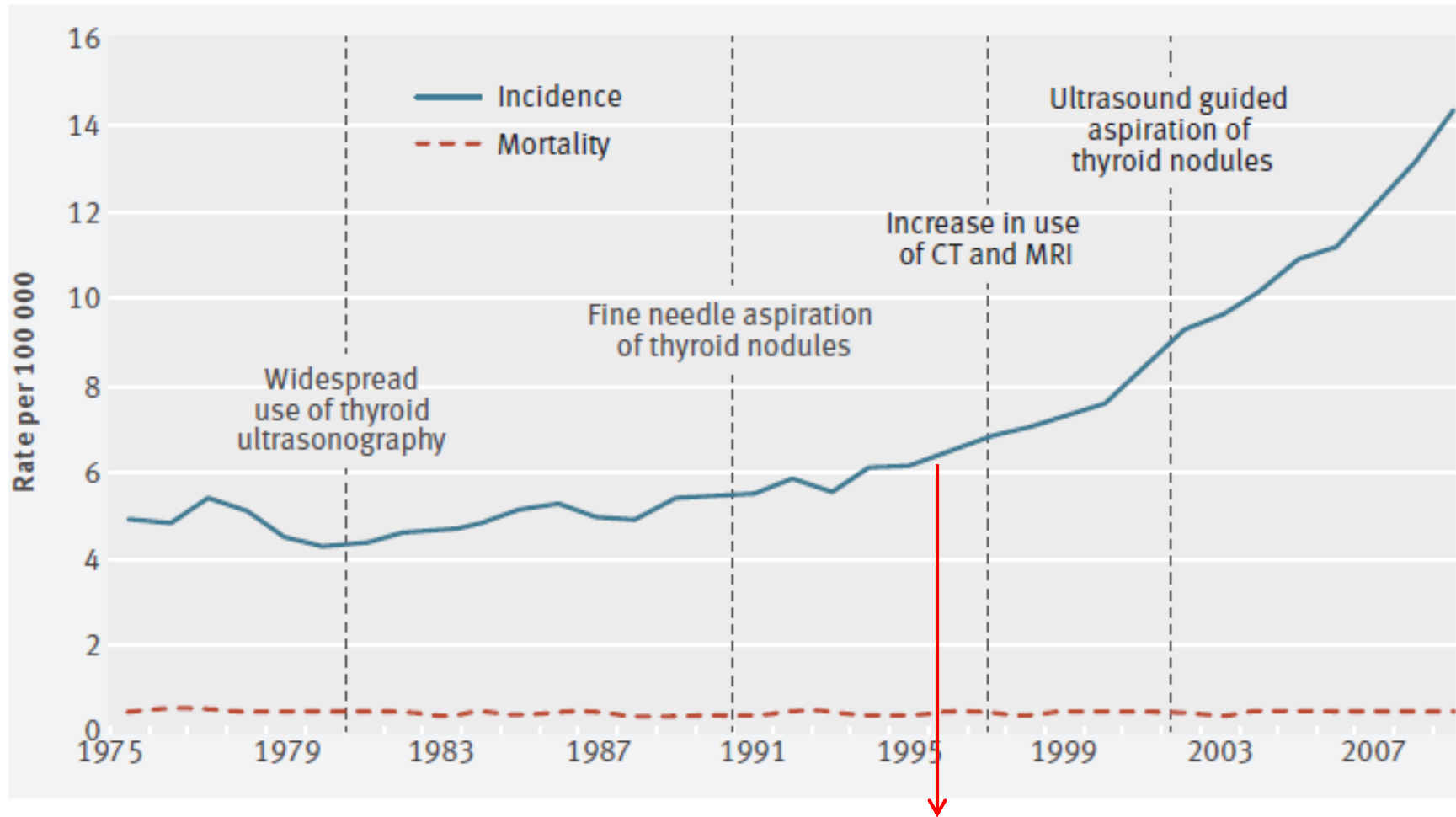
Incidence, mortality, and treatment of different types of thyroid cancer (TC) in the US

Type	% of TC	Change in mortality in last 30 yrs	Lethality	Treatment	Benefits on survival
Papillary	85%	Unchanged	1-2/1000 in 20 yrs	Thyroidectomy, I ₁₃₁ , hormone replacement	Unclear
Follicular	11%	Unchanged	10-20% at 10 yrs	Thyroidectomy, hormone replacement	moderate survival increase
Medullary	3%	Unchanged	25-50% at 10 yrs	Thyroidectomy, hormone replacement	Some pts can be cured by surgery
Anaplastic	1%	Unchanged	90% at 5 yrs	Thyroidectomy, chemo, hormone replacement	Prolongs survival by months

Very different risk, similarly aggressive treatment

No evidence of increased exposure to known or novel risk factors, at least not to the extent of explaining the steep increases in thyroid cancer incidence

Incidence and mortality from thyroid cancer in the US, 1975-2009 and advent of new technologies, Brito, BMJ, 2013



1996: The American Thyroid Association recommended ultrasound-guided FNA for the investigation of thyroid nodules

Definition of **overdiagnosis** :

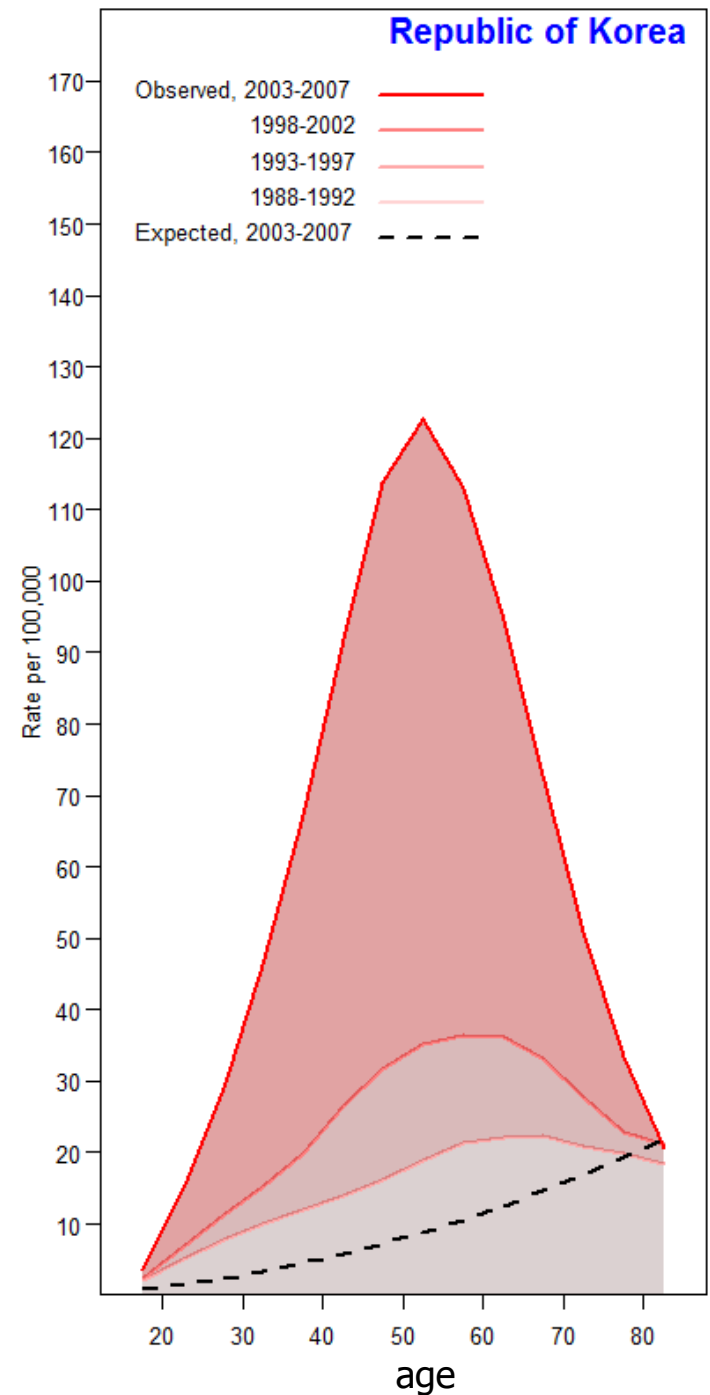
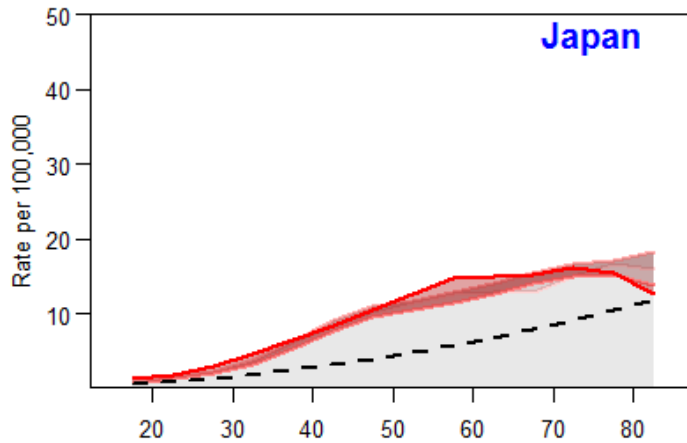
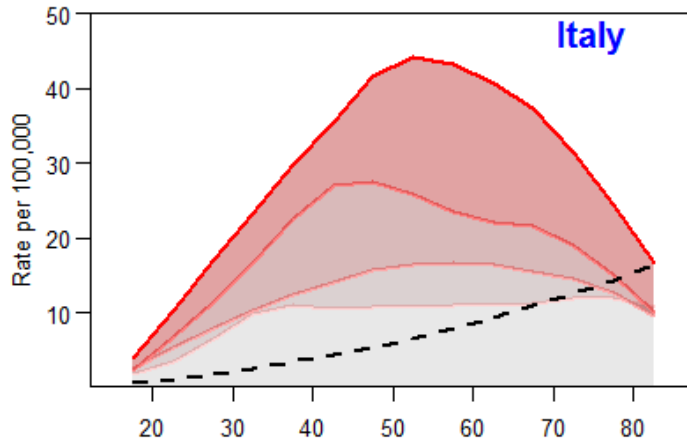
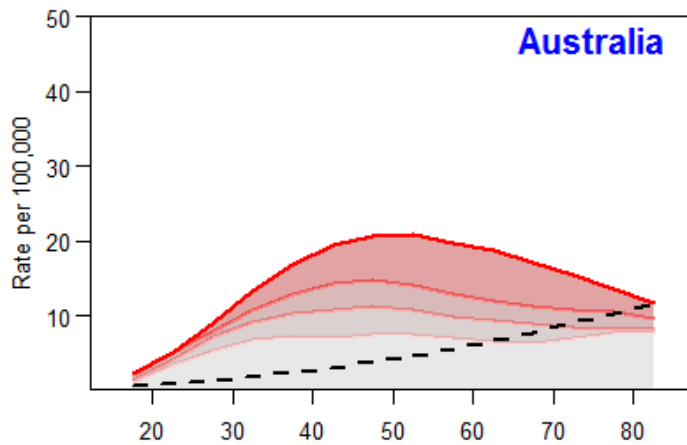
The diagnosis of a cancer that would otherwise not gone to cause symptoms or death (Welch and Black, 2010)

1) Increased organized or disorganized early detection, **intentional** or **unintentional**;

2) Existence of a **vast reservoir of latent tumours**

• **12%** of 8,619 thyroids from 15 autopsy studies showed occult papillary carcinoma, mainly <0.3cm. The prevalence was similar in males and females.

Observed
(solid lines)
and expected
(dashed lines)
age-specific
incidence
rates of
thyroid
cancer in
women



Multistage model of carcinogenicity

- For the majority of epithelial carcinomas the incidence rate increases exponentially with age (Armitage and Doll, 1954)

$$\text{rate} \propto (\text{age})^k$$

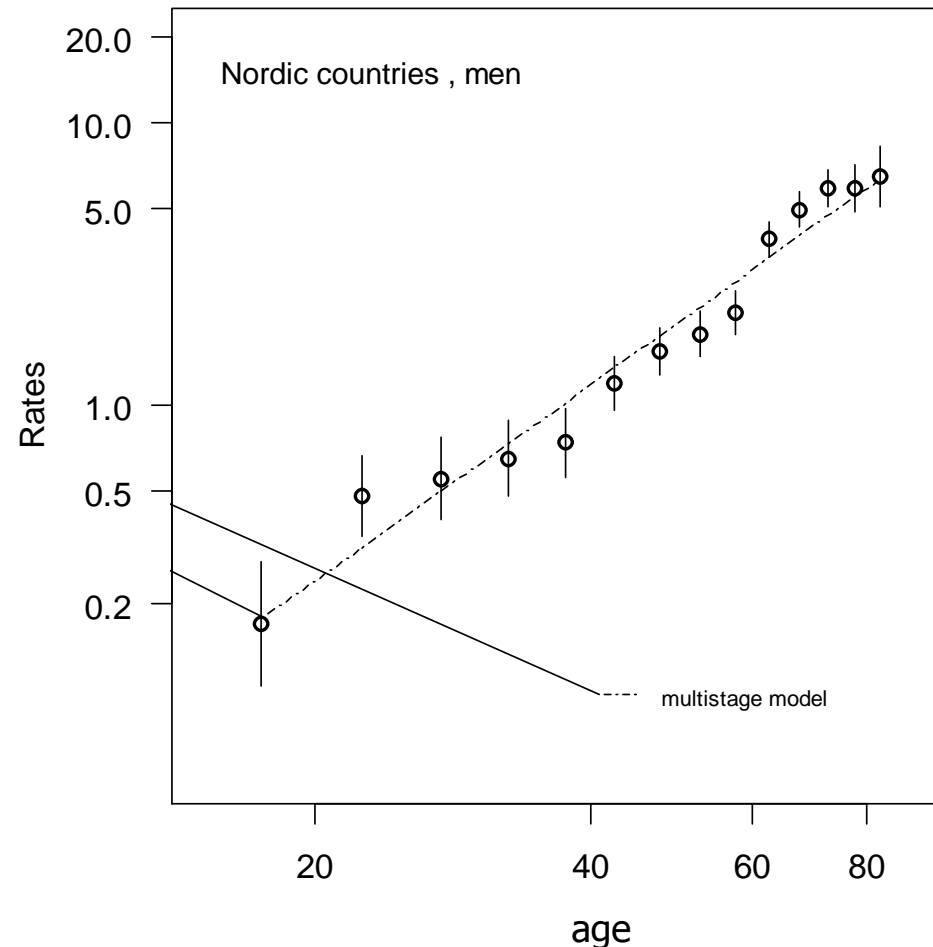
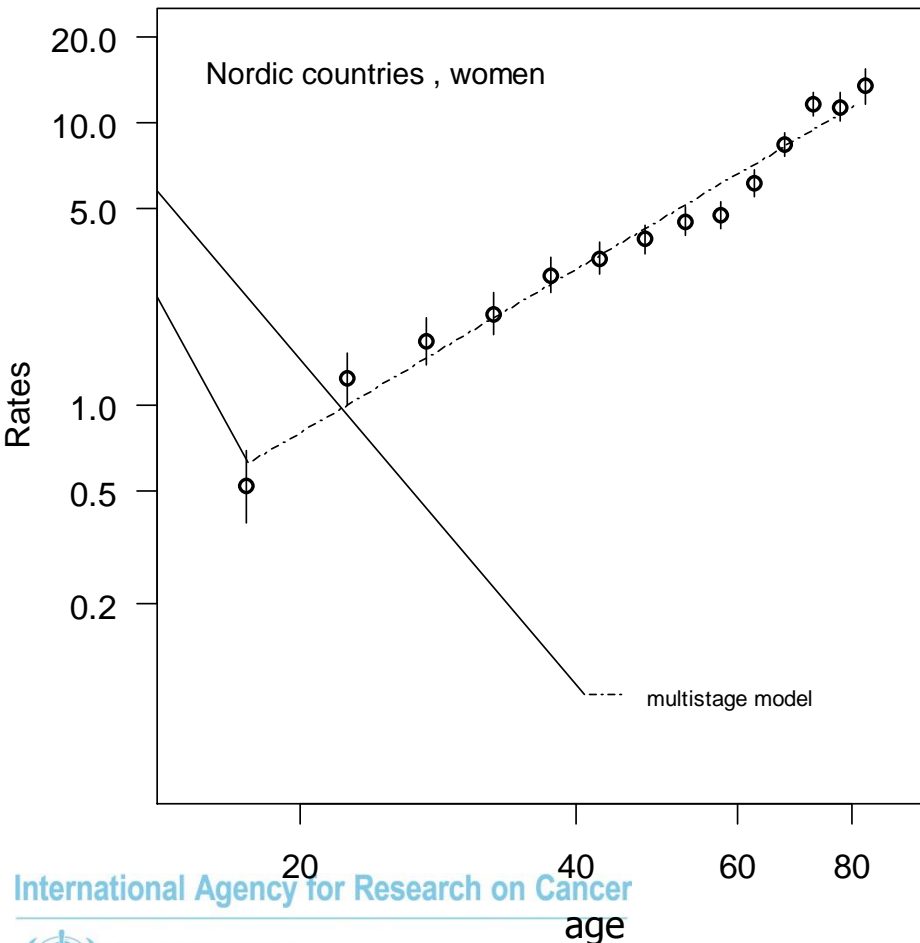
i.e.,

$$\log(\text{rate}) = c + k \cdot \log(\text{age})$$

- Implies a linear relationship between rates and age on the log-log scale
- This relationship could be distorted by changes in carcinogenic exposures or diagnostic practices

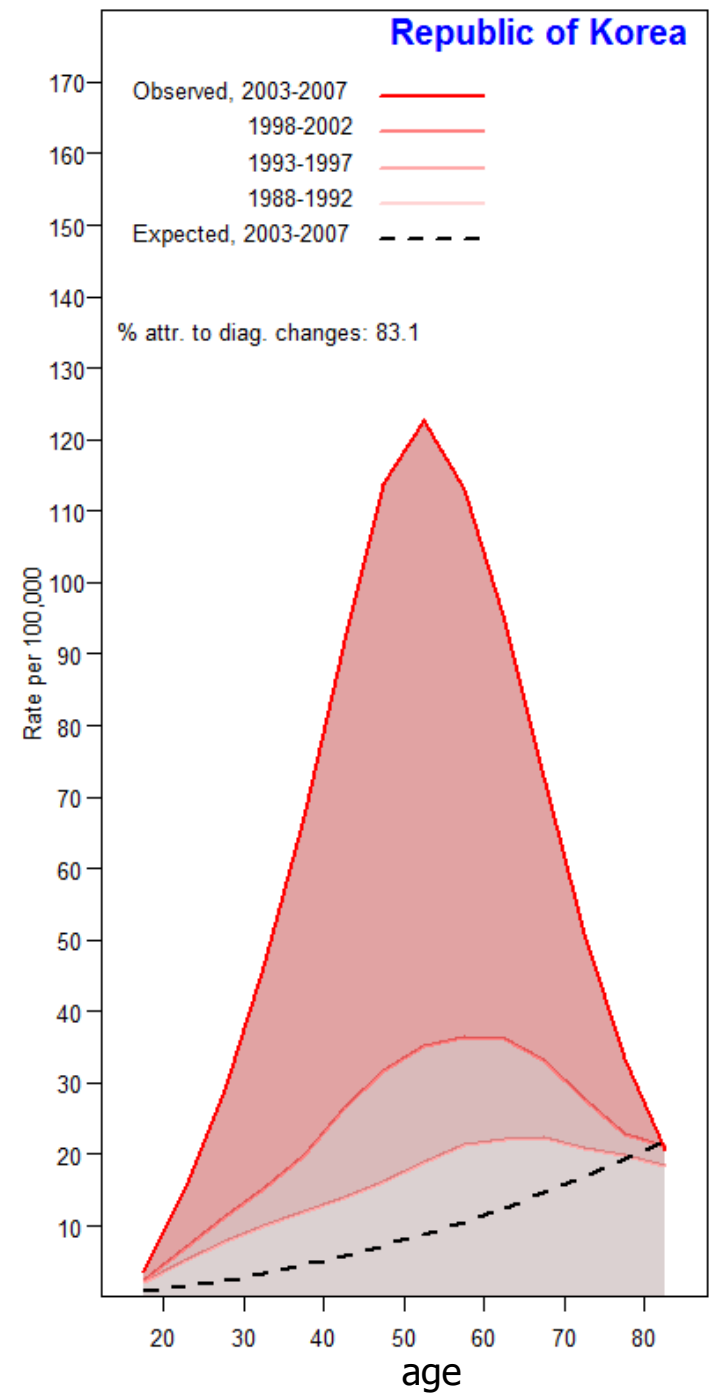
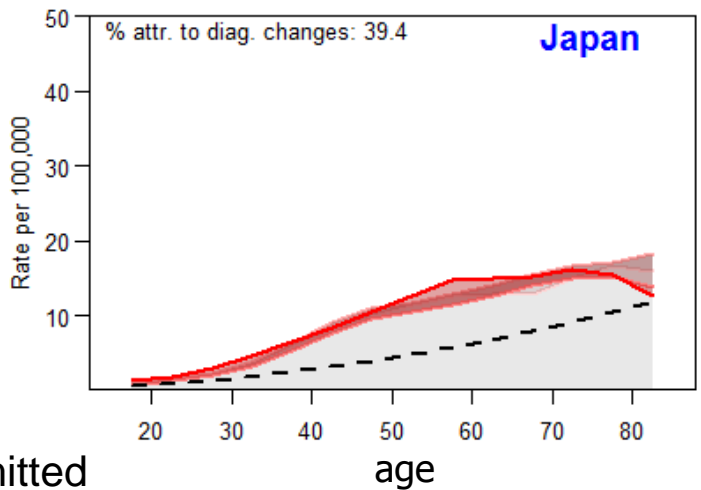
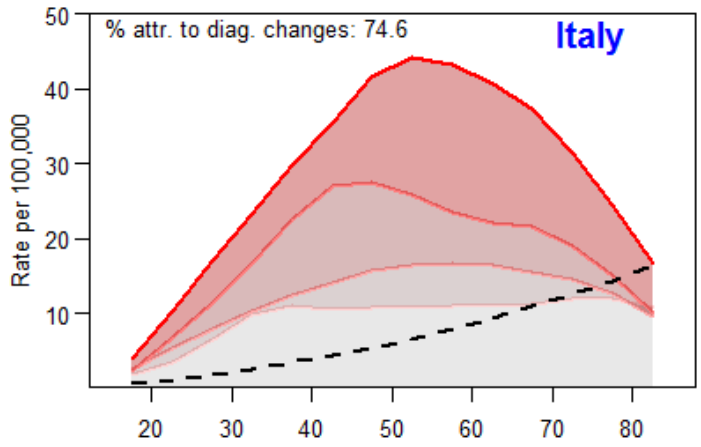
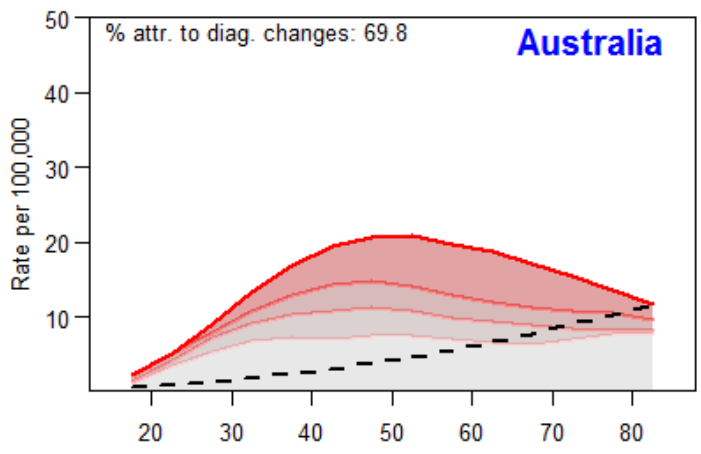
Rates per 100,000 of TC in the Nordic countries, 1958-1967 (prior to the advent of ultrasonography), log-log scale

*The risk increased proportionally to **second power of age**, in agreement to the *multistage model of carcinogenicity theory**



**Observed
(solid lines)
and expected
(dashed lines)
incidence
rates of
thyroid
cancer in
women**

**Cases in excess
of the multistage
model-based
projection are
attributed to
overdiagnosis**



Estimated fraction and number of thyroid cancer cases attributable to overdiagnosis, 1988-2007

	Cases of thyroid cancer					
	Women			Men		
	Observed	Attributable to overdiagnosis		Observed	Attributable to overdiagnosis	
	N	N	%	N	N	%
Nordic countries	13,601	5,786	42.5	4,833	438	9.1
UK	17,107	7,382	43.1	6,379	744	11.7
France	60,324	45,627	76.0	18,219	13,157	72.4
Italy	85,835	64,527	74.6	27,554	19,086	69.0
US	307,372	228,019	74.8	102,343	49,458	48.8
Australia	14,764	10,301	69.8	5,018	2,148	42.8
Japan	93,787	36,269	39.4	25,474	558	2.2
Republic of Korea*	93,461	76,898	83.1	16,605	8,170	49.2
TOTAL		474,809			93,759	

Inte

CONCLUSIONS

A large fraction of thyroid cancer diagnoses in high resource countries is likely due to overdiagnosis (**>80% in the Republic of Korea**);

The majority of the **1/2 million cases** of overdiagnosed TC underwent **total thyroidectomy and harmful treatment**;

Address the problem: avoid systematic ultrasound thyroid screening and work up of small nodules, watchful-waiting approaches, reclassification of low-risk TC;

Warning about **data interpretation** in the context of large-scale screening of the thyroid after radiation exposure due to exceptional events (e.g., Fukushima).