Late Cancer-Related Health Effects in the General Population

Thyroid Cancer

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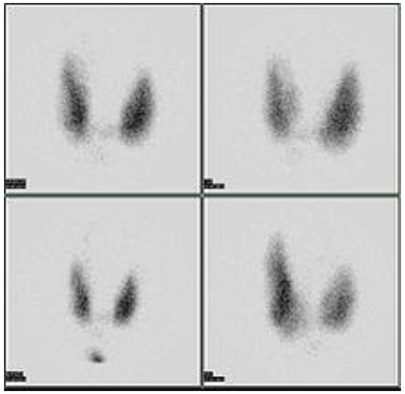
outline

- thyroid disease studies for the general population:
  - exposure in childhood and adolescence, including effect modification
  - exposure in adulthood
- summary of findings
- open questions and…
- future plans

introduction

- first reports on thyroid cancer increase after Chernobyl were met with scepticism because:
  - susceptibility of thyroid gland to internal exposure from radioactive iodine was less established, compared to external radiation exposure
  - main evidence came from studies of medically exposed populations with underlying thyroid conditions and limited data on childhood exposure



introduction (2)

- 2008 UNSCEAR reported 6,848 cases of thyroid cancer diagnosed amongst those under 18 y in 1986 between 1991 and 2005 in the whole of Belarus and Ukraine and in the 4 most affected regions of the Russian Federation

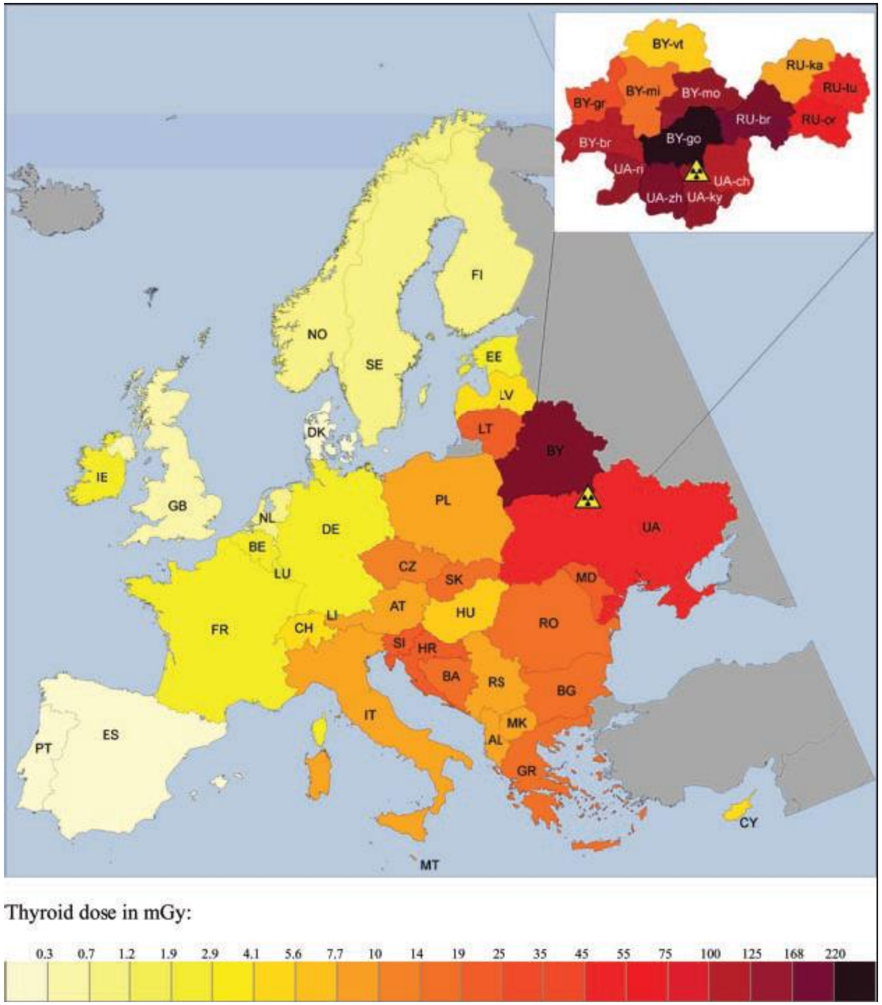
- by 2016, more than 11,000 thyroid cancer cases had been diagnosed in this group
  http://www.who.int/ionizing_radiation/chernobyl/Chernobyl-update.pdf?ua=1

- It is most likely that a fraction of these is attributable to radioiodine intake in 1986

thyroid doses in children

- average country-specific thyroid doses from Chernobyl in Europe to **children aged 1 y** at the time of the accident

Drozdovitch *et al*, 2006



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TC: exposure early in life

- study jointly led by the US NCI, Institute of Endocrinology and Metabolism (IEM), Ukraine & Republican Research Centre for Radiation Medicine and Human Ecology (RRCRM&HE), Belarus
- recent reports from Belarus:
  - Zablotska *et al, BJC,* 2010 and *Cancer,* 2015
- recent reports from Ukraine:
  - Brenner *et al, EnvHP,* 2011
  - Tronko *et al, J Radiol Prot* 2012
- individuals ≤18y.o. with thyroid radioactivity measured in April-June 1986
  - 38,543 in Belarus
  - subsample of 32,385 in Ukraine

screened cohort study: BelAm & UkrAm

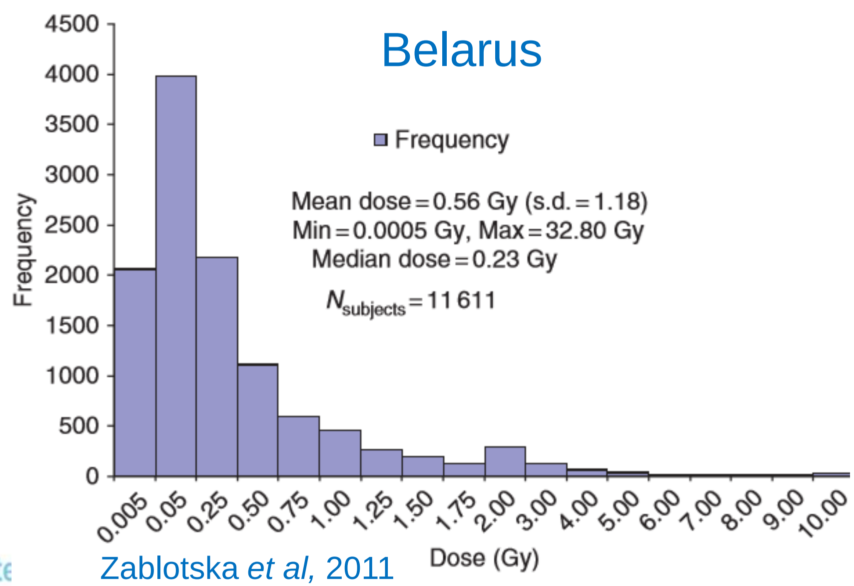
- 4 biennial screening cycles in Ukraine*:
  - 13,243 subjects screened in 1st cycle
  - from 93.8% to 76.9% in the next 3 cycles (between 2001 and 2007)
- 3 screening cycles in 1997-2008 in Belarus*:
  - 11,644 individuals were screened 1st time during 1997-2000
  - two more cycles during 2002-04 and 2004-06 (ext up to 2008)

* 5th cycle completed recently

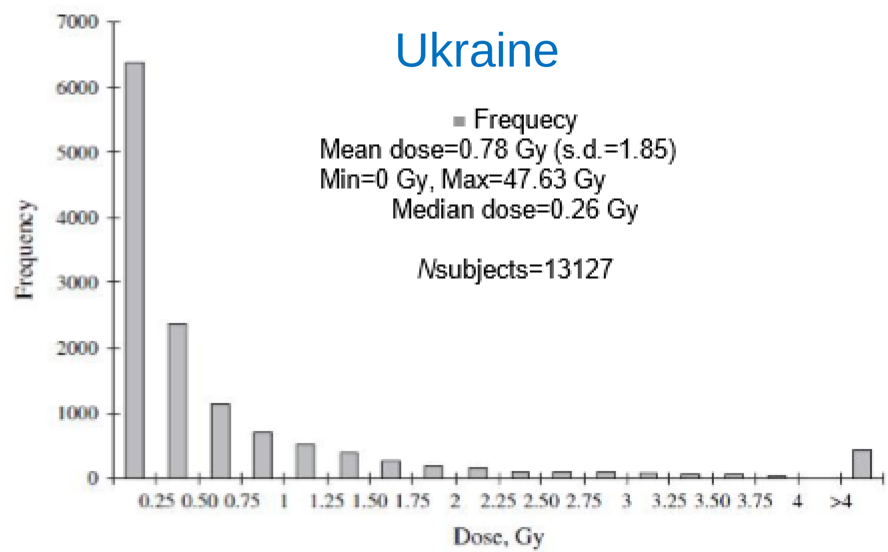
**by Belarussian decree persons under 18y are recalled annually

screened cohort study: BelAm & UkrAm (2)

- individual doses (and uncertainties) estimated based on:
  - ❖ thyroid activity measurement
  - ❖ individual data on dietary, lifestyle habits and residential history
  - ❖ environmental transfer models



Zablotska *et al*, 2011

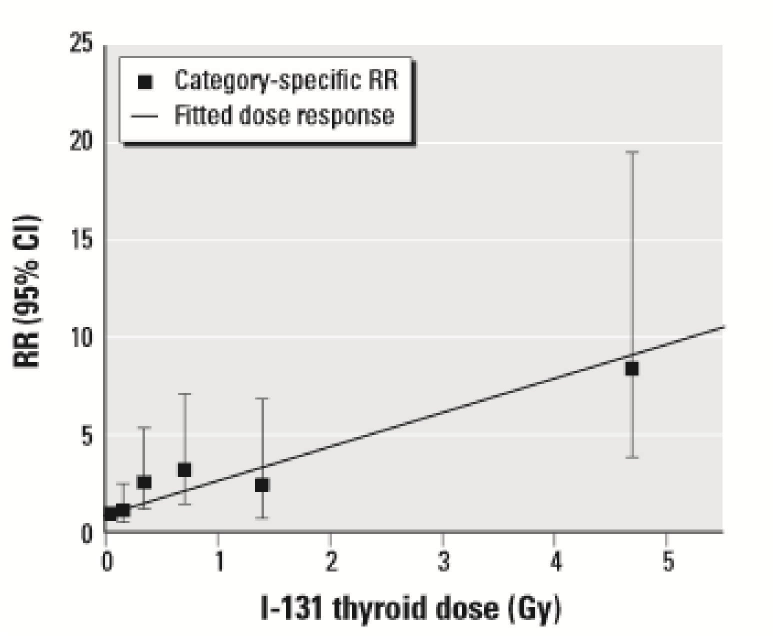


Tronko *et al*, 2006

TC: dose-response with I-131

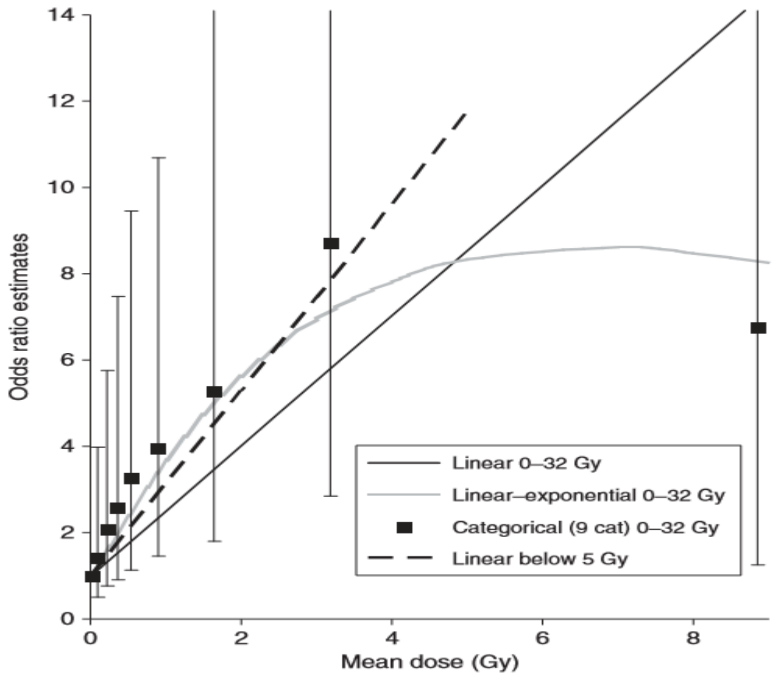
Ukraine (Brenner *et al*, 2011)

ERR/Gy 1.91 (95% CI: 0.43-6.34)



Belarus (Zablotska *et al*, 2010)

<5Gy: EOR/Gy 2.15 (95% CI: 0.81-5.47)



TC: latency

- very early onset (first cases appeared only 3 to 4 years after the accident) was unexpected based on existing knowledge from externally exposed populations*

* Ron *et al*, 1995; Veiga *et al*, 2016

Caution: the first cases demonstrated very clear clinical symptoms, they were not detected by screening

Photo: http://renaissanceresearch.blogspot.fr/2006_04_01_archive.html

TC: effect modifiers

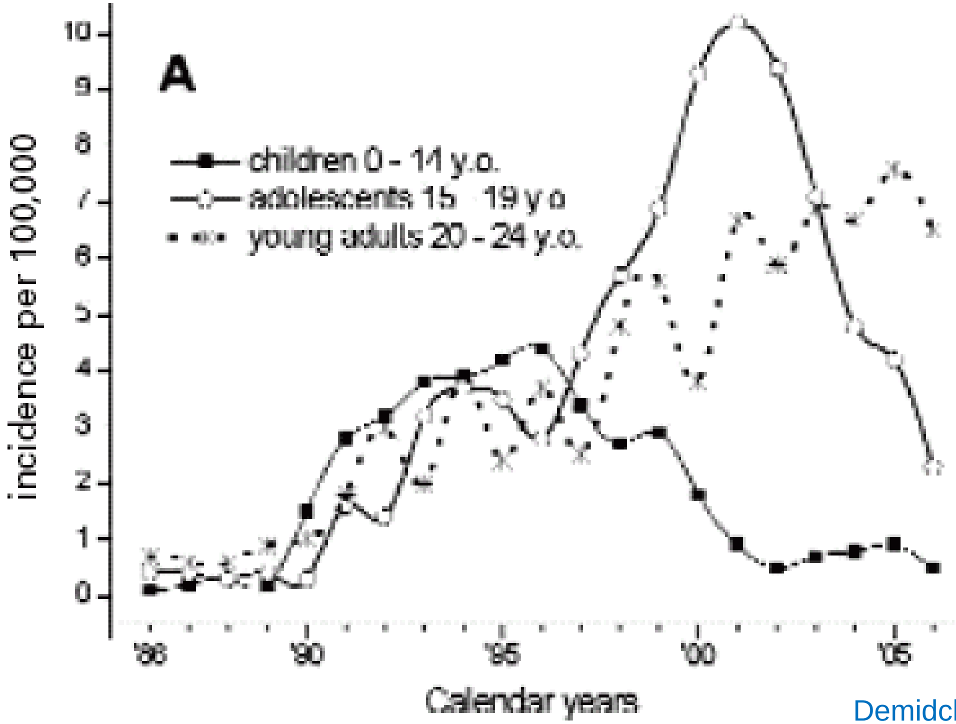
- age at exposure and gender

Reference	Ratio ERR/Gy girls/boys	Age at exposure effect
Cardis *et al*, 2005	0.9 *p=0.9*	NA
Kopecky *et al, 2006*	NA	No monotone trend with increasing age; *p=0.7*
Tronko *et al*, 2006	7.5 *p=0.14*	ERR decreased with increasing age at exposure; *p=0.6*
Brenner *et al*, 2011	2.2 *p=0.9*	ERR decreased with increasing age at exposure; *p=0.4*
Zablotska *et al,* 2010	*3.0* *p=0.13*	No significant effect of age at exposure; *p=0.9*
Ron *et al,* 1995	2 *p=0.07*	ERR decreased with increasing age at exposure; *p=0.004*
Veiga *et al*, 2016	*0.8* *p=0.37*	ERR varied significantly with age at exposure; *p=* 0.001

- effect of gender not clear because most of TC diagnosed at very young age (mean age ATD-11.7 (Demidchik et al 2006))
- overall, risk decreases with increasing age at exp. although trends are not always significant or monotonous

TC: effect modifiers (2)

- risk pattern over time



Demidchik, Saenko and Yamashita, 2007

- I-131-related risk persisted more than 20 y after exposure, with no evidence of decrease Brenner *et al*, 2011

TC: effect modifiers (3)

- iodine deficiency and iodine supplementation

Consumption of potassium iodide	OR at 1 Gy (95% CI)	
	Highest two tertiles of soil iodine	Lowest tertile of soil iodine
No	3.5 (1.8 to 7.0)	10.8 (5.6 to 20.8)
Yes	1.1 (0.3 to 3.6)	3.3 (1.0 to 10.6)

Cardis *et al*, 2005

- in Belarus, diffuse goitre and thyroid enlargement were modifiers of TC risk (Zablotska *et al*, 2010)
- in Ukraine, data not strong enough to support a modifying effect of iodine deficiency (Brenner *et al*, 2011)
- **indicators of past stable iodine intake are difficult to reconstruct**

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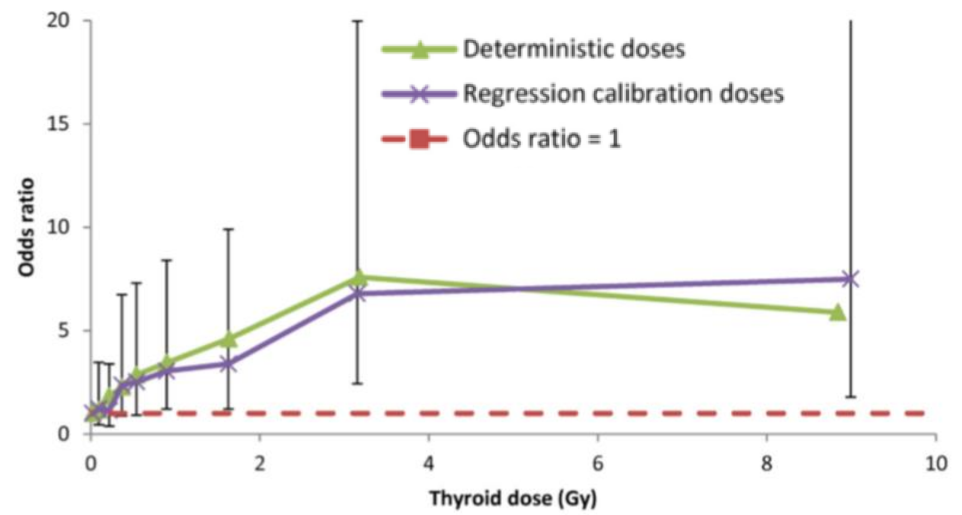
TC: role of uncertainties in dose estimates on risk

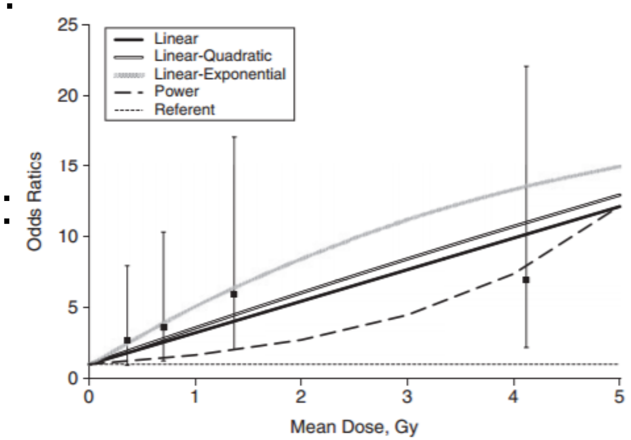
- relatively small contribution of unshared classical dose error
- effects of adjusting for dose error were minimal, resulting in changes to risk estimates:
  - in Ukraine between -11% and +7% (Little *et al*, 2014)
  - In Belarus between -23% and -2% (depending on the method) (Little *et al*, 2015)



- new effort to characterise uncertainties in doses and their role on risk estimate in the IARC c-c study

non-malignant thyroid diseases
BelAm and UkrAm studies

- follicular adenoma:
  - ❖ in Ukraine (Zablotska et al, 2008) n=23:
    - ✓ ERR/Gy 2.07 (95%CI: 0.28, 10.31)
    - ✓ risk higher in women
  - ❖ in Belarus (Zablotska et al, 2015) n=38:
    - ✓ ERR/Gy 2.22 (95% CI: 0.41, 13.1)
    - ✓ similar in males and females

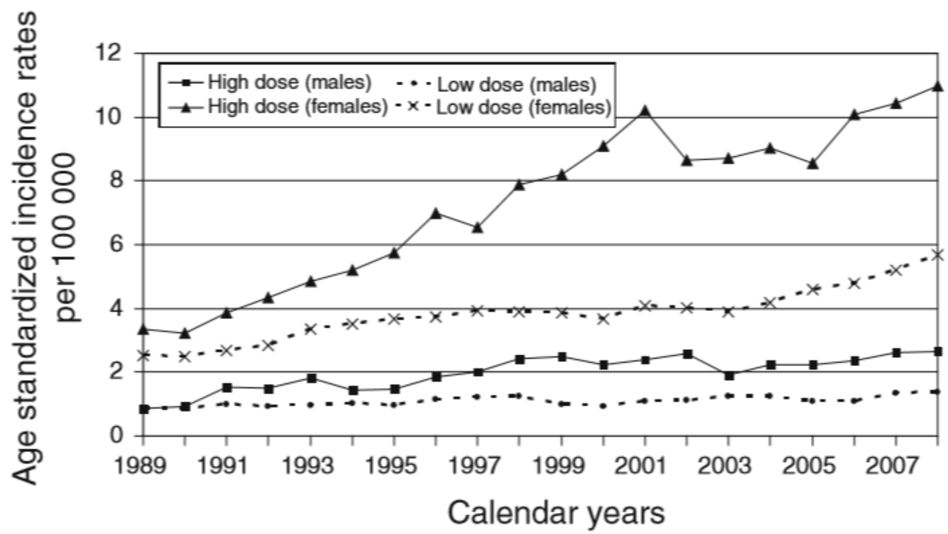


- hyperthyroidism (Hatch et al, 2010):
  - ❖ In Ukraine: n=76; no dose-response relationship
- autoimmune thyroiditis (AIT) (Tronko et al, 2008):
  - ❖ in Ukraine: no dose-response relationship for AIT; significant association between elevated ATPO levels and ^{131}I

TC: exposure in adulthood

- recent studies of residents of contaminated territories >18 y at the time of accident:
  - ❖ ecological study in Ukraine compared TC incidence rates – between high and low exposure regions in 1989-2007 (Fuzik *et al*, 2011)
  - ❖ incidence rate ratios in females was significantly higher in high exposure regions in those exposed at ages of 20–49 years, in males, this tendency was less clear

(Fuzik *et al*, 2011)



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TC: exposure in adulthood (2)

- in Russia (Ivanov *et al,* 2012):
  - TC incidence in the contaminated territories of Bryansk, Kaluga, Oryol and Tula evaluated in 1991-2008
  - no dose-response relationship found in exposed adults based on average residential doses
- caution:
  - possible surveillance bias
  - no individual dosimetry, doses intend to be low
- In Finland (Auvinen *et al,* 2013):
  - cancer incidence data obtained for 1988-2007 for the cohort divided into 4 exposure categories (the lowest <0.1 mSv and the highest 0.5 mSv)
  - weak, non-significant positive relation was observed in females
- No convincing evidence of effect of exposure as an adult

TC: risks after exposure in childhood and adolescence

summary of most informative analytical studies

Study	Ascertainment period	Number of cases	Number of controls/ size of study population/PY	ERR* at 1 Gy (95% CI)
Chernobyl studies				
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 *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)
Brenner *et al*, 2011	2001-2007	65	12,514	1.91 (0.43–6.34)
Zablotska *et al*, 2010	1996-2004	133	11,611	3.16 (1.49 – 6.95)
		85		2.15 (0.81 - 5.47)
Exposure in utero				
Hatch *et al*, *2009*	2003-2006	7	2,582	11.7 (NE – 1,982)
External exposures - *Pooled analyses*				
Ron *et al*. 1995		458	1.400.000 PY	7.7 (2.1-28.7)
Veiga *et al*. 2016		927	3.400.000 PY	5.5 (4.1–7.5)

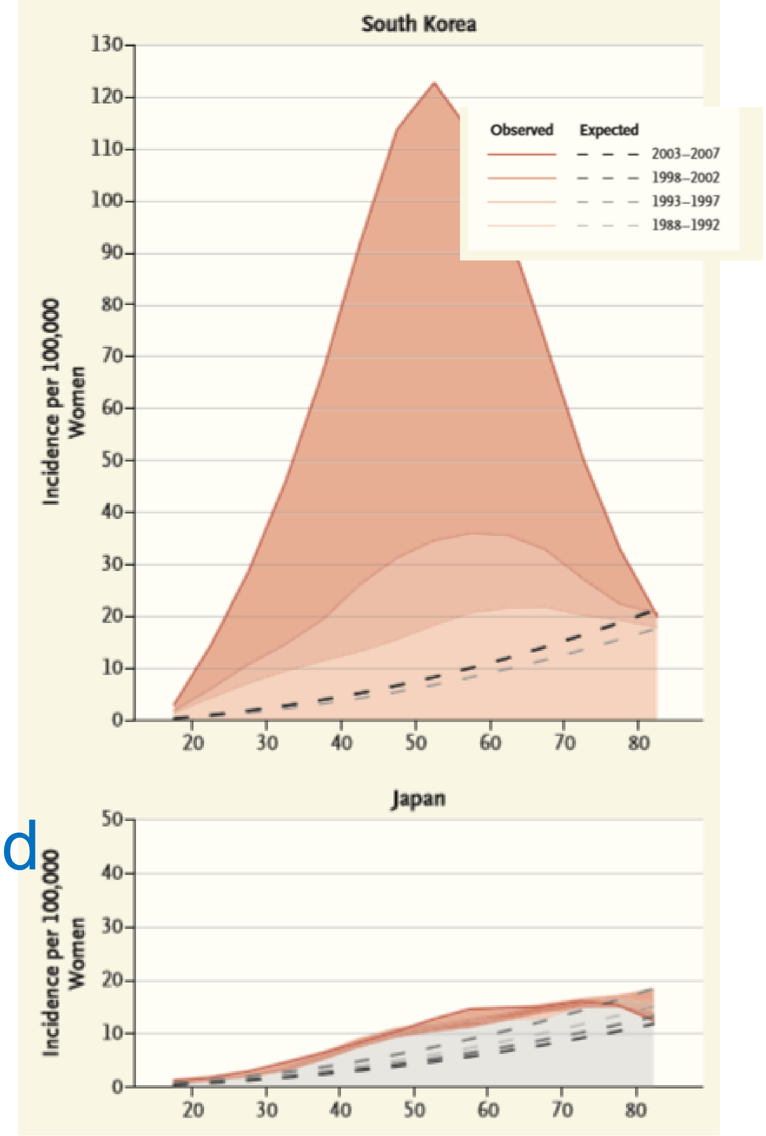
*ERR=excess relative risk

TC and screening

- effect of large scale screening efforts in contaminated areas:
  - ❖ *absolute rate of thyroid cancer increases in a screened population*
  - ❖ *ERR estimate can be biased upward, if there is a correlation between thyroid dose and frequency of screening*
  - ❖ BelAm and UkrAm cohort studies provided an estimate of the risk where confounding effect of screening is unlikely (all subjects were screened, regardless of dose)
- however:
  - ? whether the detection of additional small thyroid cancers affects the excess radiation risks
  - ? whether these small tumours are induced by radiation to the same extent as large tumours

worldwide: rise in thyroid cancer incidence

- estimated number of cases attributable to increased thyroid-gland surveillance:
  - in women:
    - ✓ 90% in South Korea;
    - ✓ 50% in Japan
  - in men:
    - ✓ 70% in South Korea;
    - ✓ less than 25% in Japan



"careful data interpretation needed in the context of screening after radiation exposure"

Vaccarella *et al*, 2016

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from Chernobyl to Fukushima

SHAMISEN
Nuclear Emergency Situations
Improvement of Medical and
Health Surveillance

- subtask 1.2: Critical review of long-term medical surveillance programmes

→ to provide a set of lessons learned from medical surveillance on physical and mental health of populations exposed to fallout from the Chernobyl and Fukushima accidents

→ recommendations for setting up criteria to:
  - justify long-term medical surveillance programmes of affected populations
  - evaluate their effectiveness

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OPERRA OPEN PROJECT FOR EUROPEAN RADIATION RESEARCH AREA

summary

- risks following exposure to I-131 are somewhat smaller, but compatible with estimates from external irradiation
- latency period less than 5 years
- sensitivity to I-131 in children is much grater compared to adults
- I-131-related risk persists nearly 3 decades after Chernobyl accident
- most of observed thyroid malignancies are papillary carcinomas

there is more to be learned…

- about the impact of:
  - gender,
  - age at exposure, including in adulthood,
  - stable iodine intake
  - increased surveillance
  - uncertainties in doses on risk estimates…
- there is a need for studies to better understand natural history of thyroid cancer (progression and regression of thyroid tumours over life span)
- **importance of international cooperation in science is explicitly recognised and has been proven after Chernobyl**

CO-CHER: setting the scene for future research on Chernobyl

- development of a long-term research programme with agreed research priorities
- Chernobyl Research Programme highlights:
  - establishment of Chernobyl Life Span cohort
  - convening a multinational body - International Chernobyl Research Committee
  - conducting prioritized multidisciplinary studies
  - **more info: http://co-cher.iarc.fr/**


Thank you!
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