Thyroid cancer: incidence, prevention possibilities and early detection options (screening – lessons learnt from Fukushima accident)

Richard Wakeford
Professor in Epidemiology
Institute of Population Health and Dalton Nuclear Institute
The University of Manchester, UK
(Richard.Wakeford@manchester.ac.uk)

MANCHESTER 1824

Chornobyl Workshop, Stockholm, 25 April 2016

The University of Manchester Centre for Occupational and Environmental Health

Chornobyl – 26 April 1986

MANCHESTER 1824

The University of Manchester
Centre for Occupational and
Environmental Health

Radioactivity Released

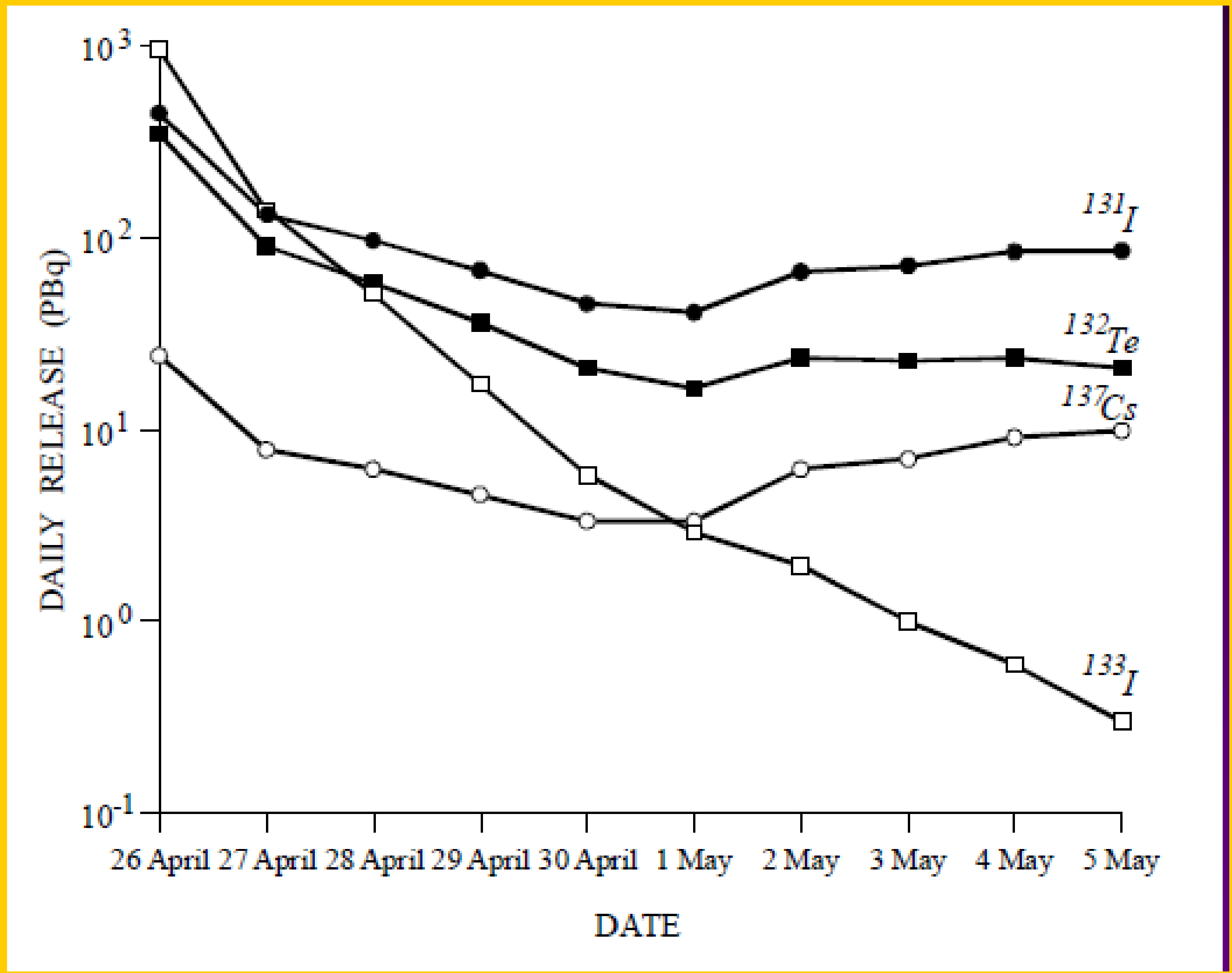
- Total activity release of ~14 EBq
- ~50% of the activity released was as radioisotopes of noble gases, and
- 1.8 EBq of ^{131}I,
- 85 PBq of ^{137}Cs,
- 10 PBq of ^{90}Sr,
- 0.1 PBq of Pu α-emitting isotopes.

Nuclear Weapons Testing

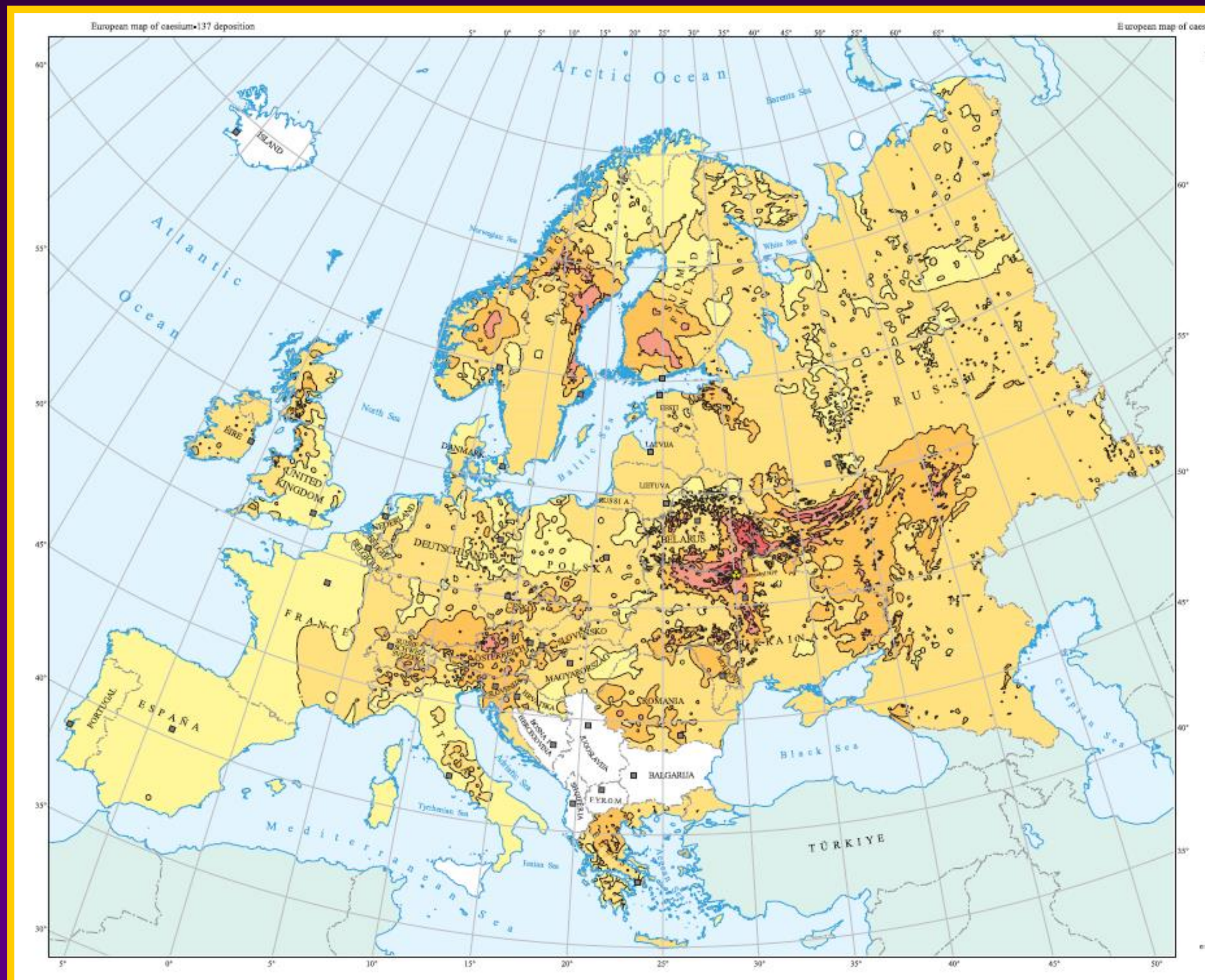
Comparison of Activity Releases (PBq) from Atmospheric Nuclear Weapons Testing and the Chornobyl Accident

Radionuclide	Nuclear Weapons Testing (PBq)	Chornobyl Accident (PBq)
I-131	675 000	1 800
Cs-137	948	85
Sr-90	622	10
Pu (α-activity)	11	0.1

Release of Radionuclides



Chornobyl Contamination



MANCHESTER 1824

The University of Manchester
Centre for Occupational and
Environmental Health

Chornobyl Contamination

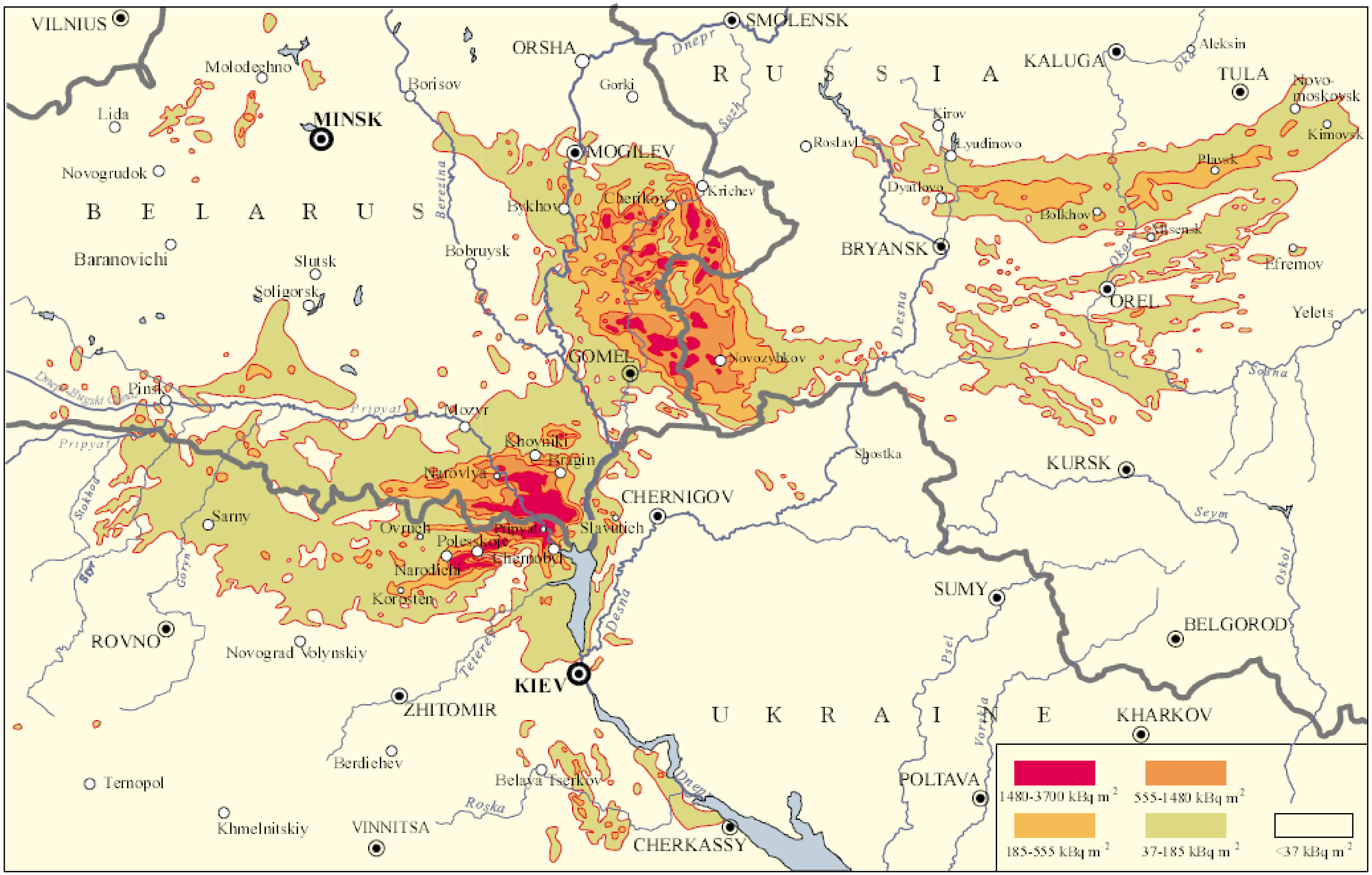


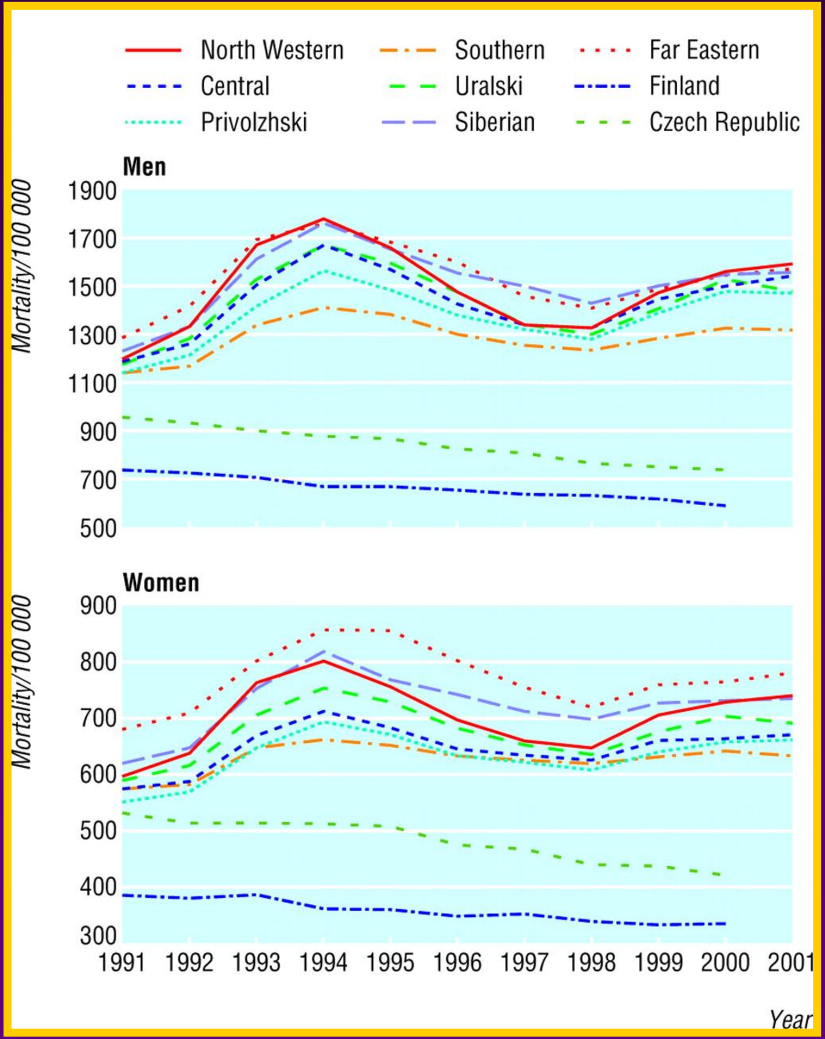
Figure VI. Surface ground deposition of caesium-137 released in the Chernobyl accident [I1, I3].

MANCHESTER 1824

The University of Manchester Centre for Occupational and Environmental Health

Evacuation of Heavily Contaminated Areas

Age Standardised Mortality from All Causes by District of Russia



MANCHESTER 1824

The University of Manchester Centre for Occupational and Environmental Health

Chornobyl – Predicted Health Consequences

(Ilyin *et al.*, *J Radiol Prot* 1990; **10**: 3-29)

"A statistically significant excess over the spontaneous level is unlikely to be detectable for these effects [cancer, hereditary effects and teratogenic effects]. A possible exception may be thyroid disorders."

L A Ilyin *et al.* of the Academy of Medical Sciences of the USSR, November 1989.

MANCHESTER 1824

The University of Manchester Centre for Occupational and Environmental Health

Predicted Thyroid Cancers (1986-2015)

(Ilyin *et al.*, *J Radiol Prot* 1990; **10**: 3-29)

Table 8. Possible late effects of thyroid exposure among the population in the central European regions of the USSR.

Republic	Oblasts	Population (millions)	Collective dose (10^4 man-Sv)		Possible consequences	
			Thyroid	Whole body	Malignant tumours	Fatal cancer
Ukrainian SSR	Central	13.6	19.9	9.2	195	20
	Western	8.3	1.2	0.8	12	1
	Eastern	14.5	2.5	1.5	25	2
	Southern	14.6	2.8	0.9	28	3
	Total	51.0	26.6	12.3	260	26
Byelorussian SSR	South Eastern	3.0	7.7	8.5	78	8
	North Western	7.0	1.2	1.9	13	1
	Total	10.0	9.0	10.4	91	9
RSFSR	Central	9.8	9.7	8.0	97	10
Moldavian SSR		4.1	0.4	0.4	4	0
Overall total		74.9	45.7	31.1	452	45

Thyroid Cancer Incidence in Europe

Predicted Number of Radiation-induced and Background Cases (Exposure at **All Ages**)

(Cardis *et al.*, *Int J Cancer* 2006; **119**: 1224-35)

Country Grouping	Average Thyroid Dose in 1986 (mSv) (0-4 years of age)	Number of Cases during 1986-2005		Number of Cases during 1986-2065	
		Radiation-Induced* (% of background)	Background	Radiation-Induced* (% of background)	Background
1	1	60 (0.03%)	224 000	800 (0.08%)	950 000
2	7	125 (0.12%)	105 000	1900 (0.41%)	460 000
3	19	300 (0.33%)	91 000	5100 (1.3%)	400 000
4	63	60 (1.0%)	6 000	**1100 (4.1%)**	27 000
5	201	**400 (3.5%)**	11 500	**6800 (13.9%)**	49 000
Total	11	945 (0.22%)	437 500	15 700 (0.83%)	1 886 000

* Predicted using BEIR VII risk model

MANCHESTER 1824

The University of Manchester Centre for Occupational and Environmental Health

Thyroid Cancer Incidence in Europe

Predicted Numbers of Radiation-induced and Background Cases (Exposure at **<15 Years of Age**)

(Cardis *et al.*, *Int J Cancer* 2006; **119**: 1224-35)

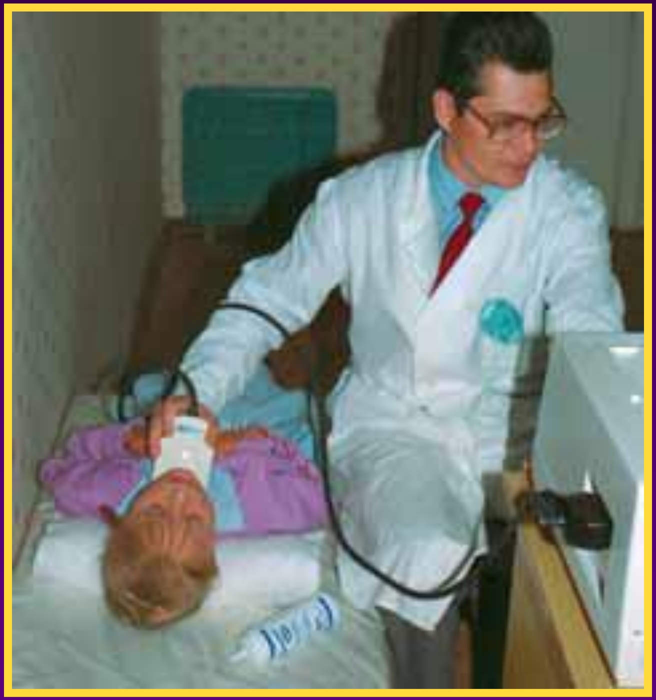
Country Grouping	Average Thyroid Dose in 1986 (mSv) (0-4 years of age)	Number of Cases during 1986-2005		Number of Cases during 1986-2065	
		Radiation-Induced* (% of background)	Background	Radiation-Induced* (% of background)	Background
1	1	30 (0.20%)	15 000	700 (0.16%)	440 000
2	7	80 (1.1%)	7 000	1700 (0.77%)	220 000
3	19	200 (4.0%)	5 000	4600 (2.2%)	210 000
4	63	**40 (13%)**	300	**1000 (7.1%)**	14 000
5	201	**250 (42%)**	600	**6100 (24.4%)**	25 000
Total	11	600 (2.2%)	27 900	14 100 (1.6%)	909 000

*Predicted using BEIR VII risk model

MANCHESTER 1824

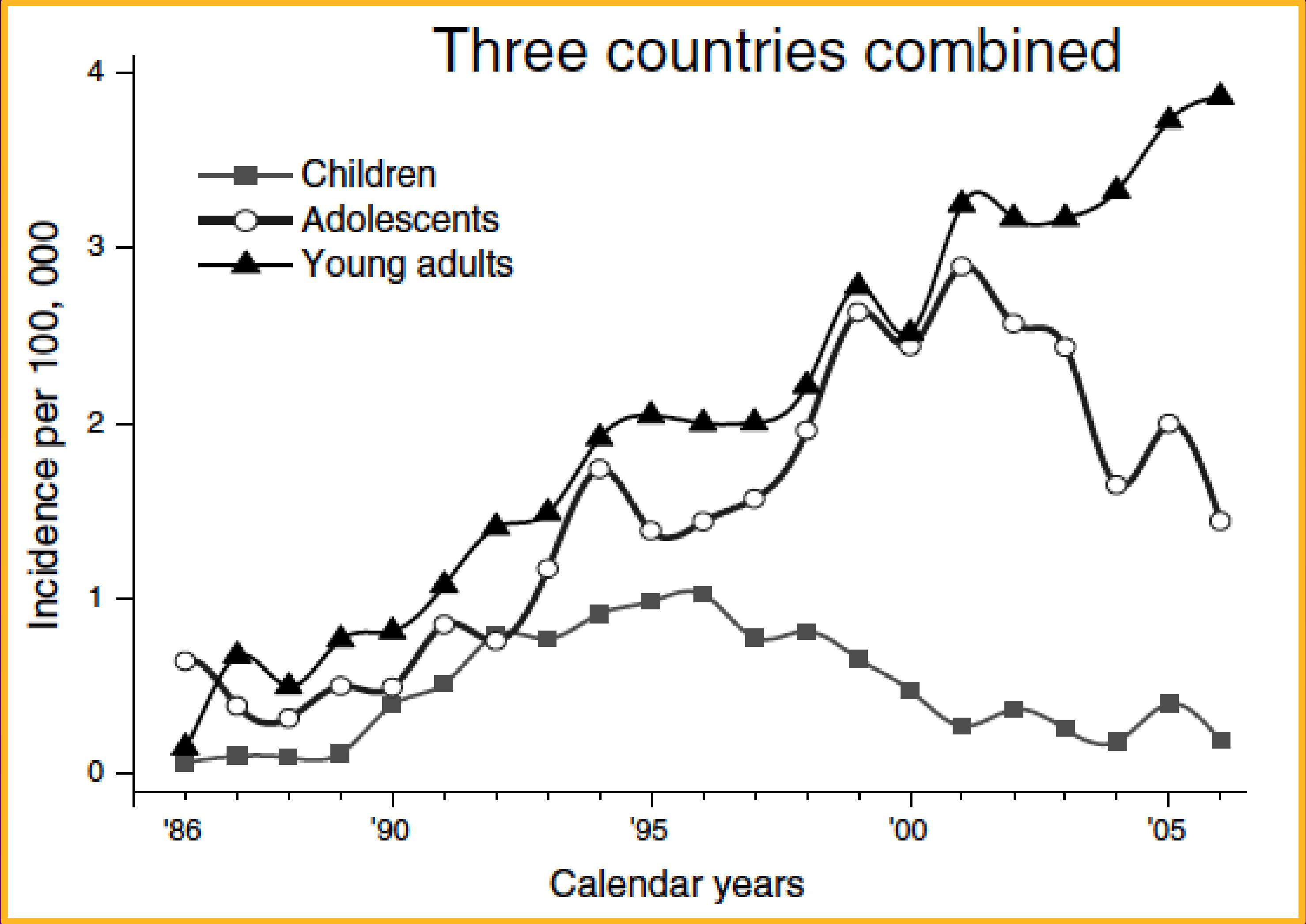
The University of Manchester Centre for Occupational and Environmental Health

Thyroid Cancer



Chornobyl – Thyroid Cancer

(Yamashita, *Health Phys* 2014; **106**: 166-80)



MANCHESTER 1824

The University of Manchester Centre for Occupational and Environmental Health

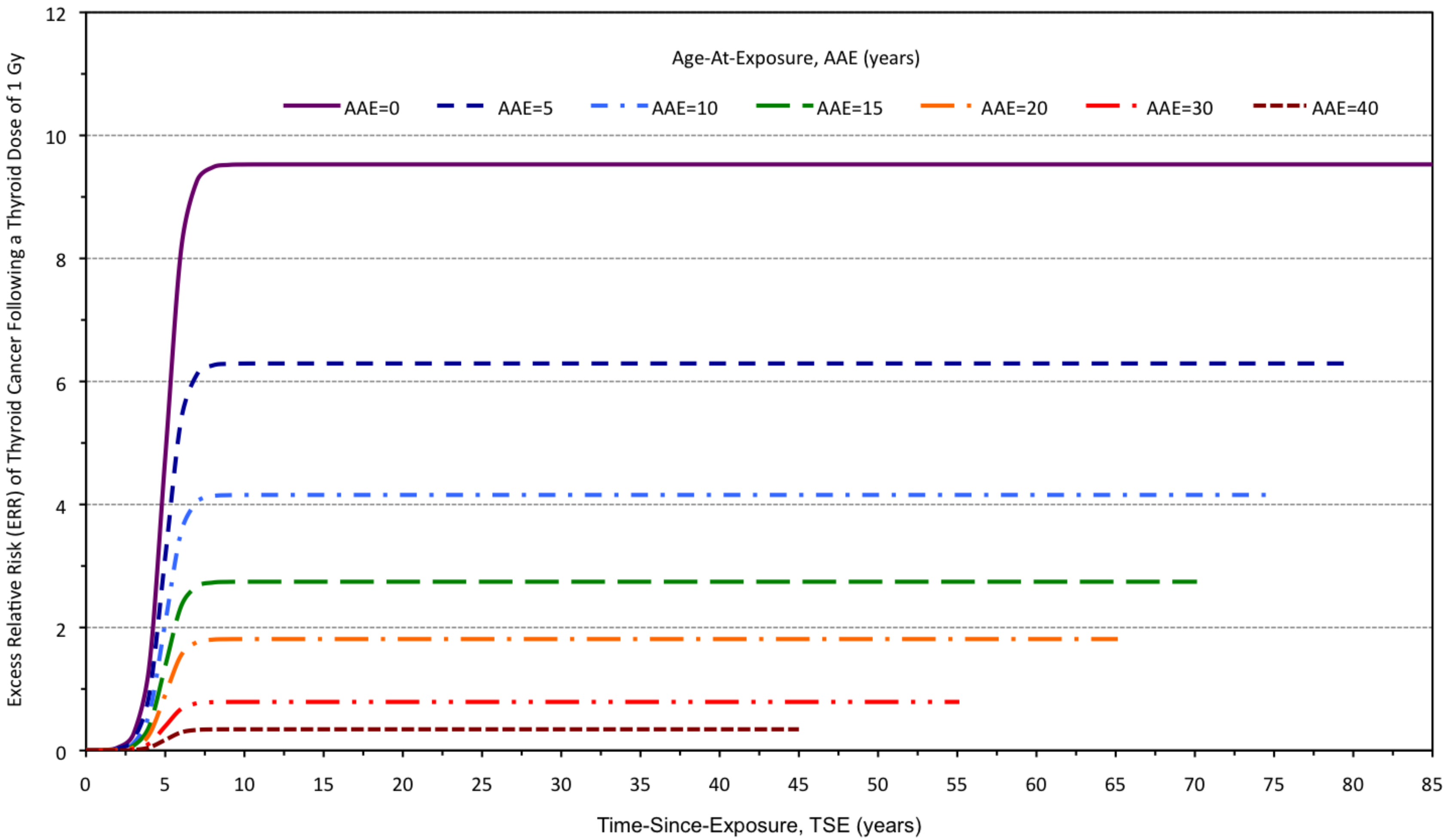
Chornobyl – Thyroid Cancer

(UNSCEAR 2008 Report, Vol. II, Annex D)

- Tens of thousands of children in heavily contaminated areas of the former USSR received high thyroid doses (>1 Gy) as a result of the release of radioiodine (mainly ^{131}I) during the Chornobyl reactor accident.
- >4000 excess thyroid cancers have already occurred with the likelihood of many more to come as the exposed population ages.

BEIR VII/NCI Thyroid Cancer Risk Model

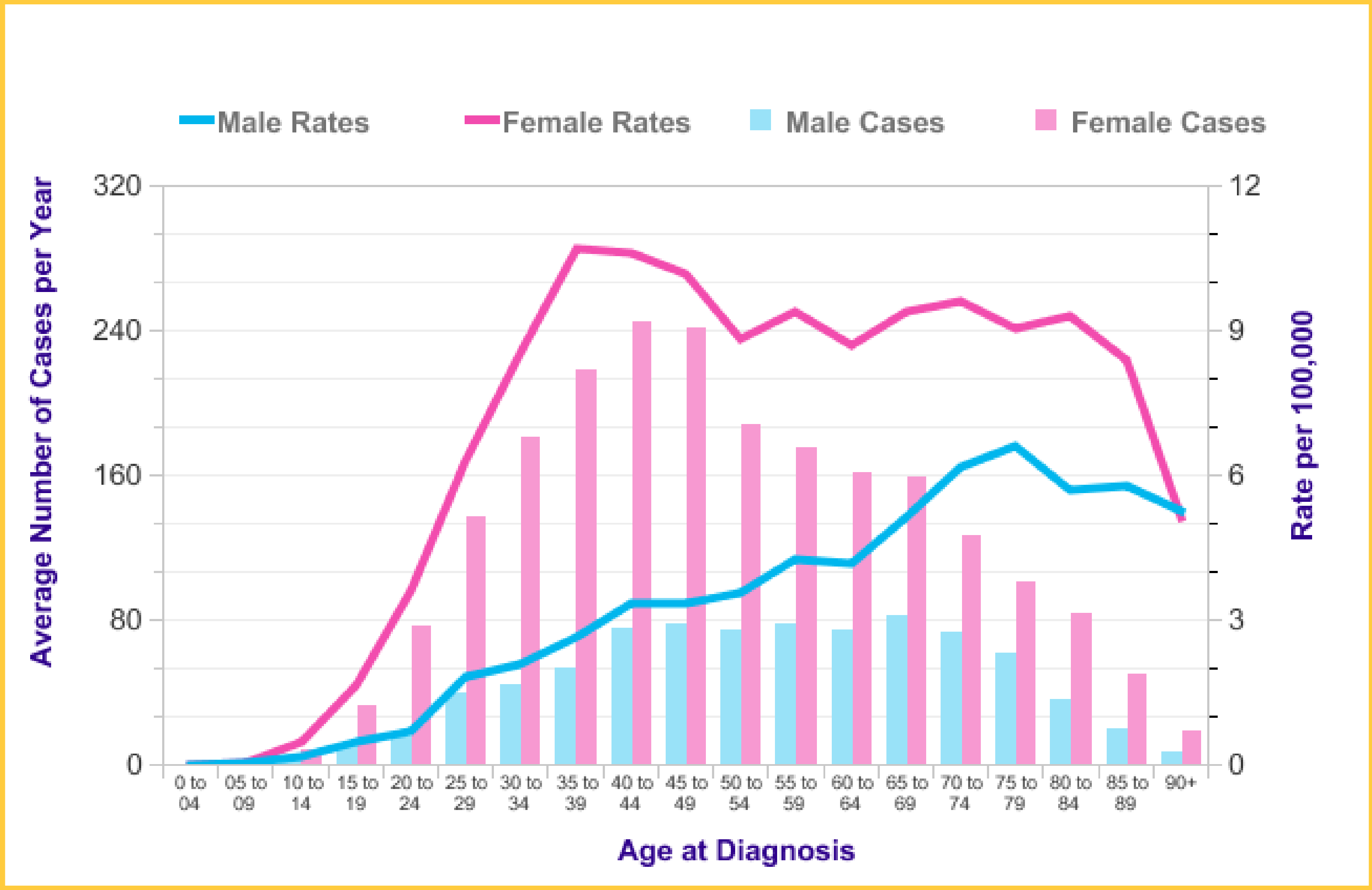
(Berrington de González *et al*., *J Radiol Prot* 2012; **32**: 205-22)



MANCHESTER 1824

The University of Manchester Centre for Occupational and Environmental Health

Thyroid Cancer: Numbers of New Cases and Age-specific Incidence Rates, UK, 2011-13



MANCHESTER 1824

The University of Manchester Centre for Occupational and Environmental Health

Chornobyl – Thyroid Cancer

- The eventual number of excess cases of thyroid cancer will largely depend on how long the excess risk persists and how (and if) the ERR varies with time since exposure.
- A dose-related excess of thyroid cancer is still present among the Japanese atomic bomb survivors 55 years after exposure, although some evidence exists for a decrease in ERR.

Thyroid Cancer

(Ron *et al.*, *Radiat Res* 1995; **141**: 259-277)

- Atomic bomb survivors and therapeutically irradiated patients demonstrate that the thyroid glands of children are very sensitive to radiation-induced cancer.
- Ron *et al.* (1995) conducted a pooled analysis of seven externally irradiated groups. For those exposed before the age of 15 years the ERR coefficient was 7.7 (95% CI: 2.1, 28.7) Gy^{-1}.

Thyroid Cancer

- Case-control and cohort studies in the heavily contaminated areas of the former USSR have been able to estimate dose-response relationships for thyroid cancer.
- Studies of Belarusian and Ukrainian cohorts have been especially informative because thyroid dose <u>measurements</u> were made soon after the accident and there are regular <u>uniform</u> screenings of the study subjects.

Thyroid Cancer
(<15 years of age at exposure)

Exposure	Study	ERR/Gy (95% CI)
External	Pooled Analysis Ron *et al.*, *Radiat Res* 1995; **141**: 259-277	7.7 (2.1, 29)
Chornobyl	Case-control (Belarus & Russia) Cardis *et al.*, *J Natl Cancer Inst* 2005; **97**: 724-32	4.5 (1.2, 7.8)
Chornobyl	Cohort* (Ukraine) Tronko *et al.*, *J Natl Cancer Inst* 2006; **98**: 897-903 * <18 years of age at exposure	5.2 (1.7, 27)
Chornobyl	Cohort* (Belarus) Zablotska *et al.*, *Br J Cancer* 2011; **104**: 181-187 * <18 years of age at exposure	2.2 (0.8, 5.5)
Chornobyl	Cohort* (Ukraine) Brenner *et al.*, *Environ Health Perspect* 2011; **119**: 933-939 * <18 years of age at exposure	1.9 (0.4, 6.3)

Chornobyl – Thyroid Dose Uncertainties

(Likhtarov *et al.*, *Health Phys* 2014; **106**: 370-96)
(Drozdovitch *et al.*, *Radiat Res* 2015; **184**: 203-18)
(Little *et al.*, *Plos ONE* 2014; **9**(1): e85723)
(Little *et al.*, *PLoS ONE* 2015; **10**(10): e0139826)

- Much effort has been expended on estimating thyroid doses, and a new dose dataset has recently been derived.
- Taking account of uncertainties:
- Ukraine

  ERR/Gy = 4.93 (95% CI: 1.67, 19.90)
- Belarus

  ERR/Gy = 1.48 (95% CI: 0.53, 3.87)

Chornobyl – Thyroid Cancer

- Risk estimates from studies of thyroid cancer following Chornobyl contamination are broadly compatible with predictions from external irradiation studies.
- Evidence exists for a modifying effect of iodine deficiency at the time of exposure (increases risk), and of stable iodine supplementation after exposure (decreases risk).
- Other uncertainties: effects of short-lived isotopes of iodine (e.g. ^{133}I), screening for thyroid disease, etc..

Signature of Radiation Exposure?

(Heβ *et al. PNAS* 2011; **108**: 9595-9600)

- Study of genomic alterations in radioiodine exposed and unexposed groups of young papilliary thyroid cancer patients.
- Found raised gain of 7q11.22-11.23 and over-expression of CLIP2 gene in exposed group.
- Radiation-specific molecular markers?
- Confirmation of the findings is required.

Other Thyroid Diseases

- Thyroid benign nodules and cysts show a dose-related excess among the Japanese atomic bomb survivors 55 years after exposure.
- Evidence of a dose-related excess of benign thyroid tumours in the Ukrainian cohort.
- It seems likely that a substantial excess of cases of thyroid diseases other than cancer will occur as a result of exposure to radioiodine from Chernobyl.

Fukushima Dai-ichi
12 March 2011 – Unit 1

Radionuclides Released during Fukushima Accident

Radionuclide	Releases to Atmosphere during March 2011 (PBq)*	In Liquid Released into Pacific Ocean during 26 March to 30 September 2011 (PBq)
Noble Gases (mainly Xe-133)	500	-
I-131	500	11
Cs-134	10	3.5
Cs-137	10	3.6

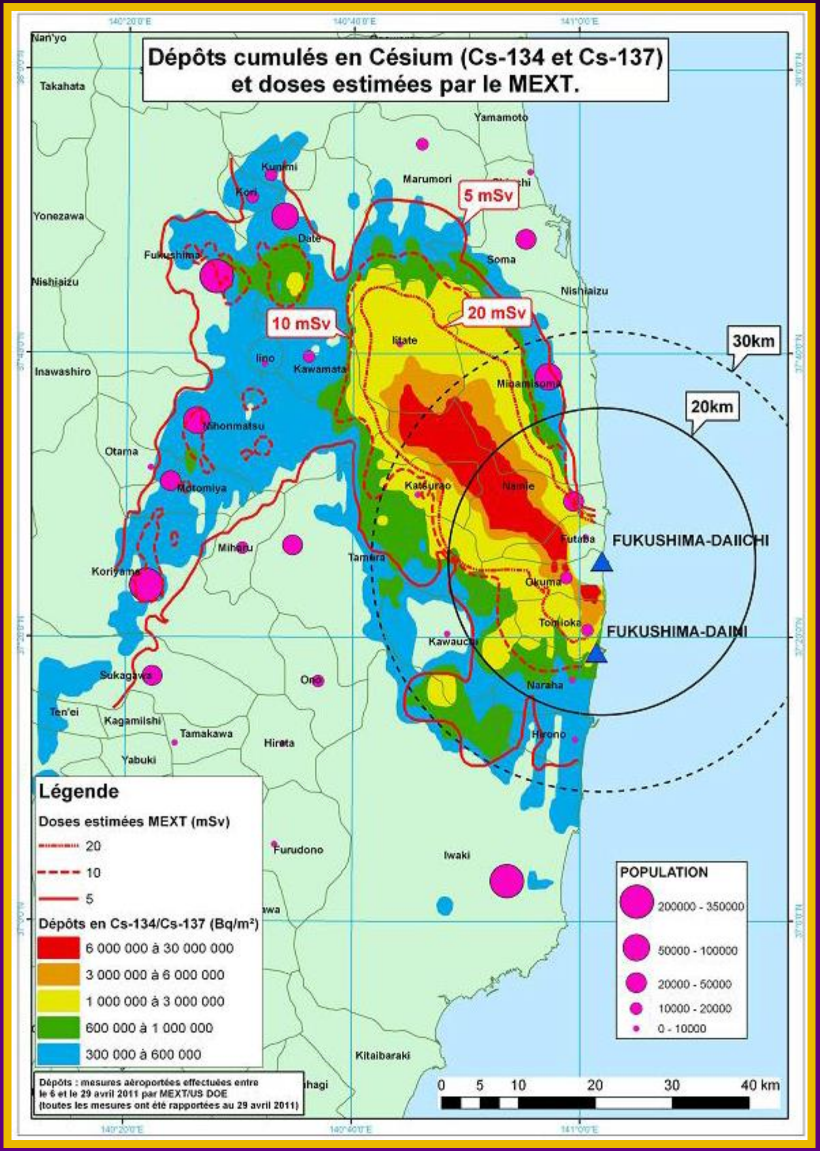
* 20% from Unit 1, 40% from Unit 2 (peak on 15 March), and 40% from Unit 3 (peak on 16 March).

Radionuclide half-lives ($t_{½}$): ^{133}Xe, ~5 days; ^{131}I, ~8 days; ^{134}Cs, ~2 years; ^{137}Cs, ~30 years.

MANCHESTER 1824

The University of Manchester Centre for Occupational and Environmental Health

Fukushima Contamination



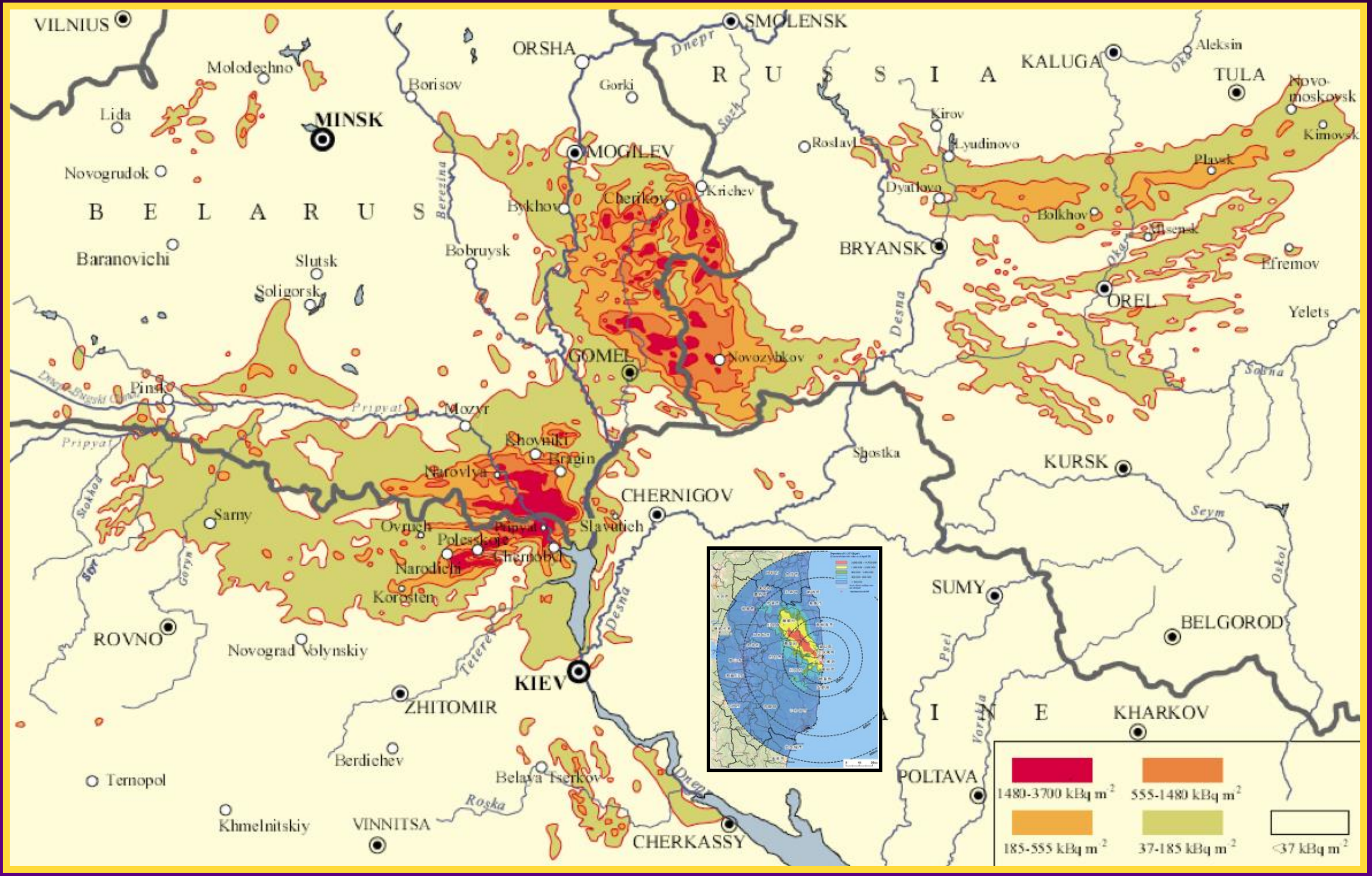
MANCHESTER 1824

The University of Manchester Centre for Occupational and Environmental Health

Comparison of ^{137}Cs Contamination around Chornobyl with that around Fukushima (inset)

The two areas shown are approximately to the same scale.

The orange/red areas around Chornobyl correspond approximately to the green/yellow/red areas around Fukushima in level of contamination.



MANCHESTER
1824

The University of Manchester
Centre for Occupational and
Environmental Health

WHO First Year Dose Assessment

- Committed effective dose
  - 10-50 mSv in most affected areas
  - 1-10 mSv in rest of Fukushima Prefecture
  - 0.1-1 mSv in rest of Japan
- Committed thyroid dose
  - 10-100 mSv in most affected areas
    - 100-200 mSv for infant 1 year of age
  - 1-10 mSv in rest of Japan

Risks to General Population

(WHO Expert Group, 2013)

- For an *infant* in the *most affected location*, the ***ERR*** of leukaemia over a lifetime is 7%; of breast cancer, 4%; of thyroid cancer, 70%; and of all solid cancers, 4%.
- The ***EAR*** of leukaemia over a lifetime (the **LAR**) is <0.05%; of breast cancer, <0.5%; of thyroid cancer, ~0.5%; and of all solid cancers, ~1%.
- The risks are less than this for other ages at exposure and other locations.

Thyroid Cancer in Fukushima

(Tsuda *et al. Epidemiol* 2016; **27**: 316-22)
(Wakeford et al., *Epidemiol* 2016; **27**: e20-e21)
(Wakeford, *J Radiol Prot* 2016; **36**: E1-E5)

- ~300 000 thyroid ultrasound examinations of Fukushima Prefecture residents ≤18 years
- Number of thyroid cancers detected by screening programme was 110, ~30 times more than might be expected from Japanese incidence rates.
- However, cannot compare prevalence found by an intensive screening programme with incidence in the absence of such a programme.

Thyroid Screening

(Jacob *et al*., *Radiat Environ Biophys* 2014; **53**:391-401)

- "Based on the results presented here, it is expected that the ultrasonography survey of residents of Fukushima Prefecture will increase thyroid cancer incidence compared with thyroid cancer incidence in 2007 in Japan drastically."
- 105 (95% CI: 30, 258) background cases expected from first screening in Fukushima.

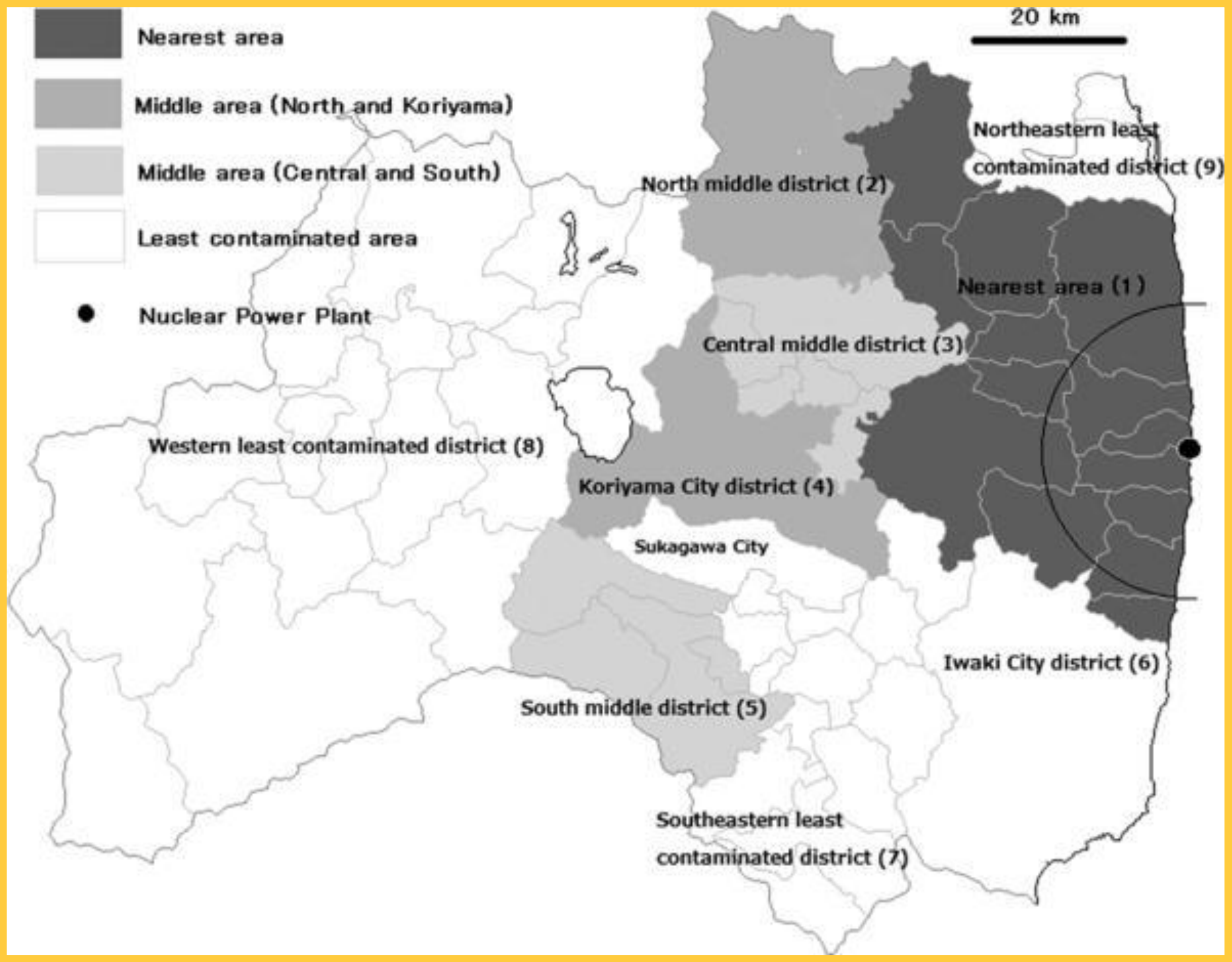
Thyroid Cancer in Fukushima

(Tsuda *et al. Epidemiol* 2016; **27**: 316-22)
(Wakeford et al., *Epidemiol* 2016; **27**: e20-e21)
(Wakeford, *J Radiol Prot* 2016; **36**: E1-E5)

- Cases found at a uniform rate within 3 years of exposure.
- Thyroid doses insufficiently high.
- No significant variation of prevalence across the prefecture, despite heterogeneous levels of contamination.
- The detected cases are occurring in those exposed as teenagers, <u>not</u> as young children.

Fukushima Prefecture

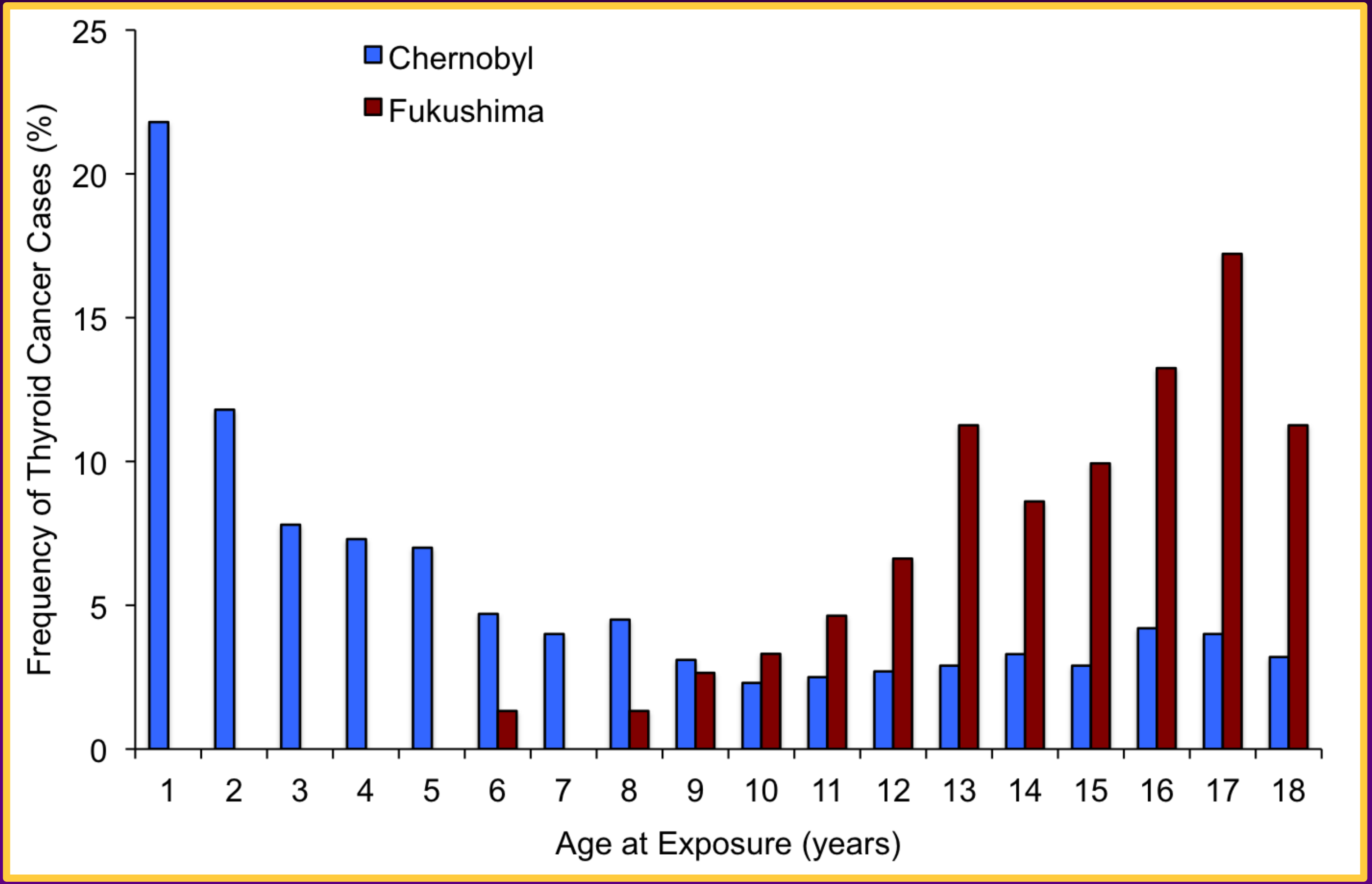
(Tsuda *et al. Epidemiol* 2016; **27**: 316-22)



MANCHESTER 1824

The University of Manchester Centre for Occupational and Environmental Health

Thyroid Cancer
Chornobyl *vs* Fukushima

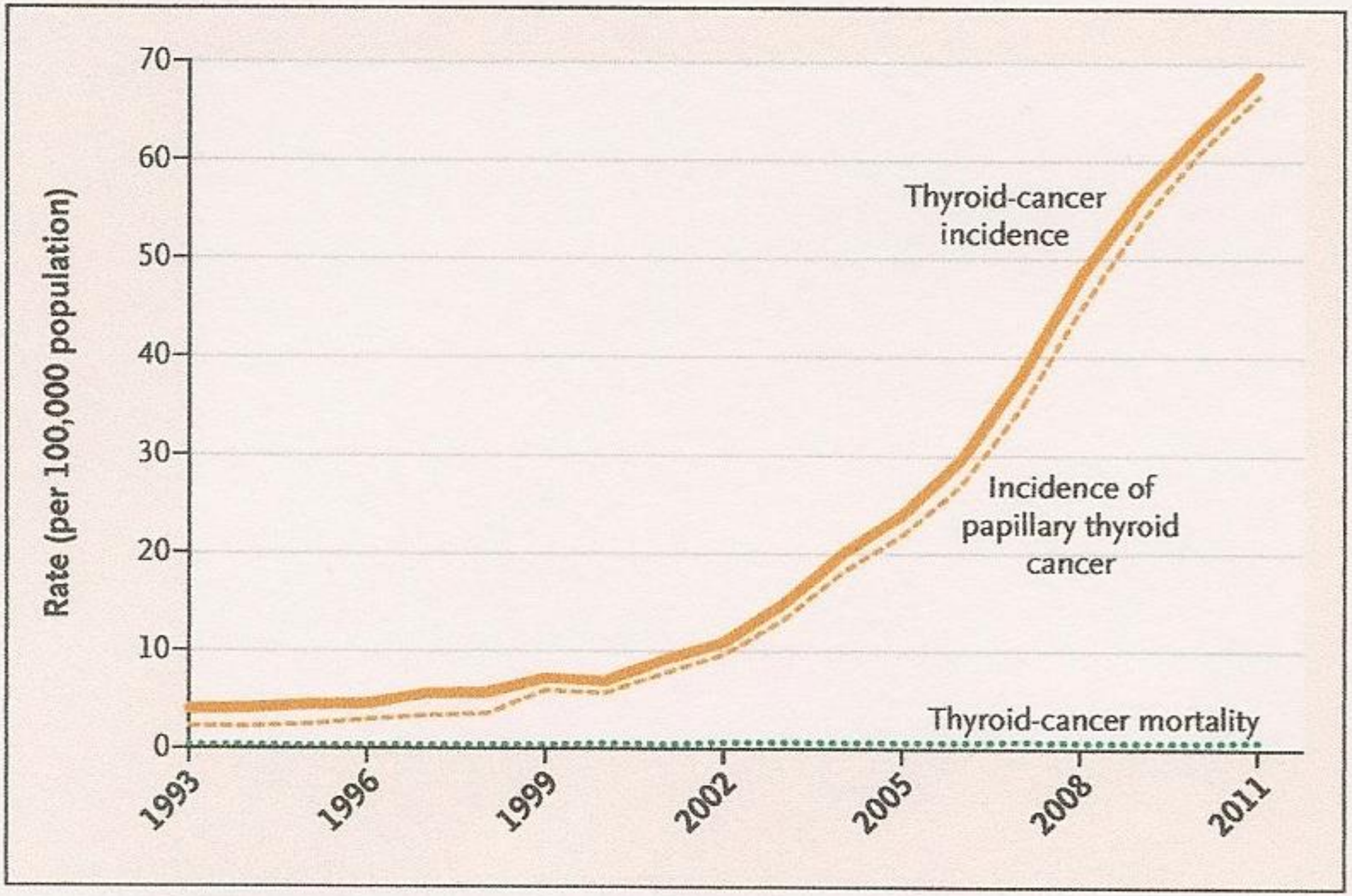


MANCHESTER 1824

The University of Manchester Centre for Occupational and Environmental Health

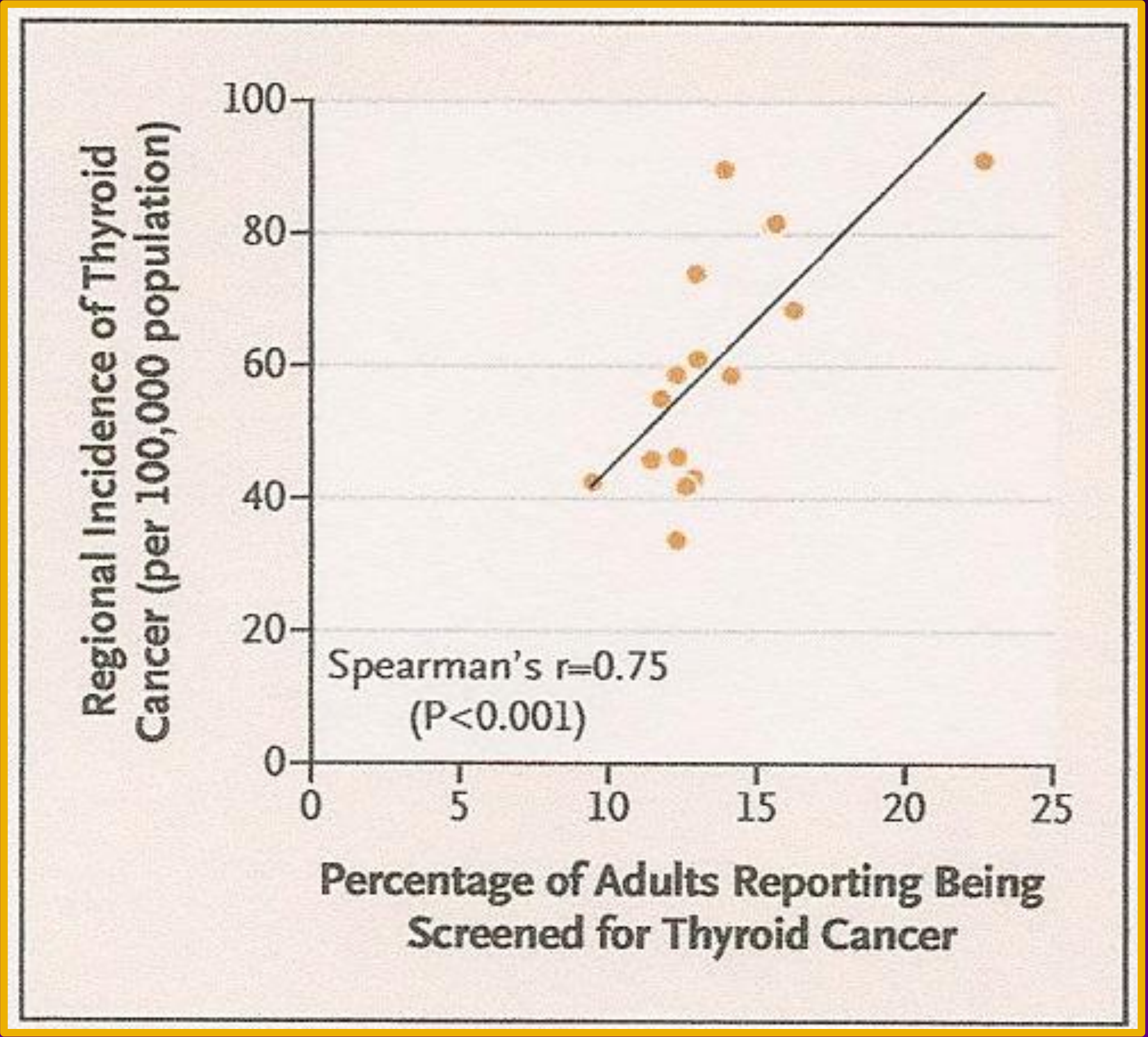
Thyroid Cancer, South Korea

(Ahn *et al.*, *New Eng J Med* 2014; **371:** 1765-7)



Thyroid Cancer, South Korea

(Ahn *et al.*, *New Eng J Med* 2014; **371:** 1765-7)



MANCHESTER 1824

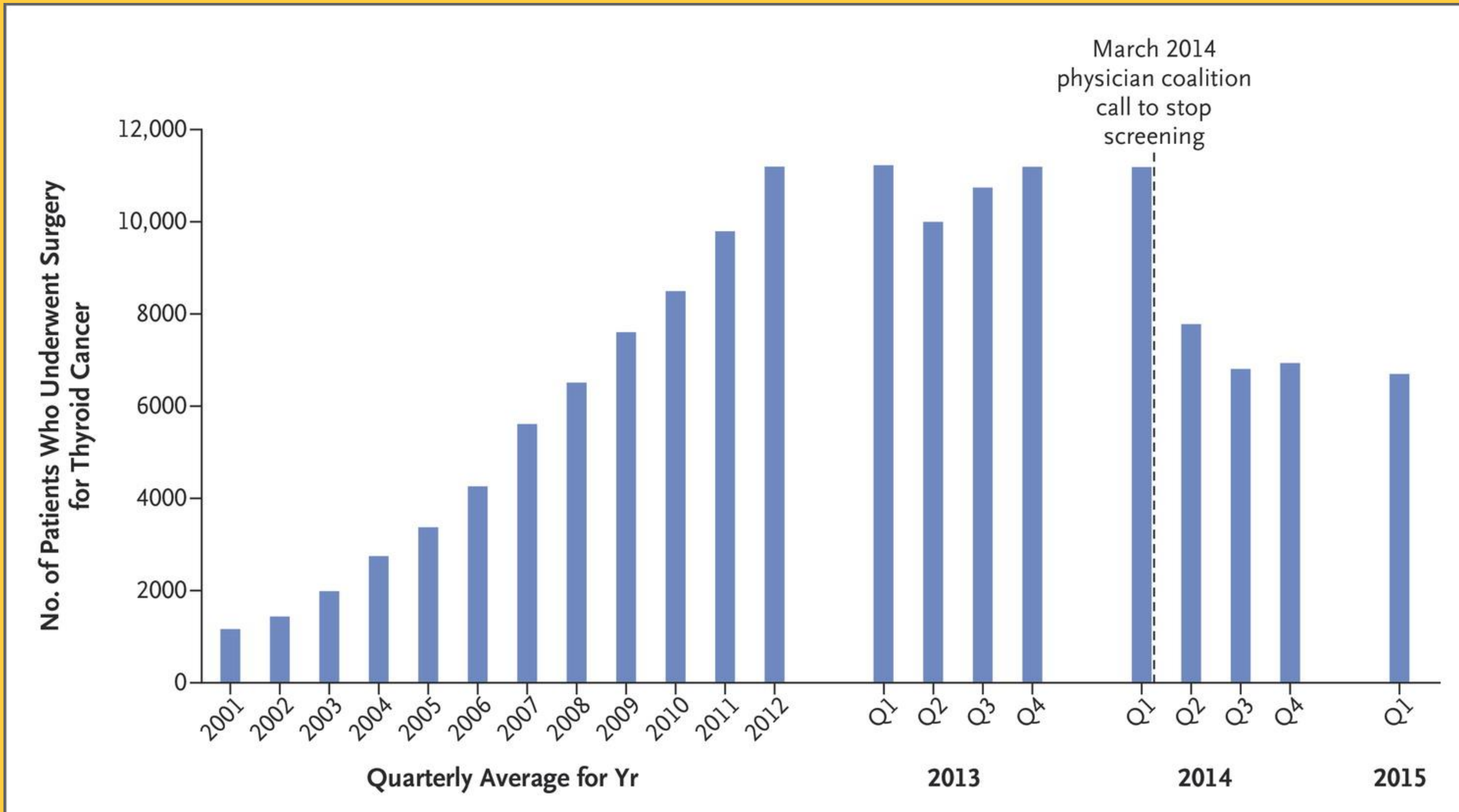
The University of Manchester Centre for Occupational and Environmental Health

Thyroid Screening

"Screening may be of value, but only if groups with a sufficiently high prevalence of thyroid cancer can be identified to offset the adverse effects of unnecessary treatment due to false positive results."
(Bucci *et al.*, *J Clin Endocrinol Metab* 2001; 86: 3711–6)

Thyroid Cancer, South Korea

(Ahn & Welch, *N Engl J Med* 2015; **373**: 389-90)



Hanford, Washington State, USA

MANCHESTER 1824

The University of Manchester Centre for Occupational and Environmental Health

I-131 and Hanford

(Davis *et al.*, *JAMA* 2004; **292**: 2600-13)

- 27 PBq I-131 released to atmosphere from Hanford during 1944-57.
- Davis *et al.* (2004) conducted a historical cohort study of nearly 3500 people born near Hanford during 1940-46, with individual dose estimates; mean thyroid dose 174 mGy.
- Non-significant ERR coefficient of 0.7 Gy^{-1}.

Conclusions

- Clear excess of thyroid cancer among those exposed as children in heavily contaminated areas of the former USSR – many 1000s of excess cases can be expected, but just how many depends on future levels of risk.
- Intensive thyroid screening in Fukushima has led to an increase in the detection of background cases of thyroid cancer– a radiation-related excess <u>may</u> be found, but there is no reliable evidence for this at present.

FIN