Results of Thyroid Ultrasound Examination in the Fukushima Health Management Survey

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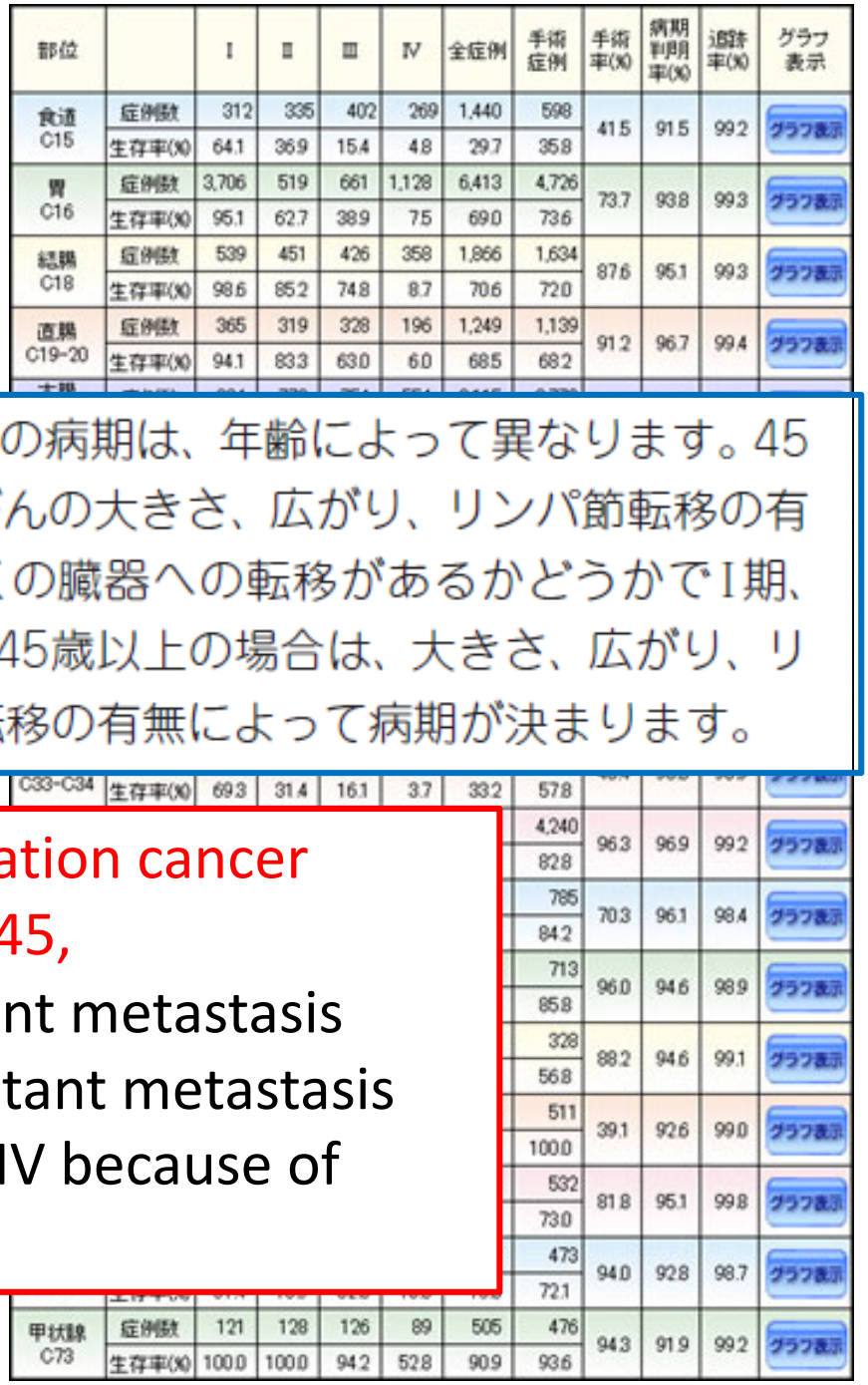
Background of necessity of thyroid ultrasound examination survey in Fukushima

- **The Japanese general public became particularly concerned with the possibility of an increased risk of childhood thyroid cancer similar to that observed following the Chernobyl nuclear accident.**
- **Although radiation exposure level in Fukushima is deemed to be much lower than that in Chernobyl, the survey was required not only for scientific perspective but also for social demand.**
- **Since thyroid ultrasound examination make a high possibility of overdiagnosis, a standard protocol is desired to suppress harm of overdiagnosis even though no adequate screening guideline.**

10-year relative cancer survival rate

(National Cancer Research Center HP)



部位		I	II	III	IV	全症例	手術症例	手術率(%)	病期判明率(%)	追跡率(%)	グラフ表示
食道 C15	症例数	312	335	402	269	1,440	598	41.5	91.5	99.2	グラフ表示
	生存率(%)	64.1	36.9	15.4	4.8	29.7	35.8				
胃 C16	症例数	3,706	519	661	1,128	6,413	4,726	73.7	93.8	99.3	グラフ表示
	生存率(%)	95.1	62.7	38.9	7.5	69.0	73.6				
結腸 C18	症例数	539	451	426	358	1,866	1,634	87.6	95.1	99.3	グラフ表示
	生存率(%)	98.6	85.2	74.8	8.7	70.6	72.0				
直腸 C19-20	症例数	365	319	328	196	1,249	1,139	91.2	96.7	99.4	グラフ表示
	生存率(%)	94.1	83.3	63.0	6.0	68.5	68.2				
C33-C34	生存率(%)	69.3	31.4	16.1	3.7	33.2	57.8				
							4,240	96.3	96.9	99.2	グラフ表示
							82.8				
							78.5	70.3	96.1	98.4	グラフ表示
							84.2				
							71.3	96.0	94.6	98.9	グラフ表示
							85.8				
							32.8	88.2	94.6	99.1	グラフ表示
							56.8				
							51.1	39.1	92.6	99.0	グラフ表示
							100.0				
							53.2	81.8	95.1	99.8	グラフ表示
							73.0				
							47.3	94.0	92.8	98.7	グラフ表示
							72.1				
甲状腺 C73	症例数	121	128	126	89	505	476	94.3	91.9	99.2	グラフ表示
	生存率(%)	100.0	100.0	94.2	52.8	90.9	93.6				

乳頭がん、濾胞がんの病期は、年齢によって異なります。45歳未満の場合には、がんの大きさ、広がり、リンパ節転移の有無には関係なく、遠くの臓器への転移があるかどうかでI期、II期に分類されます。45歳以上の場合は、大きさ、広がり、リンパ節や別の臓器へ転移の有無によって病期が決まります。

Thyroid differentiation cancer
Under the age of 45,
Stage Ⅰ No distant metastasis
Stage Ⅱ With distant metastasis
No stage III stage IV because of good prognosis

Gastric cancer 69%
- Stage Ⅰ 95%
- Stage Ⅱ 63%
- Stage Ⅲ 39%
- Stage Ⅳ 8%

Colon Cancer 70%
- Stage Ⅰ 97%
- Stage Ⅱ 84%
- Stage Ⅲ 70%
- Stage Ⅳ 8%

Lung Cancer 33%
- Stage Ⅰ 69%

Pancreatic Ca 5%
- Stage Ⅰ 30%

Liver Ca 15%
- Stage Ⅰ 29%

Thyroid Ca 91%
- Stage Ⅰ 100%
- Stage Ⅱ 100%
- Stage Ⅲ 94%
- Stage Ⅳ 53%

Prevalence of Latent Thyroid Carcinoma in Autopsy Cases

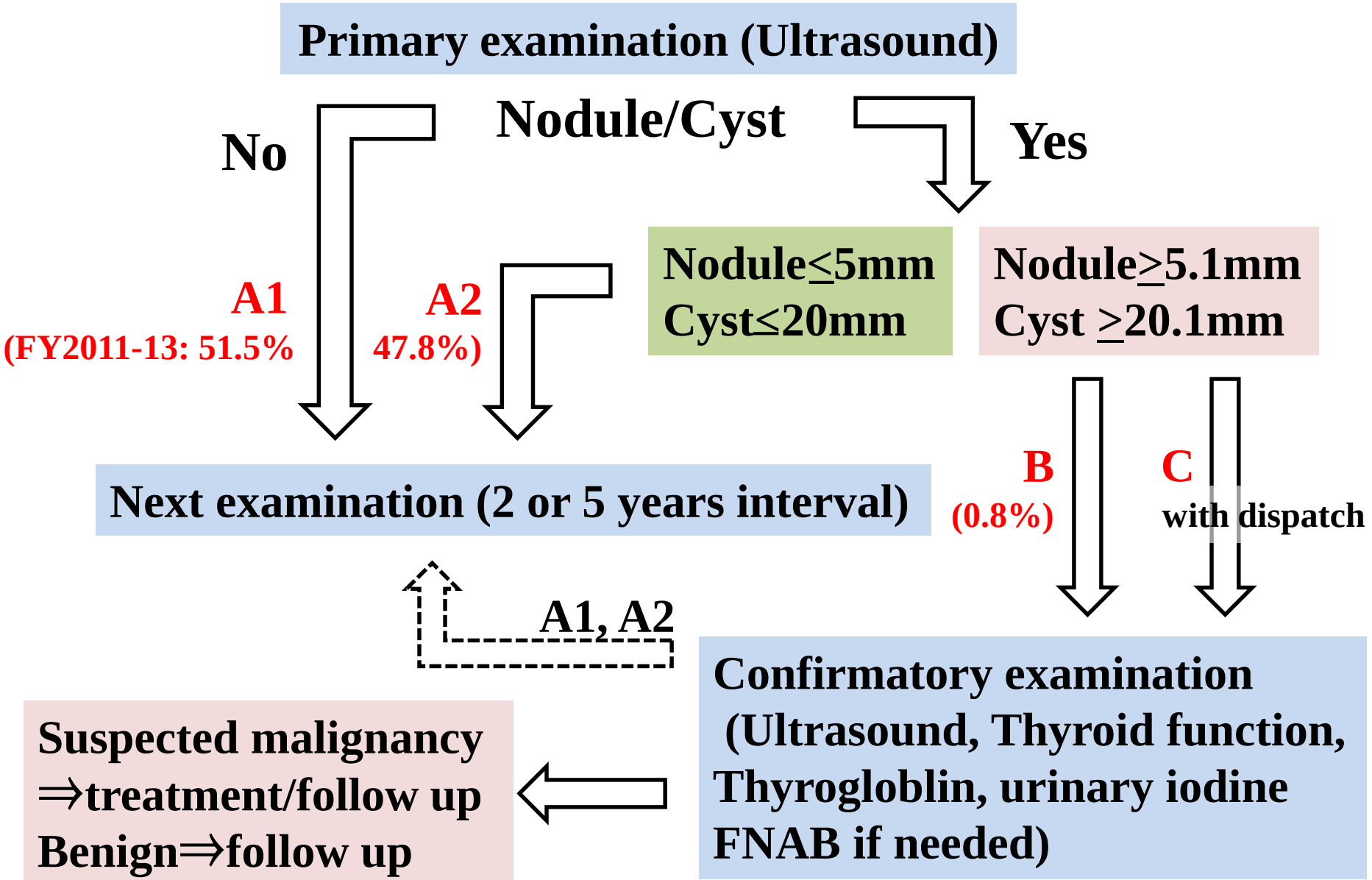
Study and Year of Publication	Location	Median Year When Autopsies Were Performed	Study Population	Median Age at Death (years)	Female (%)	Whole/Partial Examination of the Gland and No. of Slices Examined per Gland	No. of Autopsies Examined	No. of iDTCs	Prevalence of iDTC (%)
Lang et al,[30] 1988	Hannover, Germany	1987	Autopsies in patients > 15 years of age with no clinically manifest carcinoma of the thyroid	61	44	Partial, NR	1,020	62	6.08
Martinez-Tello et al,[31] 1993 (1)	Madrid, Spain	1993	Autopsies performed at the Hospital Central de la Cruz Roja	68	45	Partial, 2*	625	31	4.96
Martinez-Tello et al,[31] 1993 (2)	Madrid, Barcelona, and Zaragoza, Spain	1993	Consecutive autopsies with no thyroid-related diseases	58	34	Whole, 35	100	22	22.00
Mitselou et al,[32] 2002	Epirus, Greece	1999	Forensic cases without any clinical thyroid disease history	56	26	Partial, 4-6*	160	12	7.50
Mortensen et al,[33] 1955	Minnesota, United States	1952	Hospital routine consecutive postmortem examination; excluded patients with clinical evidence of thyroid disorder	> 60	32	Partial, 1*	821	13	1.58
Neuhold et al,[34] 2001	Vienna, Austria	2001	Consecutive hospital autopsies with no clinical manifestation of thyroid carcinoma	66	52	Whole, NR	118	10	8.47
Nielsen and Zetterlund,[35] 1985	Jonkoping, Sweden	1981	Consecutive hospital autopsies without prior surgery	72	42	Partial, 2*	498	27	5.42
Ottino et al,[36] 1989	La Plata, Argentina	1986	Consecutive hospital autopsies	58	41	Whole, 24*	100	11	11.00
Pingitore,[37] 1982	Tuscany and Lig Italy						111	4	3.60
Sampson et al,[38] 1974	Minnesota, Unit States		residents				157	8	5.10
Seta and Takahashi,[39] 1976	Iwate, Japan	1976	Unselected autopsies	40	52	Whole, 120-180	379	58	15.30
Siegal and Modan,[40] 1981	Tel-Hashomer and Kfar Saba, Israel	1977	Consecutive hospital autopsies in adults	68	46	Partial, 6*	260	17	6.54
Silverberg and Vidone,[41] 1966	Connecticut, United States	1965	Unselected hospital autopsies in patients > 20 year of age	64	39	Partial, 5-6*	300	8	2.67
Sobrinho-Simoes et al,[42] 1979	Porto, Portugal	1975	Consecutive hospital autopsies in which entire thyroid gland was available	53	44	Partial, 2*	600	40	6.67
Solares et al,[43] 2005	Guatemala City, Guatemala	2000	Consecutive autopsies with a cause of death not related to thyroid disease	41	23	Partial, 1*	150	3	2.00
Tanriover et al,[44] 2011	Marmara, Turkey	2007	Forensic autopsies in people with no history of thyroid disease	45	14	Partial, 2*	108	4	3.70
Thorvaldsson et al,[45] 1992	Reykjavik, Iceland	1985	Consecutive forensic autopsies in people without history of thyroid surgery or radiation treatment	52	20	Whole, 19	199	13	6.53
Yamamoto et al,[47] 1990	Tokushima, Japan	1984	Hospital consecutive autopsies	61	39	Partial, 2*	408	46	11.27
Yatani et al,[48] 1981 (1)	Mie, Japan	1981	Unselected autopsies; routine autopsy examination	50	40	Partial, NR	1,102	27	2.45
Yatani et al,[48] 1981 (2)	Mie, Japan	1981	Unselected autopsies; exhaustive autopsy examination	50	44	Whole, NR	68	18	26.47

Whole examination average: 11.2%

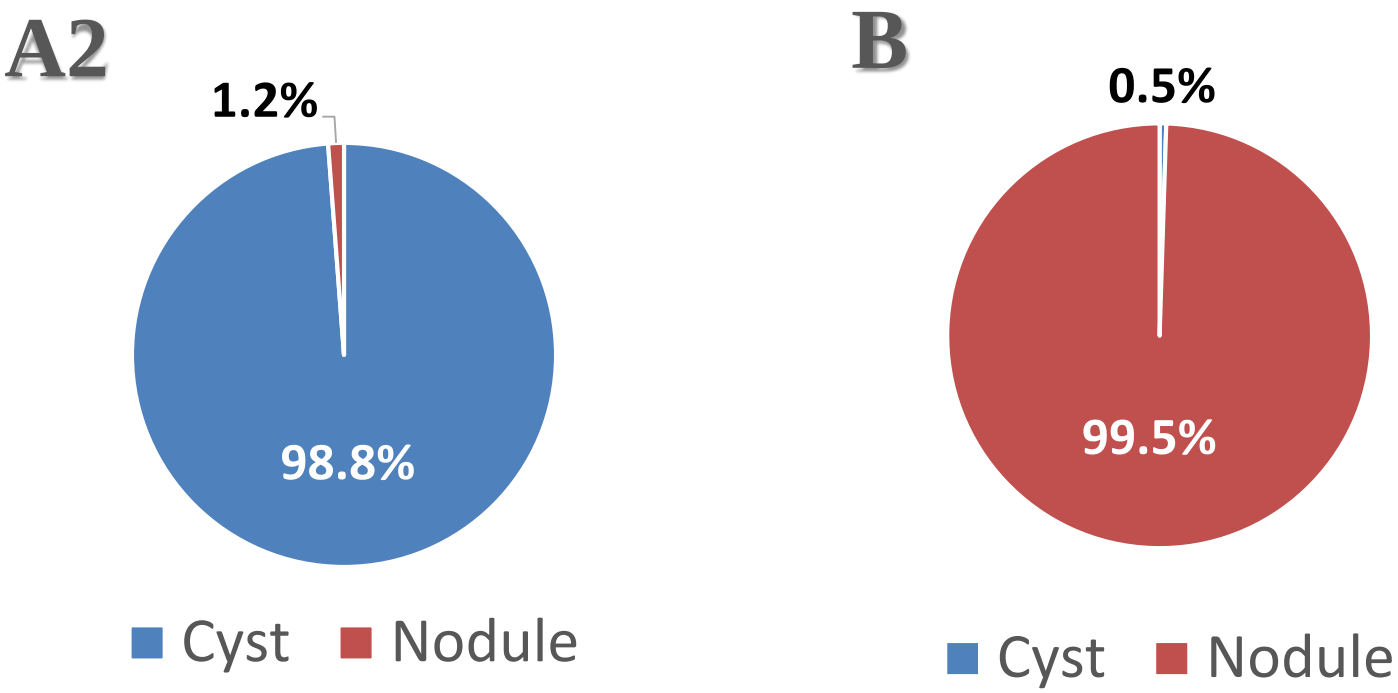
Abbreviations: iDTC, incidental differentiated thyroid cancer; NR, not reported.
*Number of slices examined when no grossly macroscopic lesions were visible; additional slices were examined when macroscopic lesions were present.

Flow Chart of Thyroid Ultrasound Examination

(**Endcr J** 2016, 63: 315-21)



Percentage of Cyst and Nodule in two category

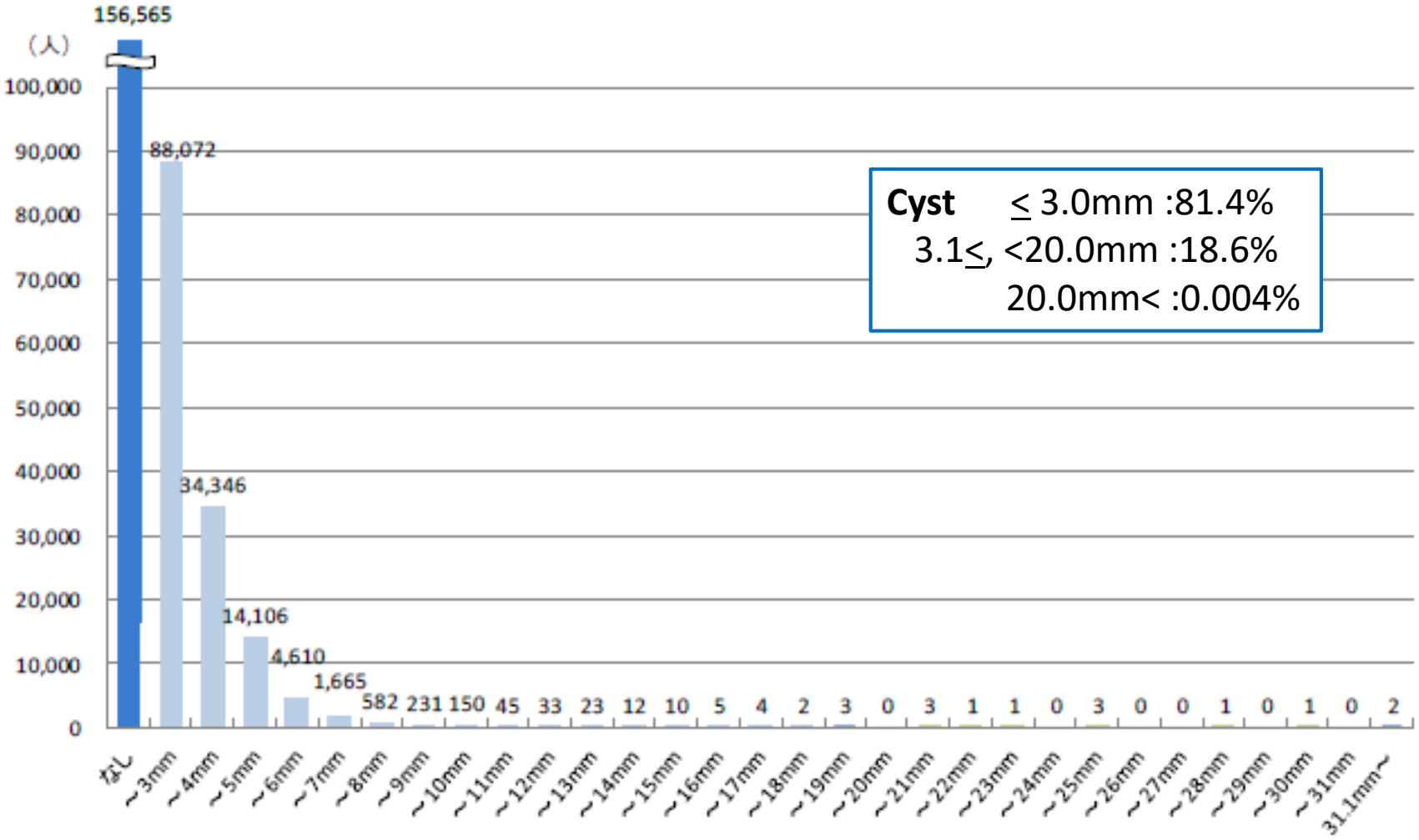


98.8% of A2 is Cyst, in contrast 99.5% of B is Nodule.

（http://fukushima-mimamori.jp/ March 31, 2015）

Size distribution of thyroid cysts detected by US among 300,476 children (FY2011-13, PBS)

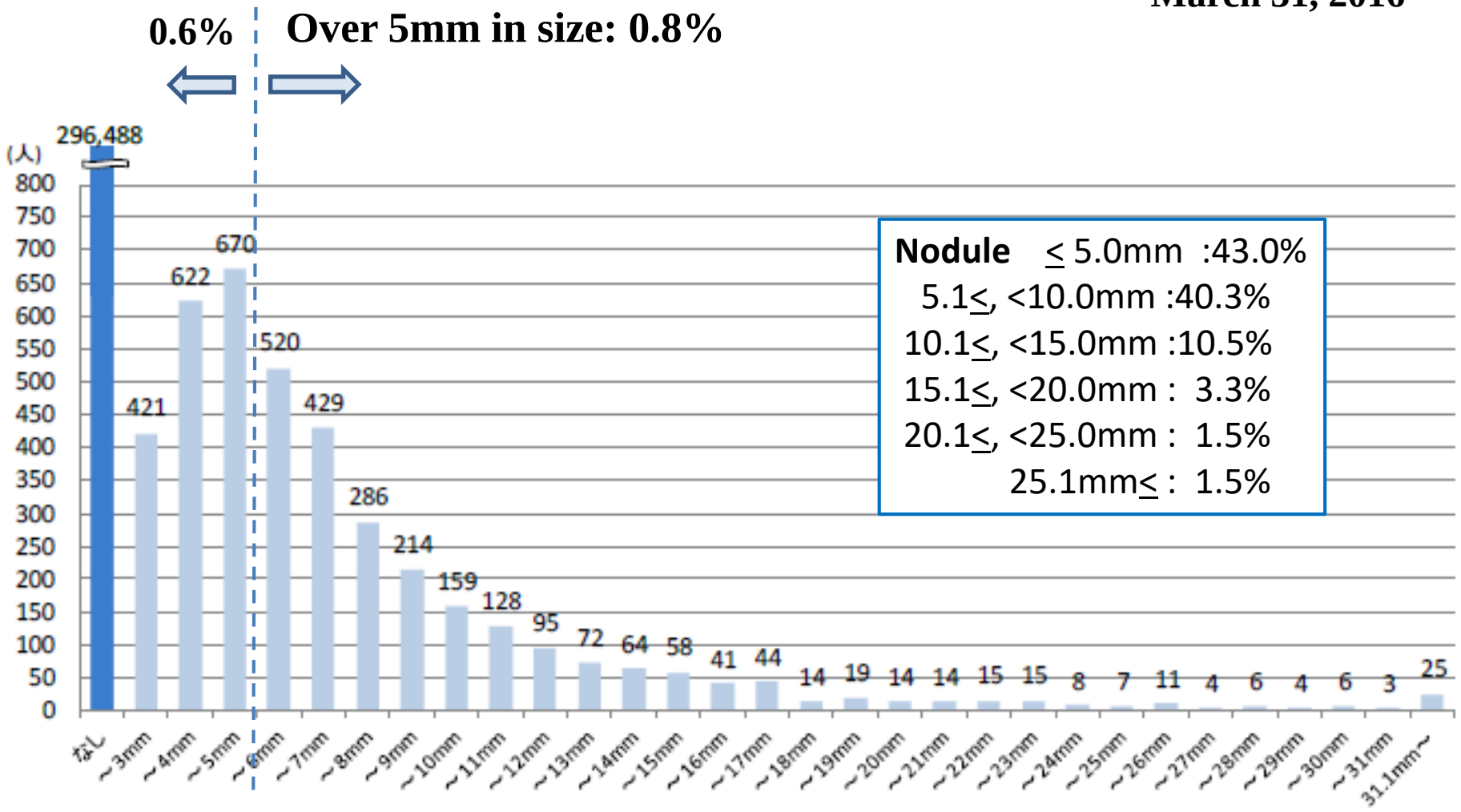
March 31, 2016



(http://fukushima-mimamori.jp/)

Size distribution of thyroid nodules detected by US among 300,476 children (FY2011-2013, PBS)

March 31, 2016



（http://fukushima-mimamori.jp/）

Malignant or suspicious cases detected by US-FNAB

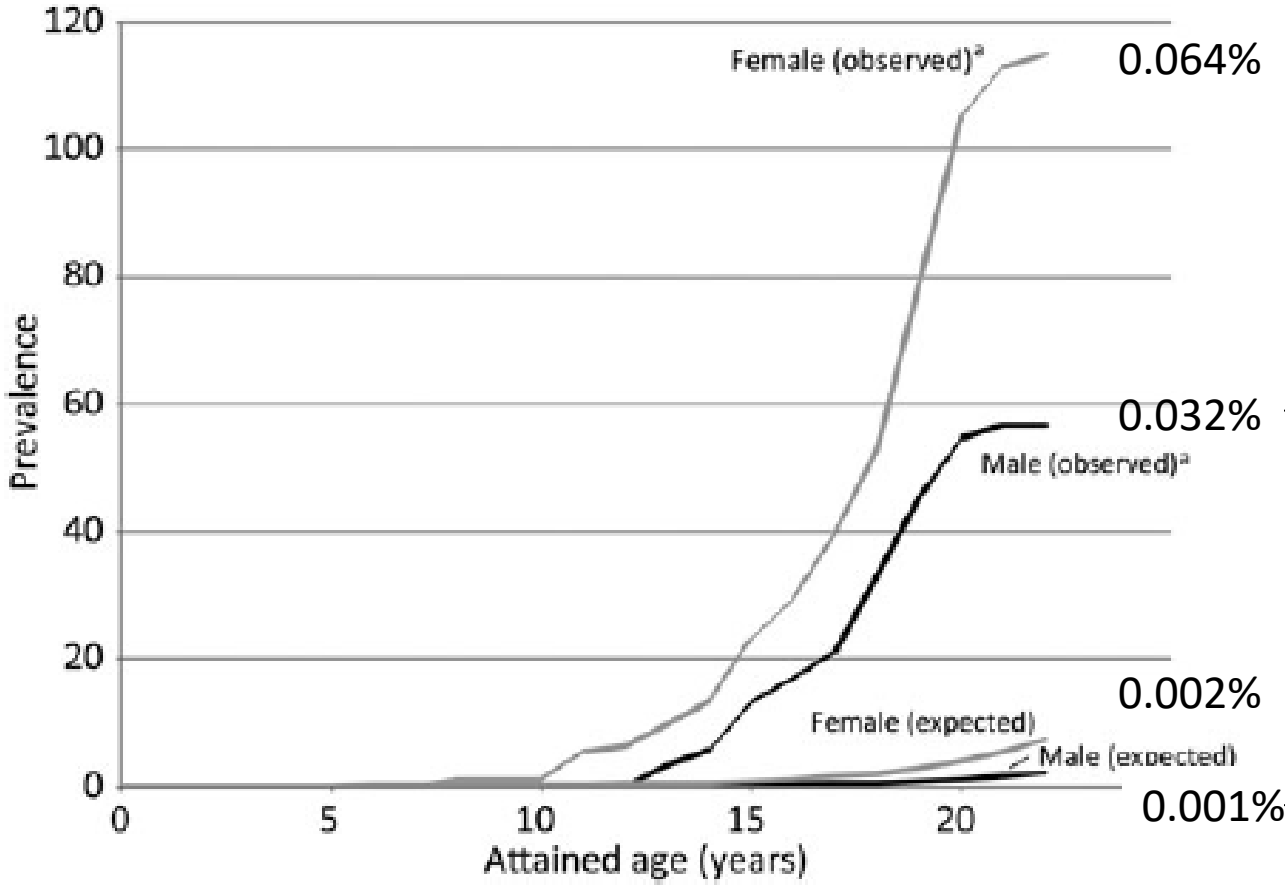
Comparison preliminary baseline (PBLS) with first full-scale survey (FFSS)

	PBLS (FY2011-13)	FFSS (FY2014-15)
Number of cases	116	69
Gender (Male : Female)	39:77	31:37
Mean age (±SD)	17.3 (±2.7) y/o	16.9 (±3.3) y/o
Age at the time of disaster	6-18	5-18
Mean tumor size (±SD)	13.9 (±7.8) mm	11.0 (±5.6) mm
(min-max)	5.1-45.0 mm	5.3-35.6 mm
Number of surgical cases	102	44
Pathological diagnosis		
benign nodule	1	0
papillary thyroid carcinoma	100	43
poorly differentiated TC	1	0
others	0	1

（http://fukushima-mimamori.jp/ Feb 20, 2017）

Quantification of the increase in thyroid cancer prevalence in Fukushima after the nuclear disaster in 2011—a potential overdiagnosis?

Katanoda K et al.
Jpn J Clin Oncol 46: 284-86, 2016



0.064%
0.032%
0.002%
0.001%

O/E ratio (Observed/ Expected ratio)

26.6

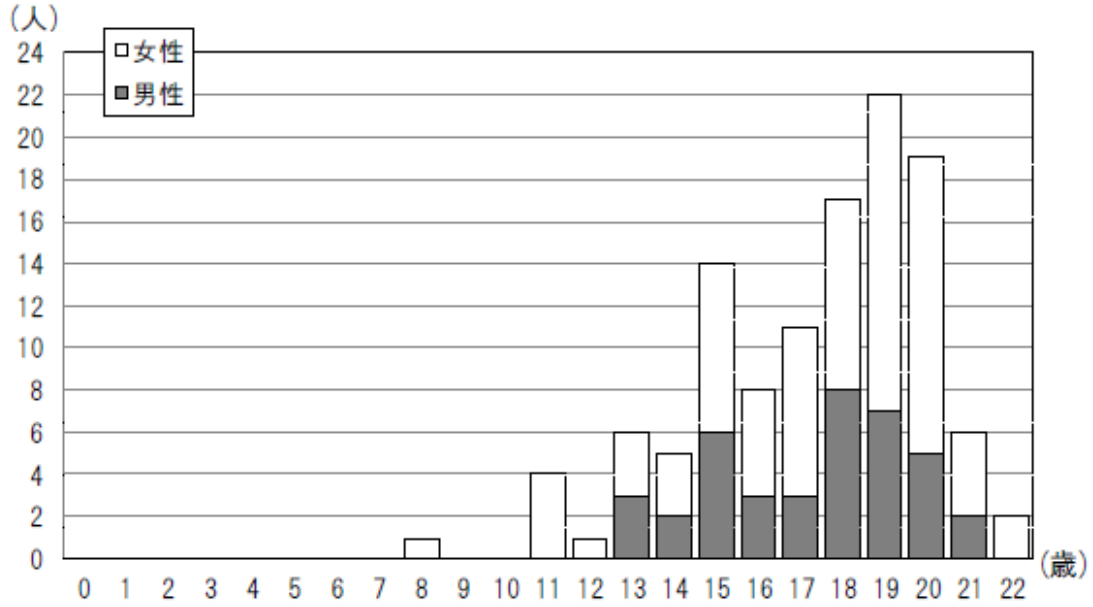
46.1

Total O/E ratio

30.8

Figure 1. Age-specific prevalence of thyroid cancer in Fukushima Prefecture, expected in 2010 and observed as of the end of April 2015. [a]Confirmed by aspiration biopsy (including suspected malignancy). The detected number was corrected for screening rate.

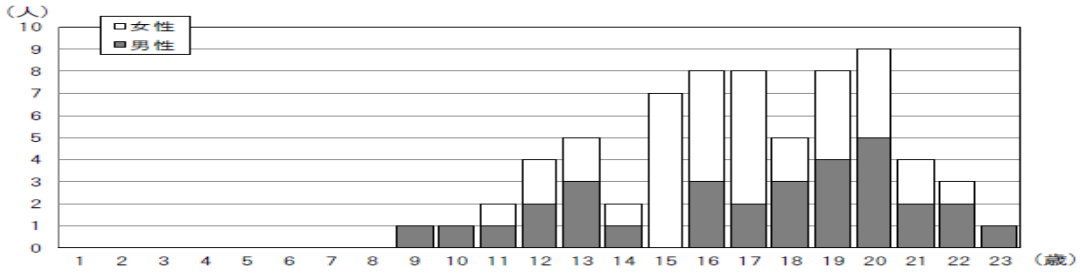
Age distribution and Sex ratio for Malignant or Suspicious Cases (age at diagnosis in confirmatory exam.)



Female

Male

PBLS (FY2011-13)



first FSS (FY2014-15)

(http://fukushima-mimamori.jp/ Dec 27, 2016)

Comparison of childhood thyroid cancer prevalence among 3 areas based on external radiation dose after the Fukushima Daiichi nuclear power plant accident

The Fukushima health management survey

Medicine®

Ohira T et.al. Medicine 2016; 95:35

Age- and Sex-adjusted ORs of thyroid cancer according to location group by first 4 months external doses estimated by the FHMS

Table 2

Age- and sex-adjusted ORs and 95% CIs of thyroid cancer according to location group by first 4-month external radiation doses estimated by The Fukushima Health Management Survey.

	Group A*	Group B†	Group C‡
N	4,192	213,564	82,720
Women, %	50.5	49.4	49.8
Age at the time of the nuclear accident, y (SD)	9.4 (5.4)	9.0 (5.1)	8.6 (4.8)
Age at the time of screening, y (SD)	10.2 (5.4)	10.6 (5.1)	11.2 (4.9)
Duration from the time of the nuclear accident to the time of screening, y (SD)	0.8 (0.6)	1.7 (0.7)	2.6 (0.5)
No. of cases	2	76	34
Prevalence proportion per 100,000 people	47.7	35.6	41.1
Crude OR (95% CI)	1.16 (0.28–4.83)	0.87 (0.58–1.30)	Reference
Age- and sex-adjusted OR (95% CI)§	1.49 (0.36–6.23)	1.00 (0.67–1.50)	Reference
Multivariable-adjusted OR (95% CI)¶	1.01 (0.22–4.63)	0.82 (0.51–1.34)	Reference

Group A: of 5 mSv or more is more than or equal to 1%.

Group B: of 5 mSv or more is less than 1% and of 1 mSv or less is less than 99.9%.

Group C: of 1 mSv or less is more than 99.9%.

Age- and Sex-adjusted ORs of thyroid cancer according to location group by first year thyroid doses estimated by WHO

from the nuclear accident
after the 2011 Great East Japan
Earthquake and Tsunami
based on a preliminary dose estimation

World Health Organization

Group 1: WHO dose estimation, relatively highest thyroid organ dose area.
Group 2: WHO dose estimation, middle thyroid dose area.
Group 3: WHO dose estimation, relatively lowest dose area.

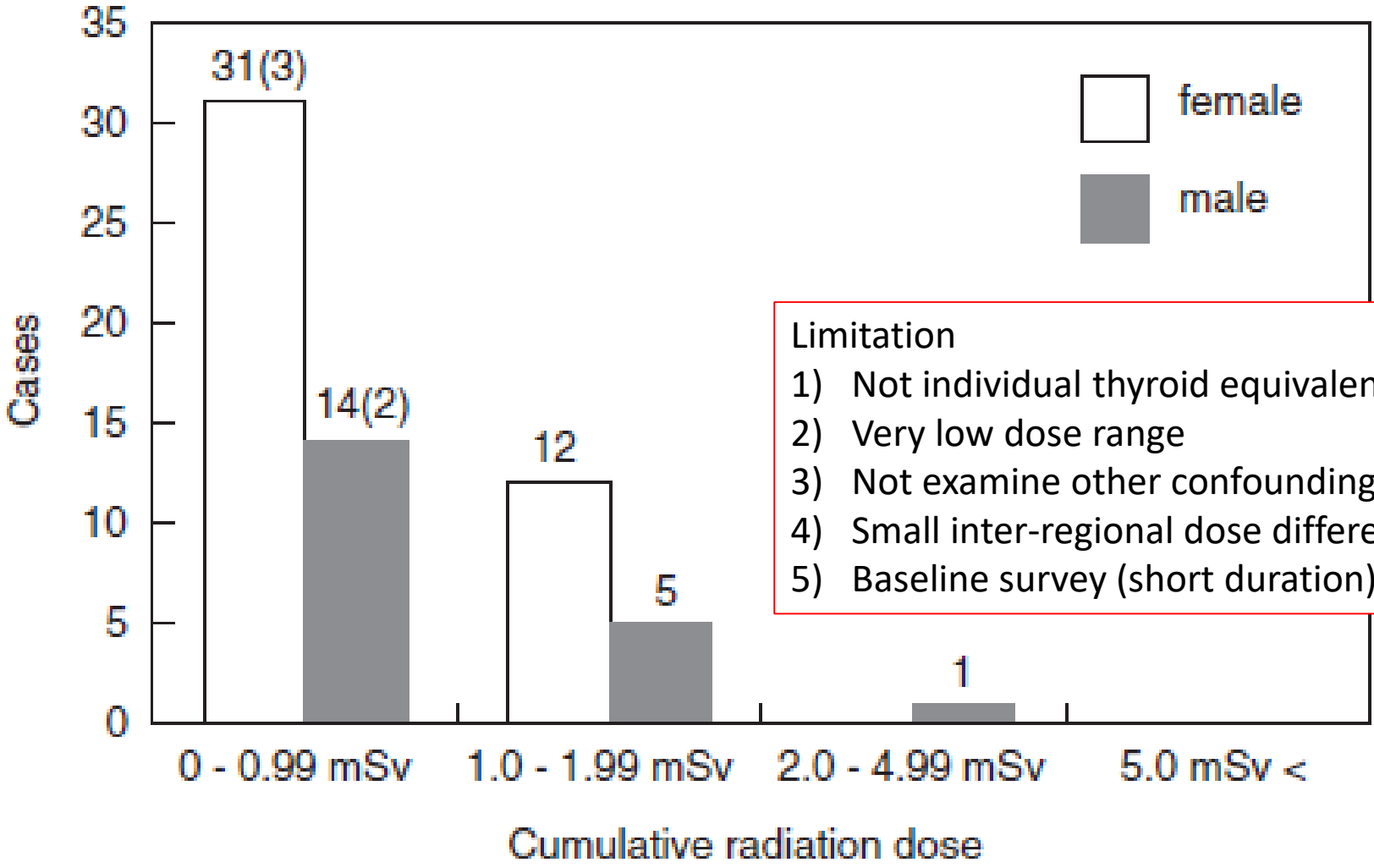
Table 3

Age- and sex-adjusted ORs and 95% CIs of thyroid cancer according to location group by first year thyroid doses estimated by WHO.

	Group 1*	Group 2†	Group 3‡
N	4,192	147,830	148,454
Women, %	50.5	49.4	49.8
Age at the time of the nuclear accident, y (SD)	9.4 (5.4)	9.1 (5.2)	8.7 (4.9)
Age at the time of screening, y (SD)	10.2 (5.4)	10.6 (5.2)	11.0 (4.9)
Duration from the time of the nuclear accident to the time of screening, y (SD)	0.8 (0.6)	1.5 (0.6)	2.3 (0.7)
No. of cases	2	52	58
Prevalence proportion per 100,000 people	47.7	35.2	39.1
Crude OR (95% CI)	1.22 (0.30–5.00)	0.90 (0.62–1.31)	Reference
Age- and sex-adjusted OR (95% CI)§	1.50 (0.37–6.15)	1.01 (0.69–1.47)	Reference
Multivariable-adjusted OR (95% CI)¶	1.07 (0.24–4.71)	0.84 (0.54–1.32)	Reference

* Relatively highest dose area.
† Middle dose area.
‡ Relatively lowest dose area classified by WHO estimation.[4]
§ Adjusted for age at the thyroid examination and sex.
¶ Adjusted for age at the thyroid examination, sex, and duration from the nuclear accident to the thyroid examination.
95% CI = 95% confidence interval, OR = odds ratio, SD = standard deviation, WHO = World Health Organization.

Age- and Sex-adjusted ORs of thyroid cancer according to estimated external dose range by FHMS in thyroid cancer cases



Limitation
1) Not individual thyroid equivalent dose
2) Very low dose range
3) Not examine other confounding factors
4) Small inter-regional dose differences
5) Baseline survey (short duration)

(S Suzuki et.al. Thyroid 2016; e-pub, DOI: 10.1089/thy.2015.0564,
T Ohira et.al. Medicine (Baltimore). 2016;95(35):e4472. doi: 10.1097/MD.0000000000004472.)

Overdiagnosis in Cancer

J Natl Cancer Inst 2010;102:605–613

H. Gilbert Welch, William C. Black

Cancer	Population	% With cancer (disease reservoir) (*a*)	Lifetime risk of death or metastatic disease* (*b*), %	Probability of overdiagnosis where entire disease reservoir detected† ($c = [a - b]/a$), %
Prostate	Men older than 60 y	30–70	4	87–94
Thyroid	Adults aged 50–70 y	36–100	0.1	99.7–99.9
Breast	Women aged 40–70 y	7–39	4	43–90

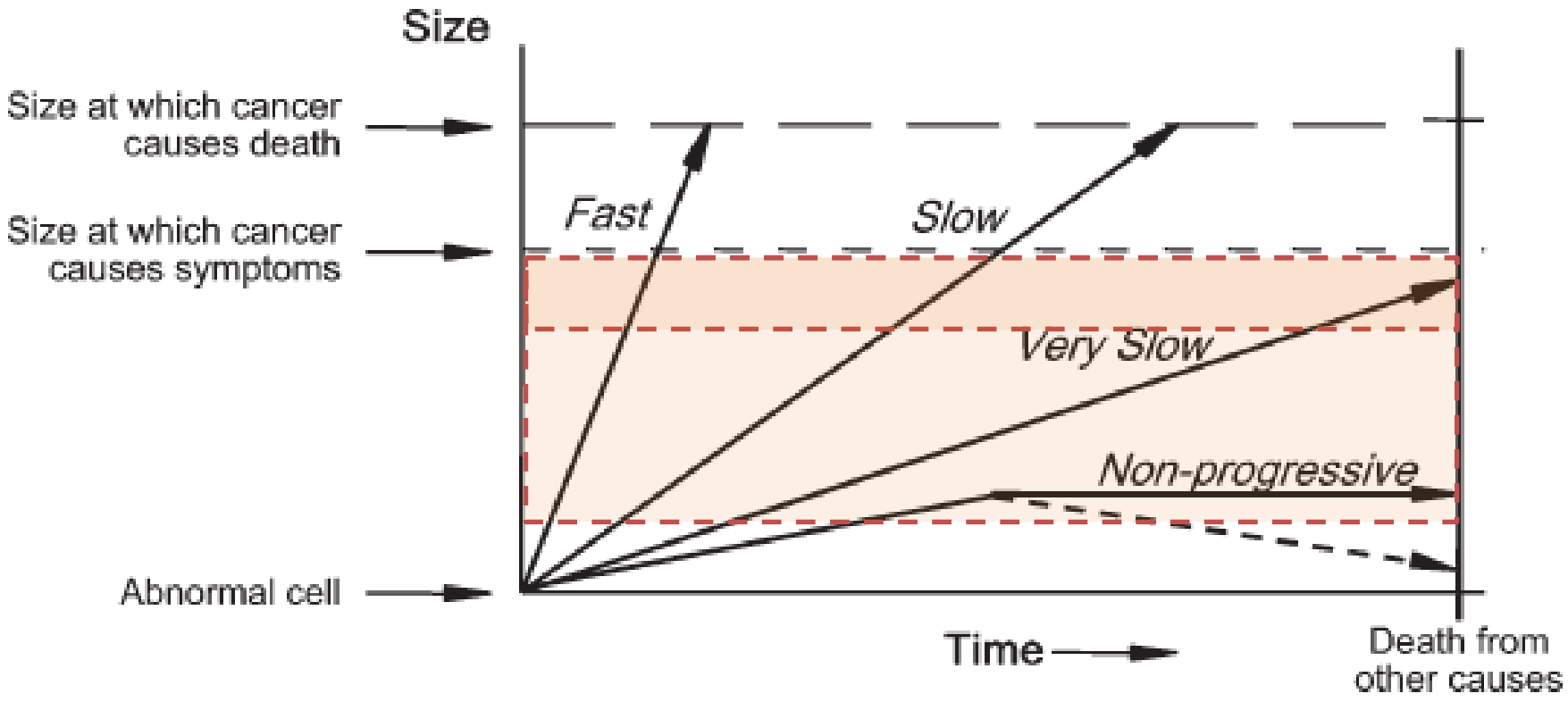


Figure 1. Heterogeneity of cancer progression. The arrow labeled "fast" represents a fast-growing cancer, one that quickly leads to symptoms

Summary of Thyroid US Examination in Fukushima Health Management Survey

- **Due to recent advances in US technology, diagnostic image quality has dramatically improved showing a tendency of increased incidence of thyroid cancers, suggesting overdiagnosis. The average detection rate of childhood thyroid cancer is around 0.038% by baseline first 3 years US screening. The similar tendency continues by following 2 years survey.**
- **The relationship between a high prevalence of thyroid cancer and radiation exposure is thought to be very unlikely because of several standpoints, such as very low doses, age and geographical distributions of the patients with thyroid cancer, etc. However precise individual estimation of thyroid equivalent dose are required to obtain epidemiological conclusion in the future.**
- **These results indicate that long term survey for the residents is necessary to reconsider a screening strategy, range, and criteria.**