DEAR EDITOR

We were very interested in the article by Ohira et al. [1]. Whereas Tsuda et al. [2], Yamamoto et al. [3], Kato [4] and Toki et al. [5] found a significant association between the occurrence of thyroid cancer and radiation following the Fukushima nuclear accidents, Ohira et al. claim no association between thyroid doses and thyroid cancer risk.

Ohira et al. [1] stratified the Fukushima prefecture into four regions defined by the quartiles of the absorbed thyroid dose distribution and assumed that the dose should have been avoided in the evacuation areas. The question arises of whether the evaluation of the thyroid dose including the evacuated municipalities can show a significant correlation. To this end, we considered the municipality-specific counts of thyroid cancers and the person-years in the Fukushima Health Management Survey (FHMS) as published in tables 1 and 2 of Yamamoto et al. [3]. Table 1 supplements this information with the total absorbed thyroid dose to 10-year-old children as estimated by UNSCEAR in the Attachments C-16 and C-18 of its 2013 Report [6]. These internal doses are compiled in the last column of Table 1, whereby the missing dose values in Attachment C-16 for the partly or completely evacuated prefectures were imputed by the dose values in Attachment C-18 taking the proportion of evacuees in the individual municipalities into account by linear interpolation.

Yamamoto et al. [3] found a considerably elevated detection rate per dose-rate of thyroid cancer below 2 μSv h–1 compared with the detection rate ratio from unrestricted data. We built on this finding by performing a segmented regression analysis [7] to determine an optimum dose (mGy) beyond which the slope of the detection rate by dose changes significantly. The dashed light blue elements in Fig. 1 present the corresponding change point analysis based on the deviance criterion [8]. The optimum thyroid absorbed dose of this change point is 21 mGy, 95% confidence interval (CI) 17–24. The detection rate ratio (DRR) below 21 mGy is 1.154 per mGy, 95% CI 1.044–1.277, P value 0.0053, and the residual DRR above 21 mGy is 1.003. The odds ratio and the P value for the interaction (change of slope) are 0.869, 95% CI 0.783–0.965, and 0.0083, respectively. This means that the overall effect is driven by the strong effect below 21 mGy. The solid blue line in Fig. 1 depicts this change point model. The solid black line in Fig. 1 indicates the overall association between the thyroid cancer occurrence and the thyroid absorbed dose in all 59 municipalities of Fukushima after the nuclear accidents. The DRR and the P value for this overall trend are 1.008, 95% CI 1.000–1.017, and 0.0445, respectively. The first- and second-order models are possible alternatives, which cannot be distinguished with certainty based on the data at hand. The presence of significant non-linearity does not mean that a simple linear overall model is inappropriate. If the simple linear model is not significant, this is not evidence of no effect [9].

The raw detection rate (DR′ = cases/person-years) and of the adjusted detection rate (DR′ = RR’ × cases/person-years), where superscript ‘0’ means the counts of cases (n = 142) and person-years (n = 1 865 957) at zero dose can be determined using table 1 in Lubin et al. [10]. These data are compiled in Table 2 and depicted in Fig. 2 comparing the detection rates of Lubin et al. and Yamamoto et al. DRRs per mGy, 95% CIs and P values of the trends in Fig. 2 are 1.0067, 1.0000–1.017, and 0.0001 for Lubin et al. [10], and 1.0100, 1.0006–1.0196 and 0.0379 for Yamamoto et al. [3]. Therefore, the meta-analysis of Lubin et al. and the FHMS yield consistent relative risks of the order of magnitude of 1% per 1 mGy thyroid absorbed dose in 10-year-old children. Yamamoto et al. found an association between radiation and thyroid cancer within 5 years after the Fukushima nuclear accidents. In contrast, Lubin et al. state ‘Although data were limited, fitted RRs in the restricted data appeared compatible with a minimum latency of 5 to 10 years.’ Veiga et al. support this finding [11]. However, these estimates of the minimum latency are based on few observations and cannot entirely exclude the possibility of earlier disease onset in (unnoticed) highly exposed or particularly sensitive children, see also paragraph 2.2 Induction and latent period, point prevalence, incidence...
Table 1. FHMS basic data of the combined first and second screening rounds [3]: municipality, person-years, thyroid cancers, detection rate and UNSCEAR (2013) total thyroid absorbed dose of 10-year-old children (mGy) in the first year after Fukushima derived from the UNSCEAR 2013 Report Attachments C-16 and C018 [6]

| Location no. | Municipality          | Person-years | Thyroid cancers | Detection rate per 100 000 | Total thyroid dose for 10-year-old children (mGy)\(^a\) |
|--------------|-----------------------|--------------|-----------------|-----------------------------|-----------------------------------------------------|
| 1            | Kawamata Machi        | 5790         | 2               | 34.54                       | 29.04                                               |
| 2            | Namie Machi           | 8304         | 4               | 48.17                       | 83.75                                               |
| 3            | Iitate Mura           | 2502         | 0               | 0.00                        | 55.92                                               |
| 4            | Minamisoma Shi        | 29 333       | 6               | 20.45                       | 35.32                                               |
| 5            | Date Shi              | 30 411       | 9               | 29.59                       | 22.61                                               |
| 6            | Tamura Shi            | 17 133       | 5               | 29.18                       | 19.42                                               |
| 7            | Hirano Machi          | 2359         | 0               | 0.00                        | 41.19                                               |
| 8            | Naraha Machi          | 3401         | 0               | 0.00                        | 85.26                                               |
| 9            | Tomioka Machi         | 6812         | 1               | 14.68                       | 121.31                                              |
| 10           | Kawauchi Mura         | 755          | 1               | 132.45                      | 41.32                                               |
| 11           | Okuma Machi           | 5933         | 3               | 50.56                       | 112.68                                              |
| 12           | Futaba Machi          | 2475         | 0               | 0.00                        | 28.72                                               |
| 13           | Katsurao Mura         | 521          | 0               | 0.00                        | 67.17                                               |
| 14           | Fukushima Shi         | 146 213      | 22              | 15.05                       | 24.73                                               |
| 15           | Nihonmatsu Shi        | 29 623       | 6               | 20.25                       | 27.41                                               |
| 16           | Motomiya Shi          | 17 788       | 2               | 41.87                       | 23.96                                               |
| 17           | Otama Mura            | 4777         | 4               | 22.39                       | 22.82                                               |
| 18           | Koriyama Shi          | 192 018      | 43              | 15.88                       | 24.72                                               |
| 19           | Koeri Machi           | 6298         | 1               | 15.88                       | 24.72                                               |
| 20           | Kunimi Machi          | 4808         | 0               | 0.00                        | 19.61                                               |
| 21           | Ten-Ei Mura           | 3009         | 0               | 0.00                        | 20.47                                               |
| 22           | Shirakawa Shi         | 36 846       | 7               | 19.00                       | 18.81                                               |
| 23           | Nishigo Mura          | 12 499       | 2               | 16.00                       | 19.69                                               |
| 24           | Iinumizaki Mura       | 3954         | 1               | 25.29                       | 18.08                                               |
| 25           | Miharu Machi          | 9695         | 1               | 10.31                       | 19.87                                               |
| 26           | Iwaki Shi             | 195 333      | 31              | 15.87                       | 31.16                                               |
| 27           | Sukagava Shi          | 48 513       | 5               | 10.31                       | 18.82                                               |
| 28           | Sonma Shi             | 20 546       | 1               | 4.87                        | 17.47                                               |
| 29           | Kagamihashi Machi     | 8262         | 1               | 12.10                       | 17.85                                               |
| 30           | Shinchi Machi         | 4515         | 0               | 0.00                        | 17.26                                               |
| 31           | Nakajima Mura         | 3524         | 1               | 28.38                       | 16.39                                               |
| 32           | Yabuki Machi          | 11 354       | 1               | 8.81                        | 16.86                                               |
| 33           | Ishikawa Machi        | 9559         | 1               | 10.46                       | 14.80                                               |
| 34           | Yamatsuri Machi       | 3500         | 0               | 0.00                        | 15.99                                               |
| 35           | Asakawa Machi         | 4840         | 0               | 0.00                        | 16.36                                               |
| 36           | Hirata Mura           | 3929         | 1               | 25.45                       | 16.30                                               |
| 37           | Tanagura Machi        | 10 042       | 2               | 19.92                       | 17.30                                               |
| 38           | Hanawa Machi          | 5526         | 1               | 18.10                       | 16.23                                               |
| 39           | Samegawa Mura         | 2317         | 0               | 0.00                        | 16.39                                               |
| 40           | Ono Machi             | 6237         | 0               | 0.00                        | 16.54                                               |
| 41           | Tamakawa Mura         | 4513         | 0               | 0.00                        | 16.49                                               |
| 42           | Furudono Machi        | 3677         | 0               | 0.00                        | 16.37                                               |
| 43           | Hisoemata Mura        | 306         | 0               | 0.00                        | 15.32                                               |
| 44           | Minamiaizu Machi      | 8288         | 0               | 0.00                        | 15.45                                               |
| 45           | Kaneyama Machi        | 612          | 0               | 0.00                        | 15.41                                               |
| 46           | Showa Mura            | 447          | 0               | 0.00                        | 15.80                                               |
| 47           | Mishima Machi         | 574          | 0               | 0.00                        | 15.97                                               |
| 48           | Shinogu Machi         | 3047         | 1               | 32.82                       | 15.40                                               |
| 49           | Kitakata Shi          | 26 455       | 3               | 11.34                       | 18.44                                               |
| 50           | Nishiuai Machi        | 2968         | 0               | 0.00                        | 15.58                                               |
| 51           | Todami Machi          | 2220         | 1               | 45.05                       | 16.03                                               |
| 52           | Inawashiro Machi      | 8435         | 1               | 11.86                       | 16.53                                               |
| 53           | Bandai Machi          | 1893         | 0               | 0.00                        | 16.61                                               |
| 54           | Kitashibara Mura      | 1752         | 0               | 0.00                        | 19.46                                               |
| 55           | Aizuimastu Machi      | 11 713       | 1               | 8.34                        | 16.10                                               |
| 56           | Aizuabage Machi       | 9570         | 1               | 10.45                       | 19.90                                               |
| 57           | Yanai Machi           | 1755         | 0               | 0.00                        | 15.91                                               |
| 58           | Aizuikawamura Shino    | 67 951       | 8               | 11.77                       | 16.64                                               |
| 59           | Yugawa Mura           | 2342         | 1               | 42.70                       | 18.46                                               |

\(^{a}\)Derived from the UNSCEAR 2013 Report Attachments C-16 and C-18 [6]
Table 2. Dose ranges, range-specific mean values of dose, thyroid cancer cases, person-years and detection rates (DR raw and DR adjusted) derived from the study of Lubin et al. [10] and detection rate (DR) from the study of Yamamoto et al. [3]

| Dose range (mGy) | Lubin et al. (2017) | Yamamoto et al. (2019) |
|------------------|--------------------|------------------------|
|                  | Mean (mGy) | Cases | Person-years | DR | DR' | Mean (mGy) | Cases | Person-years | DR |
| 0                | 0          | 142   | 1 868 957    | 7.6 | 7.6 | –           | –     | –           | –  |
| 1–4              | 2          | 24    | 367 606      | 6.5 | 8.1 | –           | –     | –           | –  |
| 4–20             | 9          | 30    | 587 614      | 5.1 | 9.2 | 17          | 47    | 386 111     | 12.2 |
| 20–40            | 25         | 13    | 345 748      | 3.8 | 6.6 | 26          | 128   | 663 088     | 19.3 |
| 40–60            | 49         | 54    | 315 014      | 17.1 | 15.3 | 46          | 1     | 5616        | 17.8 |
| 60–80            | 68         | 31    | 256 456      | 12.1 | 10.7 | 67          | 0     | 521         | 0.0  |
| 80–100           | 88         | 32    | 242 247      | 13.2 | 13.5 | 85          | 4     | 11 705      | 34.2 |
| 100–120          | 107        | 20    | 136 943      | 14.6 | 19.1 | 113         | 3     | 5933        | 50.6 |
| 120–140          | 126        | 21    | 149 525      | 14.0 | 20.0 | 121         | 1     | 6812        | 14.7 |
| 140–160          | 146        | 13    | 73 824       | 17.6 | 28.6 | –           | –     | –           | –  |
| 160–190          | 177        | 14    | 113 582      | 12.3 | 18.3 | –           | –     | –           | –  |
| **Total**        | 394        | 4 454 516 | –           | –     | –   | 184        | 1 079 786 | –           | –  |

Fig. 1. Association between thyroid cancer detection rate and thyroid absorbed dose (mGy) in 59 municipalities of Fukushima after the nuclear accidents (see Table 1). Thick solid black line: overall Poisson regression of the detection rate on the absorbed dose. Dashed blue lines: estimation of optimum change point of segmented regression [7]. Solid blue line, segmented Poisson regression of the detection rate on the absorbed dose allowing for an optimum change of slope at 21 mGy; outlying data point Kawauchi Mura not shown; circle area is proportional to expected thyroid cancer cases; PBLSP, Primary Base Line Screening Program, FFSSP First Full-Scale Screening Program.

In summary, our findings contradict the conclusion of Ohira et al. stating 'No dose-dependent pattern emerged from the geographical distribution of absorbed doses by municipality, as estimated by UNSCEAR, and the detection of thyroid cancer among participants within 4–6 years after the accident' [1]. We conjecture that the negative finding by Ohira et al. [1] may partly be due to a too coarse exposure proportion and incidence rate, and detection rate' in Yamamoto et al. [3].
stratification, the neglect of the evacuation areas and the disregard of the non-linearity of the association between radiation dose and thyroid cancer in the FHMS.

CONFLICT OF INTEREST
The authors declare that they have no known conflicts of interest.

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