Peer Review File

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Reviewer Comments:

You mention screening as a possible explanation.

(1) Describe when or what time period screening was performed in the different countries.

Response: Thanks for the reviewer' good comments.

In Korea, TC incidence had a ten-fold increase between 1996 and 2010, after the initiation of an opportunistic but widespread national screening program in middle-aged people in 1990s.

Actually, in China, since 1988, there are amount of literature about ultrasound diagnosis of thyroid nodule and the ultrasound has been widely used for the examination for neck tumors since 1990s (**Chinese Journal of Radiology 1998, 32(9); Chinese Journal of Medical Imaging Technology 1998, 3(3); Chinese Journal of Medical Imaging Technology 1998, 6(6)**) and the incidence has increased three times from 1988 to 2009 (**Sun JW, et al. Epidemiological Study on Thyroid Cancer in China. China Cancer,2013,09:690-693**).

In Japan, the incidence rates of incidentally-detected thyroid cancer consistently increased especially after 2001, for all sex and age groups. The rate of incidentally-detected thyroid cancer increased from 0.1 and 0.1 per 100 000 person-years among men and women in 1992-1994 to 2.0 and 4.9, respectively, in 2010-2012. However, the mortality rates among both sexes during the period leveled off, which suggests that the thyroid cancer incidence rate increased with incidental detection after 2001 in Osaka, Japan. (**Toyoda Y, Tabuchi T, Nakata K, et al. Increase in incidental detection of thyroid cancer in Osaka, Japan. Cancer Sci. 2018;00:1–5.**)

(2) Was that on a national basis?

Response: China, Japan and Korea are three neighboring countries with similar genetic backgrounds and similar culture and a high economic level, and have relatively complete cancer registry data in East Asian countries. We can see the increasing trend of thyroid and cancer among both sexes in the three countries (Figure 2).

(3) Were both genders and all age groups included.

Response: This incidence of thyroid cancer is increasing in both males and females in China, Japan and Korea (Figure 2). In Figure 4 the incidence at all age group have also an increasing trend for all sex(Figure 4A, 4B and 4C).

(4) How does screening fit with your findings?

Response:

In our study, an increasing trend in TC incidence rates was observed among males from China (10.3%), Japan (4.7%), and the Republic of Korea (20.8%) and among females from China (9.4%), Japan (3.5%), and the Republic of Korea (20.5%). But the mortality is decreasing among males and females in the three countries except the slight increase among Chinese males (0.7%) and Korean females (0.1%). The contradictory finding is called "overdiagnosis" with the introduction and improvement of new diagnostic procedures including ultrasonography, computed tomography, and magnetic resonance imaging which can result in increases in detection of small papillary lesions which may have existed in the large reservoir of asymptomatic, nonlethal diseases related to the thyroid gland (**Reference 5: Vaccarella S, Dal ML, Laversanne M, et al. The impact of diagnostic changes on the rise in thyroid cancer incidence: A population-based study in selected high-resource countries. Thyroid 2015;25:1127–36. Reference 31: Davies L, Morris LG, Haymart M, et al. American Association of Clinical Endocrinologists and American College of Endocrinology disease state clinical review: the increasing incidence of thyroid cancer. Endocr Pract 2015;21:686–96.**).

(5). Statistical analysis - Joinpoint analysis:

The authors should also add, that when joinpoints were detected, annual percentage changes were calculated for each linear segment. The common abbreviation for annual percent change is APC, but since the authors already use this to indicate age-period-cohort, they should use another abbreviation (or no abbreviation at all, as in Table 1).

Response: Thanks for the reviewer' good comments.

We have replaced the "APC" with the "age-period-cohort" (no abbreviation as in Table 1) in 13 places in the revised manuscript and add annual percentage changes calculated for each linear segment in Figure 2 and 3.

(6). Figure 2 and 3:

The scale of the y-axis should start at 0 for all figures (this is easy to change in the Joinpoint software). In addition, the authors could try to use the same scale for some of the figures, to make it easier to compare the incidence levels between countries and genders.

Response: Thanks for the reviewer' good comments. We have corrected the scale of the y-axis at 0 for the figures produced by Joinpoint software. To make it easier to compare the incidence and mortality levels between countries and genders, we used the same scale from 0 to 110 by 5 for incidence between countries and genders, and the same scale from 0 to 0.72 by 0.04 for mortality (as shown in Figure 2 and 3).

(7). Figure 5 (and text at page 10-11):

The authors should also add a table with results (RRs and 95 % CIs) as discussed on page 10-11, for age, time period and birth cohort, for each country.

Response: Thanks for the reviewer' good comments.
We have added a table 3 with age-period-cohort results (RRs and 95 % CIs).

(8). Line 253: "TC incidence decreased in a few countries such as Norway and Sweden (21)".
This reference is outdated, see e.g. Carlberg et al. BMC Cancer (2016) 16:426.
The authors should discuss the potential carcinogenesis of radiofrequency radiation, see Figures 9 and 10 in that article.
It would be of interest with similar Fig 9 for the different countries.

Response: Thanks for the reviewer' constructive comments.
We have deleted the word "TC incidence decreased in a few countries such as Norway and Sweden (21)" according to the updated literature by Carlberg et al (BMC Cancer (2016) 16:426).
We have added some about the potential carcinogenesis of radiofrequency radiation in the discussion part. The added content is as follows in line 357-367 in the discussion part in the manuscript: "Furthermore, other than ionizing radiation (mostly medical radiation), exposure to the radiofrequency electromagnetic fields (RF-EMFs) due to the use of mobile and cordless phones should also be considered in the context [50]. The carcinogenic effect of RF-EMFs radiation was evaluated by International Agency for Research on Cancer (IARC) and RFEMFs were categorized from mobile phones and from other devices that emit similar non-ionizing electromagnetic fields in the frequency range 30 kHz – 300 GHz as Group 2B, i.e., 'possibly' carcinogenic to humans [51, 52]. Additionally, thyroid gland exposure to RF-EMFs has increased, especially during the last one or two decades. And the thyroid gland was one of the organs with the highest exposure in both near-filed and far-field. Compared to mobile feature phones, smartphones potentially provide higher RF-EMF exposure [50]."