Point-by-Point Responses to Reviewers' Comments
Response to the Comments from Reviewer #1.

Regarding the complementary comments,
I think the problem detractors will point out is that rates of small clinically detected tumors also went up (which you rightly point out could be either misclassification or inaccurate insurance claims). I think an additional effective argument here might be to add that 8-9mm tumors are just too small for any patient to notice or physician to find at such high rates. To be palpable or cause symptoms at such a size they would have to all be located at the isthmus (easier to feel) or external surface of the thyroid (also easier to feel), or be invading/pressing on the trachea or recurrent nerve or esophagus (not likely for every single one of these tumors). It falls into the category of what Gil Welch has taught me to label as - 'possible, but not particularly plausible'. The clinically detected rates going up as they did is likely reflective of more complex changes in medical practice than can be seen in higher level data reviews, and also the problems you point out of misclassification and insurance claim issues.

Response: We appreciate the reviewer for such a nice suggestion. We paraphrased what is suggested and added it in the Discussion Section (page.17, Line3 ~ 9) as follows;
"Practically, 8-9 mm tumours are just too small for any patient to notice or physician to find at such high rates. To be palpable or cause symptoms at such a size they would have to be all located at the isthmus or external surface of the thyroid, or be invading/pressing on the trachea or recurrent nerve or esophagus, which is extremely unlikely.."

We also incorporated minor wording changes in that paragraph to improve logical flow of the ideas with a hope to better persuade the detractors

Regarding the comment on Supplementary Tables 3 and 4;
2. I like the supplemental tables 3 and 4 (incorrectly labeled in the discussion text as supplemental tables 2 and 3). They help the reader feel confident in your sampling methods. Waiting until the discussion seems late to bring them up. Consider mentioning them in the methods or results.

Response: As recommended, we added commentary remarks regarding the Supplemental Tables 3 and 4 (after correcting the Table numbering, of course) to the Methods Section from the Discussion Section, as follows (Page 9, paragraph 2, Lines 10~14);
"To check if the NEST database would be representative of the National Cancer Incidence Database (KNCI DB), we compared the age and sex distribution (Supplementary Table 1) and the estimated age-standardized incidence rate of thyroid cancer (Supplementary Table 2). The results were quite comparable with the results from KNCI DB for each given year."

Regarding the comments on the way of presenting the result;
3. There are just so many results, it was a really a struggle for me to cognitively shift gears every time I was looking at a new way to organize the counts, rates, and changes. Are we really helping the reader learn something by showing the data so many different ways? This is an editorial and authorial decision, of course, but I have a few thoughts.
Would it help if it was explained in the text what the value is of seeing an absolute number instead of a proportion, etc.? Or, another idea - maybe the tables and figures could be notarized in the 'white space' to help the reader see why each way of looking at the data adds something unique to the paper? This may not be fixable (in some ways, it is the curse of epidemiology that I always struggle with as an author, myself), but worth thinking about. Also, I know it may not be something the editors want in their journal, but if it spurs discussion, about how best to present the results, then I will have helped.

Response: We fully agree that it is really a challenging issue. In this paper, by showing the graphic figures, we tried to visualize the dramatic increase in the thyroid cancer incidence, which occurred over a very short time span, according to the routes of detection. To improve the readability, we switch the order of showing the bar in each category in Figures 3A, 3B, and 3C. We also modified the result to improve the readability. (For example, the proportion of lymph node involvement was represented as the its numerator and denominator (numerator/denominator)) (Page 12, Line 8-17). In addition, in the revised manuscript, we decided to separate out the Figure 3C from the others. We re-numbered it as Figure 4 because it dealt with slightly different issue of "absolute change over time in incidence rate of regional stage thyroid cancer by degree of extension and lymph node involvement".

Regarding the comments on the issue of reporting relative survival rates of >100%;
4. In the discussion, reporting relative survival rates of >100% may not be easily understandable to readers not closely familiar with the various kinds of survival calculations. You may want to take a minute to explain it, such as by saying 'rates are >100% because the life tables used to make the calculation are not exactly representative of those undergoing the screening - those undergoing screening are healthier than the general population'. Alternatively, you could truncate the rates at 100%.

Response: As suggested, we explained it by adding a new line on Page16 (Paragraph 1, Lines 10-13), as follows;
"This finding of >100% relative survival rates means that thyroid cancer patients who were more likely to get thyroid cancer screening might be healthier and have lower risk of dying than the general population, even in those with regional stage thyroid cancer by SEER summary stage"

Regarding the comments on the phrase, 'the truth seems to be the opposite"
5. Page 16 line 21: 'the truth seems to be the opposite" is not followed immediately by a strong argument of why the truth is opposite. Consider rephrasing to strengthen /clarify the argument or altering the flow of the discussion.

Response: As you recommended, we rephrase the sentences to clarify the arguments. We largely revised the discussion (Page16, paragraph 2, Line 19 ~ Page 17, paragraph 2, Line 18)

Regarding the typo on Page 16 line 25
6. Page 16 line 25 : typo - "and the most" was probably meant to be "and most"

Response: The previous sentences were deleted while editing the text according to the comment #5.

Regarding the typo on 'one of the first to show a direct association'
7. Page 17 line 24: 'one of the first to show a direct association' of routes of detection, or is this actually better stated to be

'the first'? I don't know of another study that is quite like this one, but have not done an in depth literature search. There are others that were similar, and it would be polite to reference them for example a 2014 study authored by Udelsman in the journal Thyroid that correlated the density of surgeons, endocrinologists and insurance claims for ultrasound with rates of thyroid cancer in the U.S. might be a good one.

Response: As recommended, we rephrased 'one of the first to show a direct association' to read as 'shows a direct association' and we added a few lines on page 18 to cite the study authored by Udelsman, as follows (Page17, paragraph 3, Lines 21~ Page.18 Line2):
"Our study shows a direct association at the individual level between the routes of thyroid cancer detection and an increase in thyroid cancer rates through the medical record review. On the other hand, previous studies showed only indirect and ecological association between ultrasonography uses and the incidence of thyroid cancer.[8, 27]."

Regarding on the more detailed description of potential contributors to thyroid cancer epidemic in the Discussion Section.
8. Page 18, lines 24-29: "Although many experts suggested that the increase in the incidence of thyroid cancer was mainly due to the increasing utilization of imaging tools for thyroid cancer screening…", this is an oversimplification of what we now recognize about how thyroid cancers are detected (and of what Dr. Welch and I said in the discussion section of the paper referenced for this statement). The problem starts at the macro level, with how health care is paid for at the system level, and extends all the way down to the microscopic level, with how pathology specimens are processed these days compared to how they were examined 30 years ago. You will help readers understand the complexity of the problem by indicating this more fully. I was the head of a task force that looked at this and published a review paper in 2015 in the journal Endocrine Practice outlining the known contributors (and non contributors) to the increasing incidence of thyroid cancer, and there was also another similar paper written in 2013 in the Journal of Cancer Epidemiology with the first author Pellegriti. Both have good reference lists to show the other work that has been done to illuminate the various ways thyroid cancers can be detected.

Response: We totally agreed with you that thyroid cancer epidemic in Korea is not only the problem at the microscopic or physician level, but also reflects the problem of the health care system in Korea. As recommended, we extensively revised the Discussion Section (Page 18 Line 20~21; Page 19 Line 15~20; Page 20 Line 1~ 4; Page 20 Line 7~8; Page 20 Line 11~14). We described the possible causes of thyroid cancer epidemic in more details and described the detailed mechanism for increasing thyroid cancer corresponds to our cases in South Korea as follows:
"There have been debates regarding the cause of the rising incidence of thyroid cancer in the past decade, as well summarized in recent reviews.[29,30]" (Page 18 Line 20~21)
"To date, the only confirmed risk factor for the thyroid cancer is exposure to the ionizing radiation.[35] In Korea, however, there were no discernible sources of additional radiation exposures other than the medicinal use of radioisotopes and such diagnostic procedures as CT scan.[11, 29, 36] Even if there were some increase in thyroid cancer incidence by all those environmental causes, their contributions seems to be very small." (Page 19 Line 15~20)
"This issue of overdetection starts at the macro level, with how health care is paid for at the system level, and extends all the way down to the microscopic level, with how pathological specimens are processed these days compared to how they were examined 30 years ago.[29,30]" (Page 20 Line 1~ 4)
"Many hospitals and clinicians encouraged routine health check-up programs, which include thyroid cancer screening as an option with additional fee, not covered by the National Health Insurance." (Page 20 Line 6~ 8)
"At the microscopic level, more careful pathologic examination of resected thyroid specimens could well have contributed to the increase of thyroid cancer to some extent.[37] But, it alone doesn't seem to explain the magnitude of thyroid cancer epidemic in Korea." (Page 20 Line 11~14)

Regarding the typo on Page 21 line 22
9. Page 20 line 22: typo - "provides an evidence" should be revised to "provides evidence that'.

Response: As recommended, we changed "provides and evidence" to "provides evidence that".
(Page21, paragraph 1, Line 7)

Regarding the typo on Page 22 line 4
10. Page 20 line 33: typo "conserted" is spelled 'concerted"'.

Response: As recommended, we changed "conserted" to "concerted".
(Page21, paragraph 1, Line 12)

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