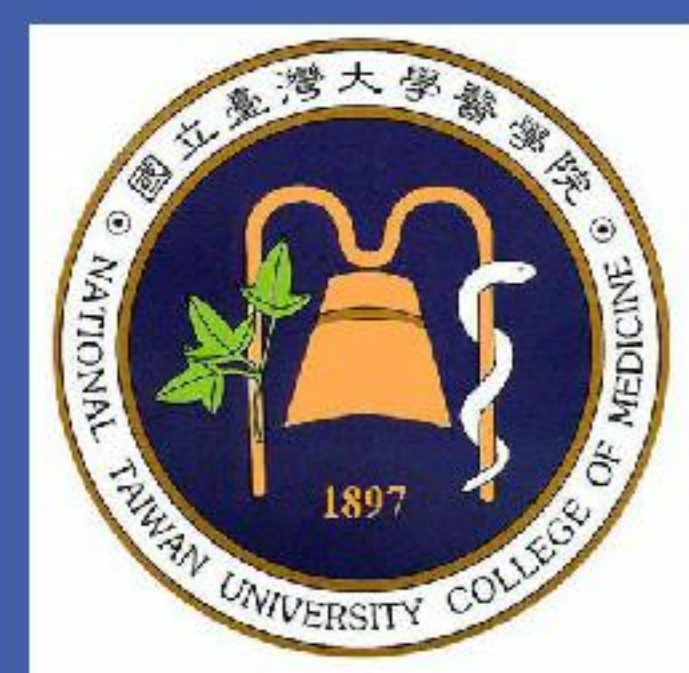# Sitagliptin Use and Thyroid Cancer Risk in Patients with Type 2 Diabetes

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Background

Whether sitagliptin may increase thyroid cancer risk has not been investigated in the Asian populations.

Purpose

To evaluate the risk of thyroid cancer with regards to sitagliptin use in patients with type 2 diabetes mellitus in the Taiwanese population.

Methods

The reimbursement database of the National Health Insurance in Taiwan was used. Figure 1 shows the procedures in recruiting a cohort of patients with newly diagnosed type 2 diabetes mellitus during the period from 1999 to 2008 (original sample). They should have been followed for at least 6 months after March 1, 2009, the date when sitagliptin was approved for reimbursement. Follow-up started on the first prescription of sitagliptin or comparators on or after March 1, 2009, and ended on December 31, 2011, at the time of a new diagnosis of thyroid cancer, or on the date of the last reimbursement record. The treatment effect (for ever versus never users, and for tertiles of cumulative duration of therapy) was estimated by Cox regression incorporated with the inverse probability of treatment weighting using propensity score. Propensity score was created by logistic regression based on baseline characteristics including age, sex, diabetes duration, hypertension, chronic obstructive pulmonary disease, heart failure, nephropathy, eye disease, dyslipidemia, stroke, ischemic heart disease, peripheral arterial disease, obesity, benign thyroid disease, insulin, sulfonylurea, metformin, meglitinide, acarbose, pioglitazone and rosiglitazone. Sensitivity analyses were conducted by using a 1:1 matched-pair sample based on 8 digits of propensity scores (matched sample).

Results

The incidence of thyroid cancer by sitagliptin exposure and hazard ratios comparing exposed to unexposed in the original sample and the matched sample are shown in Table 1. Findings in the original sample and the matched sample were fairly similar. The incidences for users within the first year (in the first and second tertiles) were higher than never users but the incidence was lower for users of more than one year (third tertile) when compared to never users. The overall hazard ratios suggested a higher risk associated with sitagliptin use, though not statistically significant in the matched sample analysis. When analyzed by the tertiles of cumulative duration, a significantly increased risk could be observed for the first and second tertiles, and the risk became neutral when sitagliptin use was >14 months in the third tertile.

Conclusions

Sitagliptin use is associated with an increased risk of thyroid cancer, especially during the first year of its treatment. The increased risk within a short-term of cumulative duration of exposure probably precludes a mechanism involving de novo development of thyroid cancer. Future studies are required to confirm the findings of the present study.

Acknowledgments

Figure 1. Flowchart showing the procedures in selecting the original sample into the study
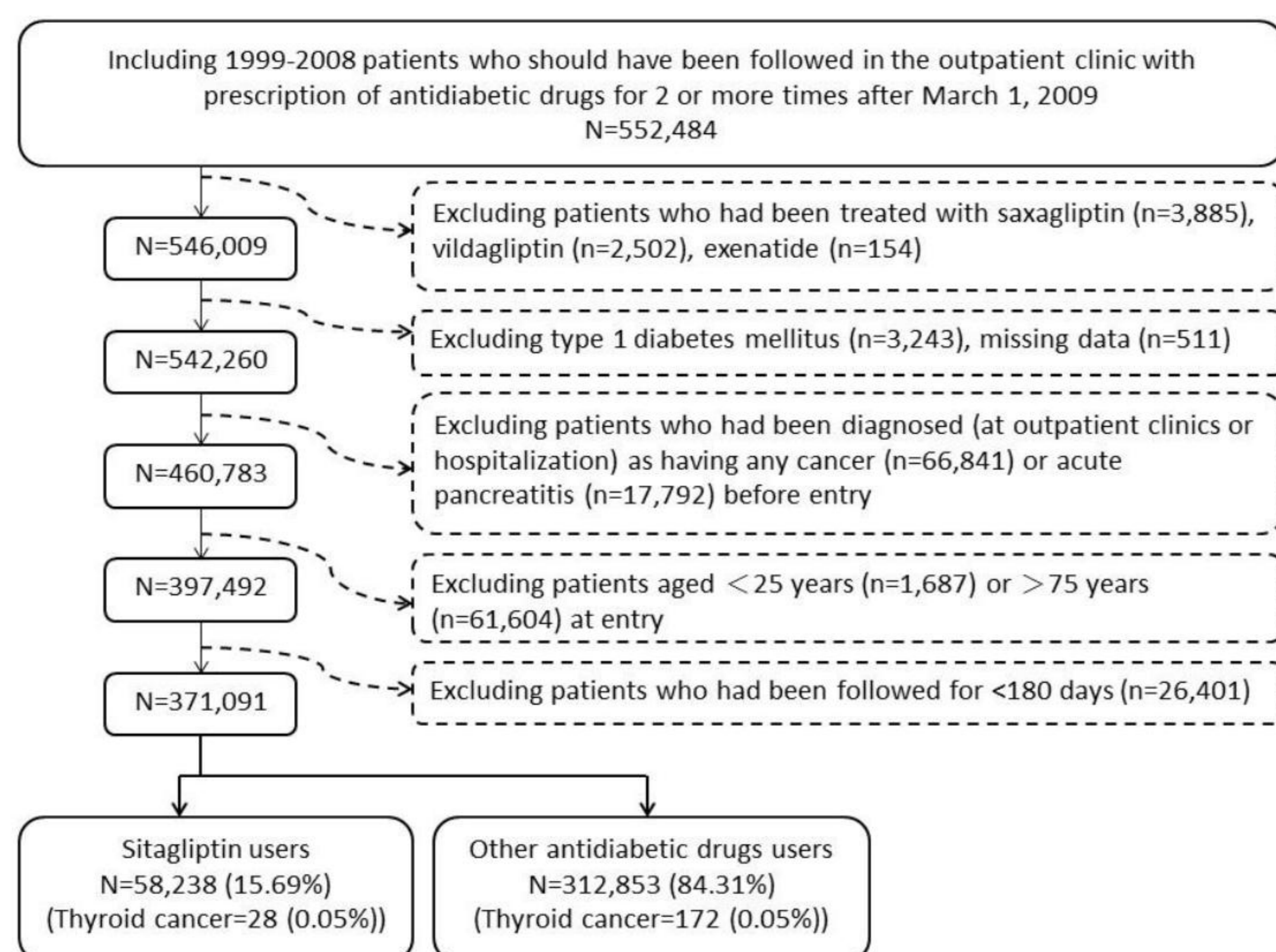

Table 1. Incidence of thyroid cancer by sitagliptin exposure and hazard ratios comparing exposed to unexposed in the original sample and the matched sample, respectively

Sitagliptin use	Case number	Incident thyroid cancer	%	Person-years	Incidence rate (per 100,000 person-years)	Hazard ratio (95% Confidence interval)	P
I. Original sample							
Never users	312853	172	0.05	777260.24	22.13	1.000	
Ever users	58238	28	0.05	95424.71	29.34	1.516 (1.011-2.271)	0.0439
Tertiles of cumulative duration of sitagliptin therapy (months)							
Never users	312853	172	0.05	777260.24	22.13	1.000	
< 6.53	18287	9	0.05	25343.96	35.51	1.995 (1.015-3.919)	0.0451
6.53-14.00	20161	14	0.07	29760.78	47.04	2.516 (1.451-4.364)	0.0010
> 14	19790	5	0.03	40319.97	12.40	0.595 (0.244-1.449)	0.2530
II. Matched sample							
Never users	57659	31	0.05	141851.35	21.85	1.000	
Ever users	57659	28	0.05	94698.12	29.57	1.462 (0.866-2.466)	0.1551
Tertiles of cumulative duration of sitagliptin therapy (months)							
Never users	57659	31	0.05	141851.35	21.85	1.000	
< 6.53	18066	9	0.05	25104.96	35.85	1.936 (0.906-4.137)	0.0881
6.53-14.00	19978	14	0.07	29578.69	47.33	2.301 (1.208-4.386)	0.0113
> 14	19615	5	0.03	40014.47	12.50	0.574 (0.222-1.483)	0.2516