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Incidence of Pancreatic Malignancy and Thyroid Neoplasm in Type 2 Diabetes Mellitus Patients who Initiate Exenatide Compared to Other Antihyperglycemic Drugs

Final Report-Updated

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Summary of Corrections

This revised report describes the corrections to the "intent-to-treat" analyses presented in the original report dated 19 December 2012, including the main analyses (Tables 4, 5) and the sensitivity analyses (Tables 4a, 4b, 5a, 5b). All changes are marked in bold italics.

The person-time allocation in Tables 4, 4b, 5, and 5b of the original report was miscalculated. The person-time was allocated on the basis of a person's total cumulative duration of exenatide use or other antidiabetic drug (OAD) use at the end of follow-up, in which a person only contributed his/her person-time to the category (duration of follow-up) that he/she ultimately reached, rather than contributing person-time to each category of duration of follow-up for which he/she qualified.

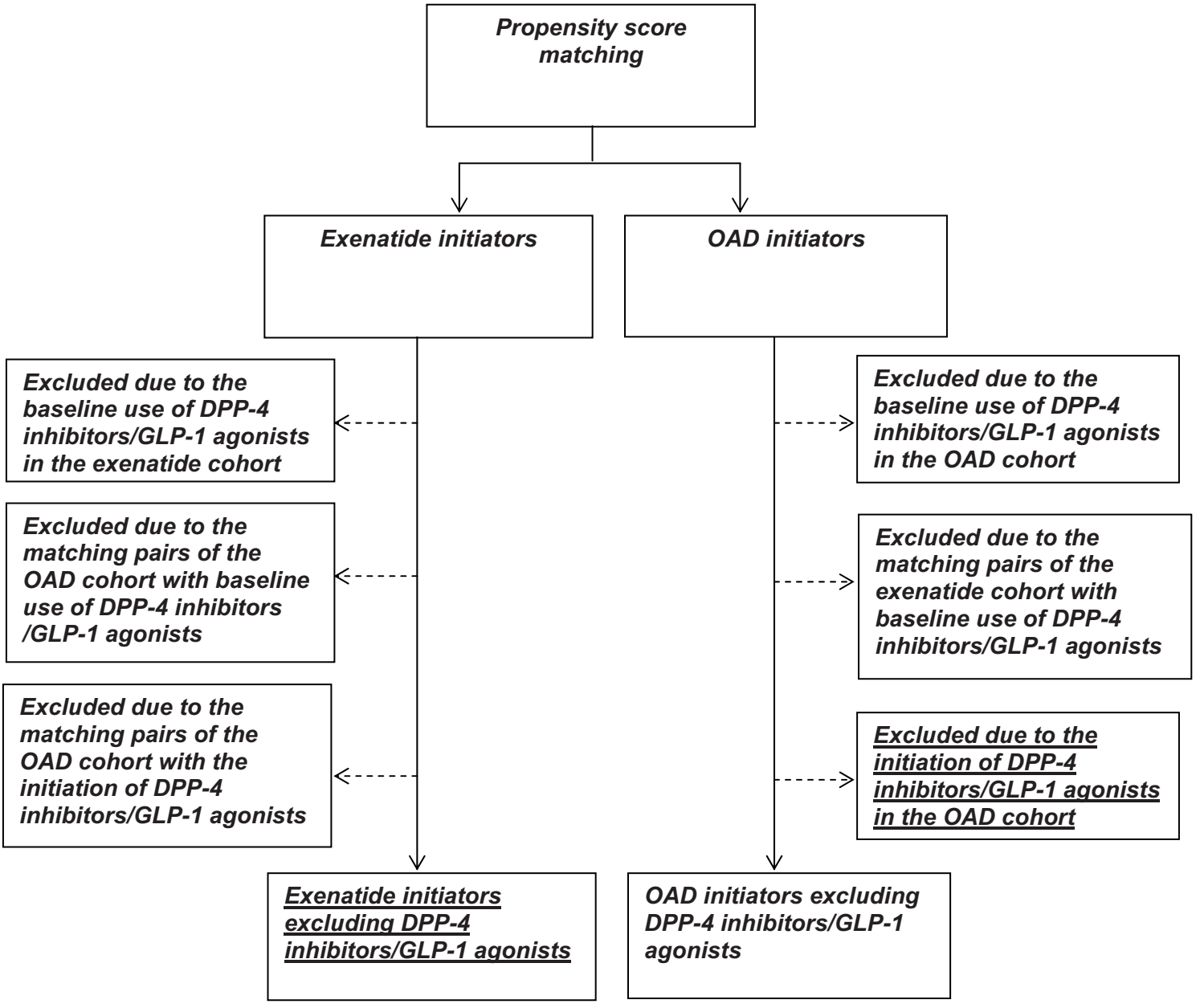
To correctly allocate the person-time for the intent-to-treat analyses, we revised the analyses presented in Tables 4, 4b, 5, and 5b and classified the person-time into categories of 1 to <2 years, ≥2 years to < 3 years, and ≥3 years based on time since initiation. For each person, his or her experience in the 1 to <2 years of follow-up was allocated to that category, with subsequent experience allocated to subsequent categories (e.g., ≥2 years to < 3 years). Thus, some patients contributed person-time to different categories of follow-up duration.

This reallocation of person-time required the rechecking of the covariates for imbalance across categories of duration of follow-up and updated covariate data are in Tables 1.6.1a, 1.6.1b, 1.6.2a, and 1.6.2b. We revised these tables based on the new person-time allocations and found no additional covariates imbalanced and the corrected analyses were adjusted for the same covariates as the previous analysis. The corrections of Tables 4, 4b, 5 and 5b did not affect the results in the overall analyses, but affected the results that were stratified by duration of follow-up. The corrected results showed that the crude and adjusted hazard ratios remained essentially unchanged, but the incidence rates by duration of follow-up decreased in categories with less than 2 years duration of follow-up due to the increase in person-years and were closer to the overall incidence rate.

In Tables 4a and 5a for the analysis comparing the risk of cancer outcomes in exenatide initiators with initiators of DPP-4 inhibitors/GLP-1 receptor agonists only, the original report presented the results based on a subset of cohorts without removing patients with baseline use of DPP-4 inhibitors/GLP-1 receptor agonists. These patients should have been excluded in the sensitivity analysis. The following flow chart shows the steps of excluding patients with baseline use of DPP-4 inhibitors/GLP-1 receptor agonist in the exenatide and OAD cohorts. In

the corrected analysis, patients in the boxes with underlined texts were compared. The results showed only a slight difference after correction.

In all, the corrections yielded comparable relative estimates of effect and did not alter the conclusions of this study, although the estimates of incidence rates in categories with short duration of follow-up decreased.



1. Executive Summary

This was a retrospective cohort study of pancreatic malignancy and thyroid neoplasm involving comparisons of patients who initiated exenatide with patients who initiated other antidiabetes drugs (OADs). The data were derived from health insurance claims from the Life Sciences Research Database (LSRD) and the Impact National Benchmark Database. Within these 2 databases, patients were accrued from 01 June 2005 through 31 July 2010 with follow-up extending to 31 December 2010. Patients with baseline dispensings for the same drug or drug class that qualified them for entry into the cohort were excluded. Furthermore, those who had claims for pancreatic or thyroid neoplasms during the baseline period were also excluded.

Exenatide initiators were matched in a variable ratio to initiators of OADs using propensity scores. Outcomes of interest included pancreatic cancer, thyroid cancer, and benign thyroid neoplasm, identified on the basis of algorithms consisting of specific patterns of health insurance claims data. The algorithms were validated against a set of cases that were initially identified from the claims data and confirmed through medical chart review. Patients were followed for a new occurrence of pancreatic cancer or thyroid neoplasm from one-year after drug initiation (i.e., excluding the first year of follow-up as a lag period) to the end of follow-up period (31 December 2010) or disenrollment of health plan.

Two approaches were used to estimate the absolute and relative incidence of pancreatic cancer and thyroid neoplasm between the study cohorts. The first, a time-fixed analysis, categorized all follow-up time according to the initial exposure status (i.e., the patient's first dispensing). The second approach involved measuring cumulative dose and duration of exenatide exposure. Incidence rates (IR) and corresponding 95% confidence intervals (CIs) in the exenatide cohort, overall, by periods of cumulative dose and duration were estimated and contrasted with rates among person-time unexposed to exenatide.

In the final cohorts, the combined databases included 18,932 persons in the matched exenatide cohort and 27,691 in the matched OAD cohort. Baseline characteristics, such as gender, age, and year of cohort entry, as well as the occurrence of baseline diagnoses, procedures, and medication dispensings were generally balanced between the cohorts after matching on the propensity score, though a few variables required adjustment in models due to slight remaining imbalances.

In the LSRD there were 7 cases of pancreatic cancer among the exenatide initiators and 6 cases of pancreatic cancer in the OAD cohort (Executive Summary Table 1). The Impact database had 3 cases of pancreatic cancer in the exenatide cohort and 5 cases of pancreatic cancer among patients in the OAD cohort. In the LSRD, the overall IR was 0.3 (95% CI: 0.1-0.7) cases of pancreatic cancer per 1,000 person-years among

exenatide initiators and 0.2 (95% CI: 0.1-0.4) cases of pancreatic cancer per 1,000 person-years among OAD initiators (adjusted hazard ratio [HR] 1.4; 95% CI 0.4-4.2. ***Allowing for a 1-year lag, the IRs in both cohorts fluctuated with duration of follow-up due to few cases from which to draw inference.*** Similar IR results were found in the Impact database; however, the outcomes were sparser.

Executive Summary Table 1 (Report Table 4). Incidence of Algorithm-identified Pancreatic Cancer Among Exenatide Initiators and Other Antidiabetes Drug Initiators (Overall and by Follow-Up Since Treatment Initiation)----Time-Fixed Analysis (Excluding People with Baseline DPP-4 Inhibitors/GLP-1 Receptor Agonist Use and/or Events and Person-time in the First Year after Drug Initiation)

Variables	Events	Person-years	IR	95% CI	Unadjusted[+]		Adjusted*	
					HR	95% CI	HR	95% CI
Life Sciences Research Database								
Overall[‡]								
Exenatide	7	20,300.2	0.3	(0.1 - 0.7)	1.5	(0.5 - 4.6)	1.4	(0.4 - 4.2)
OADs	6	29,865.6	0.2	(0.1 - 0.4)	Ref.		Ref.	
1 to <2 years								
Exenatide	4	9,691.9	0.4	(0.1 - 1.1)	1.2	(0.3 - 4.9)	1.1	(0.3 - 4.4)
OADs	4	14,033.3	0.3	(0.1 - 0.7)	Ref.		Ref.	
≥2 years to <3 years								
Exenatide	0	6,151.2	0.0	(0.0 - 0.5)	NC		NC	
OADs	1	8,774.6	0.1	(0.0 - 0.6)	Ref.		Ref.	
≥3 years								
Exenatide	3	4,457.1	0.7	(0.1 - 2.0)	5.1	(0.5 - 51.2)	6.0	(0.5 - 66.7)
OADs	1	7,057.7	0.1	(0.0 - 0.8)	Ref.		Ref.	
Impact National Benchmark Database								
Overall[‡]								
Exenatide	3	11,527.9	0.3	(0.1 - 0.8)	0.8	(0.2 - 3.4)	0.8	(0.2 - 3.6)
OADs	5	16,577.4	0.3	(0.1 - 0.7)	Ref.		Ref.	
1 to <2 years								
Exenatide	0	5,654.2	0.0	(0.0 - 0.5)	NC		NC	
OADs	4	8,147.3	0.5	(0.1 - 1.3)	Ref.		Ref.	
≥2 years to <3 years								
Exenatide	3	3,494.1	0.9	(0.2 - 2.5)	NC		NC	
OADs	0	4,923.5	0.0	(0.0 - 0.6)	Ref.		Ref.	
≥3 years								
Exenatide	0	2,379.7	0.0	(0.0 - 1.3)	NC		NC	
OADs	1	3,506.5	0.3	(0.0 - 1.6)	Ref.		Ref.	

Abbreviations: IR=Incidence rate per 1,000 person-years; HR= Hazard ratio; Ref.=Reference; NC= Not calculable.

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins.

[+]The unadjusted models are based on the propensity score matched cohorts, but do not adjust for any other variables.

****Adjusted for imbalanced variables, including cohort initiation in 2006, metformin, sulfonylureas, and/or thiazolidinediones use during the baseline period, number diabetes drug dispensings, days from the start of the initiation period until initiation date, and number of drugs dispensed.***

[‡]The duration here is the time since one-year post drug initiation

In the LSRD, there were 8 cases of thyroid cancer among the exenatide initiators and 7 cases of the same cancer among the OAD initiators (Executive Summary Table 2). The Impact database also had 8 thyroid cases in the exenatide cohort, and 9 thyroid cases among the OAD initiators. In the LSRD, the overall IR for thyroid cancer among exenatide initiators was 0.4 (95% CI: 0.2 – 0.8) per 1,000 person-years and 0.2 (95% CI: 0.1 – 0.5) per 1,000 person-years among OAD initiators. The overall, unadjusted HR of thyroid cancer among exenatide initiators compared to OAD initiators was 1.8 (95% CI: 0.6 – 5.0) and the adjusted HR was 2.0 (95% CI: 0.7 – 5.6**).** ***When stratified across follow-up, the IRs in both cohorts fluctuated. Similar results were found in the Impact database.***

Executive Summary Table 2 (Report Table 5). Incidence of Algorithm-identified Thyroid Cancer among Exenatide Initiators and Other Antidiabetes Drug Initiators (Overall and by Follow-Up Since Treatment Initiation)----Time-Fixed Analysis (Excluding People with Baseline DPP-4 Inhibitors/GLP-1 Receptor Agonist Use and/or Events and Person-time in the First Year after Drug Initiation)

	Events	Person-years	IR	95% CI	Unadjusted[+]		Adjusted*	
					HR	95% CI	HR	95% CI
Life Sciences Research Database								
Overall[‡]								
Exenatide	8	20,288.7	0.4	(0.2 - 0.8)	1.8	(0.6 - 5.0)	2.0	(0.7 - 5.6)
OADs	7	29,856.5	0.2	(0.1 - 0.5)	Ref.		Ref.	
1 to <2 years								
Exenatide	3	9,693.2	0.3	(0.1 - 0.9)	1.0	(0.2 - 4.7)	1.1	(0.2 - 5.1)
OADs	4	14,030.0	0.3	(0.1 - 0.7)	Ref.		Ref.	
≥2 years to <3 years								
Exenatide	3	6,146.6	0.5	(0.1 - 1.4)	2.5	(0.4 - 15.6)	2.7	(0.4 - 17.7)
OADs	2	8,770.9	0.2	(0.0 - 0.8)	Ref.		Ref.	
≥3 years								
Exenatide	2	4,449.0	0.4	(0.1 - 1.6)	3.6	(0.3 - 41.3)	3.7	(0.3 - 43.7)
OADs	1	7,055.6	0.1	(0.0 - 0.8)	Ref.		Ref.	
Impact National Benchmark Database								
Overall[‡]								
Exenatide	8	11,515.5	0.7	(0.3 - 1.4)	1.3	(0.5 - 3.3)	1.3	(0.5 - 3.4)
OADs	9	16,556.1	0.5	(0.2 - 1.0)	Ref.		Ref.	
1 to <2 years								
Exenatide	3	5,648.5	0.5	(0.1 - 1.6)	0.6	(0.2 - 2.4)	0.6	(0.2 - 2.5)
OADs	7	8,141.5	0.9	(0.3 - 1.8)	Ref.		Ref.	
≥2 years to <3 years								
Exenatide	3	3,490.2	0.9	(0.2 - 2.5)	1.9	(0.3 - 11.7)	1.9	(0.3 - 12.0)
OADs	2	4,916.3	0.4	(0.0 - 1.5)	Ref.		Ref.	
≥3 years								
Exenatide	2	2,376.9	0.8	(0.1 - 3.0)	NC		NC	
OADs	0	3,498.3	0.0	(0.0 - 0.9)	Ref.		Ref.	

Abbreviations: IR=Incidence rate per 1,000 person-years; HR= Hazard ratio; Ref.=Reference; NC= Not calculable.

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins.

+The unadjusted models are based on the propensity score matched cohorts, but do not adjust for any other variables.

****Adjusted for imbalanced variables, including South census region, cohort initiation in 2005, metformin, sulfonylureas, and/or thiazolidinediones use during the baseline period, and number of drugs dispensed***

‡The duration here is the time since one-year post drug initiation

In the analysis of cumulative exposure in the LSRD, there were no clear trends in the IRs of pancreatic cancer when assessing increasing cumulative exenatide exposure, and the 95% CIs were overlapping. Furthermore, compared to non-use, there were no clear trends among the relative risks (RRs) for pancreatic cancer with longer cumulative use of exenatide. In analyses adjusting for imbalanced covariates between cohorts following propensity score matching, the RRs were slightly closer to the null. There were fewer cases of pancreatic cancer in the Impact database, making the results more difficult to interpret.

When examining the effect of cumulative exenatide use compared to non-use on the incidence of thyroid cancer there was no clear trend in the IRs and RRs with longer exenatide use in the LSRD and Impact database.

These analyses do not support or refute the presence of an increased incidence of pancreatic or thyroid cancers among exenatide initiators when compared to other antidiabetes drug initiators. There were differences in the direction and strength of point estimates between the two databases. Determining the underlying reasons (e.g., chance, unmeasured confounding, detection bias, and/or protopathic bias) for variability is challenging given the small number of outcomes.

2. Introduction

Diabetes is a major public health concern globally and especially in the US. According to the US Centers for Disease Control and Prevention, over 23 million people in the US have diabetes[1]. Type 2 diabetes (T2D) accounts for 90-95% of diagnosed cases of diabetes and is associated with older age, obesity, family history of diabetes, gestational diabetes, impaired glucose metabolism, physical inactivity, and certain ethnic groups such as African Americans, Hispanics, and American Indians. Diabetes is a leading cause of blindness, end-stage renal disease and non-traumatic lower limb amputation, and is a major risk factor for coronary artery disease and stroke [2]. Interventions that improve glycemic control reduce microvascular complications involving the eyes, kidneys and nerves, and may reduce macrovascular complications such as myocardial infarction[3].

Many of the traditional diabetes medications (such as sulfonylureas [SU], metformin, α-glucosidase inhibitors, thiazolidinediones [TZDs], and insulin) lower blood glucose, but they may also cause hypoglycemia, gastrointestinal symptoms, or weight gain. The American Diabetes Association recommends a hemoglobin A1c goal of less than 7%, but many patients with diabetes are unable to achieve this goal by using combinations of drugs, diet, and exercise. Most patients with T2D will eventually require combination therapy to maintain glycemic control. Several newer treatments have been developed that provide valuable alternatives to improve long-term glycemic control for T2D [4]. Exenatide is one of the newer treatment alternatives available (initially approved by the

Food and Drug Administration on 28 April 2005). Exenatide is a glucagon-like peptide-1 (GLP-1) receptor agonist that enhances glucose-dependent insulin secretion by pancreatic beta cells, suppresses inappropriately elevated glucagon secretion, and slows gastric emptying. The drug is delivered via injection in twice-daily or extended release (i.e., once-per-week) formulations.

Review of recent data on the newer antidiabetes agents has noted signals of pancreatitis and pancreatic and thyroid malignancies with GLP-1 receptor agonists. Acute pancreatitis has been reported as a rare adverse effect of exenatide therapy principally though passive post-marketing surveillance; however, this association was not supported by recent pharmacoepidemiologic studies [5-7]. Liraglutide, another GLP-1 receptor agonist, was found to increase the risk of benign C-cell hyperplasia in rodents exposed to doses similar to approved doses for humans. However, rodents receiving doses 8 times above approved levels were more likely to develop malignant C-cell carcinomas, leading to concern about the occurrence of medullary thyroid cancer (MTC), a C-cell cancer that produces excessive calcitonin, in humans receiving GLP-1 receptor agonist therapy [8].

Indeed, in rodent toxicology studies, C-cell hyperplasia and C-cell carcinoma (the rodent equivalent of human MTC) were detected within animals exposed to the long-acting GLP-1 receptor agonist class (e.g., liraglutide and exenatide once weekly). A GLP-1 receptor-mediated mode of action has been proposed with respect to carcinogenicity in the rodent thyroid [9]. In the thyroid of various species, including rodents, monkeys, and humans, GLP-1 receptors are expressed only on C-cells, and not on other thyroid cell types [10]. Accordingly, across multiple preclinical studies of all GLP-1 receptor agonists in rodents, which included near-lifetime treatment with high doses, there was no evidence of an increase in thyroid tumors of cell types other than C-cells.

Data, both from clinical studies (approximately 4,300 patient-years of exposure) and post-marketing exposure (approximately 2.2 million patient-years), have shown no evidence for an increased risk of thyroid malignancy in general; no cases of medullary thyroid cancer have been reported with either exenatide formulation. In primates, there is no detectable stimulation of calcitonin release by GLP-1 receptor activation. Calcitonin concentrations were not elevated in human subjects with diabetes following up to 2 years of clinical exposure to liraglutide or exenatide once-weekly.

This study aims to clarify these conflicting data by estimating the association between exenatide use and the occurrence of pancreatic cancer and thyroid neoplasm.

3. Objectives

The objectives of this study were to estimate the absolute and relative incidence of claims-based algorithm-identified pancreatic cancer and thyroid neoplasm (including

benign and malignant thyroid neoplasm) among exenatide initiators relative to initiators of other antidiabetic drugs (OADs).

3.1. Primary Objectives

- To estimate the absolute and relative incidence of newly diagnosed pancreatic cancer among initiators of exenatide compared to matched initiators of OADs, overall and by duration of follow-up and drug exposure—assessing events one-year after drug initiation.
- To estimate the absolute and relative incidence of newly diagnosed thyroid cancer among initiators of exenatide compared to matched initiators of OADs, overall and by duration of follow-up and drug exposure—assessing events one-year after drug initiation.

3.2. Secondary Objectives

- To estimate the absolute incidence of benign thyroid neoplasm, MTC and non-MTC neoplasms in initiators of exenatide and OADs—assessing events one-year after drug initiation.

4. Methods

This was a retrospective cohort study designed to compare the incidence of pancreatic malignancy and thyroid neoplasm among initiators of exenatide and among initiators of OADs. The exposure group (exenatide cohort) was matched to the comparison group (OAD cohort) using propensity scores. Each outcome was identified by an algorithm developed using claims data. The primary analyses included a time-fixed analysis for pancreatic cancer and thyroid cancer, in which the follow-up time was categorized according to the initial exposure status. The secondary analyses included the time-fixed analytic approach for the subgroups of thyroid neoplasm (MTC, non-MTC, and benign thyroid neoplasm) and analyses of cumulative exposure for pancreatic cancer and thyroid cancer that categorized person-time based on the cumulative dose or duration of exenatide use. Additionally, sensitivity analyses were conducted to evaluate the effect of residual confounding on the main study results, and evaluate the presence of detection bias.

4.1. Data Sources

The data sources included person-identifiable and de-identified health insurance claims data from the Life Sciences Research Database (LSRD, formerly Normative Health Information) and de-identified claims data from the Impact National Benchmark Database. The LSRD contains eligibility, pharmacy claims, and medical claims data from a large US health plan affiliated with OptumInsight. In 2011, there were 12.7 million

members with enrollment, medical and pharmacy claims. The individuals covered by this health plan are geographically diverse across the United States. The age and gender distribution of the LSRD population approximates that of the US population for all age categories through 64 years. For persons aged 65 years or older, the LSRD database has proportionately fewer members than does the US population. In this database, we combined the patient-identifiable population with the de-identified population to increase the sample size.

The Impact database contains comprehensive, de-identified US healthcare claims that, like the LSRD, are representative of the non-elderly, insured population in the US. The database contains inpatient, outpatient, and pharmacy claims, lab results, and enrollment information on more than 28 million lives since 2004. Approximately 73% of all patients in the database have both medical and pharmacy benefits and, on average, 27.8 months of enrollment and claims information.

4.2. Institutional Review Board / Privacy Board Approvals

This study used identifiable and de-identified insurance claims data. To comply with HIPAA Privacy Regulations, we sought a Waiver of Patient Authorization for access to protected health information from a Privacy Board and approval from an Institutional Review Board for general study oversight, including use of the de-identified claims data. Confidentiality of patient records was maintained at all times. This study report contains aggregate data only and does not identify individual patients or physicians.

4.3. Study Population

The study population consisted of patients included in the LSRD or the Impact database with at least 9 months of continuous enrollment in the underlying health insurance plan between 01 September 2004 and 31July 2010. Patients were eligible for cohort entry starting on 01 June 2005 (the date of exenatide launch). Initiators of exenatide or OADs were included in the study according to the following inclusion and exclusion criteria:

4.3.1. Inclusion criteria

- Had complete medical and pharmacy benefits and 9 months of continuous enrollment in the health plan prior to cohort entry date, and
- Had a diagnosis of T2D (ICD-9-CM 250.x0, 250.x2) during the 9-month baseline period, inclusive of the cohort entry date, and
- Had a dispensing of at least one antidiabetes drug other than the initiating drug during the 9-month baseline period, inclusive of the cohort entry date.

4.3.2. Exclusion criteria

- Had a diagnosis of T2D but had no dispensings of antidiabetes drugs during the 9-month baseline period inclusive of cohort entry date, or
- Had a dispensing of exenatide during the 9-month baseline period inclusive of cohort entry date in the OAD cohort, or
- Had a dispensing of a drug from the same class as the initiating drug during the 9-month baseline period, or
- Had claims associated with pancreatic and thyroid neoplasm (including benign and malignant neoplasm) during the 9-month baseline period.

4.4. Study Cohorts

4.4.1. Initiators of Exenatide

The pharmacy claims were searched for the initiation of exenatide. The date of cohort eligibility was defined by the date of the first dispensing of exenatide, without an exenatide dispensing in the prior 9-months (exclusive of cohort entry date), but with at least one OAD dispensing in the prior 9-month period inclusive of cohort entry date. The rationale for requiring that patients are taking at least one other OAD was to limit cohort membership to patients initiating exenatide (or an OAD in the OAD cohort) as add-on therapy with the aim of improving comparability of patient characteristics across the exposure cohorts.

4.4.2. Comparison Cohort: OADs Initiators

A contemporaneous comparison cohort of new users of OADs was identified in the same fashion as exenatide initiators. The date of cohort entry was defined by the date of the first dispensing of an OAD with no dispensing of the same drug or drug class in the prior 9-month period (exclusive of cohort entry date), but with at least one different OAD dispensing in the prior 9-month period (inclusive of cohort entry date). The OADs of interest are listed in Appendix I. Dipeptidyl peptidase-4 (DPP-4 inhibitors)/ Glucagon-like peptide-1 (GLP-1) receptor agonists were not included in the primary analysis as DPP-4 inhibitors/GLP-1 receptor agonists have a similar mechanism of action as exenatide and have been reported to be associated with pancreatic and thyroid cancer [8]. Instead, we chose a comparison cohort of OAD users who we assumed were not at increased risk of thyroid or pancreatic neoplasm as a result of the antidiabetes medication regimen.

For patients using multiple antidiabetes medications during the study period, we preferentially chose users of exenatide first, such that a person who initiated exenatide and metformin during the study period was assigned to the exenatide cohort even if s/he initiated exenatide later than metformin. This hierarchical cohort selection process allowed exenatide-exposed person-time to be attributed to the exenatide cohort in the primary analysis. Although handling cohort creation in this way can result in immortal

person-time bias [11], in previous work we observed no material bias with this approach in similar cohorts [12].

4.5. Exclusion of Patients with Baseline Use of DPP-4 Inhibitors or GLP-1 Receptor Agonists

We excluded patients with baseline use of DPP-4 inhibitors or GLP-1 receptor agonists (other than exenatide) following propensity score matching, but before identifying the outcomes and beginning the outcome analyses. These patients were excluded from the analysis because of concern around masking a class effect; however, these patients also may be a more representative cohort with regards to comorbidities and diabetes severity.

4.6. Exposure Measures

Exposure to exenatide (and OADs) was defined in a time-fixed and a time-dependent manner. The time-fixed exposure to exenatide and OADs was based on the exposure status at the time of drug initiation. This analysis allowed for attribution of remote events (i.e., pancreatic/thyroid cancers occurring at least one year after initiation of the study drugs) to the initial exposure. The dynamic nature of exposure to exenatide was also measured to allow for the assessment of the risk associated with cumulative exposure to exenatide. In this analysis, exposure was classified by ascertaining the time-dependent cumulative dose and duration of exposure across the study period. The cumulative dose of exenatide exposure was calculated according to the number of dispensings, days supplied, and dosage formulation of the product—taken as the sum of the micrograms of each twice-daily dose over all doses dispensed to the patient. Cumulative duration was measured by summing the days-supply across unique exenatide dispensings over time, including a grace period to allow for modest non-adherence. Patients who refilled a study drug within 31 days following the end of days-supply of the previous dispensing were considered continuing users of the drug. Cumulative dose and duration were not calculated for OADs while all the person-time for each OAD was pooled together and classified as unexposed.

4.7. Outcome Identification

4.7.1. Claims Identification of Outcomes

The primary outcomes were newly diagnosed pancreatic cancer and thyroid neoplasm occurring at least one year following cohort entry. We identified outcomes using validated algorithms that defined patterns of claims that were highly suggestive of true thyroid or pancreatic neoplasm (based on diagnosis and procedure codes from the claims data). We began with algorithms defined *a priori,* which we then validated within the subset of the LSRD where medical records were available for abstraction. The algorithms were then modified to improve their validity (measured by the positive

predictive value). Next, we used the revised algorithms for case ascertainment in all segments of the data: the patient identifiable and de-identified segments of the LSRD and Impact databases. The details of the algorithms are in Appendix II and Appendix III. Details of the validation process follow in Sections 4.7.2 through 4.7.5.

4.7.2. Review of Claims Profiles

When identifying cases using the predetermined algorithms, each potential case was assigned a case date corresponding to the first date of diagnosis in the claims data. A chronological listing of claims data (claims profiles) of the identified cases in the identifiable portion of the LSRD database were extracted from 3 months before and 9 months after the claims-based diagnosis date. A clinical consultant performed a detailed review of the claims profiles and decided which claim corresponded to the facility or provider with the medical record most likely to contain the information necessary for case adjudication. Upon the review of claims profiles, the reviewer selected two providers (primary and alternative) for each case in order to maximize the chance to abstract available medical records. Records were first sought from the primary provider and, if not available, subsequently the alternate provider. The order of preference for choosing types of providers for medical record abstraction (primary and alternate) was as follows:

1. The hospital where the patient was diagnosed or treated for pancreatic cancer or thyroid neoplasm;
2. The surgeon associated with pancreatectomy or thyroidectomy;
3. Medical specialists (e.g. endocrinologist, oncologist) who treated the patients for pancreatic cancer or thyroid neoplasm;
4. Other (e.g. consultation, primary care physician).

Once primary providers were identified, they were contacted with a request for their patient's medical record. The date of the claims line corresponding to a provider was set as the date of service. This review process was blinded to study drug exposure.

4.7.3. Medical Record Abstraction

The medical record abstraction forms were developed to collect information from the 9 months prior to the date of service through 2 months after the date of service in order to collect enough information for case adjudication. The abstraction forms (Appendix IV) were reviewed and finalized by the clinical experts in pancreatic cancer and thyroid neoplasm. The abstractors were trained to use the abstraction forms and to blind the protected health information (PHI) items and study exposures. The corresponding providers were contacted and asked to participate in the study by mailing the copies of the IRB and Privacy Board approvals and a brief description of the study. Medical

record abstractors then followed-up with the providers to ask permission to access specific patients' medical records for the purpose of collecting data related to the outcome of interest.

The medical records of the potential cases from both cohorts identified from the claims algorithms and screened by profile review were sought. We included patients matched and unmatched on the propensity score (in order to provide enough information for algorithm development and revision given the rare occurrence of pancreatic cancer and thyroid neoplasm).

Abstractors blinded medical records electronically and quality control on a 10% sample of medical records. The blinded photocopies of medical records were returned to OptumInsight. Research associates at OptumInsight also performed a quality check on a random 10% sample of the blinded medical records to ensure the identifiable information was completely blinded before forwarding the de-identified records to an adjudicator for review.

4.7.4. Adjudication of Outcomes

A medical record adjudication form was developed for each outcome (Appendix IV) to include the criteria necessary for the confirmation of the neoplasms of interest. Each adjudication panel comprised 2 adjudicators; the pancreatic cancer panel comprised one oncologist in pancreatic cancer and one general oncologist, and the thyroid cancer panel comprised one specialist in thyroid neoplasm and one general oncologist. Each panel focused on the adjudication of study outcomes among the patient-identifiable subset in the LSRD. The adjudication elements were ultimately the responsibility of the independent adjudicators and included key diagnostic questions, case status, event onset date, and tumor stage. Discrepant adjudications were resolved by consensus among the adjudicators with an OptumInsight senior scientist/clinician serving as mediator. All the reviewers were blinded to exposure status as described in Section 4.6.3. Each medical record was adjudicated as a definite, probable, possible or non-diagnostic case. Only definite and probable cases were considered confirmed cases and included in the analyses that gave rise to the case algorithms (Section 4.7.5).

4.7.5. Algorithm-Based Identification of Outcomes

After adjudication of potential outcomes, the positive predictive value (PPV) was estimated for the algorithms developed *a priori* (the relaxed algorithms). In response to the observation that the algorithms developed *a priori* could plausibly be improved, these algorithms were revised into more restrictive case definitions according to the medical records/profiles review and clinical knowledge. Please see Appendix III for the restrictive algorithms. The restrictive algorithms required the presence of the surgery, chemotherapy, and radiotherapy, and the absence of corresponding benign neoplasms.

The PPV of each restrictive algorithm was also calculated. The restrictive algorithms with the highest PPVs were used to identify the outcomes of interest in this study.

4.8. Potential Cofounders

A broad range of baseline (i.e., leading up to cohort entry) characteristics including demographics, diagnoses, medical procedures, drug use, and health care utilization was derived from the claims data.

Demographics

- Age, sex, race
- Geographic area
- Cohort entry year

Diabetes severity indicators

- Use of oral antidiabetes medication
- Dispensings of one, 2, or 3 study medications within 45 days of cohort entry
- Peripheral neuropathy
- Nephropathy
- Retinopathy

Cardiovascular disease indicators

- Hypertension
- Hyperlipidemia
- Hypertriglyceridemia
- Ischemic heart disease
- Myocardial infarction
- Congestive heart failure
- Stroke

Other

- Health care utilization (e.g. the number of days hospitalized in prior 9 months, hospitalization within 45 days of the cohort entry date, number of different ICD-9 diagnoses, number of different drugs dispensed, number of physician visits, emergency department visits and costs of facility and pharmacy, etc.)

Additionally, the 100 most prevalent drug classes dispensed to exenatide initiators relative to the comparator cohorts, along with the 100 most prevalent diagnoses (at the 3-digit ICD-9-CM level) and 100 most prevalent procedures were included.

4.9. Statistical Analysis

4.9.1. Baseline Characteristics

The baseline characteristics, such as demographics, medical conditions (e.g., baseline malignancies), procedures, drug dispensings, and health care utilization measures, were described among the exenatide and OAD cohorts. Continuous variables were summarized by mean and standard deviation or median and interquartile range and categorical variables were summarized by frequency and percentage.

4.9.1.1. Propensity Score Development and Matching

Each exenatide initiator was matched to up to 2 OAD initiators (including 1:1 and 1:2) on the estimated propensity score with the aim of achieving balance between comparison groups in terms of all identified predictors of exenatide initiation. Variables for inclusion in the propensity models were selected based on *a priori* knowledge (e.g. clinical plausibility), prevalence of the variable (e.g. the 100 most prevalent diagnoses), statistical significance, and c-statistics between exenatide initiators and OAD initiators. First, the 10 variables with the highest c-statistic as well as a set of clinically important variables (e.g., metformin use in baseline, number of physician visits, number of laboratory tests) were forced into the model. Second, time indicators (i.e., calendar quarter) were created to assess the interactions between calendar year and the 10 variables most predictive of exenatide initiation, based on univariate c-statistic, to accommodate changes in the way that antidiabetes drugs were used over time. Variables with time interaction terms having a p-value <0.1 were forced into the model. The propensity scores were estimated using an unconditional logistic regression model by including the forced variables and via a stepwise selection process for the remaining predictors of exenatide initiation with a p-value of 0.2 for model entry and 0.3 for retaining.

The propensity score was the fitted value of the probability of being a member of the exenatide cohort, given membership in the study population and the covariate pattern. Each subject was assigned a propensity score, and each exenatide initiator was matched up to 2 OAD initiators using a greedy matching algorithm performed to the 8th digit of the propensity score first and to 7th, 6th up to the 1st digit. A commonly used approach, a greedy matching algorithm matches a treated patient (i.e., exenatide initiator) to an untreated patient (OAD initiator) based on propensity scores, ensuring that the patients' scores equal each other starting at a certain level of precision and decreasing until all treated patients are matched [13;14].

4.9.1.2. Control for Residual Confounding and Time-Varying Covariates

After matching, "trimming" was performed in the patients who were assigned extreme values of the propensity score in order to exclude subjects who were apparently not candidates for exenatide use or who were absolute candidates for exenatide use. Patients with the lowest 2% of propensity scores in the exenatide cohorts and their matched OADs initiators were excluded. Similarly, the patients with the top 2% of propensity scores in OAD cohorts and their matched exenatide initiators were excluded. This "trimming" was done with the aim of reducing the impact of unmeasured confounding.

While the propensity score matching accounted for most of the measured confounding, residual confounding remained due to some minor differences in measured characteristics after matching. Covariate imbalance was defined as an absolute standardized difference > 0.1 (difference between the 2 mean values divided by the standard deviation)[15]. These remaining imbalances were identified and adjusted for in the outcome analyses.

For the analysis of cumulative dose and duration, we defined a set of time-varying covariates representing use of each OAD within in each stratum of cumulative duration or dose. These covariates were included in the analysis of cumulative exposure regression models.

4.9.2. Time-Fixed Analyses

4.9.2.1. Person-time

At-risk person-time for each outcome was calculated from one-year post drug initiation until the first occurrence of a study outcome (i.e., pancreatic cancer or thyroid neoplasm), disenrollment from the health plan, or the end of the study period (31 December 2010). Person-time within the first year following the cohort entry date was not considered at-risk for the primary analysis as the outcomes occurring during this period were unlikely to be affected by use of the initiated medications given the expected long latency period of the outcomes. For each study event, the follow-up was censored for that outcome at the first occurrence of that specific study event, but we continued to follow patients for the other outcomes. Follow-up person-time, starting one-year after drug initiation, was summed and characterized with respect to exenatide and OAD initiators, in totality and stratified by duration of follow-up. The categories for duration of follow-up were as follows: 1 to <2 years, ≥2 years to < 3 years, and ≥3 years. This classification was based on person-time, such that for each person, his or her experience in the 1 to <2 years of follow-up was allocated to that category, with subsequent experience as allocated to subsequent categories (e.g., ≥2 years to < 3

years). Thus, some patients contributed person-time to different categories of follow-up duration. The person-time for each type of newly diagnosed thyroid neoplasm was estimated for the 2 cohorts, in totality and by subgroups of thyroid neoplasm (e.g., benign tumor, MTC, and non-MTC neoplasms).

4.9.2.2. Incidence Rate and Rate Ratio Estimation

For each cohort, we tabulated the number of outcome events and corresponding person-time overall and per stratification of follow-up duration. The incidence rate (IR) of each outcome observed one year following drug initiation was calculated as the number of events divided by the corresponding sum of the person-years at-risk. Similarly, the incidence rate of each outcome in the subgroups of patients with and without concurrent use of insulins in the compared cohorts was also calculated. Concurrent use of insulins and the study exposure (e.g., exenatide) was defined as the use of insulin within 32 days before and after cohort entry. Any insulin use beyond the 32 days window was defined as non-concurrent use with exenatide or OADs.

Kaplan-Meier plots for pancreatic and thyroid cancer were provided to depict the cumulative probability of event-free time among the propensity score matched cohorts. Cox proportional hazards regression models were used to estimate the HRs and 95% CIs of newly diagnosed pancreatic cancer and thyroid neoplasm among exenatide initiators compared with OADs initiators, by study outcomes, and by the duration of follow-up. Additional adjustment occurred through the stratification of models by duration and the analyses with DPP-4 inhibitors/GLP-1 receptor agonists removed.

Because covariate balance achieved through propensity score matching may not hold when the data are aggregated across matching ratios (1:1 vs. 1:2 exenatide to OAD matching), all regression models were conditioned on the matching ratio. Moreover, because the standardized differences (a measure of covariate balance across exposure groups) were calculated without regard to the matching ratio, some covariate imbalances identified may be false positives in that they may not be differentially distributed across exposure, conditional on the matching ratio—only in the aggregate. Thus, we took a conservative approach to identifying covariates to include in the regression models, because covariates that are imbalanced in the aggregate are not imbalanced when the regression models were conditioned on the matching ratio.

The IRs and HRs were estimated separately in the LSRD and the Impact database. The results were not pooled, because there were inconsistent estimates across databases.

4.9.2.3. Sensitivity Analysis

A sensitivity analysis was conducted to evaluate the potential bias of excluding events occurring within the first year of drug initiation by repeating the analysis excluding only events occurring within the first 6 months after study entry (i.e., including events that

occur 7–12 months after initiation). The estimates that included the outcomes during the first 6 months after drug initiation were assumed to reflect outcomes that cannot be affected by recent antidiabetes drug initiation. To observe any changes in estimates, we added the additional duration category of 6 months post-initiation through the end of 12 months of follow-up.

Another sensitivity analysis was performed to compare the incidence of pancreatic and thyroid cancer among patients who initiated exenatide compared with patients who initiated DPP-4 inhibitors/GLP-1 receptor agonists only, patients who initiated OADs excluding DPP-4 inhibitors/GLP-1 receptor agonists, and patients who initiated OADs including DPP-4 inhibitors/GLP-1 receptor agonists. This sensitivity analysis was conducted to test the hypothesis that the effects of exenatide and DPP-4 inhibitors/GLP-1 receptor agonists on the occurrence of pancreatic and thyroid cancer are similar.

Additionally, we conducted a sensitivity analysis to quantify the effects of potential residual confounding on the association between exenatide exposure and pancreatic cancer or thyroid cancer. One of the potential sources of residual confounding is unmeasured confounding. Extreme obesity was considered a potential unmeasured confounder for the association between exenatide and outcomes of interest, as extremely obese subjects are more likely than normal weight patients to develop pancreatic or thyroid cancer[16], and may be more likely to use exenatide given that exenatide is preferentially prescribed to patients with poorly-controlled diabetes. A similar analysis was also conducted for smoking, another potential unmeasured confounder considered.

The prevalence of smoking or obesity among exenatide initiators, OAD initiators and overall were estimated from the data collected during the Amylin-sponsored study[6] of exenatide and acute pancreatitis by constructing a study population with the same eligibility criteria as the present study. We applied the rule-out approach presented by Schneeweiss et al [17] to explore the effect of residual confounding over a wide range of relative risks of the unmeasured confounder and the disease/outcome (RR_{CD}) and the odds ratio between the unmeasured confounder and the exposure (OR_{CE}). Generated figures show how strong an unmeasured confounder must be to explain fully the observed findings, or the apparent relative risk (ARR).

4.9.3. Analysis of Cumulative Exposure

4.9.3.1. Person-time

Among the exenatide initiators, the person-time of each person was classified into different ranges of cumulative dose and duration of exenatide use. This classification was designed so that persons could contribute to multiple categories of cumulative dose or duration, according that person's actual use (see the Statistical Analysis Plan for

details). The stratification of cumulative dose and duration was determined according to the distribution of the observed values. For patients with multiple outcomes, person-time for each outcome was censored and calculated separately. Person-time, including that accumulated within the first year following the cohort entry date, was summed and characterized with respect to exenatide use by the categories of cumulative duration and dose. The person-time of all OADs was considered as a whole and for those unexposed to exenatide use (i.e., non-use). The incidence rates and corresponding 95% CIs were calculated within strata of cumulative dose and duration of exenatide use and all OADs as a group.

4.9.3.2. Incidence Rate and Relative Risk Estimation

Poisson regression models were used to estimate relative risk (RRs) and 95% CIs for each outcome (pancreatic and thyroid cancer) comparing different categories of cumulative dose and duration of exenatide use to non-use of exenatide (principally, current use of OADs). Cumulative dose and duration were treated as a time-dependent exposure in the model with each person potentially having multiple records. Cases were counted beginning one year after cohort entry.

To address potential residual confounding introduced when patients switch drug regimens during follow-up, the dynamic use of concomitant antidiabetes drugs across different time periods was captured and treated as time-dependent covariates in the Poisson regression model, along with any covariates that were imbalanced within that category of use, based on tabulations. We assumed that the discontinuation or switching of OADs represented a change of diabetes severity or indication for drug use. We also assumed that this adjustment did not reflect any mediators or colliders; otherwise, the estimates would be biased [18].

All of these analyses were conducted only for outcomes of pancreatic and thyroid cancer within the matched cohorts with the removal of DPP-4 inhibitors/GLP-1 receptor agonists and were conducted separately in LSRD and the Impact database. We reported the databases separately. It should be noted that the 2 databases might represent 2 different populations with discrepant coding systems. To explore the reasons for any database heterogeneity, we compared the characteristics of the subjects included in the 2 databases.

5. Results

5.1. Cohort accrual

From 01 June 2005 through 31 July 2010, there were 69,178 patients with at least one dispensing of exenatide and 1,119,511 patients with at least one dispensing of any other antidiabetes drugs in the LSRD. After applying the exclusion criteria, there were 31,459 exenatide users and 947,252 OAD users who were removed because they were:

continuously enrolled for less than 9 months, without first line treatment with OADs or were without a diagnosis of type II diabetes, or not a new user with existing initiating drug use. We excluded 228 exenatide users and 804 OAD users who had a diagnosis of pancreatic and thyroid neoplasm in the 9 months before cohort entry. In total, 208,946 patients met the inclusion and exclusion criteria for cohort entry, among whom 37,491 were exenatide initiators and 171,455 OAD initiators (Figure 1).

In the Impact database, there were 36,437 exenatide users with at least one dispensing of exenatide and 649,229 OAD users with at least one dispensing of any other antidiabetes drugs. After applying for the inclusion and exclusion criteria, there were 14,352 exenatide users and 535,862 OAD users removed because they were: not continuously enrolled for at least 9 months, without first line treatment with OADs other than initiating drugs or without a diagnosis of type II diabetes, or not a new user with existing initiating drug use. We excluded 164 exenatide users and 581 OAD users who had a diagnosis of pancreatic and thyroid neoplasm in the 9 months before cohort entry. In total, 134,707 patients met the inclusion and exclusion criteria for cohort entry, among whom 21,921 were exenatide initiators and 112,786 OAD initiators (Figure 2).

5.1.1. Matched Cohorts by Propensity Score

After propensity score matching and trimming the extreme values of propensity score, 31,301 exenatide initiators were matched to 49,783 OAD initiators in the LSRD based on the demographics, baseline dispensings, underlying conditions, baseline procedures and health care utilization. In the Impact database, 16,206 exenatide initiators were matched to 25,385 OAD initiators.

5.1.2. Matched Cohorts with DPP-4 Inhibitors/GLP-1 Receptor Agonists and Their Matched Pairs Removed

After the initial matching, but before identification or analysis of outcomes, it was deemed necessary to remove patients and their matches with DPP-4 inhibitors/GLP-1 receptor agonists use in the baseline period. This change decreased the cohorts to 11,978 in the matched exenatide cohort and 17,594 in the matched OAD cohort in the LSRD (Table 1.1a) and decreased the matched exenatide cohort to 6,954 and the matched OAD cohort 10,097 in the Impact database (Table 1.1b). (NOTE: All further tables present the data pre- and post-matching without DPP-4 inhibitor/GLP-1 receptor agonist initiators in baseline.) Tables comparing characteristics of the cohorts pre- and post-matching also present characteristics of the unmatched exenatide initiators.

5.2. Baseline Characteristics

In the LSRD, over 60% of each of the matched cohorts were aged 50 and older, and had more females than males (Table 1.1a). Nearly 60% of patients in each of the matched cohorts were from the South. After matching, standardized differences between cohorts across covariates were less than 0.10 without regard to the matching ratio, with the exception of the 2006 cohort entry year, which was adjusted for in subsequent models using data from the LSRD. Similar to initiators in the LSRD, matched exenatide and OAD initiators in the Impact data were more likely to be over the age of 50 (>68%) (Table 1.1b). However, the number of males and females were nearly equal between the two cohorts, and most matched cohort members were from the Northeast of the United States. The post-matching standardized differences (aggregated across matching ratios) between cohorts across levels of covariates exceeded 0.10 for patients in the South (the exenatide cohort had more patients from the South (20.0%) versus the OAD cohort (15.9%)), and the 2005 cohort entry year (there were slightly more matched OAD initiators (13.9%) than exenatide initiators (10.2%)). These variables were adjusted for in modeling involving the Impact database.

Among the matched cohorts in the LSRD, after type II diabetes, hypertension, hyperlipidemia, and disorders of lipoid metabolism were the most prevalent of identified medical conditions (Table 1.2a). Office visits and tests for hemoglobin A1c were the most prevalent procedures (Table 1.3a) while metformin, sulfonylureas, statins, and lipotropics were the most prevalent drug classes among the matched cohorts in the LSRD (Table 1.4a). After matching, metformin, sulfonylureas, and thiazolidinediones had aggregated standardized differences that were greater than 0.10, and were adjusted for in models using data from the LSRD.

In the Impact database, the most prevalent medical conditions included type II diabetes and disorders of lipoid metabolism (Table 1.2b). Lipid panels, hemoglobin, and several types of labs and office visits were some of the most prevalent procedures in the matched cohorts, while blood sugar diagnostics, statins, and metformin were the most prevalent drug classes in the Impact database. Metformin, sulfonylureas, and thiazolidinediones had aggregated standardized differences greater than 0.10 and models using the Impact data adjusted for them.

Tables 1.2.1a and 1.2.1b display the prevalence of baselines malignancies during the 9-month baseline period in the Life Sciences Research and Impact databases. Approximately 2.5% of each of the matched exenatide and OAD cohort members had a personal history of malignant neoplasm in both databases.

Tables 1.5a and 1.5b include data on healthcare utilization characteristics among the overall and matched cohorts in the LSRD and the Impact database. In the LSRD, after matching, the aggregated standardized difference for the number of diabetes drug dispensings was greater than 0.10; matched exenatide initiators had 7.5 dispensings on average during the 9-month baseline, as compared to 6.9 diabetes drug dispensings among members of the matched OAD cohort. The number of diabetes drug dispensings was subsequently adjusted for in models using data from the LSRD. After matching, similar differences for the number of diabetes drug dispensings were not found in the Impact database.

Characteristics of the matched cohorts stratified by duration of follow-up for pancreatic cancer are displayed in Tables 1.6.1a and 1.6.1b for the LSRD and Impact databases, respectively. Similarly, Tables 1.6.2a and 1.6.2b include the same characteristics by database, but for thyroid cancer. Of note, based on the aggregated standardized differences, all variables were balanced across the two study cohorts when stratified by cancer type and duration of follow-up. The only exceptions included the number of drug dispensings and the indicator variable for those patients with 5-9 drug dispensings. Rather than adjust for both variables in the models, which could lead to issues of multi-collinearity, models for both databases included only the variable for the number of drug dispensings.

Tables 2.1a and 2.1b describe the top 100 most frequently recorded diagnoses in the claims data amongst the cohort initiators during the 9-month baseline period in the LSRD and the Impact database, respectively. Tables 2.2a and 2.2b build upon tables 2.1a and 2.1b by including the ranking of the top 100 most frequently recorded procedures in the claims data in both databases. Finally, Tables 2.3a and 2.3b both describe the top 100 most frequently recorded drug dispensings among the cohort initiators in both databases.

5.3. Medical Review and Assessment of Algorithm Performance

Table 3 presents data on the medical records identified, sought, and retrieved from the LSRD for validation of the pancreatic and thyroid cancers and benign thyroid neoplasm outcomes. Of the 61 pancreatic cancer cases, 11 of the claims-identified cases were from exenatide initiators; 8 of those 11 cases (73%) were retrieved. The retrieval percentage among pancreatic cancer cases from OAD patients was 72%. There were 53 thyroid cancer cases found in the claims data, 12 of which were in the exenatide cohort and 41 from the OAD cohort. The retrieval percentages were 75% and 85% for the exenatide and OAD groups, respectively. Finally, 34 of the 38 benign thyroid neoplasms were retrieved.

Table 3.1 includes comparisons of the PPVs for each of the algorithms. In general, the restricted algorithms had higher estimated PPVs (Range: 0.75 – 0.95). Of note, the PPV for the first version of the restricted algorithm for pancreatic cancer was noticeably lower (0.65, 95% CI: 0.43 – 0.74), but increased to 0.88 (95% CI: 0.62 – 0.98) after removing patients with a claims history for selected types of cancers. The medullary thyroid cancer restricted algorithm did not identify any cases, therefore requiring the use of the relaxed algorithm, which had a suitably high PPV (0.75 (95% CI: 0.19 – 0.99)). (NOTE: Following the exclusion of DPP-4 inhibitors/GLP-1 receptor agonists users in baseline, several outcomes were excluded from this analysis, including one case of medullary thyroid cancer.)

Table 3.2 stratifies the cancer cases by their tumor stage based on the review of the charts.

In order to assess whether differential detection occurred with exenatide use, pancreatic diagnostic tests and disease diagnosis stratified by cohort were evaluated during follow-up in Tables 3.3a and 3.3b for the LSRD and the Impact database, respectively. There were no discernable differences in pancreatic cancer diagnoses between the exenatide and OAD cohorts during follow-up in the LSRD. Similar negligible differences among some pancreatic diagnostic tests were found in the Impact database. Tables 3.4a and 3.4b present diagnosis and diagnostic testing for thyroid cancer by cohort in the LSRD and the Impact database, respectively. Again, only slight differences in diagnostic tests were found.

Table 3.5 describes the algorithm-identified pancreatic and thyroid cancer cases by chart confirmation status. Three of the pancreatic cancer cases identified by the algorithm were found not to be cases after chart review. Two of the algorithm-identified thyroid cancer cases were not cases as determined by chart review. Because the plan for the study was to identify outcomes on the basis of algorithms, these apparently misclassified cases remain in the analysis as cases.

5.4. Time-Fixed Analysis

Incidence rates (IRs) and hazard rates (HRs) for pancreatic cancer in both databases are presented in Table 4. The HRs were presented as unadjusted and adjusted for covariates imbalanced after propensity-score matching. The analyses were stratified by duration of follow-up and excluded events and person-time in the first year after drug initiation, as well as users of DPP-4 inhibitors/GLP-1 receptor agonists at baseline. In the LSRD, there were 7 cases of pancreatic cancer for an overall IR of 0.3 (95% CI: 0.1-0.7) cases of pancreatic cancer per 1,000 person-years among exenatide initiators and, based on 6 cases of pancreatic cancer, the overall IR was 0.2 (95% CI: 0.1-0.4) cases of pancreatic cancer per 1,000 person-years among OAD initiators. ***When examining the incidence of pancreatic cancer across duration of follow up (allowing for a 1-year***

lag), there was no obvious pattern of the IRs observed in either cohort given that there were no cases in some categories. Similar IR results were found in the Impact database; however, there were more categories of follow-up without cases of pancreatic cancer among exenatide or OAD initiators. The data were not pooled due to the heterogeneity of the estimates between databases.

The Kaplan Meier curves for pancreatic cancer comparing exenatide initiators to OAD initiators did not demonstrate clear differences in time to the diagnosis of pancreatic cancer in either database (Figure 3a and 3b). Indeed, the risk difference between the cohorts was minute (0.0001).

Table 4a presents comparisons of the pancreatic cancer rates among exenatide initiators compared to 3 sub-groups of OAD initiators: OAD initiators including DPP-4 inhibitors/GLP-1 receptor agonists, OADs excluding DPP-4 inhibitors/GLP-1 receptor agonists (i.e., the comparison seen in Table 4), and only DPP-4 inhibitors/GLP-1 receptor agonists. In both databases, the HRs were higher when excluding DPP-4 inhibitors/GLP-1 receptor agonists from the OAD categories.

Table 4b expands on the analysis of the IRs and HRs for pancreatic cancer by including exenatide and OAD initiators with at least one day to 6 months of follow-up, or more than 6 and less than 12 months of follow-up after cohort initiation. ***The IRs for pancreatic cancer in the OAD initiators were highest among those with follow-up of at least 1 day through the first year, though the number of cases was small in some categories. A consistent decreasing pattern was not observed in the IRs across duration of follow-up for the exenatide cohort, In the Impact database, the patterns of the IRs across duration of follow-up in both cohorts were not apparent given that there were no cases of pancreatic cancer in some categories of duration.***

The IRs and HRs for thyroid cancer stratified by duration of follow-up are shown in Table 5. Again, the HRs were presented as unadjusted and adjusted for covariates imbalanced after propensity-score matching. In the LSRD, the overall IR for thyroid cancer among exenatide initiators was 0.4 (95% CI: 0.2 – 0.8) per 1,000 person-years and 0.2 (95% CI: 0.1 – 0.5) per 1,000 person-years among OAD initiators. The overall unadjusted HR of thyroid cancer among exenatide initiators compared to OAD initiators was 1.8 (95% CI: 0.6 – 5.0) and the adjusted HR was 2.0 (95% CI: 0.7 – 5.6), based on 8 and 7 thyroid cancer cases among exenatide and OAD initiators, respectively***. When stratified across follow-up, no obvious pattern of the IRs was observed in either cohort.*** Similar results were found in the Impact database. The data were not pooled due to the heterogeneity of the estimates between databases.

The Kaplan Meier curves for time to diagnosis of thyroid cancer for the two cohorts in the LSRD and Impact databases are displayed in Figures 4a and 4b, respectively.

Table 5a presents comparisons of the IRs and HRs of thyroid cancer among exenatide initiators compared to 3 sub-groups of OAD initiators: OAD initiators including DPP-4 inhibitors/GLP-1 receptor agonists, OADs excluding DPP-4 inhibitors/GLP-1 receptor agonists (i.e., the comparison seen in Table 5), and only DPP-4 inhibitors/GLP-1 receptor agonists. In both databases, the HRs for thyroid cancer were higher when excluding DPP-4 inhibitors/GLP-1 receptor agonists from the OAD categories compared to including the same class of antidiabetes medications in the OAD initiator population.

Table 5b expands on the analysis of the IRs and HRs for thyroid cancer by including those with follow-up between >0 to 6 months and >6 to 12 months after cohort initiation. In the LSRD, ***the IRs for thyroid cancer between exenatide and OAD initiators in the LSRD were generally similar across duration of follow-up although a slight decrease was observed in the OAD cohort. The HRs were higher in the >6 to 12 month duration category, 3.6 (95% CI: 0.7 – 19.1) and 3.5 (0.7 – 18.5) and in the ≥3 years duration category, 3.6 (95% CI: 0.3 – 41.3) and 3.7 (95% CI: 0.3 –43.7) in unadjusted and adjusted models, respectively, than in the other categories. In the Impact database, for those patients with up to 6 months of follow-up time, the incidence rates were 1.3 (95% CI: 0.5 – 2.8) for exenatide initiators and 0.9 (95% CI: 0.3 -1.9) per 1,000 person-years for OAD initiators. Among those with 6-12 months of follow-up in the Impact database, the IRs were 0.3 cases of thyroid cancer per 1,000 person-years among the exenatide cohort versus 1.1 cases per 1,000 person-years among the OAD cohort.*** There were a small number of cases in these stratified analyses, therefore the 95% CIs were overlapping. ***The HRs for thyroid cancer for persons with 6-12 months of follow-up were low for unadjusted (0.2 [95% CI: 0.0 –1.9]) and adjusted (0.3 [95% CI: 0.0 – 2.4]) models.***

The IRs and HRs for benign thyroid neoplasm for exenatide and OAD initiators were generally low (Table 6.1a). No exenatide initiators had medullary thyroid cancer in either database and there were only two cases of this disease in the OAD population (Table 6.1b). In the LSRD there were a total of 8 cases of non-medullary thyroid cancer among exenatide initiators and 5 cases among OAD initiators, for IRs of 0.4 (95% CI: 0.2 – 0.8) cases per 1,000 person-years and 0.2 (95% CI: 0.1 – 0.4) cases per 1,000 person-years, respectively (Table 6.1c). There were the same number of non-medullary thyroid cancer cases (n=8) among exenatide initiators in the Impact database, but 9 cases of this cancer among OAD initiators; the IR for exenatide initiators was 0.7 (95% CI: 0.3 – 1.4) and 0.5 (95% CI: 0.2 – 1.0) for OAD initiators.

There were no cases of pancreatic cancer among exenatide initiators with concurrent insulin use in either database (Table 6.2a). However, there were a total of 4 and 2 pancreatic cancer cases among OAD initiators with concurrent insulin use from in the LSRD and Impact database, respectively.

The incidence of thyroid cancer among exenatide initiators with concurrent insulin is shown in Table 6.2b.

5.5. Analysis of Cumulative Exposure

In the analysis of cumulative exposure in the LSRD, evaluating events beginning one-year post-drug initiation, there did not appear to be a clear trend in the IRs of pancreatic cancer across increasing cumulative time on exenatide (Table 7); the number of cases was small, making the results difficult to interpret. Compared to non-use, the unadjusted RRs for pancreatic cancer went from 1.9 (95% CI: 0.5 – 6.8) for those with up to 1 year's use of exenatide, to 1.5 (95% CI: 0.3 -7.5) for 1 to less than 2 years of exenatide use, on to 2.2 (95% CI: 0.3 – 17.9) for those with cumulative exenatide exposure of 2-3 years. However, the 95% CIs were overlapping and very wide. RRs adjusted for imbalanced variables were slightly attenuated. There were few cases of pancreatic cancer in the Impact database, making the results more difficult to interpret. The data were not pooled due to the heterogeneity of the estimates between databases.

In both databases, when examining the effect of cumulative time on exenatide compared to non-use on the incidence and risk of thyroid cancer we found no clear trends across categories of cumulative exenatide exposure (Table 8). Of note, there were fewer than 4-5 cases in most categories of duration. Similarly, there was not a clear trend among the RRs of thyroid cancer across categories of cumulative exenatide exposure in the databases. Between the two databases, there was only 1 case of thyroid cancer among exenatide initiators in categories of cumulative exposure greater than 2 years, which made the interpretation of the results more difficult.

Table 9 examines the incidence and risk of pancreatic disease stratified by cumulative dose of exenatide use versus non-use. There were few cases of pancreatic cancer in the dosage categories, and there was not a clear trend in the incidence of this cancer. Rate ratios did not consistently increase with larger cumulative dose of exenatide use versus non-use, and the 95% CIs were overlapping.

Thyroid cancer incidence was compared across cumulative exenatide dose levels and non-use in Table 10. The IRs of thyroid cancer were lowest for doses greater than 6,000 mcg in both databases; however, there were a small number of cases as well as overlapping 95% CIs for the IRs across dose levels. Compared to non-use, increasing categories of exenatide were accompanied by RRs with wide, overlapping 95% CIs for all categories.

5.6. Residual Confounding Analysis

Figures 5a and 5b display the apparent relative risk (ARR) plotted against the association (OR_{EC}) between the exposure (exenatide) and the confounder (smoking) as well as the association (RR_{CD}) between the confounder and the outcome (pancreatic

cancer), for the LSRD and Impact databases, respectively. The area to the upper right of the curve represents combinations of the RR_{CD} and the OR_{EC} required to result in the ARR or something more extreme if the un-confounded effect is 1.0. Combinations to the left of the curve represent values that are not sufficient to explain the ARR through confounding. In the case of Figure 5a, the confounding brought about by smoking would need to be more strongly associated with the exposure (OR_{EC} > 2.00) as well as with the pancreatic cancer (RR_{CD} >3 to explain the ARR of 1.5 between exenatide initiation and pancreatic cancer. In Figure 5b, data from the Impact database for pancreatic cancer indicates that while the log OR_{EC} would need to be very small to explain the association between the exposure and smoking, the log RR_{CD} would need to be at least 1.5 to explain the ARR of 0.8.

Similar to the results for the pancreatic cancer in the LSRD, Figure 6a shows that smoking would need to be associated with exenatide exposure with an OR_{EC} >4.00, assuming that smoking were also associated with thyroid cancer with a RR_{CD} >5 in order to account for the ARR between exenatide and thyroid cancer. Figure 6b for the Impact database is similar, though the associations between smoking and the exposure (i.e., OR_{EC}) and confounder (i.e., RR_{CD}) would need to be >2.00. Based on these results, smoking does not seemingly explain the ARR between exenatide initiation and pancreatic or thyroid cancer. Figures 7a (LSRD) and 7b (Impact database) examine the potential for residual confounding caused by obesity to explain the ARR between exenatide initiation and pancreatic cancer. In the case of pancreatic cancer in the LSRD, the OR_{EC} and RR_{CD} would need to be greater than 3 for obesity to account for the ARR. In the Impact database, the log RR_{CD} would need to be greater than approximately 1.5 for obesity to account for the ARR. The associations between obesity and exenatide use and thyroid cancer would need to be much larger (OR_{EC} >6.00 and RR_{CD} >3) to explain the association found in the LSRD (Figure 8a). While not as extreme, the OR_{EC} and RR_{CD} would need to be great than 2 in order for obesity to account for the ARR in the Impact database (Figure 8b). Thus, obesity appears unlikely to explain the ARR between exenatide initiation and pancreatic or thyroid cancer.

6. Discussion

This retrospective cohort study sought to quantify the incidence and risk of pancreatic and thyroid cancer among patients with new use of exenatide, a GLP-1 receptor agonist, as compared to propensity-score matched users of other antidiabetes medications. In the final cohorts, the combined databases included 18,932 in the matched exenatide cohort and 27,691 in the matched OAD cohort. Baseline characteristics, such as gender, age, and cohort entry, as well as baseline diagnosis, procedure, and medication utilization were generally balanced between the cohorts.

6.1. Findings for Pancreatic Cancer

In the time-fixed analysis, the overall IR for pancreatic cancer for exenatide and OAD initiators ranged from 0.2-0.3 cases per 1,000 person-years in the two databases. There were differences in the IRs and HRs for pancreatic cancer when stratifying by duration of follow-up; however, because there were few cases of the outcomes, the confidence intervals were wide and the results remain compatible with chance.

6.2. Findings for Thyroid Cancer

In the LSRD, the IR for thyroid cancer was 0.4 cases per 1,000 person-years for exenatide initiators and 0.2 cases per 1,000 person-years for OAD initiators, while it was 0.7 cases per 1,000 person-years for exenatide initiators and 0.5 thyroid cancer cases per 1,000 person-years for OAD users in the Impact database. Nonetheless, these differences were not statistically significant, including when evaluating both the IRs and HRs for thyroid cancer across duration of follow-up. The analyses of cumulative exposure comparing cumulative exenatide dose or duration to non-use (i.e., primarily, OAD use), showed somewhat similar findings to the time-fixed results, but again, were compatible with chance. Analyses to rule out residual confounding due to obesity and smoking did not demonstrate that such confounding could explain the results of the study. Furthermore, detection bias did not appear to occur in the study.

6.3. Potential Mechanisms

In the primary time-fixed analyses, although the IRs of pancreatic and thyroid cancer in both cohorts fluctuated with duration of follow-up, a slight decrease of IRs was observed in the OAD cohort as the duration of follow-up increased. The larger IRs closer to the start of follow-up could result from the effect of protopathic bias, or the bias introduced when symptoms or signs of the outcome lead to the exposure (i.e., “reverse causality”). Worsening glucose control is a symptom of many forms of pancreatic cancer [19;20], resulting in modification of antidiabetes drug regimens to help control worsening diabetes symptoms. Indeed, uncontrolled diabetes could necessitate switching to second and third-line medications, such as exenatide and other GLP-1 receptor agonists and DPP-4 inhibitors. Similarly, certain forms of thyroid cancer can occur concomitantly with hyperthyroidism, which can lead to worsening glucose control [21;22], though there exists some debate on the direction of this association. Nonetheless, a protopathic bias for these cancers would inflate the incidence rate away from zero, and potentially explain some of this study’s findings. Additional understanding of the length of the pre-diagnosed phase of thyroid and pancreatic cancer and assessment of patients with longer follow-up times may elucidate the presence of a protopathic bias and its potential to explain our study results.

Research has shown that extreme obesity is an important predictor of developing pancreatic or thyroid cancer [16], and obese patients may be more likely to use exenatide given that exenatide is preferentially prescribed to patients with poorly-controlled diabetes. Furthermore, smokers are more likely to develop pancreatic cancer [23], despite smoking having a seemingly protective effect on the development of thyroid cancer [24]. Unfortunately, both smoking and obesity are poorly captured by claims data. Analyses using the prevalence of smoking and obesity based on chart-abstracted data from an earlier Amylin study of exenatide and pancreatitis demonstrated that residual confounding due to unmeasured smoking or obesity could not explain the estimates found in the current study.

In 2007, the FDA issued a safety alert for exenatide and the development of acute pancreatitis, and this and other subsequent announcements about a potential link between GLP-1 receptor agonists and thyroid cancer could have led to increased surveillance and differential detection of pancreatic or thyroid cancer among exenatide users. A comparison of the percentage of exenatide and OAD patients receiving diagnoses and/or diagnostic work-ups for pancreatic and thyroid cancer did not uncover meaningful differences between the cohorts.

Because we preferentially selected exenatide use, the person-time of patients in the OAD cohort was censored at the time of an exenatide dispensing. For patients in the exenatide cohort, their person-time was not censored for the addition of OADs at the time of OADs dispensing. Although this censoring mechanism is a form of informative censoring, it was not anticipated to bias estimates because very few OAD users initiated exenatide during follow-up due to the hierarchical cohort selection.

Other studies have examined the association between exenatide and pancreatic and thyroid cancers. Despite a potential signal of disproportionality in a report summarizing serious adverse events [25], in reviews and meta-analyses, as well as in more recent observational research, a clear association between exenatide and thyroid cancers was not consistently found [7;26;27]. Nonetheless, many of the studies in the reviews/meta-analysis did not have large sample sizes or lengthy follow-up periods.

6.4. Strength and Limitations

A major strength of our study is the use of large administrative claims environments consisting of a representative sample of patients with moderately long follow-up. Commercial claims data generally have short dwell times relative to other administrative databases (e.g., Medicare); however, because of the nature of the population (diabetics), average dwell time is likely longer than the overall average dwell time of approximately 2 years. In our previous work on pancreatitis[6], we observed that patients with at least 9 months of continuous enrollment and a diagnosis of diabetes stayed in the LSRD for an average of 5 years. Indeed, using a claims environment can be a useful

and efficient method for assessing drug safety questions, and techniques such as propensity score techniques can permit careful control of confounding across myriad potential covariates. Despite the large sample size of the LSRD and Impact database, the number of thyroid and pancreatic cancer cases was low, leading to wide confidence intervals and stratified analyses without cases in some strata.

Both the LSRD and Impact database include large populations of employer-based, health insurance recipients, with comparable general characteristics. However, formulary and coverage differences inherent in the respective insurance environments could lead to differential ascertainment of case or exposure status by database and consequently affect the IRs and HRs in the constituent databases. Indeed, there were differences in the direction and strength of point estimates between databases. Despite the differences, determining the underlying reasons (e.g., unmeasured confounding) for variability is difficult to disentangle, given the small number of outcomes and the sensitivity of relative measures of effect, such as HRs, to small numbers.

This study is based on an analysis of automated medical and prescription claims. While claims data are extremely valuable for the efficient and effective examination of health care outcomes, treatment patterns, health care resource utilization, and costs, all claims databases have certain inherent limitations because the claims are collected for the purpose of payment and not research. Presence of a claim for a filled prescription does not indicate that the medication was consumed or that it was taken as prescribed. Medications filled over-the-counter or provided as samples by the physician will not be observed in the claims data. Presence of a diagnosis code on a medical claim is not positive presence of disease, as the diagnosis code may be incorrectly coded or included as rule-out criteria rather than actual disease. Duration of follow-up can be limited in the insurance claims database due to individuals changing health insurance plans.

The use of medical records as the gold standard for outcome classification is also a limitation of this analysis. Indeed, the estimated PPVs are likely an underestimate of the true PPVs if some of the medical records were inconclusive, but did in fact have either pancreatic or thyroid cancer. Therefore, these findings could be viewed as conservative estimates of the claims accuracy for identifying cases of these cancers.

6.5. Conclusions

These analyses do not support or refute the presence of an increased incidence of pancreatic or thyroid cancers among exenatide initiators when compared to other antidiabetes drug initiators. There were differences in the direction and strength of point estimates between the two different databases. Determining the underlying reasons (e.g., chance, unmeasured confounding, detection bias, and/or protopathic bias) for variability is challenging given the small number of outcomes.

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7. Tables

Table 1.1a. Characteristics of Exenatide Initiators and Other Antidiabetes Drugs (OADs) Initiators on the Date of Cohort Entry, Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonists and without 1 year of Follow-up Person Time, Life Sciences Research Database 6/1/2005-7/31/2010

Characteristic	All (N = 102,203)					Matched (N = 29,572)					Not Matched (N = 72,631)	
	Exenatide (N = 15,540)		OAD (N = 86,663)		Standardized Difference	Exenatide (N = 11,978)		OAD (N = 17,594)		Standardized Difference	Exenatide (N = 3,562)	
	N	%	N	%		N	%	N	%		N	%
Age												
≤ 39	1,442	9.3	9,997	11.5	0.07	1,148	9.6	1,911	10.9	0.04	294	8.3
40-49	3,783	24.3	17,841	20.6	0.09	2,855	23.8	4,116	23.4	0.01	928	26.1
50-59	6,415	41.3	31,165	36.0	0.11	4,792	40.0	6,932	39.4	0.01	1,623	45.6
60-69	3,436	22.1	20,026	23.1	0.02	2,742	22.9	3,942	22.4	0.01	694	19.5
≥ 70	464	3.0	7,634	8.8	0.25	441	3.7	693	3.9	0.01	23	0.6
Sex												
Male	6,971	44.9	49,770	57.4	0.25	5,627	47.0	8,315	47.3	0.01	1,344	37.7
Female	8,569	55.1	36,893	42.6	0.25	6,351	53.0	9,279	52.7	0.01	2,218	62.3
Geographic Area												
Northeast	1,031	6.6	7,325	8.5	0.07	828	6.9	1,255	7.1	0.01	203	5.7
Midwest	3,094	19.9	19,995	23.1	0.08	2,441	20.4	3,771	21.4	0.03	653	18.3
South	9,490	61.1	47,392	54.7	0.13	7,186	60.0	10,311	58.6	0.03	2,304	64.7
West	1,925	12.4	11,951	13.8	0.04	1,523	12.7	2,257	12.8	0.00	402	11.3
Cohort Entry Year												
2005	1,628	10.5	33,832	39.0	0.70	1,224	10.2	2,281	13.0	0.09	404	11.3
2006	5,860	37.7	17,784	20.5	0.39	3,753	31.3	6,422	36.5	0.11	2,107	59.2
2007	3,811	24.5	12,538	14.5	0.26	3,184	26.6	3,992	22.7	0.09	627	17.6
2008	2,762	17.8	12,541	14.5	0.09	2,429	20.3	3,027	17.2	0.08	333	9.3
2009	1,479	9.5	9,968	11.5	0.06	1,388	11.6	1,872	10.6	0.03	91	2.6

Note: OADs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins. Standardized difference is calculated by the difference between the 2 proportions divided by the pooled standard deviation.

Table 1.1b. Characteristics of Exenatide Initiators and Other Antidiabetes Drugs (OADs) Initiators on the Date of Cohort Entry, Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonists and without 1 year of Follow-up Person Time, Impact National Benchmark Database 6/1/2005-7/31/2010

Characteristic	All (N = 65,098)					Matched (N = 17,051)					Not Matched (N = 48,047)	
	Exenatide (N = 10,643)		OAD (N = 54,455)		Standardized Difference	Exenatide (N = 6,954)		OAD (N = 10,097)		Standardized Difference	Exenatide (N = 3,689)	
	N	%	N	%		N	%	N	%		N	%
Age												
≤ 39	767	7.2	5,626	10.3	0.11	532	7.7	895	8.9	0.04	235	6.4
40-49	2,516	23.6	10,245	18.8	0.12	1,587	22.8	2,224	22.0	0.02	929	25.2
50-59	4,465	42.0	20,946	38.5	0.07	2,869	41.3	4,156	41.2	0.00	1,596	43.3
60-69	2,660	25.0	14,452	26.5	0.04	1,785	25.7	2,565	25.4	0.01	875	23.7
≥ 70	235	2.2	3,186	5.9	0.19	181	2.6	257	2.5	0.00	54	1.5
Sex												
Male	5,112	48.0	32,293	59.3	0.23	3,463	49.8	5,049	50.0	0.00	1,649	44.7
Female	5,531	52.0	22,162	40.7	0.23	3,491	50.2	5,048	50.0	0.00	2,040	55.3
Geographic Area												
Northeast	6,928	65.1	39,781	73.1	0.17	4,485	64.5	6,820	67.5	0.06	2,443	66.2
Midwest	1,007	9.5	5,602	10.3	0.03	715	10.3	1,110	11.0	0.02	292	7.9
South	2,151	20.2	6,262	11.5	0.24	1,389	20.0	1,604	15.9	0.11	762	20.7
West	557	5.2	2,810	5.2	0.00	365	5.2	563	5.6	0.01	192	5.2
Cohort Entry Year												
2005	1,118	10.5	27,277	50.1	0.95	707	10.2	1,407	13.9	0.12	411	11.1
2006	4,650	43.7	11,085	20.4	0.52	2,427	34.9	3,811	37.7	0.06	2,223	60.3
2007	2,813	26.4	7,333	13.5	0.33	2,078	29.9	2,728	27.0	0.06	735	19.9
2008	1,335	12.5	4,752	8.7	0.12	1,097	15.8	1,315	13.0	0.08	238	6.5
2009	727	6.8	4,008	7.4	0.02	645	9.3	836	8.3	0.04	82	2.2

Note: OADs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins. Standardized difference is calculated by the difference between the 2 proportions divided by the pooled standard deviation.

Table 1.2a. Prevalence of Medical Conditions, Procedures and Drug Dispensings During the 9-Month Baseline Period, Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonists and without 1 year of Follow-up Person Time, Life Sciences Research Database 6/1/2005-7/31/2010

Characteristic	All (N = 102,203)					Matched (N = 29,572)					Not Matched (N = 72,631)	
	Exenatide (N = 15,540)		OAD (N = 86,663)		Stand. Diff.	Exenatide (N = 11,978)		OAD (N = 17,594)		Stand. Diff.	Exenatide (N = 3,562)	
	N	%	N	%		N	%	N	%		N	%
Medical Conditions												
Type II diabetes	15,173	97.6	81,364	93.9	0.19	11,640	97.2	17,017	96.7	0.03	3,533	99.2
Retinopathy*	878	5.6	5,272	6.1	0.02	679	5.7	1,073	6.1	0.02	199	5.6
Hypertension*	11,223	72.2	55,506	64.0	0.18	8,500	71.0	12,269	69.7	0.03	2,723	76.4
Myocardial Infarction*	187	1.2	2,099	2.4	0.09	149	1.2	253	1.4	0.02	38	1.1
Congestive Heart Failure*	490	3.2	4,533	5.2	0.10	389	3.2	651	3.7	0.02	101	2.8
Hypertriglyceridemia*	576	3.7	1,961	2.3	0.08	390	3.3	552	3.1	0.01	186	5.2
Renal disease*	2	0.0	609	0.7	0.12	2	0.0	13	0.1	0.03	0	0.0
Cerebrovascular disease*	289	1.9	3,144	3.6	0.11	236	2.0	380	2.2	0.01	53	1.5
Peripheral neuropathy*	1,827	11.8	7,252	8.4	0.11	1,299	10.8	1,773	10.1	0.03	528	14.8
Hyperlipidemia*	12,791	82.3	60,945	70.3	0.28	9,637	80.5	13,832	78.6	0.05	3,154	88.5
Ischemic heart disease*	2,058	13.2	13,045	15.1	0.05	1,624	13.6	2,377	13.5	0.00	434	12.2
Alcohol Use/Abuse	39	0.3	655	0.8	0.07	31	0.3	61	0.3	0.02	8	0.2
Smoking	326	2.1	2,733	3.2	0.07	272	2.3	420	2.4	0.01	54	1.5
Obesity	3,058	19.7	7,347	8.5	0.33	1,971	16.5	2,610	14.8	0.04	1,087	30.5
Gastroesophageal reflux disease	1,465	9.4	6,965	8.0	0.05	1,081	9.0	1,637	9.3	0.01	384	10.8
Malignant neoplasms >=2 clms	273	1.8	2,501	2.9	0.08	211	1.8	371	2.1	0.03	62	1.7
211 - Benign neoplasm of other parts of digestive system	686	4.4	3,230	3.7	0.03	516	4.3	680	3.9	0.02	170	4.8
216 - Benign neoplasm of skin	646	4.2	2,351	2.7	0.08	462	3.9	642	3.6	0.01	184	5.2
244 - Acquired hypothyroidism	2,562	16.5	9,063	10.5	0.18	1,801	15.0	2,491	14.2	0.02	761	21.4
272 - Disorders of lipoid metabolism	12,673	81.6	59,568	68.7	0.30	9,572	79.9	13,682	77.8	0.05	3,101	87.1
276 - Disorders of fluid, electrolyte, and acid-base balance	666	4.3	7,556	8.7	0.18	535	4.5	838	4.8	0.01	131	3.7
277 - Other and unspecified disorders of metabolism	934	6.0	1,746	2.0	0.20	584	4.9	656	3.7	0.06	350	9.8
285 - Other and unspecified anemias	1,098	7.1	7,593	8.8	0.06	859	7.2	1,254	7.1	0.00	239	6.7
300 - Anxiety, dissociative and somatoform disorders	921	5.9	4,009	4.6	0.06	666	5.6	979	5.6	0.00	255	7.2
305 - Nondependent abuse of drugs	433	2.8	3,716	4.3	0.08	364	3.0	566	3.2	0.01	69	1.9
311 - Depressive disorder, not elsewhere classified	949	6.1	3,976	4.6	0.07	707	5.9	997	5.7	0.01	242	6.8
327 - Organic sleep disorders	837	5.4	1,845	2.1	0.17	615	5.1	729	4.1	0.05	222	6.2

Table 1.2a. Prevalence of Medical Conditions, Procedures and Drug Dispensings During the 9-Month Baseline Period, Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonists and without 1 year of Follow-up Person Time, Life Sciences Research Database 6/1/2005-7/31/2010

Characteristic	All (N = 102,203)					Matched (N = 29,572)					Not Matched (N = 72,631)	
	Exenatide (N = 15,540)		OAD (N = 86,663)		Stand. Diff.	Exenatide (N = 11,978)		OAD (N = 17,594)		Stand. Diff.	Exenatide (N = 3,562)	
	N	%	N	%		N	%	N	%		N	%
362 - Other retinal disorders	1,559	10.0	9,121	10.5	0.02	1,198	10.0	1,820	10.3	0.01	361	10.1
372 - Disorders of conjunctiva	566	3.6	2,653	3.1	0.03	436	3.6	620	3.5	0.01	130	3.6
427 - Cardiac dysrhythmias	856	5.5	6,420	7.4	0.08	670	5.6	1,052	6.0	0.02	186	5.2
465 - Acute upper respiratory infections of multiple or unspecified sites	1,422	9.2	6,750	7.8	0.05	1,046	8.7	1,489	8.5	0.01	376	10.6
477 - Allergic rhinitis	1,410	9.1	5,871	6.8	0.09	1,037	8.7	1,435	8.2	0.02	373	10.5
496 - Chronic airway obstruction, not elsewhere classified	483	3.1	3,486	4.0	0.05	377	3.1	603	3.4	0.02	106	3.0
535 - Gastritis and duodenitis	470	3.0	2,790	3.2	0.01	369	3.1	569	3.2	0.01	101	2.8
562 - Diverticula of intestine	605	3.9	3,016	3.5	0.02	458	3.8	631	3.6	0.01	147	4.1
571 - Chronic liver disease and cirrhosis	494	3.2	2,253	2.6	0.03	366	3.1	491	2.8	0.02	128	3.6
585 - Chronic kidney disease (CKD)	459	3.0	3,625	4.2	0.07	383	3.2	577	3.3	0.00	76	2.1
600 - Hyperplasia of prostate	546	3.5	3,940	4.5	0.05	444	3.7	659	3.7	0.00	102	2.9
607 - Disorders of penis	560	3.6	3,175	3.7	0.00	456	3.8	648	3.7	0.01	104	2.9
611 - Other disorders of breast	626	4.0	2,347	2.7	0.07	442	3.7	628	3.6	0.01	184	5.2
626 - Disorders of menstruation and other abnormal bleeding from female genital tract	550	3.5	2,014	2.3	0.07	407	3.4	626	3.6	0.01	143	4.0
682 - Other cellulitis and abscess	930	6.0	5,420	6.3	0.01	697	5.8	1,078	6.1	0.01	233	6.5
702 - Other dermatoses	887	5.7	3,983	4.6	0.05	655	5.5	962	5.5	0.00	232	6.5
706 - Diseases of sebaceous glands	475	3.1	2,037	2.4	0.04	354	3.0	515	2.9	0.00	121	3.4
715 - Osteoarthrosis and allied disorders	1,851	11.9	8,329	9.6	0.07	1,389	11.6	1,931	11.0	0.02	462	13.0
716 - Other and unspecified arthropathies	429	2.8	2,402	2.8	0.00	309	2.6	487	2.8	0.01	120	3.4
723 - Other disorders of cervical region	1,039	6.7	4,668	5.4	0.05	765	6.4	1,129	6.4	0.00	274	7.7
729 - Other disorders of soft tissues	3,027	19.5	14,325	16.5	0.08	2,233	18.6	3,286	18.7	0.00	794	22.3
739 - Nonallopathic lesions, not elsewhere classified	702	4.5	2,644	3.1	0.08	506	4.2	645	3.7	0.03	196	5.5
780 - General symptoms	5,136	33.1	23,624	27.3	0.13	3,685	30.8	5,358	30.5	0.01	1,451	40.7
782 - Symptoms involving skin and other integumentary tissue	2,069	13.3	9,000	10.4	0.09	1,526	12.7	2,151	12.2	0.02	543	15.2
783 - Symptoms concerning nutrition, metabolism, and development	888	5.7	3,225	3.7	0.09	601	5.0	770	4.4	0.03	287	8.1
787 - Symptoms involving digestive system	1,368	8.8	8,918	10.3	0.05	1,078	9.0	1,654	9.4	0.01	290	8.1

Table 1.2a. Prevalence of Medical Conditions, Procedures and Drug Dispensings During the 9-Month Baseline Period, Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonists and without 1 year of Follow-up Person Time, Life Sciences Research Database 6/1/2005-7/31/2010

Characteristic	All (N = 102,203)					Matched (N = 29,572)					Not Matched (N = 72,631)	
	Exenatide (N = 15,540)		OAD (N = 86,663)		Stand. Diff.	Exenatide (N = 11,978)		OAD (N = 17,594)		Stand. Diff.	Exenatide (N = 3,562)	
	N	%	N	%		N	%	N	%		N	%
790 - Nonspecific findings on examination of blood	1,884	12.1	10,547	12.2	0.00	1,406	11.7	1,952	11.1	0.02	478	13.4
847 - Sprains and strains of other and unspecified parts of back	511	3.3	2,486	2.9	0.02	392	3.3	542	3.1	0.01	119	3.3
V58 - Encounter for other and unspecified procedure and aftercare	4,208	27.1	21,139	24.4	0.06	3,173	26.5	4,625	26.3	0.00	1,035	29.1
V70 - General medical examination	1,943	12.5	10,990	12.7	0.01	1,529	12.8	2,364	13.4	0.02	414	11.6

Stand. Diff., Standardized Difference

Note: OADs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins. Standardized difference is calculated by the difference between the 2 mean values divided by the pooled standard deviation.

* Conditions associated with diabetes severity.

Please note characteristic descriptions may be truncated in the data due to SAS limitations.

Table 1.2.1a. Prevalence of Baseline Malignances During the 9-Month Baseline Period, Life Sciences Research Database 6/1/2005−7/31/2010

Baseline Malignancies	All (N = 102,203)					Matched (N = 29,572)				
	Exenatide (N = 15,540)		OAD (N = 86,663)		Standardized Difference	Exenatide (N = 11,978)		OAD (N = 17,594)		Standardized Difference
	N	%	N	%		N	%	N	%	
Malignant neoplasm of lip	0	0.00	14	0.02	0.02	0	0.00	4	0.02	0.02
Malignant neoplasm of tongue	1	0.01	21	0.02	0.01	1	0.01	5	0.03	0.01
Malignant neoplasm of major salivary glands	3	0.02	15	0.02	0.00	3	0.03	6	0.03	0.01
Malignant neoplasm of gum	0	0.00	4	0.00	0.01	0	0.00	0	0.00	-
Malignant neoplasm of floor of mouth	0	0.00	5	0.01	0.01	0	0.00	0	0.00	-
Malignant neoplasm of other and unspecified parts of mouth	0	0.00	16	0.02	0.02	0	0.00	3	0.02	0.02
Malignant neoplasm of oropharynx	1	0.01	22	0.03	0.02	1	0.01	3	0.02	0.01
Malignant neoplasm of nasopharynx	0	0.00	13	0.02	0.02	0	0.00	1	0.01	0.01
Malignant neoplasm of hypopharynx	0	0.00	7	0.01	0.01	0	0.00	1	0.01	0.01
Malignant neoplasm of other and ill-defined sites within the lip, oral cavity, and pharynx	0	0.00	13	0.02	0.02	0	0.00	4	0.02	0.02
Malignant neoplasm of esophagus	1	0.01	29	0.03	0.02	1	0.01	2	0.01	0.00
Malignant neoplasm of stomach	1	0.01	29	0.03	0.02	1	0.01	0	0.00	0.01
Malignant neoplasm of small intestine, including duodenum	0	0.00	21	0.02	0.02	0	0.00	2	0.01	0.02
Malignant neoplasm of colon	31	0.20	343	0.40	0.04	24	0.20	48	0.27	0.01
Malignant neoplasm of rectum, rectosigmoid junction, and anus	17	0.11	228	0.26	0.04	12	0.10	30	0.17	0.02
Malignant neoplasm of liver and intrahepatic bile ducts	8	0.05	72	0.08	0.01	5	0.04	6	0.03	0.00
Malignant neoplasm of gallbladder and extrahepatic bile ducts	2	0.01	6	0.01	0.01	2	0.02	3	0.02	0.00
Malignant neoplasm of retroperitoneum and peritoneum	2	0.01	14	0.02	0.00	2	0.02	2	0.01	0.00
Malignant neoplasm of other and ill-defined sites within the digestive organs and peritoneum	0	0.00	16	0.02	0.02	0	0.00	3	0.02	0.02
Malignant neoplasm of nasal cavities, middle ear, and accessory sinuses	0	0.00	8	0.01	0.01	0	0.00	2	0.01	0.02
Malignant neoplasm of larynx	1	0.01	42	0.05	0.03	1	0.01	10	0.06	0.03
Malignant neoplasm of trachea, bronchus, and lung	15	0.10	211	0.24	0.04	12	0.10	32	0.18	0.02
Malignant neoplasm of pleura	2	0.01	8	0.01	0.00	2	0.02	1	0.01	0.01

Table 1.2.1a. Prevalence of Baseline Malignances During the 9-Month Baseline Period, Life Sciences Research Database 6/1/2005−7/31/2010

Baseline Malignancies	All (N = 102,203)					Matched (N = 29,572)				
	Exenatide (N = 15,540)		OAD (N = 86,663)		Standardized Difference	Exenatide (N = 11,978)		OAD (N = 17,594)		Standardized Difference
	N	%	N	%		N	%	N	%	
Malignant neoplasm of thymus, heart, and mediastinum	0	0.00	10	0.01	0.02	0	0.00	1	0.01	0.01
Malignant neoplasm of other and ill-defined sites within the respiratory system and intrathoracic organs	0	0.00	2	0.00	0.01	0	0.00	0	0.00	-
Malignant neoplasm of bone and articular cartilage	3	0.02	43	0.05	0.02	1	0.01	6	0.03	0.02
Malignant neoplasm of connective and other soft tissue	8	0.05	47	0.05	0.00	5	0.04	4	0.02	0.01
Malignant melanoma of skin	28	0.18	158	0.18	0.00	21	0.18	26	0.15	0.01
Other malignant neoplasm of skin	170	1.09	1,151	1.33	0.02	134	1.12	212	1.20	0.01
Malignant neoplasm of female breast	186	1.20	921	1.06	0.01	139	1.16	200	1.14	0.00
Malignant neoplasm of male breast	0	0.00	10	0.01	0.02	0	0.00	0	0.00	.
Kaposi's sarcoma	2	0.01	5	0.01	0.01	0	0.00	1	0.01	0.01
Malignant neoplasm of uterus, part unspecified	9	0.06	41	0.05	0.00	7	0.06	9	0.05	0.00
Malignant neoplasm of cervix uteri	5	0.03	38	0.04	0.01	5	0.04	8	0.05	0.00
Malignant neoplasm of body of uterus	30	0.19	111	0.13	0.02	21	0.18	25	0.14	0.01
Malignant neoplasm of ovary and other uterine adnexa	12	0.08	90	0.10	0.01	11	0.09	24	0.14	0.01
Malignant neoplasm of other and unspecified female genital organs	3	0.02	20	0.02	0.00	2	0.02	1	0.01	0.01
Malignant neoplasm of prostate	92	0.59	1,013	1.17	0.06	78	0.65	132	0.75	0.01
Malignant neoplasm of testis	6	0.04	43	0.05	0.01	5	0.04	5	0.03	0.01
Malignant neoplasm of penis and other male genital organs	1	0.01	8	0.01	0.00	1	0.01	1	0.01	0.00
Malignant neoplasm of bladder	30	0.19	233	0.27	0.02	25	0.21	43	0.24	0.01
Malignant neoplasm of kidney and other and unspecified urinary organs	24	0.15	152	0.18	0.01	21	0.18	25	0.14	0.01
Malignant neoplasm of eye	3	0.02	20	0.02	0.00	1	0.01	4	0.02	0.01
Malignant neoplasm of brain	7	0.05	70	0.08	0.01	7	0.06	13	0.07	0.01
Malignant neoplasm of other and unspecified parts of nervous system	5	0.03	22	0.03	0.00	4	0.03	8	0.05	0.01
Malignant neoplasm of other endocrine glands and related structures	16	0.10	40	0.05	0.02	14	0.12	14	0.08	0.01

Table 1.2.1a. Prevalence of Baseline Malignances During the 9-Month Baseline Period, Life Sciences Research Database 6/1/2005−7/31/2010

Baseline Malignancies	All (N = 102,203)					Matched (N = 29,572)				
	Exenatide (N = 15,540)		OAD (N = 86,663)		Standardized Difference	Exenatide (N = 11,978)		OAD (N = 17,594)		Standardized Difference
	N	%	N	%		N	%	N	%	
Malignant neoplasm of other and ill-defined sites	7	0.05	75	0.09	0.02	6	0.05	8	0.05	0.00
Secondary and unspecified malignant neoplasm of lymph nodes	12	0.08	157	0.18	0.03	7	0.06	23	0.13	0.02
Secondary malignant neoplasm of respiratory and digestive systems	10	0.06	170	0.20	0.04	8	0.07	27	0.15	0.03
Secondary malignant neoplasm of other specified sites	9	0.06	209	0.24	0.05	5	0.04	24	0.14	0.03
Malignant neoplasm without specification of site	9	0.06	127	0.15	0.03	8	0.07	12	0.07	0.00
Lymphosarcoma and reticulosarcoma and other specified malignant tumors of lymphatic tissue	23	0.15	121	0.14	0.00	18	0.15	24	0.14	0.00
Hodgkin's disease	17	0.11	66	0.08	0.01	14	0.12	12	0.07	0.02
Other malignant neoplasms of lymphoid and histiocytic tissue	28	0.18	308	0.36	0.03	20	0.17	49	0.28	0.02
Multiple myeloma and immunoproliferative neoplasms	10	0.06	84	0.10	0.01	9	0.08	7	0.04	0.01
Lymphoid leukemia	11	0.07	122	0.14	0.02	9	0.08	13	0.07	0.00
Myeloid leukemia	15	0.10	130	0.15	0.02	9	0.08	26	0.15	0.02
Monocytic leukemia	1	0.01	4	0.00	0.00	1	0.01	0	0.00	0.01
Other specified leukemia	0	0.00	4	0.00	0.01	0	0.00	2	0.01	0.02
Leukemia of unspecified cell type	3	0.02	56	0.06	0.02	2	0.02	3	0.02	0.00
Personal history of malignant neoplasm*	395	2.54	2,377	2.74	0.01	289	2.41	425	2.42	0.00

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, dipeptidyl peptidase-4 inhibitor, glucagon-like peptide-1 agonists, pramlintide, alpha-glucosidase inhibitors, and insulins. Standardized difference is calculated by the difference between the 2 proportions divided by the pooled standard deviation.

*This category is based on the presence of ICD-9 diagnosis code V10 in a patient's claims history during the 9 month baseline period.

Table 1.2b. Prevalence of Medical Conditions, Procedures and Drug Dispensings During the 9-Month Baseline Period, Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonists and without 1 year of Follow-up Person Time, Impact National Benchmark Databases 6/1/2005-7/31/2010

Characteristic	All (N = 65,098)					Matched (N = 17,051)					Not Matched (N = 48,047)	
	Exenatide (N = 10,643)		OAD (N = 54,455)		Stand. Diff.	Exenatide (N = 6,954)		OAD (N = 10,097)		Stand. Diff.	Exenatide (N = 3,689)	
	N	%	N	%		N	%	N	%		N	%
Medical Conditions												
Type II diabetes	10,373	97.5	50,266	92.3	0.24	6,734	96.8	9,687	95.9	0.05	3,639	98.6
Myocardial Infarction*	158	1.5	1,390	2.6	0.08	106	1.5	161	1.6	0.01	52	1.4
Peripheral neuropathy*	1,235	11.6	4,191	7.7	0.13	687	9.9	998	9.9	0.00	548	14.9
Alcohol Use/Abuse	20	0.2	412	0.8	0.08	11	0.2	26	0.3	0.02	9	0.2
Smoking	269	2.5	1,543	2.8	0.02	185	2.7	275	2.7	0.00	84	2.3
Obesity	2,126	20.0	4,127	7.6	0.37	981	14.1	1,386	13.7	0.01	1,145	31.0
Gastroesophageal reflux disease	813	7.6	3,276	6.0	0.06	525	7.5	695	6.9	0.03	288	7.8
Malignant neoplasms >=2 clms	193	1.8	1,550	2.8	0.07	139	2.0	213	2.1	0.01	54	1.5
Renal disease*	5	0.0	234	0.4	0.08	2	0.0	8	0.1	0.02	3	0.1
Liver disease	249	2.3	1,097	2.0	0.02	147	2.1	197	2.0	0.01	102	2.8
Acute MI (ICD9 410)*	88	0.8	849	1.6	0.07	55	0.8	88	0.9	0.01	33	0.9
110 - Dermatophytosis	715	6.7	3,273	6.0	0.03	425	6.1	618	6.1	0.00	290	7.9
211 - Benign neoplasm of other parts of digestive system	519	4.9	2,252	4.1	0.04	335	4.8	472	4.7	0.01	184	5.0
216 - Benign neoplasm of skin	474	4.5	1,664	3.1	0.07	282	4.1	420	4.2	0.01	192	5.2
272 - Disorders of lipoid metabolism	7,841	73.7	32,906	60.4	0.28	4,968	71.4	6,970	69.0	0.05	2,873	77.9
276 - Disorders of fluid, electrolyte, and acid-base balance	379	3.6	3,595	6.6	0.14	245	3.5	375	3.7	0.01	134	3.6
277 - Other and unspecified disorders of metabolism	569	5.3	769	1.4	0.22	250	3.6	255	2.5	0.06	319	8.6
285 - Other and unspecified anemias	655	6.2	3,976	7.3	0.05	432	6.2	656	6.5	0.01	223	6.0
327 - Organic sleep disorders	514	4.8	753	1.4	0.20	302	4.3	361	3.6	0.04	212	5.7
362 - Other retinal disorders	1,360	12.8	6,894	12.7	0.00	865	12.4	1,301	12.9	0.01	495	13.4
366 - Cataract	1,046	9.8	5,246	9.6	0.01	655	9.4	908	9.0	0.01	391	10.6
367 - Disorders of refraction and accommodation	563	5.3	2,823	5.2	0.00	369	5.3	614	6.1	0.03	194	5.3
372 - Disorders of conjunctiva	349	3.3	1,649	3.0	0.01	221	3.2	344	3.4	0.01	128	3.5
379 - Other disorders of eye	329	3.1	1,900	3.5	0.02	227	3.3	329	3.3	0.00	102	2.8
424 - Other diseases of endocardium	456	4.3	2,191	4.0	0.01	289	4.2	382	3.8	0.02	167	4.5
429 - Ill-defined descriptions and complications of heart disease	389	3.7	2,436	4.5	0.04	241	3.5	375	3.7	0.01	148	4.0
455 - Hemorrhoids	351	3.3	1,575	2.9	0.02	212	3.0	306	3.0	0.00	139	3.8
465 - Acute upper respiratory infections of multiple or unspecified sites	825	7.8	3,835	7.0	0.03	525	7.5	740	7.3	0.01	300	8.1

Table 1.2b. Prevalence of Medical Conditions, Procedures and Drug Dispensings During the 9-Month Baseline Period, Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonists and without 1 year of Follow-up Person Time, Impact National Benchmark Databases 6/1/2005-7/31/2010

Characteristic	All (N = 65,098)					Matched (N = 17,051)					Not Matched (N = 48,047)	
	Exenatide (N = 10,643)		OAD (N = 54,455)		Stand. Diff.	Exenatide (N = 6,954)		OAD (N = 10,097)		Stand. Diff.	Exenatide (N = 3,689)	
	N	%	N	%		N	%	N	%		N	%
466 - Acute bronchitis and bronchiolitis	866	8.1	3,778	6.9	0.05	554	8.0	778	7.7	0.01	312	8.5
473 - Chronic sinusitis	457	4.3	1,553	2.9	0.08	284	4.1	335	3.3	0.04	173	4.7
496 - Chronic airway obstruction, not elsewhere classified	338	3.2	2,036	3.7	0.03	238	3.4	332	3.3	0.01	100	2.7
562 - Diverticula of intestine	454	4.3	2,029	3.7	0.03	306	4.4	385	3.8	0.03	148	4.0
701 - Other hypertrophic and atrophic conditions of skin	366	3.4	1,258	2.3	0.07	204	2.9	306	3.0	0.01	162	4.4
702 - Other dermatoses	504	4.7	2,031	3.7	0.05	307	4.4	449	4.4	0.00	197	5.3
715 - Osteoarthrosis and allied disorders	1,202	11.3	4,608	8.5	0.10	701	10.1	1,013	10.0	0.00	501	13.6
719 - Other and unspecified disorders of joint	1,983	18.6	8,460	15.5	0.08	1,200	17.3	1,803	17.9	0.02	783	21.2
728 - Disorders of muscle, ligament, and fascia	644	6.1	2,412	4.4	0.07	367	5.3	528	5.2	0.00	277	7.5
780 - General symptoms	2,948	27.7	11,960	22.0	0.13	1,768	25.4	2,506	24.8	0.01	1,180	32.0
783 - Symptoms concerning nutrition, metabolism, and development	443	4.2	1,532	2.8	0.07	249	3.6	319	3.2	0.02	194	5.3
785 - Symptoms involving cardiovascular system	762	7.2	3,947	7.2	0.00	472	6.8	668	6.6	0.01	290	7.9
787 - Symptoms involving digestive system	759	7.1	4,583	8.4	0.05	519	7.5	748	7.4	0.00	240	6.5
799 - Other ill-defined and unknown causes of morbidity and mortality	343	3.2	1,495	2.7	0.03	190	2.7	291	2.9	0.01	153	4.1
V03 - Need for prophylactic vaccination and inoculation against bacterial diseases	402	3.8	1,757	3.2	0.03	238	3.4	402	4.0	0.03	164	4.4
V04 - Need for prophylactic vaccination and inoculation against certain viral diseases	2,038	19.1	8,172	15.0	0.11	1,357	19.5	1,926	19.1	0.01	681	18.5
V58 - Encounter for other and unspecified procedure and aftercare	1,678	15.8	8,202	15.1	0.02	1,040	15.0	1,545	15.3	0.01	638	17.3
V65 - Other persons seeking consultation	606	5.7	1,944	3.6	0.10	321	4.6	496	4.9	0.01	285	7.7
V70 - General medical examination	2,045	19.2	10,641	19.5	0.01	1,335	19.2	2,046	20.3	0.03	710	19.2
V72 - Special investigations and	2,761	25.9	12,680	23.3	0.06	1,719	24.7	2,596	25.7	0.02	1,042	28.2
V76 - Special screening for malignant neoplasms	2,801	26.3	11,501	21.1	0.12	1,751	25.2	2,612	25.9	0.02	1,050	28.5

Stand. Diff., Standardized Difference

Note: OADs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins. Standardized difference is calculated by the difference between the 2 proportions divided by the pooled standard deviation.

* Conditions associated with diabetes severity.

Please note characteristic descriptions may be truncated in the data due to SAS limitations.

Table 1.2.1b. Prevalence of Baseline Malignances During the 9-Month Baseline Period, Impact National Benchmark Databases 6/1/2005-7/31/2010

Baseline Malignancies	All (N = 65,098)					Matched (N = 17,051)				
	Exenatide (N = 10,643)		OAD (N = 54,455)		Standardized Difference	Exenatide (N = 6,954)		OAD (N = 10,097)		Standardized Difference
	N	%	N	%		N	%	N	%	
Malignant neoplasm of lip	1	0.01	6	0.01	0.00	1	0.01	0	0.00	0.02
Malignant neoplasm of tongue	3	0.03	18	0.03	0.00	0	0.00	1	0.01	0.01
Malignant neoplasm of major salivary glands	1	0.01	9	0.02	0.01	1	0.01	3	0.03	0.01
Malignant neoplasm of gum	0	0.00	5	0.01	0.01	0	0.00	0	0.00	-
Malignant neoplasm of floor of mouth	1	0.01	2	0.00	0.01	1	0.01	0	0.00	0.02
Malignant neoplasm of other and unspecified parts of mouth	1	0.01	17	0.03	0.02	1	0.01	0	0.00	0.02
Malignant neoplasm of oropharynx	0	0.00	13	0.02	0.02	0	0.00	1	0.01	0.01
Malignant neoplasm of nasopharynx	0	0.00	8	0.01	0.02	0	0.00	0	0.00	-
Malignant neoplasm of hypopharynx	1	0.01	3	0.01	0.00	0	0.00	0	0.00	-
Malignant neoplasm of other and ill-defined sites within the lip, oral cavity, and pharynx	1	0.01	8	0.01	0.00	1	0.01	0	0.00	0.02
Malignant neoplasm of esophagus	0	0.00	19	0.03	0.03	0	0.00	2	0.02	0.02
Malignant neoplasm of stomach	1	0.01	21	0.04	0.02	1	0.01	3	0.03	0.01
Malignant neoplasm of small intestine, including duodenum	0	0.00	8	0.01	0.02	0	0.00	0	0.00	-
Malignant neoplasm of colon	18	0.17	220	0.40	0.04	14	0.20	25	0.25	0.01
Malignant neoplasm of rectum, rectosigmoid junction, and anus	8	0.08	130	0.24	0.04	8	0.12	14	0.14	0.01
Malignant neoplasm of liver and intrahepatic bile ducts	2	0.02	50	0.09	0.03	1	0.01	4	0.04	0.02
Malignant neoplasm of gallbladder and extrahepatic bile ducts	0	0.00	2	0.00	0.01	0	0.00	0	0.00	-
Malignant neoplasm of retroperitoneum and peritoneum	1	0.01	11	0.02	0.01	0	0.00	2	0.02	0.02
Malignant neoplasm of other and ill-defined sites within the digestive organs and peritoneum	0	0.00	13	0.02	0.02	0	0.00	2	0.02	0.02
Malignant neoplasm of nasal cavities, middle ear, and accessory sinuses	1	0.01	10	0.02	0.01	0	0.00	0	0.00	-
Malignant neoplasm of larynx	4	0.04	29	0.05	0.01	4	0.06	5	0.05	0.00
Malignant neoplasm of trachea, bronchus, and lung	11	0.10	171	0.31	0.05	9	0.13	20	0.20	0.02
Malignant neoplasm of pleura	0	0.00	3	0.01	0.01	0	0.00	0	0.00	-
Malignant neoplasm of thymus, heart, and mediastinum	2	0.02	7	0.01	0.00	2	0.03	1	0.01	0.01

Table 1.2.1b. Prevalence of Baseline Malignances During the 9-Month Baseline Period, Impact National Benchmark Databases 6/1/2005-7/31/2010

Baseline Malignancies	All (N = 65,098)					Matched (N = 17,051)				
	Exenatide (N = 10,643)		OAD (N = 54,455)		Standardized Difference	Exenatide (N = 6,954)		OAD (N = 10,097)		Standardized Difference
	N	%	N	%		N	%	N	%	
Malignant neoplasm of other and ill-defined sites within the respiratory system and intrathoracic organs	1	0.01	2	0.00	0.01	0	0.00	0	0.00	-
Malignant neoplasm of bone and articular cartilage	3	0.03	29	0.05	0.01	1	0.01	4	0.04	0.02
Malignant neoplasm of connective and other soft tissue	5	0.05	54	0.10	0.02	4	0.06	10	0.10	0.01
Malignant melanoma of skin	21	0.20	124	0.23	0.01	17	0.24	18	0.18	0.01
Other malignant neoplasm of skin	107	1.01	633	1.16	0.02	67	0.96	111	1.10	0.01
Malignant neoplasm of female breast	105	0.99	570	1.05	0.01	63	0.91	116	1.15	0.02
Malignant neoplasm of male breast	0	0.00	7	0.01	0.02	0	0.00	1	0.01	0.01
Kaposi's sarcoma	0	0.00	11	0.02	0.02	0	0.00	3	0.03	0.02
Malignant neoplasm of uterus, part unspecified	10	0.09	21	0.04	0.02	7	0.10	5	0.05	0.02
Malignant neoplasm of cervix uteri	8	0.08	39	0.07	0.00	7	0.10	7	0.07	0.01
Malignant neoplasm of body of uterus	23	0.22	96	0.18	0.01	14	0.20	22	0.22	0.00
Malignant neoplasm of ovary and other uterine adnexa	8	0.08	51	0.09	0.01	6	0.09	7	0.07	0.01
Malignant neoplasm of other and unspecified female genital organs	1	0.01	11	0.02	0.01	0	0.00	2	0.02	0.02
Malignant neoplasm of prostate	78	0.73	565	1.04	0.03	58	0.83	62	0.61	0.03
Malignant neoplasm of testis	2	0.02	25	0.05	0.02	2	0.03	3	0.03	0.00
Malignant neoplasm of penis and other male genital organs	1	0.01	7	0.01	0.00	1	0.01	0	0.00	0.02
Malignant neoplasm of bladder	26	0.24	179	0.33	0.02	16	0.23	30	0.30	0.01
Malignant neoplasm of kidney and other and unspecified urinary organs	22	0.21	110	0.20	0.00	14	0.20	22	0.22	0.00
Malignant neoplasm of eye	1	0.01	9	0.02	0.01	0	0.00	2	0.02	0.02
Malignant neoplasm of brain	4	0.04	44	0.08	0.02	3	0.04	4	0.04	0.00
Malignant neoplasm of other and unspecified parts of nervous system	1	0.01	13	0.02	0.01	1	0.01	2	0.02	0.00
Malignant neoplasm of other endocrine glands and related structures	6	0.06	26	0.05	0.00	6	0.09	6	0.06	0.01
Malignant neoplasm of other and ill-defined sites	4	0.04	64	0.12	0.03	3	0.04	6	0.06	0.01

Table 1.2.1b. Prevalence of Baseline Malignances During the 9-Month Baseline Period, Impact National Benchmark Databases 6/1/2005-7/31/2010

Baseline Malignancies	All (N = 65,098)					Matched (N = 17,051)				
	Exenatide (N = 10,643)		OAD (N = 54,455)		Standardized Difference	Exenatide (N = 6,954)		OAD (N = 10,097)		Standardized Difference
	N	%	N	%		N	%	N	%	
Secondary and unspecified malignant neoplasm of lymph nodes	4	0.04	88	0.16	0.04	3	0.04	13	0.13	0.03
Secondary malignant neoplasm of respiratory and digestive systems	3	0.03	114	0.21	0.05	3	0.04	12	0.12	0.03
Secondary malignant neoplasm of other specified sites	13	0.12	116	0.21	0.02	8	0.12	16	0.16	0.01
Malignant neoplasm without specification of site	5	0.05	92	0.17	0.04	4	0.06	10	0.10	0.01
Lymphosarcoma and reticulosarcoma and other specified malignant tumors of lymphatic tissue	9	0.08	65	0.12	0.01	6	0.09	9	0.09	0.00
Hodgkin's disease	5	0.05	39	0.07	0.01	2	0.03	6	0.06	0.01
Other malignant neoplasms of lymphoid and histiocytic tissue	22	0.21	221	0.41	0.04	14	0.20	25	0.25	0.01
Multiple myeloma and immunoproliferative neoplasms	8	0.08	71	0.13	0.02	6	0.09	8	0.08	0.00
Lymphoid leukemia	6	0.06	80	0.15	0.03	5	0.07	11	0.11	0.01
Myeloid leukemia	9	0.08	72	0.13	0.01	6	0.09	9	0.09	0.00
Monocytic leukemia	2	0.02	5	0.01	0.01	2	0.03	0	0.00	0.02
Leukemia of unspecified cell type	6	0.06	36	0.07	0.00	5	0.07	2	0.02	0.02
Personal history of malignant neoplasm*	238	2.24	1,256	2.31	0.00	144	2.07	223	2.21	0.01

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, dipeptidyl peptidase-4 inhibitor, glucagon-like peptide-1 agonists, pramlintide, alpha-glucosidase inhibitors, and insulins. Standardized difference is calculated by the difference between the 2 proportions divided by the pooled standard deviation.

*This category is based on the presence of ICD-9 diagnosis code V10 in a patient's claims history during the 9 month baseline period.

Table 1.3a. Prevalence of Procedures During the 9-Month Baseline Period that Were Included in the Propensity Score Model, Life Sciences Research Database 6/1/2005−7/31/2010

Characteristic	All (N = 102,203)					Matched (N = 29,572)					Not Matched (N = 72,631)	
	Exenatide (N = 15,540)		OAD (N = 86,663)		Stand. Diff.	Exenatide (N = 11,978)		OAD (N = 17,594)		Stand. Diff.	Exenatide (N = 3,562)	
	N	%	N	%		N	%	N	%		N	%
Procedures (CPT, HCPC, and procedure category codes)												
Status post cholecystectomy	80	0.5	482	0.6	0.01	64	0.5	88	0.5	0.00	16	0.4
Organ transplant	44	0.3	700	0.8	0.07	36	0.3	65	0.4	0.01	8	0.2
36416 - Collection of capillary blood specimen (eg, finger, heel, ear stick)	897	5.8	2,726	3.1	0.13	599	5.0	804	4.6	0.02	298	8.4
76499 - Unlisted diagnostic radiographic procedure	3,682	23.7	17,252	19.9	0.09	2,748	22.9	4,025	22.9	0.00	934	26.2
80053 - Comprehensive metabolic panel This panel must include the following: Albumin (82040) Bilirubin, total (82247) Calcium (82310) Carbon dioxide (bicarbonate) (82374) Chloride (82435) Creatinine (82565) Glucose (82947) Phosphatase, alkaline (84075) Potassium	9,153	58.9	40,956	47.3	0.23	6,830	57.0	9,497	54.0	0.06	2,323	65.2
81000 - Urinalysis, by dip stick or tablet reagent for bilirubin, glucose, hemoglobin, ketones, leukocytes, nitrite, pH, protein, specific gravity, urobilinogen, any number of these constituents; non-automated, with microscopy	1,419	9.1	7,438	8.6	0.02	1,072	8.9	1,576	9.0	0.00	347	9.7
81002 - Urinalysis, by dip stick or tablet reagent for bilirubin, glucose, hemoglobin, ketones, leukocytes, nitrite, pH, protein, specific gravity, urobilinogen, any number of these constituents; non-automated, without microscopy	2,001	12.9	10,195	11.8	0.03	1,501	12.5	2,237	12.7	0.01	500	14.0
81003 - Urinalysis, by dip stick or tablet reagent for bilirubin, glucose, hemoglobin, ketones, leukocytes, nitrite, pH, protein, specific gravity, urobilinogen, any number of these constituents; automated, without microscopy	1,949	12.5	9,792	11.3	0.04	1,509	12.6	2,102	11.9	0.02	440	12.4
82043 - Albumin; urine, microalbumin, quantitative	5,638	36.3	22,338	25.8	0.23	4,170	34.8	5,786	32.9	0.04	1,468	41.2

Table 1.3a. Prevalence of Procedures During the 9-Month Baseline Period that Were Included in the Propensity Score Model, Life Sciences Research Database 6/1/2005−7/31/2010

Characteristic	All (N = 102,203)					Matched (N = 29,572)					Not Matched (N = 72,631)	
	Exenatide (N = 15,540)		OAD (N = 86,663)		Stand. Diff.	Exenatide (N = 11,978)		OAD (N = 17,594)		Stand. Diff.	Exenatide (N = 3,562)	
	N	%	N	%		N	%	N	%		N	%
82044 - Albumin; urine, microalbumin, semiquantitative (eg, reagent strip assay)	1,175	7.6	4,144	4.8	0.12	843	7.0	1,117	6.3	0.03	332	9.3
82306 - Calcifediol (25-OH Vitamin D-3)	600	3.9	1,250	1.4	0.15	464	3.9	446	2.5	0.08	136	3.8
82550 - Creatine kinase (CK), (CPK); total	1,484	9.5	6,803	7.8	0.06	1,036	8.6	1,531	8.7	0.00	448	12.6
82565 - Creatinine; blood	800	5.1	4,192	4.8	0.01	581	4.9	841	4.8	0.00	219	6.1
82570 - Creatinine; other source	4,730	30.4	17,624	20.3	0.23	3,413	28.5	4,734	26.9	0.04	1,317	37.0
82607 - Cyanocobalamin (Vitamin B-12);	811	5.2	2,870	3.3	0.09	584	4.9	763	4.3	0.03	227	6.4
82948 - Glucose; blood, reagent strip	1,329	8.6	5,820	6.7	0.07	984	8.2	1,334	7.6	0.02	345	9.7
83036 - Hemoglobin; glycosylated (A1C)	12,682	81.6	59,663	68.8	0.30	9,584	80.0	13,624	77.4	0.06	3,098	87.0
83721 - Lipoprotein, direct measurement; LDL cholesterol	1,044	6.7	3,523	4.1	0.12	712	5.9	1,022	5.8	0.01	332	9.3
84153 - Prostate specific antigen (PSA); total	2,129	13.7	13,918	16.1	0.07	1,717	14.3	2,487	14.1	0.01	412	11.6
84403 - Testosterone; total	949	6.1	2,431	2.8	0.16	636	5.3	758	4.3	0.05	313	8.8
84550 - Uric acid; blood	1,203	7.7	5,011	5.8	0.08	865	7.2	1,111	6.3	0.04	338	9.5
84681 - C-peptide	793	5.1	1,554	1.8	0.18	489	4.1	555	3.2	0.05	304	8.5
85025 - Blood count; complete (CBC), automated (Hgb, Hct, RBC, WBC and platelet count) and automated differential WBC count	5,271	33.9	28,011	32.3	0.03	4,018	33.5	5,752	32.7	0.02	1,253	35.2
85027 - Blood count; complete (CBC), automated (Hgb, Hct, RBC, WBC and platelet count)	905	5.8	5,426	6.3	0.02	686	5.7	1,000	5.7	0.00	219	6.1
87086 - Culture, bacterial; quantitative colony count, urine	1,034	6.7	5,316	6.1	0.02	797	6.7	1,200	6.8	0.01	237	6.7
88305 - Level IV - Surgical pathology, gross and microscopic examination Abortion - spontaneous/missed Artery, biopsy Bone marrow, biopsy Bone exostosis Brain/meninges, other than for tumor resection Breast, biopsy, not requiring microscopic evaluation of surgica	2,074	13.3	9,924	11.5	0.06	1,545	12.9	2,123	12.1	0.03	529	14.9
89240 - Unlisted miscellaneous pathology test	3,439	22.1	17,756	20.5	0.04	2,627	21.9	3,905	22.2	0.01	812	22.8

Table 1.3a. Prevalence of Procedures During the 9-Month Baseline Period that Were Included in the Propensity Score Model, Life Sciences Research Database 6/1/2005−7/31/2010

Characteristic	All (N = 102,203)					Matched (N = 29,572)					Not Matched (N = 72,631)	
	Exenatide (N = 15,540)		OAD (N = 86,663)		Stand. Diff.	Exenatide (N = 11,978)		OAD (N = 17,594)		Stand. Diff.	Exenatide (N = 3,562)	
	N	%	N	%		N	%	N	%		N	%
90732 - Pneumococcal polysaccharide vaccine, 23-valent, adult or immunosuppressed patient dosage, when administered to individuals 2 years or older, for subcutaneous or intramuscular use	752	4.8	2,965	3.4	0.07	550	4.6	723	4.1	0.02	202	5.7
91000 - Esophageal intubation and collection of washings for cytology, including preparation of specimens (separate procedure)	822	5.3	3,629	4.2	0.05	672	5.6	836	4.8	0.04	150	4.2
92004 - Ophthalmological services: medical examination and evaluation with initiation of diagnostic and treatment program; comprehensive, new patient, one or more visits	716	4.6	3,690	4.3	0.02	554	4.6	822	4.7	0.00	162	4.5
92012 - Ophthalmological services: medical examination and evaluation, with initiation or continuation of diagnostic and treatment program; intermediate, established patient	902	5.8	4,770	5.5	0.01	688	5.7	994	5.6	0.00	214	6.0
92015 - Determination of refractive state	1,711	11.0	7,378	8.5	0.08	1,272	10.6	1,789	10.2	0.01	439	12.3
92250 - Fundus photography with interpretation and report	883	5.7	4,217	4.9	0.04	671	5.6	966	5.5	0.00	212	6.0
97100 - Gait analysis	778	5.0	1,918	2.2	0.15	587	4.9	774	4.4	0.02	191	5.4
99000 - Handling and/or conveyance of specimen for transfer from the physician's office to a laboratory	1,659	10.7	6,942	8.0	0.09	1,221	10.2	1,685	9.6	0.02	438	12.3
99203 - Office or other outpatient visit for the evaluation and management of a new patient, which requires these 3 key components: A detailed history; A detailed examination; Medical decision making of low complexity.	2,673	17.2	12,444	14.4	0.08	2,015	16.8	2,769	15.7	0.03	658	18.5

Table 1.3a. Prevalence of Procedures During the 9-Month Baseline Period that Were Included in the Propensity Score Model, Life Sciences Research Database 6/1/2005−7/31/2010

Characteristic	All (N = 102,203)					Matched (N = 29,572)					Not Matched (N = 72,631)	
	Exenatide (N = 15,540)		OAD (N = 86,663)		Stand. Diff.	Exenatide (N = 11,978)		OAD (N = 17,594)		Stand. Diff.	Exenatide (N = 3,562)	
	N	%	N	%		N	%	N	%		N	%
99211 - Office or other outpatient visit for the evaluation and management of an established patient, that may not require the presence of a physician. Usually, the presenting problem(s) are minimal. Typically, 5 minutes are spent performing or supervising these	1,451	9.3	6,163	7.1	0.08	1,031	8.6	1,496	8.5	0.00	420	11.8
99212 - Office or other outpatient visit for the evaluation and management of an established patient, which requires at least 2 of these 3 key components: A problem focused history; A problem focused examination; Straightforward medical decision making. Counselin	3,810	24.5	17,848	20.6	0.09	2,774	23.2	4,128	23.5	0.01	1,036	29.1
99213 - Office or other outpatient visit for the evaluation and management of an established patient, which requires at least 2 of these 3 key components: An expanded problem focused history; An expanded problem focused examination; Medical decision making of low	12,316	79.3	63,102	72.8	0.15	9,365	78.2	13,621	77.4	0.02	2,951	82.8
99214 - Office or other outpatient visit for the evaluation and management of an established patient, which requires at least 2 of these 3 key components: A detailed history; A detailed examination; Medical decision making of moderate complexity. Counseling and/o	13,074	84.1	61,713	71.2	0.31	9,888	82.6	14,285	81.2	0.04	3,186	89.4
99215 - Office or other outpatient visit for the evaluation and management of an established patient, which requires at least 2 of these 3 key components: A comprehensive history; A comprehensive examination; Medical decision making of high complexity. Counseling	3,498	22.5	14,159	16.3	0.16	2,516	21.0	3,542	20.1	0.02	982	27.6

Table 1.3a. Prevalence of Procedures During the 9-Month Baseline Period that Were Included in the Propensity Score Model, Life Sciences Research Database 6/1/2005−7/31/2010

Characteristic	All (N = 102,203)					Matched (N = 29,572)					Not Matched (N = 72,631)	
	Exenatide (N = 15,540)		OAD (N = 86,663)		Stand. Diff.	Exenatide (N = 11,978)		OAD (N = 17,594)		Stand. Diff.	Exenatide (N = 3,562)	
	N	%	N	%		N	%	N	%		N	%
99232 - Subsequent hospital care, per day, for the evaluation and management of a patient, which requires at least 2 of these 3 key components: An expanded problem focused interval history; An expanded problem focused examination; Medical decision making of moder	805	5.2	10,536	12.2	0.25	656	5.5	1,038	5.9	0.02	149	4.2
99243 - Office consultation for a new or established patient, which requires these 3 key components: A detailed history; A detailed examination; and Medical decision making of low complexity. Counseling and/or coordination of care with other providers or agencies	1,965	12.6	9,181	10.6	0.06	1,466	12.2	2,173	12.4	0.00	499	14.0
99244 - Office consultation for a new or established patient, which requires these 3 key components: A comprehensive history; A comprehensive examination; and Medical decision making of moderate complexity. Counseling and/or coordination of care with other provid	3,356	21.6	12,411	14.3	0.19	2,375	19.8	3,396	19.3	0.01	981	27.5
99245 - Office consultation for a new or established patient, which requires these 3 key components: A comprehensive history; A comprehensive examination; and Medical decision making of high complexity. Counseling and/or coordination of care with other providers	1,933	12.4	6,208	7.2	0.18	1,307	10.9	1,745	9.9	0.03	626	17.6
99283 - Emergency department visit for the evaluation and management of a patient, which requires these 3 key components: An expanded problem focused history; An expanded problem focused examination; and Medical decision making of moderate complexity. Counseling	830	5.3	5,587	6.4	0.05	663	5.5	1,047	6.0	0.02	167	4.7

Table 1.3a. Prevalence of Procedures During the 9-Month Baseline Period that Were Included in the Propensity Score Model, Life Sciences Research Database 6/1/2005−7/31/2010

Characteristic	All (N = 102,203)					Matched (N = 29,572)					Not Matched (N = 72,631)	
	Exenatide (N = 15,540)		OAD (N = 86,663)		Stand. Diff.	Exenatide (N = 11,978)		OAD (N = 17,594)		Stand. Diff.	Exenatide (N = 3,562)	
	N	%	N	%		N	%	N	%		N	%
99284 - Emergency department visit for the evaluation and management of a patient, which requires these 3 key components: A detailed history; A detailed examination; and Medical decision making of moderate complexity. Counseling and/or coordination of care with o	944	6.1	7,087	8.2	0.08	756	6.3	1,224	7.0	0.03	188	5.3
99396 - Periodic comprehensive preventive medicine reevaluation and management of an individual including an age and gender appropriate history, examination, counseling/anticipatory guidance/risk factor reduction interventions, and the ordering of appropriate imm	2,457	15.8	9,057	10.5	0.16	1,795	15.0	2,499	14.2	0.02	662	18.6
A7035 - Headgear used with positive airway pressure device	1,021	6.6	2,233	2.6	0.19	686	5.7	816	4.6	0.05	335	9.4
E0601 - Continuous airway pressure (CPAP) device	733	4.7	1,761	2.0	0.15	478	4.0	593	3.4	0.03	255	7.2
015 - Lens and Cataract Procedures	208	1.3	1,481	1.7	0.03	170	1.4	270	1.5	0.01	38	1.1
017 - Lesion Destruction Retina/Choroid	202	1.3	1,425	1.6	0.03	154	1.3	275	1.6	0.02	48	1.3
020 - Intraocular Therapeutic Procedure	93	0.6	668	0.8	0.02	78	0.7	111	0.6	0.00	15	0.4
062 - Other Diagnostic Cardiovascular Procedure	643	4.1	4,368	5.0	0.04	501	4.2	779	4.4	0.01	142	4.0
063 - Nonoperative Therapeutic Cardiovascular Procedure	9,661	62.2	47,498	54.8	0.15	7,316	61.1	10,607	60.3	0.02	2,345	65.8
107 - Extracorporeal Lithotripsy Urinary	68	0.4	234	0.3	0.03	44	0.4	56	0.3	0.01	24	0.7
148 - Other Fractures/Dislocation Procedure	75	0.5	497	0.6	0.01	51	0.4	89	0.5	0.01	24	0.7
151 - Excision Semilunar Cartilage Knee	106	0.7	361	0.4	0.04	73	0.6	101	0.6	0.00	33	0.9
154 - Arthroplasty not Hip or Knee	95	0.6	273	0.3	0.04	60	0.5	79	0.4	0.01	35	1.0
155 - Arthrocentesis	1,040	6.7	3,914	4.5	0.09	748	6.2	1,041	5.9	0.01	292	8.2
156 - Aspiration Joints/Soft Tissue	364	2.3	1,265	1.5	0.06	256	2.1	341	1.9	0.01	108	3.0
165 - Breast Biopsy/Breast Diagnostic procedure	67	0.4	319	0.4	0.01	50	0.4	80	0.5	0.01	17	0.5
169 - Debride Wound/Infection/Burn	695	4.5	4,870	5.6	0.05	533	4.4	832	4.7	0.01	162	4.5
174 - Nonoperative Therapeutic Skin/Breast Procedure	546	3.5	2,744	3.2	0.02	401	3.3	638	3.6	0.02	145	4.1

Table 1.3a. Prevalence of Procedures During the 9-Month Baseline Period that Were Included in the Propensity Score Model, Life Sciences Research Database 6/1/2005−7/31/2010

Characteristic	All (N = 102,203)					Matched (N = 29,572)					Not Matched (N = 72,631)	
	Exenatide (N = 15,540)		OAD (N = 86,663)		Stand. Diff.	Exenatide (N = 11,978)		OAD (N = 17,594)		Stand. Diff.	Exenatide (N = 3,562)	
	N	%	N	%		N	%	N	%		N	%
180 - Other CT Scan	1,265	8.1	7,603	8.8	0.02	938	7.8	1,426	8.1	0.01	327	9.2
182 - Mammography	2,809	18.1	10,113	11.7	0.18	2,032	17.0	2,857	16.2	0.02	777	21.8
185 - Upper Gastrointestinal X-Ray	78	0.5	531	0.6	0.01	63	0.5	103	0.6	0.01	15	0.4
192 - Diagnostic Ultrasound Head/Neck	972	6.3	4,594	5.3	0.04	694	5.8	945	5.4	0.02	278	7.8
193 - Echocardiogram	1,781	11.5	11,562	13.3	0.06	1,338	11.2	2,082	11.8	0.02	443	12.4
199 - Electroencephalogram (EEG)	78	0.5	813	0.9	0.05	64	0.5	84	0.5	0.01	14	0.4
201 - Cardiac Stress Tests	1,854	11.9	8,838	10.2	0.06	1,372	11.5	1,997	11.4	0.00	482	13.5
202 - Electrocardiogram	4,780	30.8	28,752	33.2	0.05	3,666	30.6	5,394	30.7	0.00	1,114	31.3
208 - Radioisotope Pulmonary Scan	81	0.5	522	0.6	0.01	55	0.5	80	0.5	0.00	26	0.7
210 - Other Radioisotope Scan	193	1.2	1,178	1.4	0.01	144	1.2	220	1.3	0.00	49	1.4
212 - Diagnostic Physical Therapy	427	2.7	1,778	2.1	0.05	302	2.5	454	2.6	0.00	125	3.5
215 - Other Physical Therapy/Rehabilitation	2,017	13.0	6,670	7.7	0.17	1,412	11.8	1,929	11.0	0.03	605	17.0
218 - Psychiatric Evaluation/Therapy	1,003	6.5	3,815	4.4	0.09	695	5.8	988	5.6	0.01	308	8.6
220 - Ophthalmologic/Otologic Diagnosis/Treatment	5,096	32.8	24,459	28.2	0.10	3,831	32.0	5,474	31.1	0.02	1,265	35.5
222 - Blood Transfusion	43	0.3	848	1.0	0.09	38	0.3	77	0.4	0.02	5	0.1
226 - Other Diagnostic Radiology	6,873	44.2	33,326	38.5	0.12	5,106	42.6	7,374	41.9	0.01	1,767	49.6
227 - Other Diagnostic Procedure Evaluation/Consult	15,492	99.7	85,779	99.0	0.09	11,931	99.6	17,515	99.6	0.01	3,561	100
228 - Prophylactic Vaccinations	4,247	27.3	17,862	20.6	0.16	3,215	26.8	4,539	25.8	0.02	1,032	29.0
231 - Other Therapeutic Procedure	4,413	28.4	21,825	25.2	0.07	3,189	26.6	4,650	26.4	0.00	1,224	34.4
232 - Anesthesia	2,128	13.7	12,018	13.9	0.01	1,576	13.2	2,318	13.2	0.00	552	15.5
L00 - Orthotic Procedures	964	6.2	3,884	4.5	0.08	698	5.8	1,016	5.8	0.00	266	7.5

Stand. Diff., Standardized Difference; CPT, Current Procedural Terminology; HCPC, Centers for Medicare and Medicaid Services Common Procedure Coding System

Note: OADs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins. Standardized difference is calculated by the difference between the 2 mean values divided by the pooled standard deviation.

Please note characteristic descriptions may be truncated in the data due to SAS limitations.

Table 1.3b. Prevalence of Procedures During the 9-Month Baseline Period that Were Included in the Propensity Score Model, Impact National Benchmark Database 6/1/2005−7/31/2010

Characteristic	All (N = 65,098)					Matched (N = 17,051)					Not Matched (N = 48,047)	
	Exenatide (N = 10,643)		OAD (N = 54,455)		Stand. Diff.	Exenatide (N = 6,954)		OAD (N = 10,097)		Stand. Diff.	Exenatide (N = 3,689)	
	N	%	N	%		N	%	N	%		N	%
Procedures (CPT, HCPC, and procedure category codes)												
Status post cholecystectomy	50	0.5	250	0.5	0.00	25	0.4	47	0.5	0.02	25	0.7
Coronary revascularization	260	2.4	1,791	3.3	0.05	171	2.5	240	2.4	0.01	89	2.4
71010 - Radiologic examination, chest; single view, frontal	670	6.3	5,136	9.4	0.12	449	6.5	674	6.7	0.01	221	6.0
73630 - Radiologic examination, foot; complete, minimum of three views	522	4.9	2,075	3.8	0.05	317	4.6	448	4.4	0.01	205	5.6
80051 - Electrolyte panel This panel must include the following: Carbon dioxide (82374) Chloride (82435) Potassium (84132) Sodium (84295)	610	5.7	3,070	5.6	0.00	368	5.3	603	6.0	0.03	242	6.6
80053 - Comprehensive metabolic panel This panel must include the following: Albumin (82040) Bilirubin, total (82247) Calcium (82310) Carbon dioxide (bicarbonate) (82374) Chloride (82435) Creatinine (82565) Glucose (82947) Phosphatase, alkaline (84075) Potassium	4,361	41.0	17,783	32.7	0.17	2,748	39.5	3,899	38.6	0.02	1,613	43.7
80061 - Lipid panel This panel must include the following: Cholesterol, serum, total (82465) Lipoprotein, direct measurement, high density cholesterol (HDL cholesterol) (83718) Triglycerides (84478)	6,256	58.8	26,257	48.2	0.21	3,983	57.3	5,724	56.7	0.01	2,273	61.6
82043 - Albumin; urine, microalbumin, quantitative	3,628	34.1	14,500	26.6	0.16	2,266	32.6	3,413	33.8	0.03	1,362	36.9
82465 - Cholesterol, serum or whole blood, total	546	5.1	2,601	4.8	0.02	366	5.3	565	5.6	0.01	180	4.9
82550 - Creatine kinase (CK), (CPK); total	1,096	10.3	4,462	8.2	0.07	683	9.8	957	9.5	0.01	413	11.2
82570 - Creatinine; other source	2,912	27.4	11,291	20.7	0.16	1,794	25.8	2,760	27.3	0.03	1,118	30.3
82947 - Glucose; quantitative, blood (except reagent strip)	1,913	18.0	9,062	16.6	0.04	1,192	17.1	1,807	17.9	0.02	721	19.5
82948 - Glucose; blood, reagent strip	947	8.9	3,747	6.9	0.07	583	8.4	834	8.3	0.00	364	9.9

Table 1.3b. Prevalence of Procedures During the 9-Month Baseline Period that Were Included in the Propensity Score Model, Impact National Benchmark Database 6/1/2005−7/31/2010

Characteristic	All (N = 65,098)					Matched (N = 17,051)					Not Matched (N = 48,047)	
	Exenatide (N = 10,643)		OAD (N = 54,455)		Stand. Diff.	Exenatide (N = 6,954)		OAD (N = 10,097)		Stand. Diff.	Exenatide (N = 3,689)	
	N	%	N	%		N	%	N	%		N	%
82962 - Glucose, blood by glucose monitoring device(s) cleared by the FDA specifically for home use	1,600	15.0	5,768	10.6	0.13	974	14.0	1,349	13.4	0.02	626	17.0
83036 - Hemoglobin; glycosylated (A1C)	7,367	69.2	31,843	58.5	0.23	4,705	67.7	6,868	68.0	0.01	2,662	72.2
83721 - Lipoprotein, direct measurement; LDL cholesterol	809	7.6	3,110	5.7	0.08	477	6.9	735	7.3	0.02	332	9.0
84153 - Prostate specific antigen (PSA); total	1,164	10.9	6,963	12.8	0.06	817	11.7	1,167	11.6	0.01	347	9.4
84436 - Thyroxine; total	596	5.6	2,154	4.0	0.08	355	5.1	471	4.7	0.02	241	6.5
84450 - Transferase; aspartate amino (AST) (SGOT)	1,315	12.4	5,583	10.3	0.07	808	11.6	1,212	12.0	0.01	507	13.7
84478 - Triglycerides	489	4.6	2,011	3.7	0.05	315	4.5	473	4.7	0.01	174	4.7
85025 - Blood count; complete (CBC), automated (Hgb, Hct, RBC, WBC and platelet count) and automated differential WBC count	3,344	31.4	15,417	28.3	0.07	2,141	30.8	3,108	30.8	0.00	1,203	32.6
85027 - Blood count; complete (CBC), automated (Hgb, Hct, RBC, WBC and platelet count)	817	7.7	5,052	9.3	0.06	551	7.9	922	9.1	0.04	266	7.2
88305 - Level IV - Surgical pathology, gross and microscopic examination Abortion - spontaneous/missed Artery, biopsy Bone marrow, biopsy Bone exostosis Brain/meninges, other than for tumor resection Breast, biopsy, not requiring microscopic evaluation of surgica	1,361	12.8	6,183	11.4	0.04	857	12.3	1,277	12.6	0.01	504	13.7
90806 - Individual psychotherapy, insight oriented, behavior modifying and/or supportive, in an office or outpatient facility, approximately 45 to 50 minutes face-to-face with the patient;	512	4.8	1,755	3.2	0.08	297	4.3	415	4.1	0.01	215	5.8
92014 - Ophthalmological services: medical examination and evaluation, with initiation or continuation of diagnostic and treatment program; comprehensive, established patient, one or more visits	2,672	25.1	12,521	23.0	0.05	1,656	23.8	2,491	24.7	0.02	1,016	27.5

Table 1.3b. Prevalence of Procedures During the 9-Month Baseline Period that Were Included in the Propensity Score Model, Impact National Benchmark Database 6/1/2005−7/31/2010

Characteristic	All (N = 65,098)					Matched (N = 17,051)					Not Matched (N = 48,047)	
	Exenatide (N = 10,643)		OAD (N = 54,455)		Stand. Diff.	Exenatide (N = 6,954)		OAD (N = 10,097)		Stand. Diff.	Exenatide (N = 3,689)	
	N	%	N	%		N	%	N	%		N	%
92226 - Ophthalmoscopy, extended, with retinal drawing (eg, for retinal detachment, melanoma), with interpretation and report; subsequent	439	4.1	2,176	4.0	0.01	272	3.9	401	4.0	0.00	167	4.5
92250 - Fundus photography with interpretation and report	754	7.1	3,080	5.7	0.06	456	6.6	657	6.5	0.00	298	8.1
93005 - Electrocardiogram, routine ECG with at least 12 leads; tracing only, without interpretation and report	664	6.2	3,163	5.8	0.02	427	6.1	619	6.1	0.00	237	6.4
93010 - Electrocardiogram, routine ECG with at least 12 leads; interpretation and report only	1,213	11.4	8,331	15.3	0.11	777	11.2	1,245	12.3	0.04	436	11.8
97001 - Physical therapy evaluation	791	7.4	2,751	5.1	0.10	470	6.8	641	6.3	0.02	321	8.7
99203 - Office or other outpatient visit for the evaluation and management of a new patient, which requires these 3 key components: A detailed history; A detailed examination; Medical decision making of low complexity. Counseling and/or coordination of care with	1,483	13.9	6,013	11.0	0.09	953	13.7	1,288	12.8	0.03	530	14.4
99205 - Office or other outpatient visit for the evaluation and management of a new patient, which requires these 3 key components: A comprehensive history; A comprehensive examination; Medical decision making of high complexity. Counseling and/or coordination of	515	4.8	1,642	3.0	0.09	290	4.2	401	4.0	0.01	225	6.1
99211 - Office or other outpatient visit for the evaluation and management of an established patient, that may not require the presence of a physician. Usually, the presenting problem(s) are minimal. Typically, 5 minutes are spent performing or supervising these	1,158	10.9	4,243	7.8	0.11	663	9.5	920	9.1	0.01	495	13.4

Table 1.3b. Prevalence of Procedures During the 9-Month Baseline Period that Were Included in the Propensity Score Model, Impact National Benchmark Database 6/1/2005−7/31/2010

Characteristic	All (N = 65,098)					Matched (N = 17,051)					Not Matched (N = 48,047)	
	Exenatide (N = 10,643)		OAD (N = 54,455)		Stand. Diff.	Exenatide (N = 6,954)		OAD (N = 10,097)		Stand. Diff.	Exenatide (N = 3,689)	
	N	%	N	%		N	%	N	%		N	%
99212 - Office or other outpatient visit for the evaluation and management of an established patient, which requires at least 2 of these 3 key components: A problem focused history; A problem focused examination; Straightforward medical decision making. Counselin	2,776	26.1	11,944	21.9	0.10	1,687	24.3	2,527	25.0	0.02	1,089	29.5
99213 - Office or other outpatient visit for the evaluation and management of an established patient, which requires at least 2 of these 3 key components: An expanded problem focused history; An expanded problem focused examination; Medical decision making of low	8,681	81.6	41,549	76.3	0.13	5,527	79.5	8,078	80.0	0.01	3,154	85.5
99214 - Office or other outpatient visit for the evaluation and management of an established patient, which requires at least 2 of these 3 key components: A detailed history; A detailed examination; Medical decision making of moderate complexity. Counseling and/o	8,799	82.7	37,930	69.7	0.31	5,588	80.4	8,015	79.4	0.02	3,211	87.0
99215 - Office or other outpatient visit for the evaluation and management of an established patient, which requires at least 2 of these 3 key components: A comprehensive history; A comprehensive examination; Medical decision making of high complexity. Counseling	2,217	20.8	8,404	15.4	0.14	1,315	18.9	1,876	18.6	0.01	902	24.5

Table 1.3b. Prevalence of Procedures During the 9-Month Baseline Period that Were Included in the Propensity Score Model, Impact National Benchmark Database 6/1/2005−7/31/2010

Characteristic	All (N = 65,098)					Matched (N = 17,051)					Not Matched (N = 48,047)	
	Exenatide (N = 10,643)		OAD (N = 54,455)		Stand. Diff.	Exenatide (N = 6,954)		OAD (N = 10,097)		Stand. Diff.	Exenatide (N = 3,689)	
	N	%	N	%		N	%	N	%		N	%
99232 - Subsequent hospital care, per day, for the evaluation and management of a patient, which requires at least 2 of these 3 key components: An expanded problem focused interval history; An expanded problem focused examination; Medical decision making of moder	545	5.1	5,608	10.3	0.20	343	4.9	599	5.9	0.04	202	5.5
99243 - Office consultation for a new or established patient, which requires these 3 key components: A detailed history; A detailed examination; and Medical decision making of low complexity. Counseling and/or coordination of care with other providers or agencies	1,770	16.6	7,362	13.5	0.09	1,095	15.7	1,588	15.7	0.00	675	18.3
99244 - Office consultation for a new or established patient, which requires these 3 key components: A comprehensive history; A comprehensive examination; and Medical decision making of moderate complexity. Counseling and/or coordination of care with other provid	2,687	25.2	9,061	16.6	0.21	1,557	22.4	2,186	21.6	0.02	1,130	30.6
99245 - Office consultation for a new or established patient, which requires these 3 key components: A comprehensive history; A comprehensive examination; and Medical decision making of high complexity. Counseling and/or coordination of care with other providers	1,487	14.0	4,092	7.5	0.21	780	11.2	1,075	10.6	0.02	707	19.2

Table 1.3b. Prevalence of Procedures During the 9-Month Baseline Period that Were Included in the Propensity Score Model, Impact National Benchmark Database 6/1/2005−7/31/2010

Characteristic	All (N = 65,098)					Matched (N = 17,051)					Not Matched (N = 48,047)	
	Exenatide (N = 10,643)		OAD (N = 54,455)		Stand. Diff.	Exenatide (N = 6,954)		OAD (N = 10,097)		Stand. Diff.	Exenatide (N = 3,689)	
	N	%	N	%		N	%	N	%		N	%
99284 - Emergency department visit for the evaluation and management of a patient, which requires these 3 key components: A detailed history; A detailed examination; and Medical decision making of moderate complexity. Counseling and/or coordination of care with o	761	7.2	4,746	8.7	0.06	508	7.3	775	7.7	0.01	253	6.9
99285 - Emergency department visit for the evaluation and management of a patient, which requires these 3 key components within the constraints imposed by the urgency of the patient's clinical condition and/or mental status: A comprehensive history; A comprehensi	642	6.0	5,336	9.8	0.14	414	6.0	661	6.5	0.02	228	6.2
99396 - Periodic comprehensive preventive medicine reevaluation and management of an individual including an age and gender appropriate history, examination, counseling/anticipatory guidance/risk factor reduction interventions, and the ordering of appropriate imm	2,232	21.0	9,482	17.4	0.09	1,376	19.8	2,068	20.5	0.02	856	23.2
A7035 - Headgear used with positive airway pressure device	666	6.3	1,287	2.4	0.19	344	4.9	448	4.4	0.02	322	8.7
G0108 - Diabetes outpatient self-management training services, individual, per 30 minutes	1,396	13.1	2,463	4.5	0.31	640	9.2	898	8.9	0.01	756	20.5
006 - Decompression Peripheral Nerve	68	0.6	189	0.3	0.04	37	0.5	48	0.5	0.01	31	0.8
017 - Lesion Destruction Retina/Choroid	167	1.6	1,040	1.9	0.03	109	1.6	160	1.6	0.00	58	1.6
018 - Diagnostic Procedure on Eye	810	7.6	3,989	7.3	0.01	518	7.4	718	7.1	0.01	292	7.9
048 - Insertion/Removal Cardiac Pacemaker	25	0.2	218	0.4	0.03	14	0.2	34	0.3	0.03	11	0.3
054 - Other Vascular Catheterization not Heart	241	2.3	2,233	4.1	0.10	152	2.2	234	2.3	0.01	89	2.4
062 - Other Diagnostic Cardiovascular Procedure	424	4.0	2,346	4.3	0.02	246	3.5	399	4.0	0.02	178	4.8

Table 1.3b. Prevalence of Procedures During the 9-Month Baseline Period that Were Included in the Propensity Score Model, Impact National Benchmark Database 6/1/2005−7/31/2010

Characteristic	All (N = 65,098)					Matched (N = 17,051)					Not Matched (N = 48,047)	
	Exenatide (N = 10,643)		OAD (N = 54,455)		Stand. Diff.	Exenatide (N = 6,954)		OAD (N = 10,097)		Stand. Diff.	Exenatide (N = 3,689)	
	N	%	N	%		N	%	N	%		N	%
063 - Nonoperative Therapeutic Cardiovascular Procedure	6,905	64.9	33,900	62.3	0.05	4,547	65.4	6,663	66.0	0.01	2,358	63.9
076 - Colonoscopy and Biopsy	685	6.4	2,996	5.5	0.04	436	6.3	606	6.0	0.01	249	6.7
077 - Procto/Anorectal Biopsy	40	0.4	145	0.3	0.02	26	0.4	32	0.3	0.01	14	0.4
086 - Other Hernia Repair	49	0.5	196	0.4	0.02	28	0.4	39	0.4	0.00	21	0.6
093 - Nonoperative Upper GI Therapeutic Procedure	37	0.3	280	0.5	0.03	28	0.4	45	0.4	0.01	9	0.2
102 - Ureteral Catheterization	50	0.5	178	0.3	0.02	29	0.4	32	0.3	0.02	21	0.6
107 - Extracorporeal Lithotripsy Urinary	48	0.5	132	0.2	0.04	25	0.4	28	0.3	0.01	23	0.6
162 - Operative Therapeutic Procedure on Joints	148	1.4	460	0.8	0.05	85	1.2	106	1.0	0.02	63	1.7
169 - Debride Wound/Infection/Burn	669	6.3	3,197	5.9	0.02	413	5.9	563	5.6	0.02	256	6.9
170 - Excision of Skin Lesion	1,011	9.5	4,379	8.0	0.05	607	8.7	941	9.3	0.02	404	11.0
171 - Suture Skin/Subcutaneous Tissue	139	1.3	880	1.6	0.03	86	1.2	171	1.7	0.04	53	1.4
174 - Nonoperative Therapeutic Skin/Breast Procedure	553	5.2	2,666	4.9	0.01	340	4.9	516	5.1	0.01	213	5.8
179 - CT Scan Abdomen	715	6.7	3,840	7.1	0.01	454	6.5	664	6.6	0.00	261	7.1
182 - Mammography	2,128	20.0	7,495	13.8	0.17	1,297	18.7	1,892	18.7	0.00	831	22.5
183 - Routine Chest X-Ray	2,246	21.1	13,048	24.0	0.07	1,454	20.9	2,159	21.4	0.01	792	21.5
192 - Diagnostic Ultrasound Head/Neck	709	6.7	2,694	4.9	0.07	422	6.1	526	5.2	0.04	287	7.8
193 - Echocardiogram	1,432	13.5	7,121	13.1	0.01	875	12.6	1,231	12.2	0.01	557	15.1
196 - Diagnostic Ultrasound Abdomen	741	7.0	3,941	7.2	0.01	461	6.6	664	6.6	0.00	280	7.6
201 - Cardiac Stress Tests	1,412	13.3	5,902	10.8	0.07	816	11.7	1,202	11.9	0.01	596	16.2
202 - Electrocardiogram	3,936	37.0	20,881	38.3	0.03	2,501	36.0	3,616	35.8	0.00	1,435	38.9
211 - Therapeutic Radiology	138	1.3	1,097	2.0	0.06	89	1.3	155	1.5	0.02	49	1.3
212 - Diagnostic Physical Therapy	248	2.3	1,103	2.0	0.02	160	2.3	225	2.2	0.00	88	2.4
215 - Other Physical Therapy/Rehabilitation	2,383	22.4	6,250	11.5	0.29	1,250	18.0	1,749	17.3	0.02	1,133	30.7
216 - Respitory Intubation/Mechanical Ventilation	63	0.6	365	0.7	0.01	25	0.4	41	0.4	0.01	38	1.0
220 - Ophthalmologic/Otologic Diagnosis/Treatment	4,481	42.1	21,269	39.1	0.06	2,796	40.2	4,128	40.9	0.01	1,685	45.7
226 - Other Diagnostic Radiology	3,605	33.9	15,845	29.1	0.10	2,193	31.5	3,214	31.8	0.01	1,412	38.3
227 - Other Diagnostic Procedure Evaluation/Consult	10,602	99.6	53,856	98.9	0.08	6,920	99.5	10,033	99.4	0.02	3,682	99.8
228 - Prophylactic Vaccinations	3,455	32.5	13,999	25.7	0.15	2,235	32.1	3,165	31.3	0.02	1,220	33.1

Table 1.3b. Prevalence of Procedures During the 9-Month Baseline Period that Were Included in the Propensity Score Model, Impact National Benchmark Database 6/1/2005−7/31/2010

Characteristic	All (N = 65,098)				Stand. Diff.	Matched (N = 17,051)				Stand. Diff.	Not Matched (N = 48,047)	
	Exenatide (N = 10,643)		OAD (N = 54,455)			Exenatide (N = 6,954)		OAD (N = 10,097)			Exenatide (N = 3,689)	
	N	%	N	%		N	%	N	%		N	%
231 - Other Therapeutic Procedure	2,779	26.1	12,122	22.3	0.09	1,671	24.0	2,360	23.4	0.02	1,108	30.0
233 - Other Lab	9,264	87.0	43,007	79.0	0.22	5,957	85.7	8,600	85.2	0.01	3,307	89.6
A00 - Transportation, Medical and Surgical Supplies, Administrative, Miscellaneous and Investigational	2,594	24.4	12,103	22.2	0.05	1,555	22.4	2,285	22.6	0.01	1,039	28.2
J00 - Drugs Administered Other Than Oral Method	2,396	22.5	8,637	15.9	0.17	1,461	21.0	1,978	19.6	0.04	935	25.3

Stand. Diff., Standardized Difference; CPT, Current Procedural Terminology; HCPC, Centers for Medicare and Medicaid Services Common Procedure Coding System

Note: OADs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins. Standardized difference is calculated by the difference between the 2 proportions divided by the pooled standard deviation.

Please note characteristic descriptions may be truncated in the data due to SAS limitations.

Table 1.4a. Prevalence of Drug Dispensings During the 9-Month Baseline Period that Were Included in the Propensity Score Model, Life Sciences Research Database 6/1/2005−7/31/2010

Characteristic	All (N = 102,203)					Matched (N = 29,572)					Not Matched (N = 72,631)	
	Exenatide (N = 15,540)		OAD (N = 86,663)		Stand. Diff.	Exenatide (N = 11,978)		OAD (N = 17,594)		Stand. Diff.	Exenatide (N = 3,562)	
	N	%	N	%		N	%	N	%		N	%
Drug Class												
Non-alcohol sedatives	2,609	16.8	10,941	12.6	0.12	1,917	16.0	2,691	15.3	0.02	692	19.4
Acid-suppressing drugs	2,839	18.3	13,422	15.5	0.07	2,049	17.1	3,076	17.5	0.01	790	22.2
Antipsychotics	222	1.4	1,159	1.3	0.01	169	1.4	230	1.3	0.01	53	1.5
Dipeptidyl peptidase-4	0	0.0	0	0.0	-	0	0.0	0	0.0	-	0	0.0
Metformin	12,588	81.0	47,065	54.3	0.60	9,193	76.7	12,336	70.1	0.15	3,395	95.3
Sulfonyureas	8,588	55.3	27,127	31.3	0.50	6,017	50.2	7,226	41.1	0.18	2,571	72.2
Thiazolidinediones	8,146	52.4	24,098	27.8	0.52	5,583	46.6	6,705	38.1	0.17	2,563	72.0
Non-sulfonylurea	722	4.6	2,380	2.7	0.10	446	3.7	606	3.4	0.02	276	7.7
Pramlintide	115	0.7	83	0.1	0.10	56	0.5	54	0.3	0.03	59	1.7
Alpha-glucosidase inhibitors	185	1.2	427	0.5	0.08	100	0.8	117	0.7	0.02	85	2.4
Insulin glargine	3,067	19.7	9,382	10.8	0.25	2,000	16.7	2,912	16.6	0.00	1,067	30.0
Insulins	4,380	28.2	21,594	24.9	0.07	3,071	25.6	4,910	27.9	0.05	1,309	36.7
Ace inhibitors	7,376	47.5	40,549	46.8	0.01	5,740	47.9	8,433	47.9	0.00	1,636	45.9
NSAIDs	3,594	23.1	16,970	19.6	0.09	2,674	22.3	3,968	22.6	0.01	920	25.8
Fibrates	2,267	14.6	8,522	9.8	0.15	1,628	13.6	2,202	12.5	0.03	639	17.9
Statins	9,276	59.7	44,347	51.2	0.17	7,016	58.6	9,977	56.7	0.04	2,260	63.4
Antiretroviral agents	10	0.1	162	0.2	0.03	9	0.1	21	0.1	0.01	1	0.0
Digitalis glycosides	263	1.7	2,052	2.4	0.05	208	1.7	317	1.8	0.00	55	1.5
Hypotensives, sympatholytic	389	2.5	2,512	2.9	0.02	300	2.5	516	2.9	0.03	89	2.5
Hypotensives, angiotensin receptor	4,379	28.2	16,570	19.1	0.21	3,044	25.4	4,300	24.4	0.02	1,335	37.5
Angiotensin receptor antagonist/ thiazide and	655	4.2	2,073	2.4	0.10	573	4.8	649	3.7	0.05	82	2.3
ACE inhibitor/calcium channel blocker combination	665	4.3	2,934	3.4	0.05	508	4.2	704	4.0	0.01	157	4.4
Vasodilators, coronary	623	4.0	4,182	4.8	0.04	502	4.2	761	4.3	0.01	121	3.4
Calcium channel blocking agents	2,483	16.0	14,109	16.3	0.01	1,919	16.0	2,841	16.1	0.00	564	15.8
Narcotic antitussive-1st generation antihistamine-decongestant	335	2.2	1,520	1.8	0.03	228	1.9	401	2.3	0.03	107	3.0
Narcotic antitussive-1st generation	589	3.8	2,422	2.8	0.06	440	3.7	592	3.4	0.02	149	4.2
Narcotic antitussive-expectorant combination	615	4.0	2,774	3.2	0.04	476	4.0	661	3.8	0.01	139	3.9
Decongestant-expectorant combinations	465	3.0	1,920	2.2	0.05	320	2.7	497	2.8	0.01	145	4.1
Potassium replacement	1,263	8.1	6,143	7.1	0.04	916	7.6	1,383	7.9	0.01	347	9.7
Vitamin B preparations	253	1.6	1,216	1.4	0.02	180	1.5	246	1.4	0.01	73	2.0
Vitamin D preparations	293	1.9	918	1.1	0.07	232	1.9	234	1.3	0.05	61	1.7
Proton Pump Inhibitors	402	2.6	2,022	2.3	0.02	359	3.0	470	2.7	0.02	43	1.2
Laxatives and cathartics	777	5.0	3,546	4.1	0.04	595	5.0	778	4.4	0.03	182	5.1

Table 1.4a. Prevalence of Drug Dispensings During the 9-Month Baseline Period that Were Included in the Propensity Score Model, Life Sciences Research Database 6/1/2005−7/31/2010

Characteristic	All (N = 102,203)					Matched (N = 29,572)					Not Matched (N = 72,631)	
	Exenatide (N = 15,540)		OAD (N = 86,663)		Stand. Diff.	Exenatide (N = 11,978)		OAD (N = 17,594)		Stand. Diff.	Exenatide (N = 3,562)	
	N	%	N	%		N	%	N	%		N	%
Estrogenic agents	778	5.0	2,602	3.0	0.10	524	4.4	756	4.3	0.00	254	7.1
Contraceptives, oral	374	2.4	1,198	1.4	0.08	259	2.2	397	2.3	0.01	115	3.2
Sedative-hypnotics, non-barbiturate	1,342	8.6	5,068	5.8	0.11	980	8.2	1,329	7.6	0.02	362	10.2
Anti-anxiety drugs	1,647	10.6	7,207	8.3	0.08	1,203	10.0	1,732	9.8	0.01	444	12.5
Serotonin specific reuptake inhibitor (SSRIs)	2,724	17.5	10,639	12.3	0.15	1,963	16.4	2,917	16.6	0.01	761	21.4
Tricyclic antidepressants and related non-selective reuptake inhibitors	562	3.6	2,786	3.2	0.02	414	3.5	694	3.9	0.03	148	4.2
Analgesics, narcotics	4,938	31.8	24,569	28.4	0.07	3,681	30.7	5,488	31.2	0.01	1,257	35.3
Antimigraine preparations	223	1.4	739	0.9	0.05	157	1.3	230	1.3	0.00	66	1.9
Anticonvulsants	1,760	11.3	7,646	8.8	0.08	1,318	11.0	1,931	11.0	0.00	442	12.4
Antiparkinsonism drugs, other	262	1.7	857	1.0	0.06	192	1.6	247	1.4	0.02	70	2.0
Antitussives, non-narcotic	476	3.1	1,960	2.3	0.05	350	2.9	486	2.8	0.01	126	3.5
Skeletal muscle relaxants	1,599	10.3	6,657	7.7	0.09	1,157	9.7	1,782	10.1	0.02	442	12.4
Antiemetic/antivertigo agents	344	2.2	2,018	2.3	0.01	259	2.2	406	2.3	0.01	85	2.4
Serotonin-2 antagonist/reuptake inhibitors (SARIs)	332	2.1	1,445	1.7	0.03	238	2.0	379	2.2	0.01	94	2.6
Beta-adrenergic agents	1,431	9.2	6,527	7.5	0.06	1,027	8.6	1,588	9.0	0.02	404	11.3
Beta-adrenergics and glucocorticoids combination	624	4.0	2,624	3.0	0.05	450	3.8	692	3.9	0.01	174	4.9
Alpha-adrenergic blocking agents	274	1.8	1,895	2.2	0.03	218	1.8	388	2.2	0.03	56	1.6
Beta-adrenergic blocking agents	3,134	20.2	18,005	20.8	0.02	2,419	20.2	3,622	20.6	0.01	715	20.1
Intestinal motility stimulants	288	1.9	1,850	2.1	0.02	221	1.8	323	1.8	0.00	67	1.9
Blood sugar diagnostics	9,111	58.6	39,965	46.1	0.25	6,654	55.6	9,620	54.7	0.02	2,457	69.0
Anti-hyperlipidemic - HMG CoA reductase inhibitors	2,349	15.1	10,952	12.6	0.07	2,126	17.7	2,632	15.0	0.08	223	6.3
Lipotropics	9,094	58.5	41,999	48.5	0.20	6,652	55.5	9,593	54.5	0.02	2,442	68.6
Anti-hyperlipidemic (HMG CoA reductase inhibitor) & cholesterol absorption inhibitor	376	2.4	1,367	1.6	0.06	336	2.8	399	2.3	0.03	40	1.1
Oral anticoagulants, coumarin type	458	2.9	3,218	3.7	0.04	339	2.8	528	3.0	0.01	119	3.3
Platelet aggregation inhibitors	1,017	6.5	6,412	7.4	0.03	792	6.6	1,209	6.9	0.01	225	6.3
Thyroid hormones	2,318	14.9	8,818	10.2	0.14	1,662	13.9	2,372	13.5	0.01	656	18.4
Bone resorption suppression agents	390	2.5	2,300	2.7	0.01	293	2.4	405	2.3	0.01	97	2.7
Glucocorticoids	1,645	10.6	8,150	9.4	0.04	1,228	10.3	1,849	10.5	0.01	417	11.7
Topical antifungals	1,174	7.6	5,418	6.3	0.05	902	7.5	1,269	7.2	0.01	272	7.6
Topical anti-inflammatory steroidal	1,274	8.2	5,546	6.4	0.07	948	7.9	1,331	7.6	0.01	326	9.2
Topical antibiotics	464	3.0	2,040	2.4	0.04	354	3.0	444	2.5	0.03	110	3.1

Table 1.4a. Prevalence of Drug Dispensings During the 9-Month Baseline Period that Were Included in the Propensity Score Model, Life Sciences Research Database 6/1/2005−7/31/2010

Characteristic	All (N = 102,203)					Matched (N = 29,572)					Not Matched (N = 72,631)	
	Exenatide (N = 15,540)		OAD (N = 86,663)		Stand. Diff.	Exenatide (N = 11,978)		OAD (N = 17,594)		Stand. Diff.	Exenatide (N = 3,562)	
	N	%	N	%		N	%	N	%		N	%
Miotics/other intraocular pressure reducers	445	2.9	2,841	3.3	0.02	344	2.9	535	3.0	0.01	101	2.8
Eye antibiotic-corticoid combinations	233	1.5	1,031	1.2	0.03	174	1.5	251	1.4	0.00	59	1.7
Eye antihistamines	253	1.6	867	1.0	0.06	181	1.5	219	1.2	0.02	72	2.0
Nasal antihistamine	241	1.6	657	0.8	0.07	179	1.5	222	1.3	0.02	62	1.7
Nasal anti-inflammatory steroids	1,519	9.8	5,693	6.6	0.12	1,096	9.2	1,515	8.6	0.02	423	11.9
Benign prostatic hypertrophy/micturition agents	361	2.3	2,351	2.7	0.02	305	2.5	452	2.6	0.00	56	1.6
Urinary tract antispasmodic/anti-incontinence agent	263	1.7	1,339	1.5	0.01	191	1.6	313	1.8	0.01	72	2.0
Thiazide and related diuretics	1,837	11.8	9,103	10.5	0.04	1,359	11.3	2,087	11.9	0.02	478	13.4
Potassium sparing diuretics in combination	765	4.9	3,243	3.7	0.06	541	4.5	794	4.5	0.00	224	6.3
Loop diuretics	2,158	13.9	9,651	11.1	0.08	1,562	13.0	2,210	12.6	0.01	596	16.7
Penicillins	2,880	18.5	15,059	17.4	0.03	2,191	18.3	3,297	18.7	0.01	689	19.3
Tetracyclines	681	4.4	3,453	4.0	0.02	518	4.3	733	4.2	0.01	163	4.6
Macrolides	2,899	18.7	12,922	14.9	0.10	2,166	18.1	3,064	17.4	0.02	733	20.6
Lincosamides	485	3.1	2,341	2.7	0.02	360	3.0	550	3.1	0.01	125	3.5
Quinolones	2,920	18.8	13,768	15.9	0.08	2,181	18.2	3,164	18.0	0.01	739	20.7
Cephalosporins - 1st generation	1,293	8.3	6,835	7.9	0.02	991	8.3	1,450	8.2	0.00	302	8.5
Cephalosporins - 2nd generation	296	1.9	1,345	1.6	0.03	223	1.9	315	1.8	0.01	73	2.0
Cephalosporins - 3rd generation	396	2.5	1,311	1.5	0.07	267	2.2	349	2.0	0.02	129	3.6
Nitrofuran derivatives	319	2.1	1,355	1.6	0.04	244	2.0	336	1.9	0.01	75	2.1
Antifungal agents	1,276	8.2	5,125	5.9	0.09	962	8.0	1,392	7.9	0.00	314	8.8
Antivirals, general	549	3.5	2,579	3.0	0.03	414	3.5	615	3.5	0.00	135	3.8
Durable medical equipment, miscellaneous (Group 1)	3,450	22.2	15,607	18.0	0.10	2,482	20.7	3,656	20.8	0.00	968	27.2
Diabetic supplies	794	5.1	5,497	6.3	0.05	594	5.0	936	5.3	0.02	200	5.6
2nd generation antihistamine and decongestant combinations	261	1.7	1,167	1.3	0.03	190	1.6	276	1.6	0.00	71	2.0
Antihistamines - 1st generation	789	5.1	3,714	4.3	0.04	593	5.0	914	5.2	0.01	196	5.5
Antihistamines - 2nd generation	1,588	10.2	5,557	6.4	0.14	1,110	9.3	1,538	8.7	0.02	478	13.4
Leukotriene receptor antagonists	700	4.5	2,205	2.5	0.11	492	4.1	681	3.9	0.01	208	5.8

Stand. Diff., Standardized Difference

Note: OADs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins. Standardized difference is calculated by the difference between the 2 mean values divided by the pooled standard deviation.

Please note characteristic descriptions may be truncated in the data due to SAS limitations.

Table 1.4b. Prevalence of Drug Dispensings During the 9-Month Baseline Period that Were Included in the Propensity Score Model, Impact National Benchmark Databases 6/1/2005−7/31/2010

Characteristic	All (N = 65,098)					Matched (N = 17,051)					Not Matched (N = 48,047)	
	Exenatide (N = 10,643)		OAD (N = 54,455)		Stand. Diff.	Exenatide (N = 6,954)		OAD (N = 10,097)		Stand. Diff.	Exenatide (N = 3,689)	
	N	%	N	%		N	%	N	%		N	%
Drug Class												
Non-alcohol sedatives	1,781	16.7	6,801	12.5	0.12	1,069	15.4	1,570	15.5	0.00	712	19.3
Antipsychotics	171	1.6	836	1.5	0.01	104	1.5	162	1.6	0.01	67	1.8
Dipeptidyl peptidase-4	0	0.0	0	0.0	-	0	0.0	0	0.0	-	0	0.0
Metformin	8,757	82.3	33,319	61.2	0.48	5,400	77.7	7,173	71.0	0.15	3,357	91.0
Sulfonyureas	5,854	55.0	19,153	35.2	0.41	3,336	48.0	4,040	40.0	0.16	2,518	68.3
Thiazolidinediones	5,320	50.0	15,184	27.9	0.47	3,019	43.4	3,633	36.0	0.15	2,301	62.4
Non-sulfonylurea	591	5.6	1,551	2.8	0.14	285	4.1	343	3.4	0.04	306	8.3
Pramlintide	71	0.7	47	0.1	0.09	26	0.4	30	0.3	0.01	45	1.2
Alpha-glucosidase inhibitors	143	1.3	314	0.6	0.08	62	0.9	69	0.7	0.02	81	2.2
Insulin glargine	2,312	21.7	5,894	10.8	0.30	1,119	16.1	1,657	16.4	0.01	1,193	32.3
Insulins	3,313	31.1	13,821	25.4	0.13	1,825	26.2	2,864	28.4	0.05	1,488	40.3
Ace inhibitors	5,145	48.3	26,102	47.9	0.01	3,383	48.6	4,907	48.6	0.00	1,762	47.8
NSAIDs	2,208	20.7	10,008	18.4	0.06	1,378	19.8	2,085	20.6	0.02	830	22.5
Fibrates	1,423	13.4	4,662	8.6	0.15	850	12.2	1,175	11.6	0.02	573	15.5
Statins	6,818	64.1	30,602	56.2	0.16	4,321	62.1	6,277	62.2	0.00	2,497	67.7
Antiretroviral agents	12	0.1	119	0.2	0.03	7	0.1	15	0.1	0.01	5	0.1
Digitalis glycosides	199	1.9	1,175	2.2	0.02	123	1.8	194	1.9	0.01	76	2.1
Hypotensives, sympatholytic	206	1.9	987	1.8	0.01	128	1.8	198	2.0	0.01	78	2.1
Hypotensives, angiotensin receptor antagonist	3,092	29.1	9,932	18.2	0.26	1,758	25.3	2,402	23.8	0.03	1,334	36.2
ACE inhibitor/calcium channel blocker combination	359	3.4	1,337	2.5	0.05	213	3.1	285	2.8	0.01	146	4.0
Calcium channel blocking agents	1,704	16.0	8,326	15.3	0.02	1,078	15.5	1,598	15.8	0.01	626	17.0
Vitamin D preparations	178	1.7	570	1.0	0.05	112	1.6	155	1.5	0.01	66	1.8
Folic acid preparations	236	2.2	1,246	2.3	0.00	133	1.9	204	2.0	0.01	103	2.8
Androgenic agents	197	1.9	434	0.8	0.09	117	1.7	145	1.4	0.02	80	2.2
Drugs to treat impotency	517	4.9	2,899	5.3	0.02	340	4.9	528	5.2	0.02	177	4.8
Sedative-hypnotics, non-barbiturate	867	8.1	2,842	5.2	0.12	505	7.3	677	6.7	0.02	362	9.8
Serotonin specific reuptake inhibitor (SSRIs)	2,020	19.0	6,884	12.6	0.17	1,202	17.3	1,764	17.5	0.00	818	22.2
Tricyclic antidepressants and related non-selective reuptake inhibitors	398	3.7	1,833	3.4	0.02	258	3.7	423	4.2	0.02	140	3.8
Analgesics, narcotics	3,095	29.1	13,883	25.5	0.08	1,957	28.1	2,844	28.2	0.00	1,138	30.8
Skeletal muscle relaxants	912	8.6	3,454	6.3	0.08	577	8.3	818	8.1	0.01	335	9.1
Serotonin-norepinephrine reuptake-inhibitor (SNRIs)	751	7.1	1,647	3.0	0.19	392	5.6	580	5.7	0.00	359	9.7

Table 1.4b. Prevalence of Drug Dispensings During the 9-Month Baseline Period that Were Included in the Propensity Score Model, Impact National Benchmark Databases 6/1/2005−7/31/2010

Characteristic	All (N = 65,098)					Matched (N = 17,051)					Not Matched (N = 48,047)	
	Exenatide (N = 10,643)		OAD (N = 54,455)		Stand. Diff.	Exenatide (N = 6,954)		OAD (N = 10,097)		Stand. Diff.	Exenatide (N = 3,689)	
	N	%	N	%		N	%	N	%		N	%
Serotonin-2 antagonist/reuptake inhibitors (SARIs)	218	2.0	1,054	1.9	0.01	126	1.8	210	2.1	0.02	92	2.5
Beta-adrenergics and glucocorticoids combination	525	4.9	1,948	3.6	0.07	321	4.6	458	4.5	0.00	204	5.5
Alpha-adrenergic blocking agents	241	2.3	1,133	2.1	0.01	152	2.2	200	2.0	0.01	89	2.4
Beta-adrenergic blocking agents	2,712	25.5	13,355	24.5	0.02	1,690	24.3	2,483	24.6	0.01	1,022	27.7
Intestinal motility stimulants	151	1.4	961	1.8	0.03	113	1.6	174	1.7	0.01	38	1.0
Blood sugar diagnostics	6,855	64.4	28,401	52.2	0.25	4,195	60.3	6,038	59.8	0.01	2,660	72.1
Platelet aggregation inhibitors	674	6.3	3,352	6.2	0.01	421	6.1	613	6.1	0.00	253	6.9
Thyroid hormones	1,460	13.7	5,060	9.3	0.14	868	12.5	1,253	12.4	0.00	592	16.0
Bone resorption suppression agents	280	2.6	1,503	2.8	0.01	193	2.8	252	2.5	0.02	87	2.4
Glucocorticoids	1,158	10.9	4,996	9.2	0.06	731	10.5	1,056	10.5	0.00	427	11.6
Topical local anesthetics	160	1.5	646	1.2	0.03	93	1.3	149	1.5	0.01	67	1.8
Topical anti-inflammatory steroidal	969	9.1	4,185	7.7	0.05	600	8.6	935	9.3	0.02	369	10.0
Topical antibiotics	339	3.2	1,339	2.5	0.04	212	3.0	292	2.9	0.01	127	3.4
Miotics/other intraocular pressure reducers	348	3.3	1,834	3.4	0.01	222	3.2	308	3.1	0.01	126	3.4
Eye anti-inflammatory agents	183	1.7	1,014	1.9	0.01	122	1.8	174	1.7	0.00	61	1.7
Eye antihistamines	147	1.4	591	1.1	0.03	95	1.4	132	1.3	0.01	52	1.4
Potassium sparing diuretics	297	2.8	976	1.8	0.07	160	2.3	231	2.3	0.00	137	3.7
Potassium sparing diuretics in combination	405	3.8	1,476	2.7	0.06	252	3.6	317	3.1	0.03	153	4.1
Loop diuretics	1,466	13.8	5,519	10.1	0.11	842	12.1	1,201	11.9	0.01	624	16.9
Penicillins	2,015	18.9	9,859	18.1	0.02	1,317	18.9	1,937	19.2	0.01	698	18.9
Macrolides	1,979	18.6	8,238	15.1	0.09	1,266	18.2	1,802	17.8	0.01	713	19.3
Lincosamides	298	2.8	1,326	2.4	0.02	187	2.7	276	2.7	0.00	111	3.0
Absorbable sulfonamides	547	5.1	2,223	4.1	0.05	382	5.5	471	4.7	0.04	165	4.5
Nitrofuran derivatives	164	1.5	698	1.3	0.02	105	1.5	166	1.6	0.01	59	1.6
Antifungal agents	736	6.9	2,617	4.8	0.09	464	6.7	656	6.5	0.01	272	7.4
Diabetic supplies	311	2.9	1,861	3.4	0.03	204	2.9	300	3.0	0.00	107	2.9
Antihistamines - 1st generation	350	3.3	1,290	2.4	0.06	208	3.0	275	2.7	0.02	142	3.8

Stand. Diff., Standardized Difference

Note: OADs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins. Standardized difference is calculated by the difference between the 2 proportions divided by the pooled standard deviation.

Please note characteristic descriptions may be truncated in the data due to SAS limitations.

Table 1.5a. Healthcare Utilization Characteristics of Exenatide Initiators and OADs Initiator During the 9-Month Baseline Period, Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonists and without 1 year of Follow-up Person Time, Life Sciences Research Database 6/1/2005-7/31/2010

Characteristic	All (N = 102,203)				
	Exenatide (N= 15,540)		OADs (N= 86,663)		Standardized Difference
	N	%	N	%	
One Antidiabetic Medication within 45 Days of Cohort Entry	6,307	40.6	30,985	35.8	0.10
Two Antidiabetic Medications within 45 Days of Cohort Entry	3,667	23.6	12,772	14.7	0.23
Three Antidiabetic Medications within 45 Days of Cohort Entry	2,169	14.0	4,308	5.0	0.31
Hospitalization within 45 days of Cohort Entry	245	1.6	9,128	10.5	0.38
Critical Care Evaluation and Management	146	0.9	3,114	3.6	0.18
0-4 Unique Drugs Dispensed	314	2.0	9,247	10.7	0.36
5-9 Unique Drugs Dispensed	3,808	24.5	36,757	42.4	0.39
10-14 Unique Drugs Dispensed	5,984	38.5	24,437	28.2	0.22
≥15 Unique Drugs Dispensed	5,434	35.0	16,222	18.7	0.37

Characteristic	Exenatide (N= 15,540)			OADs (N= 86,663)			Standardized Difference
	Mean	Median	IQR	Mean	Median	IQR	
Number of Diabetes Drug Dispensings[1]	7.9	7.0	4.0- 11.0	5.7	5.0	2.0- 9.0	0.43
Number of Diabetes Diagnoses[1]	4.3	4.0	2.0- 5.0	3.9	3.0	2.0- 5.0	0.11
Number of Physician Visits	7.9	7.0	4.0- 10.0	6.6	5.0	3.0- 8.0	0.20
Number of Emergency Department Visits	0.7	0.0	0.0- 0.0	0.6	0.0	0.0- 1.0	0.02
Number of Inpatient Days	0.4	0.0	0.0- 0.0	1.6	0.0	0.0- 0.0	0.20
Number of Inpatient Stays	0.1	0.0	0.0- 0.0	0.2	0.0	0.0- 0.0	0.25
Number of 3-Digit Diagnosis Codes	13.2	12.0	8.0- 17.0	12.3	10.0	6.0- 16.0	0.11
Number of Pathology/ Laboratory Codes (CPT 80048 - 89356)	14.6	11.0	6.0- 19.0	12.7	8.0	4.0- 15.0	0.10
Number of Cardiovascular Diagnostic Procedures	0.7	0.0	0.0- 1.0	0.9	0.0	0.0- 1.0	0.07
Number of Surgery Procedures	2.7	2.0	1.0- 4.0	2.3	2.0	0.0- 3.0	0.13
Number of Anesthesia Procedures	0.2	0.0	0.0- 0.0	0.2	0.0	0.0- 0.0	0.03
Medical Costs ($)	2,014.5	1,095.1	530.2- 2,367.6	2,019.0	779.6	332.1- 1,982.8	0.00

Table 1.5a. Healthcare Utilization Characteristics of Exenatide Initiators and OADs Initiator During the 9-Month Baseline Period, Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonists and without 1 year of Follow-up Person Time, Life Sciences Research Database 6/1/2005-7/31/2010

Characteristic	Exenatide (N= 15,540)			OADs (N= 86,663)			Standardized Difference
	Mean	Median	IQR	Mean	Median	IQR	
Facility Costs ($)	2,931.3	477.9	91.4- 2,143.4	5,526.1	416.9	60.7- 2,624.9	0.14
Pharmacy Costs ($)	3,301.4	2,759.5	1,541.7- 4,283.6	2,292.9	1,638.8	700.5- 3,049.6	0.35
Days from Start of Initiation Period until Initiation	682.0	601.0	345.0- 972.0	539.8	383.0	56.0- 955.0	0.31
Internal Medicine	1.9	0.0	0.0- 3.0	2.2	0.0	0.0- 3.0	0.07
Neurology	0.1	0.0	0.0- 0.0	0.1	0.0	0.0- 0.0	0.05
Neurosurgery	0.0	0.0	0.0- 0.0	0.0	0.0	0.0- 0.0	0.01
Ophthalmology	0.2	0.0	0.0- 0.0	0.2	0.0	0.0- 0.0	0.00
ENT	0.1	0.0	0.0- 0.0	0.1	0.0	0.0- 0.0	0.06
Pediatrics	0.0	0.0	0.0- 0.0	0.1	0.0	0.0- 0.0	0.10
Psychiatry	0.2	0.0	0.0- 0.0	0.1	0.0	0.0- 0.0	0.03
General Surgery	0.1	0.0	0.0- 0.0	0.2	0.0	0.0- 0.0	0.05
Cardio/Thoracic Surgery	0.0	0.0	0.0- 0.0	0.0	0.0	0.0- 0.0	0.04
Occupational/Physical/Rehab Medicine	0.1	0.0	0.0- 0.0	0.1	0.0	0.0- 0.0	0.06
Therapeutic Radiology	0.0	0.0	0.0- 0.0	0.0	0.0	0.0- 0.0	0.01
Cardiology	0.5	0.0	0.0- 0.0	0.6	0.0	0.0- 0.0	0.07
Gastroenterology	0.2	0.0	0.0- 0.0	0.2	0.0	0.0- 0.0	0.05
Hematology	0.1	0.0	0.0- 0.0	0.1	0.0	0.0- 0.0	0.05
Nephrology	0.1	0.0	0.0- 0.0	0.2	0.0	0.0- 0.0	0.10
Rheumatology	0.1	0.0	0.0- 0.0	0.1	0.0	0.0- 0.0	0.03
Endocrinology	1.1	0.0	0.0- 2.0	0.5	0.0	0.0- 0.0	0.36
Oncology	0.0	0.0	0.0- 0.0	0.1	0.0	0.0- 0.0	0.04
Emergency Medicine	0.2	0.0	0.0- 0.0	0.3	0.0	0.0- 0.0	0.11
Dentistry/Orthodontics	0.0	0.0	0.0- 0.0	0.0	0.0	0.0- 0.0	0.01
Audiology	0.0	0.0	0.0- 0.0	0.0	0.0	0.0- 0.0	0.01
Speech Therapy	0.0	0.0	0.0- 0.0	0.0	0.0	0.0- 0.0	0.01
Pulmonary	0.2	0.0	0.0- 0.0	0.3	0.0	0.0- 0.0	0.06
Social Worker/Mental Health	0.2	0.0	0.0- 0.0	0.1	0.0	0.0- 0.0	0.07
Pharmacy	0.0	0.0	0.0- 0.0	0.0	0.0	0.0- 0.0	0.00
Hospital	0.0	0.0	0.0- 0.0	0.0	0.0	0.0- 0.0	0.04
Long Term Care Facility	0.0	0.0	0.0- 0.0	0.0	0.0	0.0- 0.0	0.02
Behavior Health/Substance	0.0	0.0	0.0- 0.0	0.0	0.0	0.0- 0.0	0.02
Hospice	0.0	0.0	0.0- 0.0	0.0	0.0	0.0- 0.0	0.01
Geriatrics	0.0	0.0	0.0- 0.0	0.0	0.0	0.0- 0.0	0.03
Preventative Medicine/Public Health	0.0	0.0	0.0- 0.0	0.0	0.0	0.0- 0.0	0.00

Table 1.5a. Healthcare Utilization Characteristics of Exenatide Initiators and OADs Initiator During the 9-Month Baseline Period, Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonists and without 1 year of Follow-up Person Time, Life Sciences Research Database 6/1/2005-7/31/2010

Characteristic	Matched (N = 29,572)					Not Matched (N = 72,631)	
	Exenatide (N = 11,978)		OADs (N = 17,594)		Standardized Difference	Exenatide (N= 3,562)	
	N	%	N	%		N	%
One Antidiabetic Medication within 45 Days of	5,000	41.7	7,546	42.9	0.02	1,307	36.7
Two Antidiabetic Medications within 45 Days of Cohort Entry	2,591	21.6	3,595	20.4	0.03	1,076	30.2
Three Antidiabetic Medications within 45 Days of Cohort Entry	1,362	11.4	1,555	8.8	0.08	807	22.7
Hospitalization within 45 days of Cohort Entry	231	1.9	444	2.5	0.04	14	0.4
Critical Care Evaluation and Management	116	1.0	224	1.3	0.03	30	0.8
0-4 Unique Drugs Dispensed	312	2.6	480	2.7	0.01	2	0.1
5-9 Unique Drugs Dispensed	3,441	28.7	5,817	33.1	0.09	367	10.3
10-14 Unique Drugs Dispensed	4,570	38.2	6,416	36.5	0.03	1,414	39.7
≥15 Unique Drugs Dispensed	3,655	30.5	4,881	27.7	0.06	1,779	49.9

Characteristic	Exenatide (N = 11,978)			OADs (N = 17,594)			Standardized Difference	Not Matched (N = 72,631)		
	Mean	Median	IQR	Mean	Median	IQR		Mean	Median	IQR
Number of Diabetes Drug Dispensings[1]	7.5	7	3.0- 10.0	6.9	6	3.0- 9.0	0.11	9.4	9	5.0- 13.0
Number of Diabetes Diagnoses[1]	4.1	3	2.0- 5.0	4	3	2.0- 5.0	0.03	4.9	4	3.0- 6.0
Number of Physician Visits	7.5	6	4.0- 10.0	7.3	6	4.0- 9.0	0.04	8.9	8	5.0- 11.0
Number of Emergency Department Visits	0.6	0	0.0- 0.0	0.6	0	0.0- 0.0	0.01	0.7	0	0.0- 0.0
Number of Inpatient Days	0.4	0	0.0- 0.0	0.5	0	0.0- 0.0	0.03	0.3	0	0.0- 0.0
Number of Inpatient Stays	0.1	0	0.0- 0.0	0.1	0	0.0- 0.0	0.03	0.1	0	0.0- 0.0
Number of 3-Digit Diagnosis Codes	12.9	11	7.0- 17.0	12.7	11	7.0- 16.0	0.02	14.3	13	9.0- 18.0
Number of Pathology/ Laboratory Codes (CPT 80048 - 89356)	13.9	11	6.0- 18.0	13.3	10	5.0- 17.0	0.04	17.1	14	8.0- 22.0
Number of Cardiovascular Diagnostic Procedures	0.7	0	0.0- 1.0	0.8	0	0.0- 1.0	0.02	0.8	0	0.0- 1.0
Number of Surgery Procedures	2.6	2	1.0- 4.0	2.5	2	1.0- 3.0	0.02	3	2	1.0- 4.0
Number of Anesthesia Procedures	0.2	0	0.0- 0.0	0.2	0	0.0- 0.0	0	0.2	0	0.0- 0.0
Medical Costs ($)	1,928.6	1,003.1	489.3- 2,234.6	1,920.6	955.1	440.7- 2,197.1	0	2,303.2	1,417.4	704.3- 2,779.4
Facility Costs ($)	2,920.3	435.9	81.5- 2,031.7	3,129.1	446.9	74.8- 2,168.9	0.02	2,968.3	623.5	137.8- 2,513.7
Pharmacy Costs ($)	3,082.2	2,556.1	1,368.0- 4,044.0	2,874.6	2,238.2	1,116.2- 3,733.8	0.07	4,038.6	3,413.9	2,212.4-
Days from Start of Initiation Period until Initiation Date	733.6	686.0	377.0- 1,035.0	674.2	586.0	327.0- 975.0	0.14	508.5	411.0	307.0- 656.0
Internal Medicine	1.9	0	0.0- 3.0	1.9	0	0.0- 3.0	0.01	2	1	0.0- 3.0
Neurology	0.1	0	0.0- 0.0	0.1	0	0.0- 0.0	0	0.1	0	0.0- 0.0

Table 1.5a. Healthcare Utilization Characteristics of Exenatide Initiators and OADs Initiator During the 9-Month Baseline Period, Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonists and without 1 year of Follow-up Person Time, Life Sciences Research Database 6/1/2005-7/31/2010

Characteristic	Exenatide (N = 11,978)			OADs (N = 17,594)			Standardized Difference	Not Matched (N = 72,631)		
	Mean	Median	IQR	Mean	Median	IQR		Mean	Median	IQR
Neurosurgery	0	0	0.0- 0.0	0	0	0.0- 0.0	0	0	0	0.0- 0.0
Ophthalmology	0.2	0	0.0- 0.0	0.2	0	0.0- 0.0	0.01	0.2	0	0.0- 0.0
ENT	0.1	0	0.0- 0.0	0.1	0	0.0- 0.0	0	0.1	0	0.0- 0.0
Pediatrics	0	0	0.0- 0.0	0	0	0.0- 0.0	0.01	0	0	0.0- 0.0
Psychiatry	0.2	0	0.0- 0.0	0.2	0	0.0- 0.0	0	0.2	0	0.0- 0.0
General Surgery	0.1	0	0.0- 0.0	0.1	0	0.0- 0.0	0.01	0.1	0	0.0- 0.0
Cardio/Thoracic Surgery	0	0	0.0- 0.0	0	0	0.0- 0.0	0	0	0	0.0- 0.0
Occupational/Physical/Rehab Medicine	0.1	0	0.0- 0.0	0.1	0	0.0- 0.0	0	0.1	0	0.0- 0.0
Therapeutic Radiology	0	0	0.0- 0.0	0	0	0.0- 0.0	0	0	0	0.0- 0.0
Cardiology	0.5	0	0.0- 0.0	0.5	0	0.0- 0.0	0.01	0.5	0	0.0- 0.0
Gastroenterology	0.2	0	0.0- 0.0	0.1	0	0.0- 0.0	0.02	0.2	0	0.0- 0.0
Hematology	0.1	0	0.0- 0.0	0.1	0	0.0- 0.0	0	0	0	0.0- 0.0
Nephrology	0.1	0	0.0- 0.0	0.1	0	0.0- 0.0	0.02	0.1	0	0.0- 0.0
Rheumatology	0.1	0	0.0- 0.0	0.1	0	0.0- 0.0	0	0.1	0	0.0- 0.0
Endocrinology	0.9	0	0.0- 1.0	0.7	0	0.0- 0.0	0.08	1.7	1	0.0- 0.0
Oncology	0	0	0.0- 0.0	0	0	0.0- 0.0	0	0	0	0.0- 0.0
Emergency Medicine	0.2	0	0.0- 0.0	0.2	0	0.0- 0.0	0.01	0.2	0	0.0- 0.0
Dentistry/Orthodontics	0	0	0.0- 0.0	0	0	0.0- 0.0	0	0	0	0.0- 0.0
Audiology	0	0	0.0- 0.0	0	0	0.0- 0.0	0.01	0	0	0.0- 0.0
Speech Therapy	0	0	0.0- 0.0	0	0	0.0- 0.0	0.01	0	0	0.0- 0.0
Pulmonary	0.1	0	0.0- 0.0	0.2	0	0.0- 0.0	0.01	0.2	0	0.0- 0.0
Social Worker/Mental Health	0.2	0	0.0- 0.0	0.1	0	0.0- 0.0	0.02	0.3	0	0.0- 0.0
Pharmacy	0	0	0.0- 0.0	0	0	0.0- 0.0	0	0	0	0.0- 0.0
Hospital	0	0	0.0- 0.0	0	0	0.0- 0.0	0.03	0	0	0.0- 0.0
Long Term Care Facility	0	0	0.0- 0.0	0	0	0.0- 0.0	0.01	0	0	0.0- 0.0
Behavior Health/Substance	0	0	0.0- 0.0	0	0	0.0- 0.0	0.02	0	0	0.0- 0.0
Hospice	0	0	0.0- 0.0	0	0	0.0- 0.0	0.02	0	0	0.0- 0.0
Geriatrics	0	0	0.0- 0.0	0	0	0.0- 0.0	0.01	0	0	0.0- 0.0
Preventative Medicine/Public Health	0	0	0.0- 0.0	0	0	0.0- 0.0	0.02	0	0	0.0- 0.0

[1] One counted per day

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, dipeptidyl peptidase-4 inhibitor, glucagon-like peptide-1 agonists, pramlintide, alpha-glucosidase inhibitors, and insulins. Standardized difference is calculated by the difference between the 2 proportions or 2 means divided by the pooled standard deviation.

Table 1.5b. Healthcare Utilization Characteristics of Exenatide Initiators and OADs Initiator During the 9-Month Baseline Period, Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonists and without 1 year of Follow-up Person Time, Impact National Benchmark Database 6/1/2005-7/31/2010

Characteristic	All (N = 134,711)				
	Exenatide (N = 21,922)		OADs (N = 112,789)		Standardized Difference
	N	%	N	%	
One Antidiabetic Medication within 45 Days of Cohort Entry (N,%)	8,662	39.5	41,732	37.0	0.05
Two Antidiabetic Medications within 45 Days of Cohort Entry (N,%)	5,379	24.5	17,651	15.6	0.22
Three Antidiabetic Medications within 45 Days of Cohort Entry (N,%)	3,148	14.4	6,558	5.8	0.29
Hospitalization within 45 days of Cohort Entry (N,%)	463	2.1	10,283	9.1	0.31
Critical Care Evaluation and Management (N,%)	208	0.9	3,524	3.1	0.15
0-4 Unique Drugs Dispensed (N,%)	349	1.6	9,117	8.1	0.31
5-9 Unique Drugs Dispensed (N,%)	5,340	24.4	45,144	40.0	0.34
10-14 Unique Drugs Dispensed (N,%)	8,543	39.0	34,189	30.3	0.18
>= 15 Unique Drugs Dispensed (N,%)	7,690	35.1	24,339	21.6	0.30

Characteristic	Exenatide (N = 21,922)			OADs (N = 112,789)			Standardized Difference
	Mean	Median	IQR	Mean	Median	IQR	
Number of Diabetes Drug Dispensings (1 counted per day)	8.2	7.0	4.0- 11.0	6.3	5.0	3.0- 9.0	0.37
Number of Diabetes Diagnoses (1 counted per day)	4.2	4.0	2.0- 5.0	3.6	3.0	2.0- 4.0	0.15
Number of Physician Visits	7.9	7.0	4.0- 10.0	6.7	5.0	3.0- 9.0	0.20
Number of Emergency Department Visits	0.3	0.0	0.0- 0.0	0.4	0.0	0.0- 1.0	0.14
Number of Inpatient Days	0.5	0.0	0.0- 0.0	1.8	0.0	0.0- 0.0	0.19
Number of Inpatient Stays	0.1	0.0	0.0- 0.0	0.2	0.0	0.0- 0.0	0.20
Number of 3-Digit Diagnosis Codes	12.2	11.0	7.0- 16.0	11.6	9.0	6.0- 15.0	0.08
Number of Pathology/ Laboratory Codes (CPT 80048 - 89356)	13.1	10.0	3.0- 18.0	11.0	7.0	1.0- 15.0	0.13
Number of Cardiovascular Diagnostic Procedures	1.0	0.0	0.0- 1.0	1.1	0.0	0.0- 1.0	0.05
Number of Surgery Procedures	3.0	2.0	1.0- 4.0	2.7	2.0	1.0- 4.0	0.07
Number of Anesthesia Procedures	0.2	0.0	0.0- 0.0	0.2	0.0	0.0- 0.0	0.03
Medical Costs ($)	3,089.2	1,652.2	748.9- 3,613.5	3,071.4	1,179.8	488.4- 2,977.0	0.00

Table 1.5b. Healthcare Utilization Characteristics of Exenatide Initiators and OADs Initiator During the 9-Month Baseline Period, Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonists and without 1 year of Follow-up Person Time, Impact National Benchmark Database 6/1/2005-7/31/2010

	Exenatide (N = 21,922)			OADs (N = 112,789)			Standardized Difference
Characteristic	**Mean**	**Median**	**IQR**	**Mean**	**Median**	**IQR**	
Facility Costs ($)	2085.4	0.0	0.0- 917.0	4102.5	32.3	0.0- 1,388.5	0.14
Pharmacy Costs ($)	3,373.5	2,768.0	1,557.0- 4,323.5	2,650.0	1,994.0	955.0- 3,431.2	0.20
Days from Start of Initiation Period until Initiation	689.7	615.0	336.0- 964.0	478.4	204.0	34.0- 833.0	0.43
Family/General Practice	1.5	0.0	0.0- 2.0	1.4	0.0	0.0- 2.0	0.01
Neurology	0.1	0.0	0.0- 0.0	0.1	0.0	0.0- 0.0	0.04
Ophthalmology	0.1	0.0	0.0- 0.0	0.2	0.0	0.0- 0.0	0.03
Orthopedic Surgery	0.3	0.0	0.0- 0.0	0.2	0.0	0.0- 0.0	0.08
ENT	0.1	0.0	0.0- 0.0	0.1	0.0	0.0- 0.0	0.06
Pediatrics	0.0	0.0	0.0- 0.0	0.1	0.0	0.0- 0.0	0.09
Plastic Surgery	0.0	0.0	0.0- 0.0	0.0	0.0	0.0- 0.0	0.01
Psychiatry	0.2	0.0	0.0- 0.0	0.2	0.0	0.0- 0.0	0.03
Diagnostic Radiology	0.0	0.0	0.0- 0.0	0.0	0.0	0.0- 0.0	0.04
Cardio/Thoracic Surgery	0.1	0.0	0.0- 0.0	0.1	0.0	0.0- 0.0	0.01
Urology	0.1	0.0	0.0- 0.0	0.1	0.0	0.0- 0.0	0.01
Gastroenterology	0.1	0.0	0.0- 0.0	0.2	0.0	0.0- 0.0	0.05
Endocrinology	0.9	0.0	0.0- 2.0	0.4	0.0	0.0- 0.0	0.34
Laboratory/Imaging	0.0	0.0	0.0- 0.0	0.0	0.0	0.0- 0.0	0.01
Oncology	0.1	0.0	0.0- 0.0	0.2	0.0	0.0- 0.0	0.06
Pulmonary	0.1	0.0	0.0- 0.0	0.2	0.0	0.0- 0.0	0.05
Hospital	0.3	0.0	0.0- 0.0	0.3	0.0	0.0- 0.0	0.03

Table 1.5b. Healthcare Utilization Characteristics of Exenatide Initiators and OADs Initiator During the 9-Month Baseline Period, Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonists and without 1 year of Follow-up Person Time, Impact National Benchmark Database 6/1/2005-7/31/2010

Characteristic	Matched (N = 41,593)					Not Matched (N= 93,118)	
	Exenatide (N = 16,206)		OADs (N = 25,387)		Standardized Difference	Exenatide (N = 5,716)	
	N	%	N	%		N	%
One Antidiabetic Medication within 45 Days of Cohort Entry (N,%)	6,681	41.2	10,747	42.3	0.02	1,981	34.7
Two Antidiabetic Medications within 45 Days of Cohort Entry (N,%)	3,697	22.8	5,551	21.9	0.02	1,682	29.4
Three Antidiabetic Medications within 45 Days of Cohort Entry (N,%)	1,860	11.5	2,559	10.1	0.05	1,288	22.5
Hospitalization within 45 days of Cohort Entry (N,%)	376	2.3	655	2.6	0.02	87	1.5
Critical Care Evaluation and Management (N,%)	151	0.9	262	1.0	0.01	57	1.0
0-4 Unique Drugs Dispensed (N,%)	295	1.8	566	2.2	0.03	54	0.9
5-9 Unique Drugs Dispensed (N,%)	4,743	29.3	8,153	32.1	0.06	597	10.4
10-14 Unique Drugs Dispensed (N,%)	6,286	38.8	9,684	38.1	0.01	2,257	39.5
>= 15 Unique Drugs Dispensed (N,%)	4,882	30.1	6,984	27.5	0.06	2,808	49.1

Characteristic	Exenatide (N = 16,206)			OADs (N = 25,387)			Standardized Difference	Not Matched (N= 93,118)		
	Mean	Median	IQR	Mean	Median	IQR		Mean	Median	IQR
Number of Diabetes Drug Dispensings (1 counted per day)	7.7	7.0	4.0- 10.0	7.4	7.0	4.0- 10.0	0.06	9.6	9.0	6.0- 13.0
Number of Diabetes Diagnoses (1 counted per day)	3.9	3.0	2.0- 5.0	3.8	3.0	2.0- 5.0	0.04	4.9	4.0	3.0- 6.0
Number of Physician Visits	7.5	6.0	4.0- 10.0	7.3	6.0	4.0- 9.0	0.03	9.1	8.0	5.0- 12.0
Number of Emergency Department Visits	0.3	0.0	0.0- 0.0	0.3	0.0	0.0- 0.0	0.01	0.3	0.0	0.0- 0.0
Number of Inpatient Days	0.5	0.0	0.0- 0.0	0.5	0.0	0.0- 0.0	0.02	0.6	0.0	0.0- 0.0
Number of Inpatient Stays	0.1	0.0	0.0- 0.0	0.1	0.0	0.0- 0.0	0.01	0.1	0.0	0.0- 0.0
Number of 3-Digit Diagnosis Codes	11.9	10.0	7.0- 15.0	11.7	10.0	6.0- 15.0	0.02	13.3	12.0	8.0- 17.0
Number of Pathology/ Laboratory Codes (CPT 80048 - 89356)	12.6	9.0	3.0- 17.0	12.5	9.0	3.0- 17.0	0.01	14.4	11.0	4.0- 20.0
Number of Cardiovascular Diagnostic Procedures	0.9	0.0	0.0- 1.0	0.9	0.0	0.0- 1.0	0.00	1.1	0.0	0.0- 1.0
Number of Surgery Procedures	2.9	2.0	1.0- 4.0	2.9	2.0	1.0- 4.0	0.01	3.2	2.0	1.0- 4.0
Number of Anesthesia Procedures	0.2	0.0	0.0- 0.0	0.2	0.0	0.0- 0.0	0.00	0.2	0.0	0.0- 0.0
Medical Costs ($)	2,949.4	1,524.9	692.3- 3,400.6	2,935.8	1,516.0	658.9- 3,422.9	0.00	3,485.6	2,031.5	940.2- 4,257.8
Facility Costs ($)	2,045.9	0.0	0.0- 861.0	2,120.9	0.0	0.0- 836.2	0.01	2,197.6	0.0	0.0- 1,079.3

Table 1.5b. Healthcare Utilization Characteristics of Exenatide Initiators and OADs Initiator During the 9-Month Baseline Period, Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonists and without 1 year of Follow-up Person Time, Impact National Benchmark Database 6/1/2005-7/31/2010

Characteristic	Exenatide (N = 16,206)			OADs (N = 25,387)			Standardized Difference	Not Matched (N= 93,118)		
	Mean	Median	IQR	Mean	Median	IQR		Mean	Median	IQR
Pharmacy Costs ($)	3,136.2	2,564.6	1,420.1- 4,055.5	3,012.0	2,356.1	1,237.3- 3,815.4	0.04	4,046.2	3,364.9	2,041.2-
Days from Start of Initiation Period until Initiation	728.1	674.0	350.0- 1,020.0	748.4	702.0	366.0- 1,043.0	0.04	580.9	470.0	316.0- 793.0
Family/General Practice	1.5	0.0	0.0- 2.0	1.4	0.0	0.0- 2.0	0.00	1.5	0.0	0.0- 2.0
Neurology	0.1	0.0	0.0- 0.0	0.1	0.0	0.0- 0.0	0.00	0.1	0.0	0.0- 0.0
Ophthalmology	0.1	0.0	0.0- 0.0	0.1	0.0	0.0- 0.0	0.01	0.2	0.0	0.0- 0.0
Orthopedic Surgery	0.3	0.0	0.0- 0.0	0.3	0.0	0.0- 0.0	0.00	0.4	0.0	0.0- 0.0
ENT	0.1	0.0	0.0- 0.0	0.1	0.0	0.0- 0.0	0.01	0.1	0.0	0.0- 0.0
Pediatrics	0.0	0.0	0.0- 0.0	0.0	0.0	0.0- 0.0	0.00	0.0	0.0	0.0- 0.0
Plastic Surgery	0.0	0.0	0.0- 0.0	0.0	0.0	0.0- 0.0	0.01	0.0	0.0	0.0- 0.0
Psychiatry	0.2	0.0	0.0- 0.0	0.2	0.0	0.0- 0.0	0.00	0.3	0.0	0.0- 0.0
Diagnostic Radiology	0.0	0.0	0.0- 0.0	0.0	0.0	0.0- 0.0	0.01	0.0	0.0	0.0- 0.0
Cardio/Thoracic Surgery	0.0	0.0	0.0- 0.0	0.0	0.0	0.0- 0.0	0.00	0.1	0.0	0.0- 0.0
Urology	0.1	0.0	0.0- 0.0	0.1	0.0	0.0- 0.0	0.00	0.1	0.0	0.0- 0.0
Gastroenterology	0.1	0.0	0.0- 0.0	0.1	0.0	0.0- 0.0	0.00	0.1	0.0	0.0- 0.0
Endocrinology	0.7	0.0	0.0- 1.0	0.6	0.0	0.0- 0.0	0.07	1.4	1.0	0.0- 3.0
Laboratory/Imaging	0.0	0.0	0.0- 0.0	0.0	0.0	0.0- 0.0	0.00	0.0	0.0	0.0- 0.0
Oncology	0.1	0.0	0.0- 0.0	0.1	0.0	0.0- 0.0	0.00	0.1	0.0	0.0- 0.0
Pulmonary	0.1	0.0	0.0- 0.0	0.1	0.0	0.0- 0.0	0.00	0.2	0.0	0.0- 0.0
Hospital	0.3	0.0	0.0-0.0	0.3	0.0	0.0- 0.0	0.01	0.3	0.0	0.0- 0.0

[1] One counted per day

Note: OADs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins. Standardized difference is calculated by the difference between the 2 means divided by the pooled standard deviation.

Table 1.6.1a (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Pancreatic Cancer, Life Sciences Research Database 6/1/2005 −7/31/2010

Characteristic	1 to < 2 Years					2 to < 3 Years				
	Exenatide (N = 11,986)		OADs (N = 17,603)		Stand. Diff.	Exenatide (N = 7,754)		OADs (N = 11,093)		Stand. Diff.
	N	%	N	%		N	%	N	%	
Age										
≤39 years	1,149	9.6	1,912	10.9	0.042	659	8.5	1,102	9.9	0.050
40-49 years	2,857	23.8	4,118	23.4	0.010	1,847	23.8	2,542	22.9	0.021
50-59 years	4,796	40.0	6,937	39.4	0.012	3,240	41.8	4,548	41.0	0.016
60-69 years	2,743	22.9	3,943	22.4	0.012	1,719	22.2	2,408	21.7	0.011
≥70 years	441	3.7	693	3.9	0.013	289	3.7	493	4.4	0.036
Number of Drugs Dispensed										
0-4 drugs	312	2.6	480	2.7	0.008	204	2.6	308	2.8	0.009
5-9 drugs	3,441	28.7	5,817	33.0	0.094	2,267	29.2	3,752	33.8	0.099
10-14 drugs	4,575	38.2	6,418	36.5	0.035	2,942	37.9	4,007	36.1	0.038
>14 drugs	3,658	30.5	4,888	27.8	0.061	2,341	30.2	3,026	27.3	0.064
Stroke/TIA	214	1.8	334	1.9	0.008	142	1.8	193	1.7	0.007
Myocardial Infarction	149	1.2	253	1.4	0.017	85	1.1	167	1.5	0.036
Gender - Male	5,630	47.0	8,315	47.2	0.005	3,634	46.9	5,295	47.7	0.017
Ischemic Heart Disease	1,624	13.5	2,379	13.5	0.001	1,041	13.4	1,510	13.6	0.005
Malignant neoplasm of lip	0	0.0	4	0.0	0.021	0	0.0	3	0.0	0.023
Malignant neoplasm of tongue	1	0.0	5	0.0	0.015	0	0.0	4	0.0	0.027
Malignant neoplasm of major salivary glands	3	0.0	6	0.0	0.005	3	0.0	4	0.0	0.001
Malignant neoplasm of other and unspecified parts of mouth	0	0.0	3	0.0	0.018	0	0.0	3	0.0	0.023
Malignant neoplasm of oropharynx	1	0.0	3	0.0	0.008	1	0.0	3	0.0	0.010
Malignant neoplasm of nasopharynx	0	0.0	1	0.0	0.011	0	0.0	1	0.0	0.013
Malignant neoplasm of hypopharynx	0	0.0	1	0.0	0.011	0	0.0	1	0.0	0.013
Malignant neoplasm of other and ill-defined sites within the lip, oral cavity, and pharynx	0	0.0	4	0.0	0.021	0	0.0	3	0.0	0.023
Malignant neoplasm of esophagus	1	0.0	2	0.0	0.003	0	0.0	0	0.0	-
Malignant neoplasm of stomach	1	0.0	0	0.0	0.013	0	0.0	0	0.0	-
Malignant neoplasm of small intestine, including duodenum	0	0.0	2	0.0	0.015	0	0.0	1	0.0	0.013
Malignant neoplasm of colon	24	0.2	48	0.3	0.015	16	0.2	36	0.3	0.023
Malignant neoplasm of rectum, rectosigmoid junction, and anus	12	0.1	30	0.2	0.019	8	0.1	21	0.2	0.023

Table 1.6.1a (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Pancreatic Cancer, Life Sciences Research Database 6/1/2005 −7/31/2010

Characteristic	1 to < 2 Years					2 to < 3 Years				
	Exenatide (N = 11,986)		OADs (N = 17,603)		Stand.	Exenatide (N = 7,754)		OADs (N = 11,093)		Stand.
	N	%	N	%	Diff.	N	%	N	%	Diff.
Malignant neoplasm of liver and intrahepatic bile ducts	5	0.0	6	0.0	0.004	2	0.0	4	0.0	0.006
Malignant neoplasm of gallbladder and extrahepatic bile ducts	2	0.0	3	0.0	0.000	2	0.0	2	0.0	0.005
Malignant neoplasm of retroperitoneum and peritoneum	2	0.0	2	0.0	0.004	1	0.0	2	0.0	0.004
Malignant neoplasm of other and ill-defined sites within the digestive organs and peritoneum	0	0.0	3	0.0	0.018	0	0.0	1	0.0	0.013
Malignant neoplasm of nasal cavities, middle ear, and accessory sinuses	0	0.0	2	0.0	0.015	0	0.0	2	0.0	0.019
Malignant neoplasm of larynx	1	0.0	10	0.1	0.027	1	0.0	6	0.1	0.023
Malignant neoplasm of trachea, bronchus, and lung	12	0.1	32	0.2	0.022	8	0.1	20	0.2	0.021
Malignant neoplasm of pleura	2	0.0	1	0.0	0.010	2	0.0	0	0.0	0.023
Malignant neoplasm of thymus, heart, and mediastinum	0	0.0	1	0.0	0.011	0	0.0	1	0.0	0.013
Malignant neoplasm of bone and articular cartilage	1	0.0	6	0.0	0.018	1	0.0	4	0.0	0.015
Malignant neoplasm of connective and other soft tissue	5	0.0	4	0.0	0.011	2	0.0	3	0.0	0.001
Malignant melanoma of skin	21	0.2	26	0.1	0.007	13	0.2	17	0.2	0.004
Other malignant neoplasm of skin	134	1.1	212	1.2	0.008	98	1.3	128	1.2	0.010
Malignant neoplasm of female	139	1.2	201	1.1	0.002	94	1.2	120	1.1	0.012
Kaposi's sarcoma	0	0.0	1	0.0	0.011	0	0.0	1	0.0	0.013
Malignant neoplasm of uterus, part unspecified	7	0.1	9	0.1	0.003	3	0.0	5	0.0	0.003
Malignant neoplasm of cervix uteri	5	0.0	8	0.0	0.002	2	0.0	6	0.1	0.014
Malignant neoplasm of body of uterus	22	0.2	26	0.1	0.009	15	0.2	15	0.1	0.014
Malignant neoplasm of ovary and other uterine adnexa	11	0.1	25	0.1	0.015	7	0.1	13	0.1	0.008

Table 1.6.1a (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Pancreatic Cancer, Life Sciences Research Database 6/1/2005 −7/31/2010

Characteristic	1 to < 2 Years					2 to < 3 Years				
	Exenatide (N = 11,986)		OADs (N = 17,603)		Stand.	Exenatide (N = 7,754)		OADs (N = 11,093)		Stand.
	N	%	N	%	Diff.	N	%	N	%	Diff.
Malignant neoplasm of other and unspecified female genital organs	2	0.0	2	0.0	0.004	2	0.0	2	0.0	0.005
Malignant neoplasm of prostate	78	0.7	132	0.7	0.012	60	0.8	88	0.8	0.002
Malignant neoplasm of testis	5	0.0	5	0.0	0.007	3	0.0	2	0.0	0.012
Malignant neoplasm of penis and other male genital organs	1	0.0	1	0.0	0.003	1	0.0	0	0.0	0.016
Malignant neoplasm of bladder	25	0.2	43	0.2	0.008	18	0.2	24	0.2	0.003
Malignant neoplasm of kidney and other and unspecified urinary organs	21	0.2	25	0.1	0.008	15	0.2	16	0.1	0.012
Malignant neoplasm of eye	1	0.0	4	0.0	0.012	1	0.0	2	0.0	0.004
Malignant neoplasm of brain	7	0.1	13	0.1	0.006	5	0.1	7	0.1	0.001
Malignant neoplasm of other and unspecified parts of nervous system	4	0.0	8	0.0	0.006	4	0.1	4	0.0	0.007
Malignant neoplasm of other endocrine glands and related structures	14	0.1	14	0.1	0.012	8	0.1	8	0.1	0.010
Malignant neoplasm of other and ill-defined sites	6	0.1	8	0.0	0.002	6	0.1	6	0.1	0.009
Secondary and unspecified malignant neoplasm of lymph nodes	7	0.1	23	0.1	0.024	5	0.1	14	0.1	0.020
Secondary malignant neoplasm of respiratory and digestive systems	8	0.1	27	0.2	0.026	4	0.1	16	0.1	0.030
Secondary malignant neoplasm of other specified sites	5	0.0	24	0.1	0.032	5	0.1	14	0.1	0.020
Malignant neoplasm without specification of site	8	0.1	12	0.1	0.001	6	0.1	7	0.1	0.005
Lymphosarcoma and reticulosarcoma and other specified malignant tumors of lymphatic tissue	18	0.2	24	0.1	0.004	16	0.2	17	0.2	0.013
Hodgkin's disease	14	0.1	12	0.1	0.016	6	0.1	10	0.1	0.004
Other malignant neoplasms of lymphoid and histiocytic tissue	20	0.2	49	0.3	0.024	15	0.2	36	0.3	0.026

Table 1.6.1a (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Pancreatic Cancer, Life Sciences Research Database 6/1/2005 −7/31/2010

Characteristic	1 to < 2 Years					2 to < 3 Years				
	Exenatide (N = 11,986)		OADs (N = 17,603)		Stand. Diff.	Exenatide (N = 7,754)		OADs (N = 11,093)		Stand. Diff.
	N	%	N	%		N	%	N	%	
Multiple myeloma and immunoproliferative neoplasms	9	0.1	7	0.0	0.015	6	0.1	3	0.0	0.022
Lymphoid leukemia	9	0.1	13	0.1	0.000	6	0.1	7	0.1	0.005
Myeloid leukemia	9	0.1	26	0.1	0.022	8	0.1	17	0.2	0.014
Monocytic leukemia	1	0.0	0	0.0	0.013	1	0.0	0	0.0	0.016
Other specified leukemia	0	0.0	2	0.0	0.015	0	0.0	2	0.0	0.019
Leukemia of unspecified cell type	2	0.0	3	0.0	0.000	1	0.0	2	0.0	0.004
Personal history of malignant neoplasm	289	2.4	426	2.4	0.001	190	2.5	281	2.5	0.005
	Mean	SD	Mean	SD	Stand. Diff.	Mean	SD	Mean	SD	Stand. Diff.
Number Drugs (HICLs) Dispensed	12.6	5.6	12.0	5.4	0.126	12.6	5.5	11.9	5.4	0.130
Number of Physician Visits	7.5	5.7	7.3	5.7	0.035	7.5	5.5	7.3	5.7	0.035
Number of Laboratory Tests	13.9	13.6	13.3	13.8	0.044	13.7	13.0	13.1	13.8	0.040

Table 1.6.1a (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Pancreatic Cancer, Life Sciences Research Database 6/1/2005 −7/31/2010

Characteristic	≥ 3 Years				
	Exenatide (N = 4,643)		OADs (N = 6,737)		Stand. Diff.
	N	%	N	%	
Age					
≤39 years	376	8.1	628	9.3	0.043
40-49 years	1,100	23.7	1,514	22.5	0.029
50-59 years	1,958	42.2	2,845	42.2	0.001
60-69 years	1,017	21.9	1,404	20.8	0.026
≥70 years	192	4.1	346	5.1	0.048
Number of Drugs Dispensed					
0-4 drugs	104	2.2	141	2.1	0.010
5-9 drugs	1,308	28.2	2,295	34.1	0.128
10-14 drugs	1,794	38.6	2,470	36.7	0.041
>14 drugs	1,437	30.9	1,831	27.2	0.083
Stroke/TIA	97	2.1	111	1.6	0.033
Myocardial Infarction	43	0.9	88	1.3	0.036

Table 1.6.1a (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Pancreatic Cancer, Life Sciences Research Database 6/1/2005 −7/31/2010

Characteristic	≥ 3 Years				
	Exenatide (N = 4,643)		OADs (N = 6,737)		Stand.
	N	%	N	%	Diff.
Gender - Male	2,188	47.1	3,221	47.8	0.014
Ischemic Heart Disease	590	12.7	927	13.8	0.031
Malignant neoplasm of lip	0	0.0	1	0.0	0.017
Malignant neoplasm of tongue	0	0.0	4	0.1	0.034
Malignant neoplasm of major salivary glands	1	0.0	4	0.1	0.019
Malignant neoplasm of other and unspecified parts of mouth	0	0.0	1	0.0	0.017
Malignant neoplasm of oropharynx	1	0.0	1	0.0	0.005
Malignant neoplasm of nasopharynx	0	0.0	1	0.0	0.017
Malignant neoplasm of hypopharynx	0	0.0	1	0.0	0.017
Malignant neoplasm of other and ill-defined sites within the lip, oral cavity, and pharynx	0	0.0	1	0.0	0.017
Malignant neoplasm of esophagus	0	0.0	0	0.0	-
Malignant neoplasm of stomach	0	0.0	0	0.0	-
Malignant neoplasm of small intestine, including duodenum	0	0.0	1	0.0	0.017
Malignant neoplasm of colon	9	0.2	23	0.3	0.029
Malignant neoplasm of rectum, rectosigmoid junction, and anus	4	0.1	14	0.2	0.032
Malignant neoplasm of liver and intrahepatic bile ducts	2	0.0	2	0.0	0.007
Malignant neoplasm of gallbladder and extrahepatic bile ducts	2	0.0	1	0.0	0.017
Malignant neoplasm of retroperitoneum and peritoneum	0	0.0	1	0.0	0.017

Table 1.6.1a (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of

Characteristic	≥ 3 Years				
	Exenatide (N = 4,643)		OADs (N = 6,737)		Stand.
	N	%	N	%	Diff.
Malignant neoplasm of other and ill-defined sites within the digestive organs and peritoneum	0	0.0	1	0.0	0.017
Malignant neoplasm of nasal cavities, middle ear, and accessory sinuses	0	0.0	2	0.0	0.024
Malignant neoplasm of larynx	1	0.0	4	0.1	0.019
Malignant neoplasm of trachea, bronchus, and lung	6	0.1	8	0.1	0.003
Malignant neoplasm of pleura	0	0.0	0	0.0	-
Malignant neoplasm of thymus, heart, and mediastinum	0	0.0	1	0.0	0.017
Malignant neoplasm of bone and articular cartilage	1	0.0	1	0.0	0.005
Malignant neoplasm of connective and other soft tissue	0	0.0	2	0.0	0.024
Malignant melanoma of skin	8	0.2	11	0.2	0.002
Other malignant neoplasm of skin	64	1.4	86	1.3	0.009
Malignant neoplasm of female	60	1.3	68	1.0	0.027
Kaposi's sarcoma	0	0.0	1	0.0	0.017
Malignant neoplasm of uterus, part unspecified	2	0.0	3	0.0	0.001
Malignant neoplasm of cervix uteri	1	0.0	5	0.1	0.024
Malignant neoplasm of body of	9	0.2	8	0.1	0.019
Malignant neoplasm of ovary and other uterine adnexa	5	0.1	10	0.1	0.011
Malignant neoplasm of other and unspecified female genital organs	1	0.0	0	0.0	0.021
Malignant neoplasm of prostate	36	0.8	50	0.7	0.004

Table 1.6.1a (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Pancreatic Cancer, Life Sciences Research Database 6/1/2005 −7/31/2010

Characteristic	≥ 3 Years				
	Exenatide (N = 4,643)		OADs (N = 6,737)		Stand.
	N	%	N	%	Diff.
Malignant neoplasm of testis	2	0.0	1	0.0	0.017
Malignant neoplasm of penis and other male genital organs	0	0.0	0	0.0	-
Malignant neoplasm of bladder	7	0.2	14	0.2	0.013
Malignant neoplasm of kidney and other and unspecified urinary organs	9	0.2	10	0.1	0.011
Malignant neoplasm of eye	0	0.0	2	0.0	0.024
Malignant neoplasm of brain	2	0.0	3	0.0	0.001
Malignant neoplasm of other and unspecified parts of nervous system	4	0.1	2	0.0	0.023
Malignant neoplasm of other endocrine glands and related structures	3	0.1	5	0.1	0.004
Malignant neoplasm of other and ill-defined sites	4	0.1	3	0.0	0.016
Secondary and unspecified malignant neoplasm of lymph nodes	3	0.1	8	0.1	0.018
Secondary malignant neoplasm of respiratory and digestive systems	2	0.0	5	0.1	0.013
Secondary malignant neoplasm of other specified sites	3	0.1	6	0.1	0.009
Malignant neoplasm without specification of site	4	0.1	4	0.1	0.010

Table 1.6.1a (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Pancreatic Cancer, Life Sciences Research Database 6/1/2005 −7/31/2010

Characteristic	≥ 3 Years				
	Exenatide (N = 4,643)		OADs (N = 6,737)		Stand. Diff.
	N	%	N	%	
Lymphosarcoma and reticulosarcoma and other specified	8	0.2	7	0.1	0.018
Hodgkin's disease	4	0.1	7	0.1	0.006
Other malignant neoplasms of lymphoid and histiocytic tissue	8	0.2	22	0.3	0.031
Multiple myeloma and immunoproliferative neoplasms	3	0.1	1	0.0	0.025
Lymphoid leukemia	3	0.1	4	0.1	0.002
Myeloid leukemia	4	0.1	7	0.1	0.006
Monocytic leukemia	1	0.0	0	0.0	0.021
Other specified leukemia	0	0.0	2	0.0	0.024
Leukemia of unspecified cell type	0	0.0	1	0.0	0.017
Personal history of malignant neoplasm	116	2.5	170	2.5	0.002
	Mean	**SD**	**Mean**	**SD**	**Stand. Diff.**
Number Drugs (HICLs) Dispensed	12.7	5.5	11.9	5.3	0.151
Number of Physician Visits	7.4	5.5	7.2	5.7	0.036
Number of Laboratory Tests	13.5	12.9	12.8	13.2	0.054

Stand. Diff., Standardized Difference; SD, Standard Deviation

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins. Standardized difference is calculated by the difference between the 2 proportions divided by the pooled standard deviation.

Table 1.6.1b (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Pancreatic Cancer, Impact National Benchmark Database 6/1/2005−7/31/2010

Description	1 to < 2 Years					2 to < 3 Years				
	Exenatide (N = 6,959)		OADs (N = 10,109)		Stand.	Exenatide (N = 4,448)		OADs (N = 6,423)		Stand.
	N	%	N	%	Diff.	N	%	N	%	Diff.
Age										
≤39 years	532	7.6	895	8.9	0.044	318	7.1	530	8.3	0.041
40-49 years	1,589	22.8	2,227	22.0	0.019	1,012	22.8	1,411	22.0	0.019
50-59 years	2,871	41.3	4,160	41.2	0.002	1,864	41.9	2,751	42.8	0.019
60-69 years	1,786	25.7	2,568	25.4	0.006	1,123	25.2	1,544	24.0	0.028
≥70 years	181	2.6	259	2.6	0.002	131	2.9	187	2.9	0.002
Number of Drugs Dispensed										
0-4 drugs	142	2.0	230	2.3	0.016	82	1.8	147	2.3	0.031
5-9 drugs	2,118	30.4	3,276	32.4	0.042	1,352	30.4	2,114	32.9	0.054
10-14 drugs	2,691	38.7	3,814	37.7	0.019	1,731	38.9	2,424	37.7	0.024
>14 drugs	2,008	28.9	2,789	27.6	0.028	1,283	28.8	1,738	27.1	0.040
Stroke/TIA	121	1.7	185	1.8	0.007	87	2.0	118	1.8	0.009
Gender - Male	3,464	49.8	5,052	50.0	0.004	2,183	49.1	3,230	50.3	0.024
Myocardial Infarction	106	1.5	161	1.6	0.006	62	1.4	100	1.6	0.014
Ischemic Heart Disease	981	14.1	1,420	14.0	0.001	656	14.7	894	13.9	0.024
Malignant neoplasm of lip	2	0.0	0	0.0	0.024	1	0.0	0	0.0	0.021
Malignant neoplasm of tongue	0	0.0	1	0.0	0.014	0	0.0	0	0.0	
Malignant neoplasm of major salivary glands	1	0.0	3	0.0	0.010	0	0.0	3	0.0	0.031
Malignant neoplasm of floor of	1	0.0	0	0.0	0.017	0	0.0	0	0.0	-
Malignant neoplasm of other and unspecified parts of mouth	1	0.0	0	0.0	0.017	0	0.0	0	0.0	-
Malignant neoplasm of oropharynx	0	0.0	1	0.0	0.014	0	0.0	1	0.0	0.018
Malignant neoplasm of other and ill-defined sites within the lip, oral cavity, and pharynx	1	0.0	0	0.0	0.017	1	0.0	0	0.0	0.021
Malignant neoplasm of esophagus	0	0.0	2	0.0	0.020	0	0.0	1	0.0	0.018
Malignant neoplasm of stomach	1	0.0	3	0.0	0.010	1	0.0	0	0.0	0.021
Malignant neoplasm of colon	14	0.2	25	0.2	0.010	8	0.2	14	0.2	0.009
Malignant neoplasm of rectum, rectosigmoid junction, and anus	8	0.1	14	0.1	0.007	5	0.1	7	0.1	0.001
Malignant neoplasm of liver and intrahepatic bile ducts	1	0.0	4	0.0	0.015	1	0.0	2	0.0	0.005

Table 1.6.1b (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period by Duration of Follow-Up, Pancreatic Cancer, Impact National Benchmark Database 6/1/2005−7/31/2010

Description	1 to < 2 Years					2 to < 3 Years				
	Exenatide (N = 6,959)		OADs (N = 10,109)		Stand.	Exenatide (N = 4,448)		OADs (N = 6,423)		Stand.
	N	%	N	%	Diff.	N	%	N	%	Diff.
Malignant neoplasm of retroperitoneum and peritoneum	0	0.0	2	0.0	0.020	0	0.0	1	0.0	0.018
Malignant neoplasm of other and ill-defined sites within the digestive organs and peritoneum	0	0.0	2	0.0	0.020	0	0.0	1	0.0	0.018
Malignant neoplasm of larynx	4	0.1	5	0.0	0.003	3	0.1	5	0.1	0.004
Malignant neoplasm of trachea, bronchus, and lung	9	0.1	20	0.2	0.017	6	0.1	8	0.1	0.003
Malignant neoplasm of thymus, heart, and mediastinum	2	0.0	1	0.0	0.014	2	0.0	0	0.0	0.030
Malignant neoplasm of bone and articular cartilage	1	0.0	4	0.0	0.015	1	0.0	2	0.0	0.005
Malignant neoplasm of connective and other soft tissue	4	0.1	10	0.1	0.015	3	0.1	4	0.1	0.002
Malignant melanoma of skin	17	0.2	19	0.2	0.012	11	0.2	11	0.2	0.017
Other malignant neoplasm of skin	67	1.0	112	1.1	0.014	47	1.1	77	1.2	0.013
Malignant neoplasm of female	63	0.9	116	1.1	0.024	39	0.9	76	1.2	0.030
Malignant neoplasm of male breast	0	0.0	1	0.0	0.014	0	0.0	1	0.0	0.018
Kaposi's sarcoma	0	0.0	3	0.0	0.024	0	0.0	2	0.0	0.025
Malignant neoplasm of uterus, part unspecified	7	0.1	5	0.0	0.019	2	0.0	3	0.0	0.001
Malignant neoplasm of cervix uteri	7	0.1	7	0.1	0.011	5	0.1	6	0.1	0.006
Malignant neoplasm of body of uterus	14	0.2	22	0.2	0.004	10	0.2	11	0.2	0.012
Malignant neoplasm of ovary and other uterine adnexa	6	0.1	7	0.1	0.006	3	0.1	5	0.1	0.004
Malignant neoplasm of other and unspecified female genital organs	0	0.0	2	0.0	0.020	0	0.0	0	0.0	-
Malignant neoplasm of prostate	58	0.8	62	0.6	0.026	34	0.8	36	0.6	0.025
Malignant neoplasm of testis	2	0.0	3	0.0	0.001	1	0.0	1	0.0	0.005
Malignant neoplasm of penis and other male genital organs	1	0.0	0	0.0	0.017	1	0.0	0	0.0	0.021
Malignant neoplasm of bladder	16	0.2	30	0.3	0.013	9	0.2	22	0.3	0.027

Table 1.6.1b (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period by Duration of Follow-Up, Pancreatic Cancer, Impact National Benchmark Database 6/1/2005 −7/31/2010

Description	1 to < 2 Years					2 to < 3 Years				
	Exenatide (N = 6,959)		OADs (N = 10,109)		Stand.	Exenatide (N = 4,448)		OADs (N = 6,423)		Stand.
	N	%	N	%	Diff.	N	%	N	%	Diff.
Malignant neoplasm of kidney and other and unspecified urinary organs	14	0.2	22	0.2	0.004	11	0.2	13	0.2	0.009
Malignant neoplasm of eye	0	0.0	2	0.0	0.020	0	0.0	1	0.0	0.018
Malignant neoplasm of brain	3	0.0	4	0.0	0.002	2	0.0	2	0.0	0.007
Malignant neoplasm of other and unspecified parts of nervous system	1	0.0	2	0.0	0.004	0	0.0	1	0.0	0.018
Malignant neoplasm of other endocrine glands and related structures	6	0.1	6	0.1	0.010	4	0.1	3	0.0	0.017
Malignant neoplasm of other and ill-defined sites	3	0.0	6	0.1	0.007	1	0.0	3	0.0	0.013
Secondary and unspecified malignant neoplasm of lymph nodes	3	0.0	13	0.1	0.029	1	0.0	6	0.1	0.029
Secondary malignant neoplasm of respiratory and digestive systems	3	0.0	12	0.1	0.027	1	0.0	4	0.1	0.019
Secondary malignant neoplasm of other specified sites	8	0.1	16	0.2	0.012	4	0.1	8	0.1	0.011
Malignant neoplasm without specification of site	4	0.1	10	0.1	0.015	4	0.1	3	0.0	0.017
Lymphosarcoma and reticulosarcoma and other specified malignant tumors of lymphatic tissue	6	0.1	9	0.1	0.001	4	0.1	5	0.1	0.004
Hodgkin's disease	2	0.0	6	0.1	0.015	0	0.0	5	0.1	0.039
Other malignant neoplasms of lymphoid and histiocytic tissue	14	0.2	26	0.3	0.012	8	0.2	11	0.2	0.002
Multiple myeloma and immunoproliferative neoplasms	6	0.1	8	0.1	0.002	4	0.1	4	0.1	0.010
Lymphoid leukemia	5	0.1	11	0.1	0.012	4	0.1	6	0.1	0.001
Myeloid leukemia	6	0.1	9	0.1	0.001	3	0.1	5	0.1	0.004
Monocytic leukemia	2	0.0	0	0.0	0.024	2	0.0	0	0.0	0.030
Leukemia of unspecified cell type	5	0.1	2	0.0	0.024	4	0.1	2	0.0	0.024
Personal history of malignant neoplasm	145	2.1	224	2.2	0.009	92	2.1	149	2.3	0.017

Table 1.6.1b (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators on the Date of Cohort Entry by Duration of Follow-Up, Pancreatic Cancer, Impact National Benchmark Database 6/1/2005−7/31/2010

Description	1 to < 2 Years					2 to < 3 Years				
	Exenatide (N = 6,959)		OADs (N = 10,109)		Stand.	Exenatide (N = 4,448)		OADs (N = 6,423)		Stand.
	Mean	SD	Mean	SD	Diff.	Mean	SD	Mean	SD	Diff.
Number Drugs (HICLs) Dispensed	12.6	5.5	12.0	5.2	0.115	12.6	5.5	11.9	5.2	0.132
Number of Physician Visits	7.4	5.3	7.3	5.1	0.018	7.3	5.2	7.1	5.1	0.021
Number of Laboratory Tests	12.6	13.6	12.8	14.1	0.018	12.3	13.3	12.4	13.9	0.006

Table 1.6.1b (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators on the Date of Cohort Entry During the 9-Month Baseline Period, Pancreatic Cancer, Impact National Benchmark Database 6/1/2005−7/31/2010

Description	≥ 3 Years				
	Exenatide (N = 2,590)		OADs (N = 3,664)		Stand.
	N	%	N	%	Diff.
Age					
≤39 years	180	6.9	303	8.3	0.050
40-49 years	594	22.9	792	21.6	0.032
50-59 years	1,108	42.8	1,649	45.0	0.045
60-69 years	620	23.9	791	21.6	0.056
≥70 years	88	3.4	129	3.5	0.007
Number of Drugs Dispensed					
0-4 drugs	42	1.6	82	2.2	0.045
5-9 drugs	788	30.4	1,203	32.8	0.052
10-14 drugs	1,001	38.6	1,404	38.3	0.007
>14 drugs	759	29.3	975	26.6	0.060
Stroke/TIA	48	1.9	66	1.8	0.004
Gender - Male	1,256	48.5	1,877	51.2	0.055
Myocardial Infarction	33	1.3	58	1.6	0.026
Ischemic Heart Disease	390	15.1	491	13.4	0.047
Malignant neoplasm of lip	1	0.0	0	0.0	0.028
Malignant neoplasm of tongue	0	0.0	0	0.0	-
Malignant neoplasm of major salivary glands	0	0.0	1	0.0	0.023
Malignant neoplasm of floor of	0	0.0	0	0.0	-
Malignant neoplasm of other and unspecified parts of mouth	0	0.0	0	0.0	-
Malignant neoplasm of oropharynx	0	0.0	0	0.0	-

Table 1.6.1b (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators on the Date of Cohort Entry During the 9-Month Baseline Period, Pancreatic Cancer, Impact National Benchmark Database 6/1/2005−7/31/2010

Description	≥ 3 Years				
	Exenatide (N = 2,590)		OADs (N = 3,664)		Stand.
	N	%	N	%	Diff.
Malignant neoplasm of other and ill-defined sites within the lip, oral cavity, and pharynx	1	0.0	0	0.0	0.028
Malignant neoplasm of esophagus	0	0.0	1	0.0	0.023
Malignant neoplasm of stomach	0	0.0	0	0.0	-
Malignant neoplasm of colon	5	0.2	11	0.3	0.022
Malignant neoplasm of rectum, rectosigmoid junction, and anus	3	0.1	5	0.1	0.006
Malignant neoplasm of liver and intrahepatic bile ducts	1	0.0	1	0.0	0.006
Malignant neoplasm of retroperitoneum and peritoneum	0	0.0	1	0.0	0.023
Malignant neoplasm of other and ill-defined sites within the digestive organs and peritoneum	0	0.0	1	0.0	0.023
Malignant neoplasm of larynx	2	0.1	1	0.0	0.022
Malignant neoplasm of trachea, bronchus, and lung	2	0.1	6	0.2	0.025
Malignant neoplasm of thymus, heart, and mediastinum	1	0.0	0	0.0	0.028
Malignant neoplasm of bone and articular cartilage	1	0.0	0	0.0	0.028
Malignant neoplasm of connective and other soft tissue	2	0.1	1	0.0	0.022
Malignant melanoma of skin	6	0.2	6	0.2	0.015
Other malignant neoplasm of skin	28	1.1	54	1.5	0.035
Malignant neoplasm of female	22	0.8	46	1.3	0.040
Malignant neoplasm of male breast	0	0.0	1	0.0	0.023
Kaposi's sarcoma	0	0.0	2	0.1	0.033
Malignant neoplasm of uterus, part unspecified	1	0.0	3	0.1	0.018
Malignant neoplasm of cervix uteri	3	0.1	4	0.1	0.002
Malignant neoplasm of body of uterus	6	0.2	4	0.1	0.030

Table 1.6.1b (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators on the Date of Cohort Entry During the 9-Month Baseline Period, Pancreatic Cancer, Impact National Benchmark Database 6/1/2005−7/31/2010

Description	≥ 3 Years				
	Exenatide (N = 2,590)		OADs (N = 3,664)		Stand.
	N	%	N	%	Diff.
Malignant neoplasm of ovary and other uterine adnexa	0	0.0	2	0.1	0.033
Malignant neoplasm of other and unspecified female genital organs	0	0.0	0	0.0	-
Malignant neoplasm of prostate	18	0.7	17	0.5	0.030
Malignant neoplasm of testis	0	0.0	1	0.0	0.023
Malignant neoplasm of penis and other male genital organs	1	0.0	0	0.0	0.028
Malignant neoplasm of bladder	3	0.1	11	0.3	0.040
Malignant neoplasm of kidney and other and unspecified urinary organs	9	0.3	7	0.2	0.030
Malignant neoplasm of eye	0	0.0	1	0.0	0.023
Malignant neoplasm of brain	2	0.1	1	0.0	0.022
Malignant neoplasm of other and unspecified parts of nervous system	0	0.0	0	0.0	-
Malignant neoplasm of other endocrine glands and related structures	2	0.1	2	0.1	0.009
Malignant neoplasm of other and ill-defined sites	1	0.0	1	0.0	0.006
Secondary and unspecified malignant neoplasm of lymph nodes	0	0.0	4	0.1	0.047
Secondary malignant neoplasm of respiratory and digestive systems	0	0.0	4	0.1	0.047
Secondary malignant neoplasm of other specified sites	2	0.1	5	0.1	0.018
Malignant neoplasm without specification of site	1	0.0	3	0.1	0.018
Lymphosarcoma and reticulosarcoma and other specified malignant tumors of lymphatic tissue	3	0.1	2	0.1	0.021

Table 1.6.1b (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period by Duration of Follow-Up, Pancreatic Cancer, Impact National Benchmark Database 6/1/2005 −7/31/2010

Description	≥ 3 Years				
	Exenatide (N = 2,590)		OADs (N = 3,664)		Stand.
	N	%	N	%	Diff.
Hodgkin's disease	0	0.0	3	0.1	0.040
Other malignant neoplasms of lymphoid and histiocytic tissue	7	0.3	4	0.1	0.037
Multiple myeloma and immunoproliferative neoplasms	0	0.0	1	0.0	0.023
Lymphoid leukemia	1	0.0	3	0.1	0.018
Myeloid leukemia	1	0.0	2	0.1	0.007
Monocytic leukemia	2	0.1	0	0.0	0.039
Leukemia of unspecified cell type	3	0.1	1	0.0	0.033
Personal history of malignant neoplasm	47	1.8	84	2.3	0.034
	Mean	SD	Mean	SD	Stand. Diff.
Number Drugs (HICLs) Dispensed	12.6	5.5	11.9	5.1	0.139
Number of Physician Visits	7.2	5.2	7.1	5.1	0.017
Number of Laboratory Tests	11.3	12.6	11.9	14.2	0.049

Stand. Diff., Standardized Difference; SD, Standard Deviation

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins. Standardized difference is calculated by the difference between the 2 proportions divided by the pooled standard deviation.

Table 1.6.2a (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Thyroid Cancer, Life Sciences Research Database 6/1/2005−7/31/2010

Characteristic	1 to < 2 Years					2 to < 3 Years				
	Exenatide (N = 11,986)		OADs (N = 17,605)		Stand.	Exenatide (N = 7,751)		OADs (N = 11,088)		Stand.
	N	%	N	%	Diff.	N	%	N	%	Diff.
Age										
≤39 years	1,148	9.6	1,912	10.9	0.042	658	8.5	1,101	9.9	0.050
40-49 years	2,856	23.8	4,117	23.4	0.010	1,846	23.8	2,541	22.9	0.021
50-59 years	4,797	40.0	6,935	39.4	0.013	3,240	41.8	4,546	41.0	0.016
60-69 yrears	2,744	22.9	3,946	22.4	0.011	1,718	22.2	2,406	21.7	0.011
≥70 years	441	3.7	695	3.9	0.014	289	3.7	494	4.5	0.037
Number of Drugs Dispensed										
0-4 drugs	312	2.6	481	2.7	0.008	204	2.6	308	2.8	0.009
5-9 drugs	3,442	28.7	5,819	33.1	0.094	2,268	29.3	3,753	33.8	0.099
10-14 drugs	4,573	38.2	6,421	36.5	0.035	2,937	37.9	4,006	36.1	0.037
>14 drugs	3,659	30.5	4,884	27.7	0.061	2,342	30.2	3,021	27.2	0.066
Stroke/TIA	214	1.8	333	1.9	0.008	142	1.8	192	1.7	0.008
Myocardial Infarction	149	1.2	253	1.4	0.017	85	1.1	166	1.5	0.035
Gender - Male	5,629	47.0	8,319	47.3	0.006	3,631	46.8	5,295	47.8	0.018
Ischemic Heart Disease	1,625	13.6	2,381	13.5	0.001	1,041	13.4	1,508	13.6	0.005
Malignant neoplasm of lip	0	0.0	4	0.0	0.021	0	0.0	3	0.0	0.023
Malignant neoplasm of tongue	1	0.0	5	0.0	0.015	0	0.0	4	0.0	0.027
Malignant neoplasm of major salivary glands	3	0.0	6	0.0	0.005	3	0.0	4	0.0	0.001
Malignant neoplasm of other and unspecified parts of mouth	0	0.0	3	0.0	0.018	0	0.0	3	0.0	0.023
Malignant neoplasm of oropharynx	1	0.0	3	0.0	0.008	1	0.0	3	0.0	0.010
Malignant neoplasm of nasopharynx	0	0.0	1	0.0	0.011	0	0.0	1	0.0	0.013
Malignant neoplasm of hypopharynx	0	0.0	1	0.0	0.011	0	0.0	1	0.0	0.013
Malignant neoplasm of other and ill-defined sites within the lip, oral cavity, and pharynx	0	0.0	4	0.0	0.021	0	0.0	3	0.0	0.023
Malignant neoplasm of esophagus	1	0.0	2	0.0	0.003	0	0.0	0	0.0	-
Malignant neoplasm of stomach	1	0.0	0	0.0	0.013	0	0.0	0	0.0	-
Malignant neoplasm of small intestine, including duodenum	0	0.0	2	0.0	0.015	0	0.0	1	0.0	0.013
Malignant neoplasm of colon	24	0.2	49	0.3	0.016	16	0.2	36	0.3	0.023

Table 1.6.2a (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Thyroid Cancer, Life Sciences Research Database 6/1/2005−7/31/2010

Characteristic	1 to < 2 Years					2 to < 3 Years				
	Exenatide (N = 11,986)		OADs (N = 17,605)		Stand.	Exenatide (N = 7,751)		OADs (N = 11,088)		Stand.
	N	%	N	%	Diff.	N	%	N	%	Diff.
Malignant neoplasm of rectum, rectosigmoid junction, and anus	12	0.1	30	0.2	0.019	8	0.1	21	0.2	0.023
Malignant neoplasm of liver and intrahepatic bile ducts	5	0.0	6	0.0	0.004	2	0.0	4	0.0	0.006
Malignant neoplasm of gallbladder and extrahepatic bile ducts	2	0.0	3	0.0	0.000	2	0.0	2	0.0	0.005
Malignant neoplasm of retroperitoneum and peritoneum	2	0.0	2	0.0	0.004	1	0.0	2	0.0	0.004
Malignant neoplasm of other and ill-defined sites within the digestive organs and peritoneum	0	0.0	3	0.0	0.018	0	0.0	1	0.0	0.013
Malignant neoplasm of nasal cavities, middle ear, and accessory sinuses	0	0.0	2	0.0	0.015	0	0.0	2	0.0	0.019
Malignant neoplasm of larynx	1	0.0	10	0.1	0.027	1	0.0	6	0.1	0.023
Malignant neoplasm of trachea, bronchus, and lung	12	0.1	32	0.2	0.022	8	0.1	20	0.2	0.021
Malignant neoplasm of pleura	2	0.0	1	0.0	0.010	2	0.0	0	0.0	0.023
Malignant neoplasm of thymus, heart, and mediastinum	0	0.0	1	0.0	0.011	0	0.0	1	0.0	0.013
Malignant neoplasm of bone and articular cartilage	1	0.0	6	0.0	0.018	1	0.0	3	0.0	0.010
Malignant neoplasm of connective and other soft tissue	5	0.0	4	0.0	0.011	2	0.0	3	0.0	0.001
Malignant melanoma of skin	21	0.2	26	0.1	0.007	13	0.2	17	0.2	0.004
Other malignant neoplasm of skin	134	1.1	212	1.2	0.008	98	1.3	129	1.2	0.009
Malignant neoplasm of female breast	139	1.2	200	1.1	0.002	94	1.2	119	1.1	0.013
Kaposi's sarcoma	0	0.0	1	0.0	0.011	0	0.0	1	0.0	0.013
Malignant neoplasm of uterus, part unspecified	7	0.1	9	0.1	0.003	3	0.0	5	0.0	0.003
Malignant neoplasm of cervix uteri	5	0.0	8	0.0	0.002	2	0.0	6	0.1	0.014
Malignant neoplasm of body of uterus	21	0.2	25	0.1	0.008	14	0.2	14	0.1	0.014

Table 1.6.2a (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Thyroid Cancer, Life Sciences Research Database 6/1/2005−7/31/2010

Characteristic	1 to < 2 Years					2 to < 3 Years				
	Exenatide (N = 11,986)		OADs (N = 17,605)		Stand.	Exenatide (N = 7,751)		OADs (N = 11,088)		Stand.
	N	%	N	%	Diff.	N	%	N	%	Diff.
Malignant neoplasm of ovary and other uterine adnexa	11	0.1	24	0.1	0.013	7	0.1	12	0.1	0.006
Malignant neoplasm of other and unspecified female genital organs	2	0.0	1	0.0	0.010	2	0.0	1	0.0	0.013
Malignant neoplasm of prostate	78	0.7	132	0.7	0.012	60	0.8	87	0.8	0.001
Malignant neoplasm of testis	5	0.0	5	0.0	0.007	3	0.0	2	0.0	0.012
Malignant neoplasm of penis and other male genital organs	1	0.0	1	0.0	0.003	1	0.0	0	0.0	0.016
Malignant neoplasm of bladder	25	0.2	43	0.2	0.008	18	0.2	24	0.2	0.003
Malignant neoplasm of kidney and other and unspecified urinary organs	21	0.2	25	0.1	0.008	15	0.2	16	0.1	0.012
Malignant neoplasm of eye	1	0.0	4	0.0	0.012	1	0.0	2	0.0	0.004
Malignant neoplasm of brain	7	0.1	13	0.1	0.006	5	0.1	7	0.1	0.001
Malignant neoplasm of other and unspecified parts of nervous system	4	0.0	8	0.0	0.006	4	0.1	4	0.0	0.007
Malignant neoplasm of other endocrine glands and related structures	14	0.1	14	0.1	0.012	8	0.1	8	0.1	0.010
Malignant neoplasm of other and ill-defined sites	6	0.1	8	0.0	0.002	6	0.1	6	0.1	0.009
Secondary and unspecified malignant neoplasm of lymph nodes	7	0.1	23	0.1	0.024	5	0.1	14	0.1	0.020
Secondary malignant neoplasm of respiratory and digestive systems	8	0.1	27	0.2	0.026	4	0.1	16	0.1	0.030
Secondary malignant neoplasm of other specified sites	5	0.0	24	0.1	0.032	5	0.1	14	0.1	0.020
Malignant neoplasm without specification of site	8	0.1	12	0.1	0.001	6	0.1	6	0.1	0.009
Lymphosarcoma and reticulosarcoma and other specified malignant tumors of lymphatic tissue	18	0.2	24	0.1	0.004	16	0.2	17	0.2	0.013

Table 1.6.2a (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Thyroid Cancer, Life Sciences Research Database 6/1/2005−7/31/2010

Characteristic	1 to < 2 Years					2 to < 3 Years				
	Exenatide (N = 11,986)		OADs (N = 17,605)		Stand.	Exenatide (N = 7,751)		OADs (N = 11,088)		Stand.
	N	%	N	%	Diff.	N	%	N	%	Diff.
Hodgkin's disease	14	0.1	12	0.1	0.016	6	0.1	10	0.1	0.004
Other malignant neoplasms of	20	0.2	49	0.3	0.024	15	0.2	36	0.3	0.026
Multiple myeloma and	9	0.1	7	0.0	0.015	6	0.1	3	0.0	0.022
Lymphoid leukemia	9	0.1	13	0.1	0.000	6	0.1	7	0.1	0.005
Myeloid leukemia	9	0.1	26	0.1	0.022	8	0.1	17	0.2	0.014
Monocytic leukemia	1	0.0	0	0.0	0.013	1	0.0	0	0.0	0.016
Other specified leukemia	0	0.0	2	0.0	0.015	0	0.0	2	0.0	0.019
Leukemia of unspecified cell type	2	0.0	3	0.0	0.000	1	0.0	2	0.0	0.004
Personal history of malignant neoplasm	289	2.4	426	2.4	0.001	190	2.5	280	2.5	0.005
	Mean	SD	Mean	SD	Stand. Diff.	Mean	SD	Mean	SD	Stand. Diff.
Number Drugs (HICLs) Dispensed	12.6	5.6	12.0	5.4	0.126	12.6	5.5	11.9	5.4	0.131
Number of Physician Visits	7.5	5.7	7.3	5.7	0.035	7.5	5.5	7.2	5.7	0.037
Number of Laboratory Tests	13.9	13.6	13.3	13.8	0.044	13.7	13.0	13.1	13.8	0.041

Table 1.6.2a (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Thyroid Cancer, Life Sciences Research Database 6/1/2005−7/31/2010,

Characteristic	≥ 3 Years				
	Exenatide (N= 4,638)		OADs (N = 6,734)		Stand.
	N	%	N	%	Diff.
Age					
≤39 years	374	8.1	627	9.3	0.044
40-49 years	1,099	23.7	1,512	22.5	0.029
50-59 years	1,956	42.2	2,843	42.2	0.001
60-69 years	1,017	21.9	1,405	20.9	0.026
≥70 years	192	4.1	347	5.2	0.048
Number of Drugs Dispensed					
0-4 drugs	104	2.2	141	2.1	0.010
5-9 drugs	1,307	28.2	2,296	34.1	0.128
10-14 drugs	1,790	38.6	2,468	36.6	0.040
>14 drugs	1,437	31.0	1,829	27.2	0.084
Stroke/TIA	97	2.1	110	1.6	0.034
Myocardial Infarction	43	0.9	88	1.3	0.036
Gender - Male	2,185	47.1	3,222	47.8	0.015

Table 1.6.2a (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Thyroid Cancer, Life Sciences Research Database 6/1/2005−7/31/2010

Characteristic	≥ 3 Years				
	Exenatide (N= 4,638)		OADs (N = 6,734)		Stand.
	N	%	N	%	Diff.
Ischemic Heart Disease	590	12.7	927	13.8	0.031
Malignant neoplasm of lip	0	0.0	1	0.0	0.017
Malignant neoplasm of tongue	0	0.0	4	0.1	0.034
Malignant neoplasm of major salivary glands	1	0.0	4	0.1	0.019
Malignant neoplasm of other and unspecified parts of mouth	0	0.0	1	0.0	0.017
Malignant neoplasm of oropharynx	1	0.0	1	0.0	0.005
Malignant neoplasm of nasopharynx	0	0.0	1	0.0	0.017
Malignant neoplasm of hypopharynx	0	0.0	1	0.0	0.017
Malignant neoplasm of other and ill-defined sites within the lip, oral cavity, and pharynx	0	0.0	1	0.0	0.017
Malignant neoplasm of esophagus	0	0.0	0	0.0	-
Malignant neoplasm of stomach	0	0.0	0	0.0	-
Malignant neoplasm of small intestine, including duodenum	0	0.0	1	0.0	0.017
Malignant neoplasm of colon	9	0.2	23	0.3	0.029
Malignant neoplasm of rectum, rectosigmoid junction, and anus	4	0.1	14	0.2	0.032
Malignant neoplasm of liver and intrahepatic bile ducts	2	0.0	2	0.0	0.007
Malignant neoplasm of gallbladder and extrahepatic bile ducts	2	0.0	1	0.0	0.017
Malignant neoplasm of retroperitoneum and peritoneum	0	0.0	1	0.0	0.017
Malignant neoplasm of other and ill-defined sites within the digestive organs and peritoneum	0	0.0	1	0.0	0.017
Malignant neoplasm of nasal cavities, middle ear, and accessory sinuses	0	0.0	2	0.0	0.024

Table 1.6.2a (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Thyroid Cancer, Life Sciences Research Database 6/1/2005−7/31/2010

Characteristic	≥ 3 Years				
	Exenatide (N= 4,638)		OADs (N = 6,734)		Stand.
	N	%	N	%	Diff.
Malignant neoplasm of larynx	1	0.0	4	0.1	0.019
Malignant neoplasm of trachea, bronchus, and lung	6	0.1	8	0.1	0.003
Malignant neoplasm of pleura	0	0.0	0	0.0	-
Malignant neoplasm of thymus, heart, and mediastinum	0	0.0	1	0.0	0.017
Malignant neoplasm of bone and articular cartilage	1	0.0	1	0.0	0.005
Malignant neoplasm of connective and other soft tissue	0	0.0	2	0.0	0.024
Malignant melanoma of skin	8	0.2	11	0.2	0.002
Other malignant neoplasm of skin	64	1.4	87	1.3	0.008
Malignant neoplasm of female breast	60	1.3	68	1.0	0.027
Kaposi's sarcoma	0	0.0	1	0.0	0.017
Malignant neoplasm of uterus, part unspecified	2	0.0	3	0.0	0.001
Malignant neoplasm of cervix uteri	1	0.0	5	0.1	0.024
Malignant neoplasm of body of uterus	9	0.2	8	0.1	0.019
Malignant neoplasm of ovary and other uterine adnexa	5	0.1	10	0.1	0.011
Malignant neoplasm of other and unspecified female genital organs	1	0.0	0	0.0	0.021
Malignant neoplasm of prostate	36	0.8	50	0.7	0.004
Malignant neoplasm of testis	2	0.0	1	0.0	0.017
Malignant neoplasm of penis and other male genital organs	0	0.0	0	0.0	.
Malignant neoplasm of bladder	7	0.2	14	0.2	0.013
Malignant neoplasm of kidney and other and unspecified urinary organs	9	0.2	10	0.1	0.011
Malignant neoplasm of eye	0	0.0	2	0.0	0.024
Malignant neoplasm of brain	2	0.0	3	0.0	0.001

Table 1.6.2a (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Thyroid Cancer, Life Sciences Research Database 6/1/2005−7/31/2010

Characteristic	≥ 3 Years				
	Exenatide (N= 4,638)		OADs (N = 6,734)		Stand.
	N	%	N	%	Diff.
Malignant neoplasm of other and unspecified parts of nervous system	4	0.1	2	0.0	0.023
Malignant neoplasm of other endocrine glands and related structures	3	0.1	5	0.1	0.004
Malignant neoplasm of other and ill-defined sites	4	0.1	3	0.0	0.016
Secondary and unspecified malignant neoplasm of lymph nodes	3	0.1	8	0.1	0.018
Secondary malignant neoplasm of respiratory and digestive systems	2	0.0	5	0.1	0.013
Secondary malignant neoplasm of other specified sites	3	0.1	6	0.1	0.009
Malignant neoplasm without specification of site	4	0.1	4	0.1	0.010
Lymphosarcoma and reticulosarcoma and other specified malignant tumors of lymphatic tissue	8	0.2	7	0.1	0.018
Hodgkin's disease	4	0.1	7	0.1	0.006
Other malignant neoplasms of lymphoid and histiocytic tissue	8	0.2	22	0.3	0.031
Multiple myeloma and immunoproliferative neoplasms	3	0.1	1	0.0	0.025
Lymphoid leukemia	3	0.1	4	0.1	0.002
Myeloid leukemia	4	0.1	7	0.1	0.006
Monocytic leukemia	1	0.0	0	0.0	0.021
Other specified leukemia	0	0.0	2	0.0	0.024
Leukemia of unspecified cell type	0	0.0	1	0.0	0.017
Personal history of malignant neoplasm	116	2.5	170	2.5	0.001

Table 1.6.2a (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Thyroid Cancer, Life Sciences Research Database 6/1/2005−7/31/2010

Characteristic	≥ 3 Years				
	Exenatide (N= 4,638)		OADs (N = 6,734)		Stand. Diff.
	Mean	SD	Mean	SD	
Number Drugs (HICLs) Dispensed	12.7	5.5	11.9	5.3	0.152
Number of Physician Visits	7.4	5.5	7.2	5.7	0.037
Number of Laboratory Tests	13.5	12.9	12.8	13.2	0.055

Stand. Diff., Standardized Difference; SD, Standard Deviation

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins. Standardized difference is calculated by the difference between the 2 proportions divided by the pooled standard deviation.

Table 1.6.2b (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Thyroid Cancer, Impact National Benchmark Database 6/1/2005–7/31/2010

Characteristic	1 to < 2 Years					2 to < 3 Years				
	Exenatide (N = 6,954)		OADs (N = 10,100)		Stand.	Exenatide (N = 4,443)		OADs (N = 6,415)		Stand.
	N	%	N	%	Diff.	N	%	N	%	Diff.
Age										
≤39 years	532	7.7	895	8.9	0.044	318	7.2	529	8.2	0.041
40-49 years	1,587	22.8	2,224	22.0	0.019	1,010	22.7	1,409	22.0	0.018
50-59 years	2,869	41.3	4,157	41.2	0.002	1,862	41.9	2,746	42.8	0.018
60-69 years	1,785	25.7	2,567	25.4	0.006	1,122	25.3	1,545	24.1	0.027
≥70 years	181	2.6	257	2.5	0.004	131	2.9	186	2.9	0.003
Number of Drugs Dispensed										
0-4 drugs	142	2.0	230	2.3	0.016	82	1.8	147	2.3	0.031
5-9 drugs	2,117	30.4	3,271	32.4	0.042	1,351	30.4	2,110	32.9	0.053
10-14 drugs	2,689	38.7	3,814	37.8	0.019	1,730	38.9	2,424	37.8	0.024
>14 drugs	2,006	28.8	2,785	27.6	0.028	1,280	28.8	1,734	27.0	0.040
Stroke/TIA	121	1.7	184	1.8	0.006	86	1.9	117	1.8	0.008
Gender - Male	3,463	49.8	5,050	50.0	0.004	2,181	49.1	3,229	50.3	0.025
Myocardial Infarction	106	1.5	161	1.6	0.006	62	1.4	100	1.6	0.014
Ischemic Heart Disease	981	14.1	1,419	14.0	0.002	655	14.7	893	13.9	0.023
Malignant neoplasm of lip	1	0.0	0	0.0	0.017	1	0.0	0	0.0	0.021
Malignant neoplasm of tongue	0	0.0	1	0.0	0.014	0	0.0	0	0.0	-
Malignant neoplasm of major salivary glands	1	0.0	3	0.0	0.010	0	0.0	3	0.0	0.031
Malignant neoplasm of floor of mouth	1	0.0	0	0.0	0.017	0	0.0	0	0.0	-
Malignant neoplasm of other and unspecified parts of mouth	1	0.0	0	0.0	0.017	0	0.0	0	0.0	-
Malignant neoplasm of oropharynx	0	0.0	1	0.0	0.014	0	0.0	1	0.0	0.018
Malignant neoplasm of other and ill-defined sites within the lip, oral cavity, and pharynx	1	0.0	0	0.0	0.017	1	0.0	0	0.0	0.021
Malignant neoplasm of esophagus	0	0.0	2	0.0	0.020	0	0.0	1	0.0	0.018
Malignant neoplasm of stomach	1	0.0	3	0.0	0.010	1	0.0	0	0.0	0.021
Malignant neoplasm of colon	14	0.2	25	0.2	0.010	8	0.2	14	0.2	0.009
Malignant neoplasm of rectum, rectosigmoid junction, and anus	8	0.1	14	0.1	0.007	5	0.1	7	0.1	0.001
Malignant neoplasm of liver and intrahepatic bile ducts	1	0.0	4	0.0	0.015	1	0.0	2	0.0	0.005

Table 1.6.2b (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Thyroid Cancer, Impact National Benchmark Database 6/1/2005–7/31/2010

Characteristic	1 to < 2 Years					2 to < 3 Years				
	Exenatide (N = 6,954)		OADs (N = 10,100)		Stand.	Exenatide (N = 4,443)		OADs (N = 6,415)		Stand.
	N	%	N	%	Diff.	N	%	N	%	Diff.
Malignant neoplasm of retroperitoneum and peritoneum	0	0.0	2	0.0	0.020	0	0.0	1	0.0	0.018
Malignant neoplasm of other and ill-defined sites within the digestive organs and peritoneum	0	0.0	2	0.0	0.020	0	0.0	1	0.0	0.018
Malignant neoplasm of larynx	4	0.1	5	0.0	0.003	3	0.1	5	0.1	0.004
Malignant neoplasm of trachea, bronchus, and lung	9	0.1	20	0.2	0.017	6	0.1	8	0.1	0.003
Malignant neoplasm of thymus, heart, and mediastinum	2	0.0	1	0.0	0.014	2	0.0	0	0.0	0.030
Malignant neoplasm of bone and articular cartilage	1	0.0	4	0.0	0.015	1	0.0	2	0.0	0.005
Malignant neoplasm of connective and other soft tissue	4	0.1	10	0.1	0.015	3	0.1	4	0.1	0.002
Malignant melanoma of skin	17	0.2	18	0.2	0.014	11	0.2	11	0.2	0.017
Other malignant neoplasm of skin	67	1.0	111	1.1	0.013	47	1.1	77	1.2	0.013
Malignant neoplasm of female breast	63	0.9	116	1.1	0.024	39	0.9	76	1.2	0.030
Malignant neoplasm of male breast	0	0.0	1	0.0	0.014	0	0.0	1	0.0	0.018
Kaposi's sarcoma	0	0.0	3	0.0	0.024	0	0.0	2	0.0	0.025
Malignant neoplasm of uterus, part unspecified	7	0.1	5	0.0	0.019	2	0.0	3	0.0	0.001
Malignant neoplasm of cervix uteri	7	0.1	7	0.1	0.011	5	0.1	6	0.1	0.006
Malignant neoplasm of body of uterus	14	0.2	22	0.2	0.004	10	0.2	11	0.2	0.012
Malignant neoplasm of ovary and other uterine adnexa	6	0.1	7	0.1	0.006	3	0.1	5	0.1	0.004
Malignant neoplasm of other and unspecified female genital organs	0	0.0	2	0.0	0.020	0	0.0	0	0.0	.
Malignant neoplasm of prostate	58	0.8	62	0.6	0.026	34	0.8	36	0.6	0.025
Malignant neoplasm of testis	2	0.0	3	0.0	0.001	1	0.0	1	0.0	0.005
Malignant neoplasm of penis and other male genital organs	1	0.0	0	0.0	0.017	1	0.0	0	0.0	0.021
Malignant neoplasm of bladder	16	0.2	30	0.3	0.013	9	0.2	22	0.3	0.027

Table 1.6.2b (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Thyroid Cancer, Impact National Benchmark Database 6/1/2005–7/31/2010

Characteristic	1 to < 2 Years					2 to < 3 Years				
	Exenatide (N = 6,954)		OADs (N = 10,100)		Stand.	Exenatide (N = 4,443)		OADs (N = 6,415)		Stand.
	N	%	N	%	Diff.	N	%	N	%	Diff.
Malignant neoplasm of kidney and other and unspecified urinary organs	14	0.2	22	0.2	0.004	11	0.2	13	0.2	0.009
Malignant neoplasm of eye	0	0.0	2	0.0	0.020	0	0.0	1	0.0	0.018
Malignant neoplasm of brain	3	0.0	4	0.0	0.002	2	0.0	2	0.0	0.007
Malignant neoplasm of other and unspecified parts of nervous system	1	0.0	2	0.0	0.004	0	0.0	1	0.0	0.018
Malignant neoplasm of other endocrine glands and related structures	6	0.1	6	0.1	0.010	4	0.1	3	0.0	0.017
Malignant neoplasm of other and ill-defined sites	3	0.0	6	0.1	0.007	1	0.0	3	0.0	0.013
Secondary and unspecified malignant neoplasm of lymph nodes	3	0.0	13	0.1	0.029	1	0.0	6	0.1	0.029
Secondary malignant neoplasm of respiratory and digestive systems	3	0.0	12	0.1	0.027	1	0.0	4	0.1	0.019
Secondary malignant neoplasm of other specified sites	8	0.1	16	0.2	0.012	4	0.1	8	0.1	0.011
Malignant neoplasm without specification of site	4	0.1	10	0.1	0.015	4	0.1	3	0.0	0.017
Lymphosarcoma and reticulosarcoma and other specified malignant tumors of lymphatic tissue	6	0.1	9	0.1	0.001	4	0.1	5	0.1	0.004
Hodgkin's disease	2	0.0	6	0.1	0.015	0	0.0	5	0.1	0.039
Other malignant neoplasms of lymphoid and histiocytic tissue	14	0.2	25	0.2	0.010	8	0.2	11	0.2	0.002
Multiple myeloma and immunoproliferative neoplasms	6	0.1	8	0.1	0.002	4	0.1	4	0.1	0.010
Lymphoid leukemia	5	0.1	11	0.1	0.012	4	0.1	6	0.1	0.001
Myeloid leukemia	6	0.1	9	0.1	0.001	3	0.1	5	0.1	0.004
Monocytic leukemia	2	0.0	0	0.0	0.024	2	0.0	0	0.0	0.030
Leukemia of unspecified cell type	5	0.1	2	0.0	0.024	4	0.1	2	0.0	0.024
Personal history of malignant neoplasm	144	2.1	223	2.2	0.009	92	2.1	149	2.3	0.017

Table 1.6.2b (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Thyroid Cancer, Impact National Benchmark Database 6/1/2005–7/31/2010

Characteristic	1 to < 2 Years					2 to < 3 Years				
	Exenatide (N = 6,954)		OADs (N = 10,100)		Stand.	Exenatide (N = 4,443)		OADs (N = 6,415)		Stand.
	Mean	SD	Mean	SD	Diff.	Mean	SD	Mean	SD	Diff.
Number Drugs (HICLs) Dispensed	12.6	5.5	12.0	5.2	0.115	12.6	5.5	11.9	5.2	0.131
Number of Physician Visits	7.4	5.3	7.3	5.1	0.018	7.3	5.2	7.1	5.1	0.021
Number of Laboratory Tests	12.6	13.6	12.8	14.1	0.018	12.3	13.3	12.4	13.9	0.006

Table 1.6.2b (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Thyroid Cancer, Impact National Benchmark Database 6/1/2005–7/31/2010

Characteristic	≥ 3 Years				
	Exenatide (N= 2,588)		OADs (N = 3,657)		Stand.
	N	%	N	%	Diff.
Age					
≤39 years	180	7.0	302	8.3	0.049
40-49 years	593	22.9	790	21.6	0.032
50-59 years	1,108	42.8	1,648	45.1	0.045
60-69 years	619	23.9	789	21.6	0.056
≥70 years	88	3.4	128	3.5	0.005
Number of Drugs Dispensed					
0-4 drugs	42	1.6	82	2.2	0.045
5-9 drugs	787	30.4	1,200	32.8	0.052
10-14 drugs	1,001	38.7	1,402	38.3	0.007
>14 drugs	758	29.3	973	26.6	0.060
Stroke/TIA	48	1.9	66	1.8	0.004
Gender - Male	1,255	48.5	1,875	51.3	0.056
Myocardial Infarction	33	1.3	58	1.6	0.026
Ischemic Heart Disease	389	15.0	492	13.5	0.045
Malignant neoplasm of lip	1	0.0	0	0.0	0.028
Malignant neoplasm of tongue	0	0.0	0	0.0	-
Malignant neoplasm of major salivary glands	0	0.0	1	0.0	0.023
Malignant neoplasm of floor of mouth	0	0.0	0	0.0	-
Malignant neoplasm of other and unspecified parts of mouth	0	0.0	0	0.0	-

Table 1.6.2b (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Thyroid Cancer, Impact National Benchmark Database 6/1/2005−7/31/2010

Characteristic	≥ 3 Years				
	Exenatide (N= 2,588)		OADs (N = 3,657)		Stand.
	N	%	N	%	Diff.
Malignant neoplasm of oropharynx	0	0.0	0	0.0	-
Malignant neoplasm of other and ill-defined sites within the lip, oral cavity, and pharynx	1	0.0	0	0.0	0.028
Malignant neoplasm of esophagus	0	0.0	1	0.0	0.023
Malignant neoplasm of stomach	0	0.0	0	0.0	.
Malignant neoplasm of colon	5	0.2	11	0.3	0.022
Malignant neoplasm of rectum, rectosigmoid junction, and anus	3	0.1	5	0.1	0.006
Malignant neoplasm of liver and intrahepatic bile ducts	1	0.0	1	0.0	0.006
Malignant neoplasm of retroperitoneum and peritoneum	0	0.0	1	0.0	0.023
Malignant neoplasm of other and ill-defined sites within the digestive organs and peritoneum	0	0.0	1	0.0	0.023
Malignant neoplasm of larynx	2	0.1	1	0.0	0.022
Malignant neoplasm of trachea, bronchus, and lung	2	0.1	6	0.2	0.025
Malignant neoplasm of thymus, heart, and mediastinum	1	0.0	0	0.0	0.028
Malignant neoplasm of bone and articular cartilage	1	0.0	0	0.0	0.028
Malignant neoplasm of connective and other soft tissue	2	0.1	1	0.0	0.022
Malignant melanoma of skin	6	0.2	6	0.2	0.015
Other malignant neoplasm of skin	28	1.1	54	1.5	0.035
Malignant neoplasm of female breast	22	0.9	46	1.3	0.040
Malignant neoplasm of male breast	0	0.0	1	0.0	0.023
Kaposi's sarcoma	0	0.0	2	0.1	0.033
Malignant neoplasm of uterus, part unspecified	1	0.0	3	0.1	0.018
Malignant neoplasm of cervix uteri	3	0.1	4	0.1	0.002

Table 1.6.2b (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Thyroid Cancer, Impact National Benchmark Database 6/1/2005–7/31/2010

Characteristic	≥ 3 Years				
	Exenatide (N= 2,588)		OADs (N = 3,657)		Stand.
	N	%	N	%	Diff.
Malignant neoplasm of body of uterus	6	0.2	3	0.1	0.038
Malignant neoplasm of ovary and other uterine adnexa	0	0.0	2	0.1	0.033
Malignant neoplasm of other and unspecified female genital organs	0	0.0	0	0.0	-
Malignant neoplasm of prostate	18	0.7	17	0.5	0.030
Malignant neoplasm of testis	0	0.0	1	0.0	0.023
Malignant neoplasm of penis and other male genital organs	1	0.0	0	0.0	0.028
Malignant neoplasm of bladder	3	0.1	11	0.3	0.041
Malignant neoplasm of kidney and other and unspecified urinary organs	9	0.3	7	0.2	0.030
Malignant neoplasm of eye	0	0.0	1	0.0	0.023
Malignant neoplasm of brain	2	0.1	1	0.0	0.022
Malignant neoplasm of other and unspecified parts of nervous system	0	0.0	0	0.0	-
Malignant neoplasm of other endocrine glands and related structures	2	0.1	2	0.1	0.009
Malignant neoplasm of other and ill-defined sites	1	0.0	1	0.0	0.006
Secondary and unspecified malignant neoplasm of lymph nodes	0	0.0	4	0.1	0.047
Secondary malignant neoplasm of respiratory and digestive systems	0	0.0	4	0.1	0.047
Secondary malignant neoplasm of other specified sites	2	0.1	5	0.1	0.018
Malignant neoplasm without specification of site	1	0.0	3	0.1	0.018

Table 1.6.2b (Revised). Selected Characteristics of the Matched Exenatide Initiators and Other Antidiabetes Drug Initiators During the 9-Month Baseline Period, by Duration of Follow-Up, Thyroid Cancer, Impact National Benchmark Database 6/1/2005–7/31/2010

Characteristic	≥ 3 Years				
	Exenatide (N= 2,588)		OADs (N = 3,657)		Stand.
	N	%	N	%	Diff.
Lymphosarcoma and reticulosarcoma and other specified malignant tumors of lymphatic tissue	3	0.1	2	0.1	0.021
Hodgkin's disease	0	0.0	3	0.1	0.041
Other malignant neoplasms of lymphoid and histiocytic tissue	7	0.3	4	0.1	0.037
Multiple myeloma and immunoproliferative neoplasms	0	0.0	1	0.0	0.023
Lymphoid leukemia	1	0.0	3	0.1	0.018
Myeloid leukemia	1	0.0	2	0.1	0.007
Monocytic leukemia	2	0.1	0	0.0	0.039
Leukemia of unspecified cell type	3	0.1	1	0.0	0.033
Personal history of malignant neoplasm	47	1.8	84	2.3	0.034
	Mean	SD	Mean	SD	Stand. Diff.
Number Drugs (HICLs) Dispensed	12.6	5.5	11.9	5.1	0.139
Number of Physician Visits	7.2	5.2	7.1	5.1	0.017
Number of Laboratory Tests	11.3	12.6	11.9	14.2	0.049

Stand. Diff., Standardized Difference; SD, Standard Deviation

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins. Standardized difference is calculated by the difference between the 2 proportions divided by the pooled standard deviation.

Table 2.1a. The Top 100 Most Frequently Recorded Diagnoses among Exenatide Initiators and OADs Initiators in the 9-Month Baseline Period, Life Sciences Research Database 6/1/2005-7/31/2010

ICD-9-CM Code	Description	Exenatide N = 31,301			OADs N = 49,783		
		Rank	Count	Percent	Rank	Count	Percent
250	Diabetes mellitus	1	31,301	100	1	49,783	100
272	Disorders of lipoid metabolism	2	25,090	80.2	2	39,438	79.2
401	Essential hypertension	3	23,467	75.0	3	36,962	74.2
780	General symptoms	4	9,901	31.6	4	15,298	30.7
786	Symptoms involving respiratory system and other chest symptoms	5	8,461	27.0	5	13,496	27.1
V58	Encounter for other and unspecified procedure and aftercare	6	8,384	26.8	6	13,007	26.1
V76	Special screening for malignant neoplasms	7	8,328	26.6	7	12,987	26.1
V72	Special investigations and examinations	8	7,432	23.7	8	11,627	23.4
278	Overweight, obesity and other hyperalimentation	9	6,337	20.2	12	8,411	16.9
719	Other and unspecified disorders of joint	10	5,991	19.1	9	9,381	18.8
729	Other disorders of soft tissues	11	5,881	18.8	10	9,152	18.4
V04	Need for prophylactic vaccination and inoculation against certain viral diseases	12	5,415	17.3	11	8,649	17.4
724	Other and unspecified disorders of back	13	5,068	16.2	13	7,846	15.8
244	Acquired hypothyroidism	14	4,592	14.7	15	6,953	14.0
414	Other forms of chronic ischemic heart disease	15	4,346	13.9	14	6,955	14.0
V70	General medical examination	16	4,241	13.5	16	6,838	13.7
789	Other symptoms involving abdomen and pelvis	17	4,102	13.1	17	6,432	12.9
782	Symptoms involving skin and other integumentary tissue	18	3,944	12.6	18	6,069	12.2
790	Nonspecific findings on examination of blood	19	3,704	11.8	19	5,708	11.5
530	Diseases of esophagus	20	3,588	11.5	21	5,525	11.1
715	Osteoarthrosis and allied disorders	21	3,563	11.4	20	5,539	11.1
461	Acute sinusitis	22	3,481	11.1	22	5,276	10.6
599	Other disorders of urethra and urinary tract	23	3,258	10.4	23	5,004	10.1
466	Acute bronchitis and bronchiolitis	24	2,990	9.6	26	4,682	9.4
726	Peripheral enthesopathies and allied syndromes	25	2,980	9.5	28	4,588	9.2
362	Other retinal disorders	26	2,976	9.5	24	4,865	9.8
787	Symptoms involving digestive system	27	2,923	9.3	27	4,604	9.2
366	Cataract	28	2,860	9.1	25	4,738	9.5
465	Acute upper respiratory infections of multiple or unspecified sites	29	2,721	8.7	29	4,348	8.7
477	Allergic rhinitis	30	2,682	8.6	31	4,110	8.3
794	Nonspecific abnormal results of function studies	31	2,641	8.4	30	4,112	8.3
722	Intervertebral disc disorders	32	2,426	7.8	32	3,698	7.4

Table 2.1a. The Top 100 Most Frequently Recorded Diagnoses among Exenatide Initiators and OADs Initiators in the 9-Month Baseline Period, Life Sciences Research Database 6/1/2005-7/31/2010

ICD-9-CM Code	Description	Exenatide N = 31,301			OADs N = 49,783		
		Rank	Count	Percent	Rank	Count	Percent
785	Symptoms involving cardiovascular system	33	2,314	7.4	35	3,552	7.1
788	Symptoms involving urinary system	34	2,299	7.3	37	3,393	6.8
285	Other and unspecified anemias	35	2,287	7.3	34	3,656	7.3
784	Symptoms involving head and neck	36	2,248	7.2	33	3,684	7.4
493	Asthma	37	2,178	7.0	39	3,286	6.6
365	Glaucoma	38	2,159	6.9	36	3,534	7.1
723	Other disorders of cervical region	39	2,089	6.7	40	3,284	6.6
110	Dermatophytosis	40	2,069	6.6	38	3,363	6.8
728	Disorders of muscle, ligament, and fascia	41	2,043	6.5	41	3,149	6.3
311	Depressive disorder, not elsewhere classified	42	1,922	6.1	46	2,857	5.7
682	Other cellulitis and abscess	43	1,862	5.9	42	2,964	6.0
300	Anxiety, dissociative and somatoform disorders	44	1,841	5.9	47	2,831	5.7
V45	Other postprocedural status	45	1,794	5.7	43	2,938	5.9
327	Organic sleep disorders	46	1,768	5.6	51	2,493	5.0
427	Cardiac dysrhythmias	47	1,761	5.6	45	2,877	5.8
367	Disorders of refraction and accommodation	48	1,711	5.5	48	2,756	5.5
702	Other dermatoses	49	1,698	5.4	49	2,642	5.3
733	Other disorders of bone and cartilage	50	1,596	5.1	50	2,585	5.2
783	Symptoms concerning nutrition, metabolism, and development	51	1,579	5.0	59	2,191	4.4
793	Nonspecific (abnormal) findings on radiological and other examination of body structure	52	1,570	5.0	52	2,475	5.0
627	Menopausal and postmenopausal disorders	53	1,550	5.0	58	2,234	4.5
462	Acute pharyngitis	54	1,514	4.8	55	2,354	4.7
402	Hypertensive heart disease	55	1,465	4.7	53	2,383	4.8
692	Contact dermatitis and other eczema	56	1,462	4.7	57	2,278	4.6
727	Other disorders of synovium, tendon, and bursa	57	1,452	4.6	56	2,285	4.6
276	Disorders of fluid, electrolyte, and acid-base balance	58	1,443	4.6	54	2,366	4.8
277	Other and unspecified disorders of metabolism	59	1,421	4.5	70	1,866	3.7
424	Other diseases of endocardium	60	1,359	4.3	60	2,139	4.3
296	Episodic mood disorders	61	1,347	4.3	63	2,006	4.0
739	Nonallopathic lesions, not elsewhere classified	62	1,307	4.2	67	1,915	3.8
211	Benign neoplasm of other parts of digestive system	63	1,306	4.2	62	2,015	4.0
791	Nonspecific findings on examination of urine	64	1,233	3.9	66	1,934	3.9

Table 2.1a. The Top 100 Most Frequently Recorded Diagnoses among Exenatide Initiators and OADs Initiators in the 9-Month Baseline Period, Life Sciences Research Database 6/1/2005-7/31/2010

ICD-9-CM Code	Description	Exenatide N = 31,301			OADs N = 49,783		
		Rank	Count	Percent	Rank	Count	Percent
V03	Need for prophylactic vaccination and inoculation against bacterial diseases	65	1,227	3.9	65	1,969	4.0
428	Heart failure	66	1,223	3.9	61	2,042	4.1
721	Spondylosis and allied disorders	67	1,210	3.9	69	1,869	3.8
216	Benign neoplasm of skin	68	1,208	3.9	72	1,818	3.7
473	Chronic sinusitis	69	1,199	3.8	75	1,778	3.6
562	Diverticula of intestine	70	1,199	3.8	68	1,913	3.8
600	Hyperplasia of prostate	71	1,189	3.8	64	1,979	4.0
238	Neoplasm of uncertain behavior of other and unspecified sites and tissues	72	1,172	3.7	82	1,714	3.4
611	Other disorders of breast	74	1,152	3.7	80	1,744	3.5
357	Inflammatory and toxic neuropathy	75	1,147	3.7	73	1,805	3.6
607	Disorders of penis	76	1,134	3.6	71	1,819	3.7
703	Diseases of nail	77	1,117	3.6	81	1,717	3.4
372	Disorders of conjunctiva	78	1,110	3.5	79	1,746	3.5
429	Ill-defined descriptions and complications of heart disease	79	1,107	3.5	74	1,790	3.6
V65	Other persons seeking consultation	80	1,107	3.5	85	1,641	3.3
796	Other nonspecific abnormal findings	81	1,091	3.5	76	1,768	3.6
455	Hemorrhoids	82	1,078	3.4	87	1,631	3.3
626	Disorders of menstruation and other abnormal bleeding from female genital tract	83	1,070	3.4	86	1,633	3.3
593	Other disorders of kidney and ureter	84	1,068	3.4	78	1,749	3.5
518	Other diseases of lung	85	1,051	3.4	77	1,755	3.5
564	Functional digestive disorders, not elsewhere classified	86	1,030	3.3	93	1,537	3.1
305	Nondependent abuse of drugs	87	1,026	3.3	83	1,710	3.4
585	Chronic kidney disease (CKD)	88	987	3.2	84	1,674	3.4
280	Iron deficiency anemias	89	978	3.1	95	1,480	3.0
535	Gastritis and duodenitis	90	976	3.1	89	1,593	3.2
496	Chronic airway obstruction, not elsewhere classified	91	975	3.1	88	1,627	3.3
571	Chronic liver disease and cirrhosis	92	970	3.1	96	1,480	3.0
847	Sprains and strains of other and unspecified parts of back	93	969	3.1	91	1,549	3.1
379	Other disorders of eye	94	949	3.0	94	1,509	3.0
706	Diseases of sebaceous glands	95	935	3.0	101	1,415	2.8
356	Hereditary and idiopathic peripheral neuropathy	96	914	2.9	98	1,462	2.9
709	Other disorders of skin and subcutaneous tissue	97	906	2.9	102	1,404	2.8

Table 2.1a. The Top 100 Most Frequently Recorded Diagnoses among Exenatide Initiators and OADs Initiators in the 9-Month Baseline Period, Life Sciences Research Database 6/1/2005-7/31/2010

ICD-9-CM Code	Description	Exenatide N = 31,301			OADs N = 49,783		
		Rank	Count	Percent	Rank	Count	Percent
959	Injury, other and unspecified	98	904	2.9	103	1,391	2.8
716	Other and unspecified arthropathies	99	893	2.9	100	1,444	2.9
V67	Follow-up examination	100	890	2.8	104	1,371	2.8

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, dipeptidyl peptidase-4 inhibitor, glucagon-like peptide-1 agonists, pramlintide, alpha-glucosidase inhibitors, and insulins. Only a proportion of diagnoses in the top 100 list were retained in the propensity score model via stepwise selection.

Table 2.1b. The Top 100 Most Frequently Recorded Diagnoses among Exenatide Initiators and OADs Initiators in the 9-Month Baseline Period, Impact National Benchmark Database 6/1/2005-7/31/2010

ICD-9-CM Code	Description	Exenatide N = 16,206			OADs N = 25,385		
		Rank	Count	Percent	Rank	Count	Percent
250	Diabetes mellitus	1	16,206	100	1	25,385	100
272	Disorders of lipoid metabolism	2	11,451	70.7	2	17,701	69.7
401	Essential hypertension	3	10,731	66.2	3	16,564	65.3
786	Symptoms involving respiratory system and other chest symptoms	5	4,516	27.9	5	6,963	27.4
V76	Special screening for malignant neoplasms	6	4,134	25.5	6	6,334	25.0
780	General symptoms	7	4,120	25.4	7	6,268	24.7
V72	Special investigations and examinations	8	4,045	25.0	8	6,141	24.2
V04	Need for prophylactic vaccination and inoculation against certain viral diseases	9	3,198	19.7	9	4,931	19.4
V70	General medical examination	10	3,080	19.0	10	4,853	19.1
719	Other and unspecified disorders of joint	11	2,853	17.6	11	4,453	17.5
278	Overweight, obesity and other hyperalimentation	12	2,793	17.2	15	3,760	14.8
729	Other disorders of soft tissues	13	2,662	16.4	12	4,105	16.2
V58	Encounter for other and unspecified procedure and aftercare	14	2,528	15.6	13	3,905	15.4
414	Other forms of chronic ischemic heart disease	15	2,418	14.9	14	3,884	15.3
724	Other and unspecified disorders of back	16	2,279	14.1	16	3,565	14.0
362	Other retinal disorders	17	1,980	12.2	17	3,161	12.5
789	Other symptoms involving abdomen and pelvis	18	1,871	11.5	18	2,934	11.6
244	Acquired hypothyroidism	19	1,834	11.3	19	2,809	11.1
782	Symptoms involving skin and other integumentary tissue	20	1,706	10.5	21	2,578	10.2
715	Osteoarthrosis and allied disorders	21	1,688	10.4	20	2,596	10.2
726	Peripheral enthesopathies and allied syndromes	22	1,604	9.9	22	2,434	9.6
366	Cataract	23	1,544	9.5	23	2,418	9.5
599	Other disorders of urethra and urinary tract	24	1,479	9.1	24	2,322	9.1
530	Diseases of esophagus	25	1,421	8.8	25	2,218	8.7
790	Nonspecific findings on examination of blood	26	1,412	8.7	26	2,138	8.4
365	Glaucoma	27	1,376	8.5	27	2,114	8.3
461	Acute sinusitis	28	1,365	8.4	28	2,022	8.0
466	Acute bronchitis and bronchiolitis	29	1,326	8.2	29	2,014	7.9
787	Symptoms involving digestive system	30	1,244	7.7	30	1,907	7.5
465	Acute upper respiratory infections of multiple or unspecified sites	31	1,204	7.4	31	1,851	7.3
785	Symptoms involving cardiovascular system	32	1,142	7.0	32	1,820	7.2
493	Asthma	33	1,108	6.8	33	1,727	6.8

Table 2.1b. The Top 100 Most Frequently Recorded Diagnoses among Exenatide Initiators and OADs Initiators in the 9-Month Baseline Period, Impact National Benchmark Database 6/1/2005-7/31/2010

ICD-9-CM Code	Description	Exenatide N = 16,206			OADs N = 25,385		
		Rank	Count	Percent	Rank	Count	Percent
788	Symptoms involving urinary system	34	1,077	6.6	34	1,699	6.7
794	Nonspecific abnormal results of function studies	35	1,072	6.6	38	1,616	6.4
722	Intervertebral disc disorders	36	1,056	6.5	35	1,698	6.7
285	Other and unspecified anemias	37	1,036	6.4	37	1,673	6.6
110	Dermatophytosis	38	1,028	6.3	40	1,560	6.1
784	Symptoms involving head and neck	39	1,006	6.2	36	1,674	6.6
723	Other disorders of cervical region	40	982	6.1	41	1,511	6.0
427	Cardiac dysrhythmias	41	981	6.1	39	1,573	6.2
477	Allergic rhinitis	42	950	5.9	42	1,457	5.7
682	Other cellulitis and abscess	43	898	5.5	43	1,430	5.6
728	Disorders of muscle, ligament, and fascia	44	887	5.5	46	1,336	5.3
300	Anxiety, dissociative and somatoform disorders	45	884	5.5	44	1,361	5.4
367	Disorders of refraction and accommodation	46	855	5.3	45	1,356	5.3
733	Other disorders of bone and cartilage	47	792	4.9	51	1,181	4.7
311	Depressive disorder, not elsewhere classified	48	788	4.9	47	1,276	5.0
793	Nonspecific (abnormal) findings on radiological and other examination of body structure	49	788	4.9	49	1,214	4.8
702	Other dermatoses	50	779	4.8	53	1,165	4.6
692	Contact dermatitis and other eczema	51	774	4.8	55	1,136	4.5
727	Other disorders of synovium, tendon, and bursa	52	770	4.8	52	1,173	4.6
211	Benign neoplasm of other parts of digestive system	53	768	4.7	50	1,202	4.7
V45	Other postprocedural status	54	762	4.7	48	1,237	4.9
296	Episodic mood disorders	55	740	4.6	54	1,147	4.5
V65	Other persons seeking consultation	56	719	4.4	58	1,058	4.2
627	Menopausal and postmenopausal disorders	57	715	4.4	60	1,045	4.1
462	Acute pharyngitis	58	692	4.3	63	1,019	4.0
424	Other diseases of endocardium	59	691	4.3	56	1,069	4.2
216	Benign neoplasm of skin	60	690	4.3	61	1,036	4.1
327	Organic sleep disorders	61	690	4.3	65	982	3.9
703	Diseases of nail	62	690	4.3	64	1,017	4.0
562	Diverticula of intestine	63	679	4.2	62	1,034	4.1
402	Hypertensive heart disease	64	664	4.1	57	1,059	4.2
428	Heart failure	65	656	4.0	59	1,048	4.1
600	Hyperplasia of prostate	66	616	3.8	66	934	3.7
611	Other disorders of breast	67	609	3.8	72	907	3.6

Table 2.1b. The Top 100 Most Frequently Recorded Diagnoses among Exenatide Initiators and OADs Initiators in the 9-Month Baseline Period, Impact National Benchmark Database 6/1/2005-7/31/2010

ICD-9-CM Code	Description	Exenatide N = 16,206			OADs N = 25,385		
		Rank	Count	Percent	Rank	Count	Percent
429	Ill-defined descriptions and complications of heart disease	68	607	3.7	70	916	3.6
739	Nonallopathic lesions, not elsewhere classified	69	604	3.7	67	933	3.7
473	Chronic sinusitis	70	584	3.6	74	868	3.4
518	Other diseases of lung	71	575	3.5	73	870	3.4
276	Disorders of fluid, electrolyte, and acid-base balance	72	573	3.5	71	907	3.6
V03	Need for prophylactic vaccination and inoculation against bacterial diseases	73	573	3.5	69	919	3.6
721	Spondylosis and allied disorders	74	561	3.5	79	809	3.2
783	Symptoms concerning nutrition, metabolism, and development	75	552	3.4	85	777	3.1
277	Other and unspecified disorders of metabolism	76	550	3.4	106	673	2.7
496	Chronic airway obstruction, not elsewhere classified	77	541	3.3	77	832	3.3
379	Other disorders of eye	78	538	3.3	78	830	3.3
593	Other disorders of kidney and ureter	79	538	3.3	68	932	3.7
959	Injury, other and unspecified	80	530	3.3	90	758	3.0
372	Disorders of conjunctiva	81	527	3.3	75	837	3.3
357	Inflammatory and toxic neuropathy	82	524	3.2	89	760	3.0
791	Nonspecific findings on examination of urine	83	521	3.2	76	836	3.3
238	Neoplasm of uncertain behavior of other and unspecified sites and tissues	84	510	3.1	82	792	3.1
585	Chronic kidney disease (CKD)	85	507	3.1	81	794	3.1
847	Sprains and strains of other and unspecified parts of back	86	504	3.1	84	780	3.1
455	Hemorrhoids	87	503	3.1	83	788	3.1
799	Other ill-defined and unknown causes of morbidity and mortality	88	490	3.0	88	768	3.0
535	Gastritis and duodenitis	89	487	3.0	80	808	3.2
681	Cellulitis and abscess of finger and toe	90	482	3.0	101	689	2.7
709	Other disorders of skin and subcutaneous tissue	91	478	2.9	105	676	2.7
571	Chronic liver disease and cirrhosis	92	475	2.9	103	687	2.7
443	Other peripheral vascular disease	93	474	2.9	86	773	3.0
626	Disorders of menstruation and other abnormal bleeding from female genital tract	94	474	2.9	97	702	2.8
490	Bronchitis, not specified as acute or chronic	95	473	2.9	96	708	2.8
716	Other and unspecified arthropathies	96	473	2.9	94	734	2.9
380	Disorders of external ear	97	471	2.9	92	746	2.9
413	Angina pectoris	98	461	2.8	87	772	3.0

Table 2.1b. The Top 100 Most Frequently Recorded Diagnoses among Exenatide Initiators and OADs Initiators in the 9-Month Baseline Period, Impact National Benchmark Database 6/1/2005-7/31/2010

ICD-9-CM Code	Description	Exenatide N = 16,206			OADs N = 25,385		
		Rank	Count	Percent	Rank	Count	Percent
569	Other disorders of intestine	99	456	2.8	99	695	2.7
706	Diseases of sebaceous glands	100	441	2.7	95	724	2.9

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, dipeptidyl peptidase-4 inhibitor, glucagon-like peptide-1 agonists, pramlintide, alpha-glucosidase inhibitors, and insulins. Only a proportion of diagnoses in the top 100 list were retained in the propensity score model via stepwise selection.

Table 2.2a. The Top 100 Most Frequently Recorded Procedures among Exenatide Initiators and OAD Initiators in the 9-Month Baseline Period, Life Sciences Research Database 6/1/2005-7/31/2010

CPT or HCPC Code	Description	Exenatide N = 31,301			OADs N = 49,783		
		Rank	Count	Percent	Rank	Count	Percent
99214	Office or other outpatient visit for the evaluation and management of an established patient, which requires at least 2 of these 3 key components: A detailed history; A detailed examination; Medical decision making of moderate complexity. Counseling and/or coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of moderate to high severity. Physicians typically spend 25 minutes face-to-face with the patient and/or family.	1	25,950	82.9	1	40,797	81.9
83036	Hemoglobin; glycosylated (A1C)	2	25,220	80.6	2	39,576	79.5
99213	Office or other outpatient visit for the evaluation and management of an established patient, which requires at least 2 of these 3 key components: An expanded problem focused history; An expanded problem focused examination; Medical decision making of low complexity. Counseling and coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of low to moderate severity. Physicians typically spend 15 minutes face-to-face with the patient and/or family	3	24,383	77.9	3	38,376	77.1
80061	Lipid panel This panel must include the following: Cholesterol, serum, total (82465) Lipoprotein, direct measurement, high density cholesterol (HDL cholesterol) (83718) Triglycerides (84478)	4	22,389	71.5	4	35,182	70.7
36415	Collection of venous blood by venipuncture	5	19,168	61.2	5	30,072	60.4
80053	Comprehensive metabolic panel This panel must include the following: Albumin (82040) Bilirubin, total (82247) Calcium, total (82310) Carbon dioxide (bicarbonate) (82374) Chloride (82435) Creatinine (82565) Glucose (82947) Phosphatase, alkaline (84075) Potassium (84132) Protein, total (84155) Sodium (84295) Transferase, alanine amino (ALT) (SGPT) (84460) Transferase, aspartate amino (AST) (SGOT) (84450) Urea nitrogen (BUN) (84520)	6	17,931	57.3	6	27,951	56.1
82043	Albumin; urine, microalbumin, quantitative	7	10,947	35.0	7	16,985	34.1
85025	Blood count; complete (CBC), automated (Hgb, Hct, RBC, WBC and platelet count) and automated differential WBC count	8	10,456	33.4	8	16,606	33.4
82570	Creatinine; other source	9	8,922	28.5	9	13,548	27.2
84443	Thyroid stimulating hormone (TSH)	10	8,608	27.5	10	12,875	25.9
80050	Obstetric panel This panel must include the following: Blood count, complete (CBC), automated and automated differential WBC count (85025 or 85027 and 85004) OR Blood count, complete (CBC), automated (85027) and appropriate manual differential WBC count (85007 or 85009) Hepatitis B surface antigen (HBsAg) (87340) Antibody, rubella (86762) Syphilis test, non-treponemal antibody; qualitative (eg, VDRL, RPR, ART) (86592) Antibody screen, RBC, each serum technique (86850) Blood typing, ABO (86900) AND Blood typing, Rh (D) (86901)	11	7,925	25.3	11	12,511	25.1

Table 2.2a. The Top 100 Most Frequently Recorded Procedures among Exenatide Initiators and OAD Initiators in the 9-Month Baseline Period, Life Sciences Research Database 6/1/2005-7/31/2010

CPT or HCPC Code	Description	Exenatide N = 31,301			OADs N = 49,783		
		Rank	Count	Percent	Rank	Count	Percent
93000	Electrocardiogram, routine ECG with at least 12 leads; with interpretation and report	12	7,281	23.3	12	11,540	23.2
99212	Office or other outpatient visit for the evaluation and management of an established patient, which requires at least 2 of these 3 key components: A problem focused history; A problem focused examination; Straightforward medical decision making. Counseling and/or coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are self limited or minor. Physicians typically spend 10 minutes face-to-face with the patient and/or family.	13	7,099	22.7	14	10,973	22.0
76499	Unlisted diagnostic radiographic procedure	14	7,069	22.6	13	11,156	22.4
89240	Unlisted miscellaneous pathology test	15	6,893	22.0	15	10,874	21.8
99215	Office or other outpatient visit for the evaluation and management of an established patient, which requires at least 2 of these 3 key components: A comprehensive history; A comprehensive examination; Medical decision making of high complexity. Counseling	16	6,485	20.7	16	9,919	19.9
99244	Office consultation for a new or established patient, which requires these 3 key components: A comprehensive history; A comprehensive examination; and Medical decision making of moderate complexity. Counseling and/or coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of moderate to high severity. Physicians typically spend 60 minutes face-to-face with the patient and/or family.	17	6,108	19.5	18	9,242	18.6
80048	Basic metabolic panel (Calcium, total) This panel must include the following: Calcium (82310) Carbon dioxide (82374) Chloride (82435) Creatinine (82565) Glucose (82947) Potassium (84132) Sodium (84295) Urea nitrogen (BUN) (84520)	18	5,971	19.1	17	9,658	19.4
71020	Radiologic examination, chest, two views, frontal and lateral;	19	5,373	17.2	19	8,741	17.6
90658	Influenza virus vaccine, split virus, when administered to individuals 3 years of age and older, for intramuscular use	20	5,343	17.1	20	8,481	17.0
99203	Office or other outpatient visit for the evaluation and management of a new patient, which requires these 3 key components: A detailed history; A detailed examination; Medical decision making of low complexity. Counseling and/or coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of moderate severity. Physicians typically spend 30 minutes face-to-face with the patient and/or family.	21	5,258	16.8	22	8,136	16.3
90471	Immunization administration (includes percutaneous, intradermal, subcutaneous, or intramuscular injections); one vaccine (single or combination vaccine/toxoid)	22	5,148	16.4	21	8,137	16.3

Table 2.2a. The Top 100 Most Frequently Recorded Procedures among Exenatide Initiators and OAD Initiators in the 9-Month Baseline Period, Life Sciences Research Database 6/1/2005-7/31/2010

CPT or HCPC Code	Description	Exenatide N = 31,301			OADs N = 49,783		
		Rank	Count	Percent	Rank	Count	Percent
92014	Ophthalmological services: medical examination and evaluation, with initiation or continuation of diagnostic and treatment program; comprehensive, established patient, one or more visits	23	4,754	15.2	24	7,457	15.0
84153	Prostate specific antigen (PSA); total	24	4,677	14.9	23	7,681	15.4
99396	Periodic comprehensive preventive medicine reevaluation and management of an individual including an age and gender appropriate history, examination, counseling/anticipatory guidance/risk factor reduction interventions, and the ordering of laboratory/diagnostic procedures, established patient; 40-64 years.	25	4,626	14.8	25	7,129	14.3
82962	Glucose, blood by glucose monitoring device(s) cleared by the FDA specifically for home use	26	4,564	14.6	27	6,898	13.9
81001	Urinalysis, by dip stick or tablet reagent for bilirubin, glucose, hemoglobin, ketones, leukocytes, nitrite, pH, protein, specific gravity, urobilinogen, any number of these constituents; automated, with microscopy	27	4,282	13.7	26	7,043	14.1
82947	Glucose; quantitative, blood (except reagent strip)	28	4,153	13.3	28	6,394	12.8
99204	Office or other outpatient visit for the evaluation and management of a new patient, which requires these 3 key components: A comprehensive history; A comprehensive examination; Medical decision making of moderate complexity. Counseling and/or coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of moderate to high severity. Physicians typically spend 45 minutes face-to-face with the patient and/or family.	29	4,040	12.9	31	6,169	12.4
81003	Urinalysis, by dip stick or tablet reagent for bilirubin, glucose, hemoglobin, ketones, leukocytes, nitrite, pH, protein, specific gravity, urobilinogen, any number of these constituents; automated, without microscopy	30	4,017	12.8	30	6,351	12.8
81002	Urinalysis, by dip stick or tablet reagent for bilirubin, glucose, hemoglobin, ketones, leukocytes, nitrite, pH, protein, specific gravity, urobilinogen, any number of these constituents; non-automated, without microscopy	31	4,007	12.8	29	6,368	12.8

Table 2.2a. The Top 100 Most Frequently Recorded Procedures among Exenatide Initiators and OAD Initiators in the 9-Month Baseline Period, Life Sciences Research Database 6/1/2005-7/31/2010

CPT or HCPC Code	Description	Exenatide N = 31,301			OADs N = 49,783		
		Rank	Count	Percent	Rank	Count	Percent
88305	Level IV - Surgical pathology, gross and microscopic examination Abortion - spontaneous/missed Artery, biopsy Bone marrow, biopsy Bone exostosis Brain/meninges, other than for tumor resection Breast, biopsy, not requiring microscopic evaluation of surgical margins Breast, reduction mammoplasty Bronchus, biopsy Cell block, any source Cervix, biopsy Colon, biopsy Duodenum, biopsy Endocervix, curettings/biopsy Endometrium, curettings/biopsy Esophagus, biopsy Extremity, amputation, traumatic Fallopian tube, biopsy Fallopian tube, ectopic pregnancy Femoral head, fracture Fingers/toes, amputation, non-traumatic Gingiva/oral mucosa, biopsy Heart valve Joint, resection Kidney, biopsy Larynx, biopsy Leiomyoma(s), uterine myomectomy - without uterus Lip, biopsy/wedge resection Lung, transbronchial biopsy Lymph node, biopsy Muscle, biopsy Nasal mucosa, biopsy Nasopharynx/oropharynx, biopsy Nerve, biopsy Odontogenic/dental cyst Omentum, biopsy Ovary with or without tube, non-neoplastic Ovary, biopsy/wedge resection Parathyroid gland Peritoneum, biopsy	32	3,990	12.7	32	6,147	12.3
84439	Thyroxine; free	33	3,939	12.6	34	5,768	11.6
99243	Office consultation for a new or established patient, which requires these 3 key components: A detailed history; A detailed examination; and Medical decision making of low complexity. Counseling and/or coordination of care with other providers or agencies	34	3,815	12.2	33	5,932	11.9
93010	Electrocardiogram, routine ECG with at least 12 leads; interpretation and report only	35	3,469	11.1	35	5,675	11.4
99245	Office consultation for a new or established patient, which requires these 3 key components: A comprehensive history; A comprehensive examination; and Medical decision making of high complexity. Counseling and/or coordination of care with other providers	36	3,313	10.6	38	4,746	9.5
92015	Determination of refractive state	37	3,214	10.3	36	5,022	10.1
99000	Handling and/or conveyance of specimen for transfer from the physician's office to a laboratory	38	3,193	10.2	37	4,971	10.0
80076	Hepatic function panel This panel must include the following: Albumin (82040) Bilirubin, total (82247) Bilirubin, direct (82248) Phosphatase, alkaline (84075) Protein, total (84155) Transferase, alanine amino (ALT) (SGPT) (84460) Transferase, aspartate amino (AST) (SGOT) (84450)	39	2,916	9.3	41	4,470	9.0
93325	Doppler echocardiography color flow velocity mapping (List separately in addition to codes for echocardiography)	40	2,859	9.1	39	4,629	9.3
93320	Doppler echocardiography, pulsed wave and/or continuous wave with spectral display (List separately in addition to codes for echocardiographic imaging); complete	41	2,844	9.1	40	4,585	9.2
82550	Creatine kinase (CK), (CPK); total	42	2,843	9.1	42	4,403	8.8
93307	Echocardiography, transthoracic, real-time with image documentation (2D) with or without M-mode recording; complete	43	2,717	8.7	43	4,362	8.8

Table 2.2a. The Top 100 Most Frequently Recorded Procedures among Exenatide Initiators and OAD Initiators in the 9-Month Baseline Period, Life Sciences Research Database 6/1/2005-7/31/2010

CPT or HCPC Code	Description	Exenatide N = 31,301			OADs N = 49,783		
		Rank	Count	Percent	Rank	Count	Percent
78465	Myocardial perfusion imaging; tomographic (SPECT), multiple studies (including attenuation correction when performed), at rest and/or stress (exercise and/or pharmacologic) and redistribution and/or rest injection, with or without quantification	44	2,711	8.7	44	4,265	8.6
78478	Myocardial perfusion study with wall motion, qualitative or quantitative study (List separately in addition to code for primary procedure)	45	2,707	8.6	46	4,215	8.5
78480	Myocardial perfusion study with ejection fraction (List separately in addition to code for primary procedure)	46	2,688	8.6	47	4,190	8.4
99211	Office or other outpatient visit for the evaluation and management of an established patient, that may not require the presence of a physician. Usually, the presenting problem(s) are minimal. Typically, 5 minutes are spent performing or supervising these services.	47	2,685	8.6	49	4,024	8.1
81000	Urinalysis, by dip stick or tablet reagent for bilirubin, glucose, hemoglobin, ketones, leukocytes, nitrite, pH, protein, specific gravity, urobilinogen, any number of these constituents; non-automated, with microscopy	48	2,672	8.5	45	4,219	8.5
93015	Cardiovascular stress test using maximal or submaximal treadmill or bicycle exercise, continuous electrocardiographic monitoring, and/or pharmacological stress; with physician supervision, with interpretation and report	49	2,592	8.3	48	4,063	8.2
84436	Thyroxine; total	50	2,568	8.2	50	4,020	8.1
82948	Glucose; blood, reagent strip	51	2,500	8.0	53	3,744	7.5
84460	Transferase; alanine amino (ALT) (SGPT)	52	2,491	8.0	52	3,905	7.8
99285	Emergency department visit for the evaluation and management of a patient, which requires these 3 key components within the constraints imposed by the urgency of the patient's clinical condition and/or mental status: A comprehensive history; A comprehensive examination; and Medical decision making of high complexity. Counseling and/or coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of high severity and pose an immediate significant threat to life or physiologic function.	53	2,336	7.5	51	3,995	8.0
82248	Bilirubin; direct	54	2,316	7.4	54	3,558	7.1
84550	Uric acid; blood	55	2,240	7.2	56	3,437	6.9
82044	Albumin; urine, microalbumin, semiquantitative (eg, reagent strip assay)	56	2,220	7.1	59	3,342	6.7
87086	Culture, bacterial; quantitative colony count, urine	57	2,179	7.0	57	3,394	6.8
88142	Cytopathology, cervical or vaginal (any reporting system), collected in preservative fluid, automated thin layer preparation; manual screening under physician supervision	58	2,096	6.7	62	3,145	6.3
71010	Radiologic examination, chest; single view, frontal	59	2,068	6.6	55	3,471	7.0

Table 2.2a. The Top 100 Most Frequently Recorded Procedures among Exenatide Initiators and OAD Initiators in the 9-Month Baseline Period, Life Sciences Research Database 6/1/2005-7/31/2010

CPT or HCPC Code	Description	Exenatide N = 31,301			OADs N = 49,783		
		Rank	Count	Percent	Rank	Count	Percent
99202	Office or other outpatient visit for the evaluation and management of a new patient, which requires these 3 key components: An expanded problem focused history; An expanded problem focused examination; Straightforward medical decision making. Counseling and/or coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of low to moderate severity. Physicians typically spend 20 minutes face-to-face with the patient and/or family.	60	2,067	6.6	61	3,204	6.4
99284	Emergency department visit for the evaluation and management of a patient, which requires these 3 key components: A detailed history; A detailed examination; and Medical decision making of moderate complexity. Counseling and/or coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of high severity, and require urgent evaluation by the physician but do not pose an immediate significant threat to life or physiologic function.	61	2,052	6.6	58	3,385	6.8
85610	Prothrombin time;	62	2,046	6.5	60	3,211	6.4
97110	Therapeutic procedure, one or more areas, each 15 minutes; therapeutic exercises to develop strength and endurance, range of motion and flexibility	63	1,972	6.3	63	3,090	6.2
83721	Lipoprotein, direct measurement; LDL cholesterol	64	1,946	6.2	65	2,899	5.8
77052	Computer-aided detection (computer algorithm analysis of digital image data for lesion detection) with further physician review for interpretation, with or without digitization of film radiographic images; screening mammography (List separately in addition to code for primary procedure)	65	1,895	6.1	64	2,934	5.9
88175	Cytopathology, cervical or vaginal (any reporting system), collected in preservative fluid, automated thin layer preparation; with screening by automated system and manual rescreening or review, under physician supervision	66	1,887	6.0	71	2,836	5.7
91000	Esophageal intubation and collection of washings for cytology, including preparation of specimens (separate procedure)	67	1,824	5.8	66	2,898	5.8
83540	Iron	68	1,817	5.8	69	2,857	5.7
85027	Blood count; complete (CBC), automated (Hgb, Hct, RBC, WBC and platelet count)	69	1,813	5.8	68	2,860	5.7
A7035	Headgear used with positive airway pressure device	70	1,803	5.8	81	2,428	4.9
99205	Office or other outpatient visit for the evaluation and management of a new patient, which requires these 3 key components: A comprehensive history; A comprehensive examination; Medical decision making of high complexity. Counseling and/or coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of moderate to high severity. Physicians typically spend 60 minutes face-to-face with the patient and/or family.	71	1,783	5.7	76	2,581	5.2

Table 2.2a. The Top 100 Most Frequently Recorded Procedures among Exenatide Initiators and OAD Initiators in the 9-Month Baseline Period, Life Sciences Research Database 6/1/2005-7/31/2010

CPT or HCPC Code	Description	Exenatide N = 31,301			OADs N = 49,783		
		Rank	Count	Percent	Rank	Count	Percent
99283	Emergency department visit for the evaluation and management of a patient, which requires these 3 key components: An expanded problem focused history; An expanded problem focused examination; and Medical decision making of moderate complexity. Counseling and/or coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of moderate severity.	72	1,753	5.6	70	2,841	5.7
99232	Subsequent hospital care, per day, for the evaluation and management of a patient, which requires at least 2 of these 3 key components: An expanded problem focused interval history; An expanded problem focused examination; Medical decision making of moderate complexity. Counseling and/or coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the patient is responding inadequately to therapy or has developed a minor complication. Physicians typically spend 25 minutes at the bedside and on the patient's hospital floor or unit.	73	1,740	5.6	67	2,868	5.8
76092	Screening mammography, bilateral (two view film study of each breast)	74	1,727	5.5	75	2,608	5.2
82270	Blood, occult, by peroxidase activity (eg, guaiac), qualitative; feces, consecutive collected specimens with single determination, for colorectal neoplasm screening (ie, patient was provided 3 cards or single triple card for consecutive collection)	75	1,724	5.5	72	2,792	5.6
84403	Testosterone; total	76	1,724	5.5	79	2,447	4.9
92250	Fundus photography with interpretation and report	77	1,700	5.4	73	2,706	5.4
82607	Cyanocobalamin (Vitamin B-12);	78	1,683	5.4	78	2,532	5.1
84450	Transferase; aspartate amino (AST) (SGOT)	79	1,675	5.4	77	2,574	5.2
92012	Ophthalmological services: medical examination and evaluation, with initiation or continuation of diagnostic and treatment program; intermediate, established patient	80	1,668	5.3	74	2,657	5.3
90772	Therapeutic, prophylactic or diagnostic injection (specify substance or drug); subcutaneous or intramuscular	81	1,648	5.3	82	2,413	4.8
20610	Arthrocentesis, aspiration and/or injection; major joint or bursa (eg, shoulder, hip, knee joint, subacromial bursa)	82	1,641	5.2	80	2,444	4.9
36416	Collection of capillary blood specimen (eg, finger, heel, ear stick)	83	1,634	5.2	86	2,334	4.7
A7034	Nasal interface (mask or cannula type) used with positive airway pressure device, with or without head strap	84	1,594	5.1	100	2,072	4.2
97100	Gait Analysis	85	1,559	5.0	89	2,311	4.6
97140	Manual therapy techniques (eg, mobilization/ manipulation, manual lymphatic drainage, manual traction), one or more regions, each 15 minutes	86	1,534	4.9	84	2,389	4.8
84479	Thyroid hormone (T3 or T4) uptake or thyroid hormone binding ratio (THBR)	87	1,514	4.8	83	2,399	4.8

Table 2.2a. The Top 100 Most Frequently Recorded Procedures among Exenatide Initiators and OAD Initiators in the 9-Month Baseline Period, Life Sciences Research Database 6/1/2005-7/31/2010

CPT or HCPC Code	Description	Exenatide N = 31,301			OADs N = 49,783		
		Rank	Count	Percent	Rank	Count	Percent
82565	Creatinine; blood	88	1,492	4.8	85	2,347	4.7
99199	Unlisted special service, procedure or report	89	1,472	4.7	90	2,288	4.6
73630	Radiologic examination, foot; complete, minimum of three views	90	1,461	4.7	94	2,185	4.4
82306	Calcifediol (25-OH Vitamin D-3)	91	1,458	4.7	99	2,133	4.3
92135	Scanning computerized ophthalmic diagnostic imaging, posterior segment, (eg, scanning laser) with interpretation and report, unilateral	92	1,458	4.7	87	2,330	4.7
92004	Ophthalmological services: medical examination and evaluation with initiation of diagnostic and treatment program; comprehensive, new patient, one or more visits	93	1,449	4.6	91	2,286	4.6
97001	Physical therapy evaluation	94	1,446	4.6	93	2,192	4.4
A7037	Tubing used with positive airway pressure device	95	1,446	4.6	105	1,983	4.0
77057	Screening mammography, bilateral (2-view film study of each breast)	96	1,410	4.5	98	2,139	4.3
99223	Subsequent hospital care, per day, for the evaluation and management of a patient, which requires at least 2 of these 3 key components: A detailed interval history; A detailed examination; Medical decision making of high complexity. Counseling and/or coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the patient is unstable or has developed a significant complication or a significant new problem. Physicians typically spend 35 minutes at the bedside and on the patient's hospital floor or unit.	97	1,392	4.4	88	2,316	4.7
90732	Pneumococcal polysaccharide vaccine, 23-valent, adult or immunosuppressed patient dosage, when administered to individuals 2 years or older, for subcutaneous or intramuscular use	98	1,383	4.4	95	2,161	4.3

Table 2.2a. The Top 100 Most Frequently Recorded Procedures among Exenatide Initiators and OAD Initiators in the 9-Month Baseline Period, Life Sciences Research Database 6/1/2005-7/31/2010

CPT or HCPC Code	Description	Exenatide N = 31,301			OADs N = 49,783		
		Rank	Count	Percent	Rank	Count	Percent
82728	Ferritin	99	1,376	4.4	103	2,038	4.1
85652	Sedimentation rate, erythrocyte; automated	100	1,368	4.4	96	2,145	4.3

CPT, Current Procedural Terminology; HCPC, Centers for Medicare and Medicaid Services Common Procedure Coding System

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, dipeptidyl peptidase-4 inhibitor, glucagon-like peptide-1 agonists, pramlintide, alpha-glucosidase inhibitors, and insulins. Only a proportion of procedures in the top 100 list were retained in the propensity score model via stepwise selection. Please note descriptions may be truncated in the data due to SAS limitations.

Table 2.2b. The Top 100 Most Frequently Recorded Procedures among Exenatide Initiators and OADs Initiators in the 9-Month Baseline Period, Impact National Benchmark Database 6/1/2005-7/31/2010

CPT or HCPC Code	Description	Exenatide N = 16,206			OADs N = 25,385		
		Rank	Count	Percent	Rank	Count	Percent
99214	Office or other outpatient visit for the evaluation and management of an established patient, which requires at least 2 of these 3 key components: A detailed history; A detailed examination; Medical decision making of moderate complexity. Counseling and/or coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of moderate to high severity. Physicians typically spend 25 minutes face-to-face with the patient and/or family.	1	13,105	80.9	1	20,303	80.0
99213	Office or other outpatient visit for the evaluation and management of an established patient, which requires at least 2 of these 3 key components: An expanded problem focused history; An expanded problem focused examination; Medical decision making of low complexity. Counseling and coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of low to moderate severity. Physicians typically spend 15 minutes face-to-face with the patient and/or family	2	13,000	80.2	2	20,224	79.7
83036	Hemoglobin; glycosylated (A1C)	3	10,853	67.0	3	16,914	66.6
36415	Collection of venous blood by venipuncture	4	10,589	65.3	4	16,659	65.6
80061	Lipid panel This panel must include the following: Cholesterol, serum, total (82465) Lipoprotein, direct measurement, high density cholesterol (HDL cholesterol) (83718) Triglycerides (84478)	5	9,199	56.8	5	14,298	56.3
80053	Comprehensive metabolic panel This panel must include the following: Albumin (82040) Bilirubin, total (82247) Calcium (82310) Carbon dioxide (bicarbonate) (82374) Chloride (82435) Creatinine (82565) Glucose (82947) Phosphatase, alkaline (84075) Potassium	6	6,411	39.6	6	9,984	39.3
82043	Albumin; urine, microalbumin, quantitative	7	5,228	32.3	7	8,095	31.9
85025	Blood count; complete (CBC), automated (Hgb, Hct, RBC, WBC and platelet count) and automated differential WBC count	8	5,033	31.1	8	7,926	31.2
93000	Electrocardiogram, routine ECG with at least 12 leads; with interpretation and report	9	4,592	28.3	9	7,196	28.3
84443	Thyroid stimulating hormone (TSH)	10	4,440	27.4	10	6,838	26.9
82570	Creatinine; other source	11	4,187	25.8	11	6,494	25.6
99212	Office or other outpatient visit for the evaluation and management of an established patient, which requires at least 2 of these 3 key components: A problem focused history; A problem focused examination; Straightforward medical decision making. Counseling and/or coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are self limited or minor. Physicians typically spend 10 minutes face-to-face with the patient and/or family.	12	3,970	24.5	12	6,156	24.3

Table 2.2b. The Top 100 Most Frequently Recorded Procedures among Exenatide Initiators and OADs Initiators in the 9-Month Baseline Period, Impact National Benchmark Database 6/1/2005-7/31/2010

CPT or HCPC Code	Description	Exenatide N = 16,206			OADs N = 25,385		
		Rank	Count	Percent	Rank	Count	Percent
92014	Ophthalmological services: medical examination and evaluation, with initiation or continuation of diagnostic and treatment program; comprehensive, established patient, one or more visits	13	3,794	23.4	13	5,819	22.9
90658	Influenza virus vaccine, split virus, when administered to individuals 3 years of age and older, for intramuscular use	14	3,642	22.5	14	5,572	21.9
99244	Office consultation for a new or established patient, which requires these 3 key components: A comprehensive history; A comprehensive examination; and Medical decision making of moderate complexity. Counseling and/or coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of moderate to high severity. Physicians typically spend 60 minutes face-to-face with the patient and/or family.	15	3,638	22.4	15	5,447	21.5
80048	Basic metabolic panel (Calcium, total) This panel must include the following: Calcium (82310) Carbon dioxide (82374) Chloride (82435) Creatinine (82565) Glucose (82947) Potassium (84132) Sodium (84295) Urea nitrogen (BUN) (84520)	16	3,379	20.9	16	5,327	21.0
90471	Immunization administration (includes percutaneous, intradermal, subcutaneous, or intramuscular injections); one vaccine (single or combination vaccine/toxoid)	17	3,193	19.7	17	4,964	19.6
99396	Periodic comprehensive preventive medicine reevaluation and management of an individual including an age and gender appropriate history, examination, counseling/anticipatory guidance/risk factor reduction interventions, and the ordering of laboratory/diagnostic procedures, established patient; 40-64 years.	18	3,179	19.6	18	4,894	19.3
99215	Office or other outpatient visit for the evaluation and management of an established patient, which requires at least 2 of these 3 key components: A comprehensive history; A comprehensive examination; Medical decision making of high complexity. Counseling	19	3,136	19.4	19	4,758	18.7
71020	Radiologic examination, chest, two views, frontal and lateral;	20	2,837	17.5	20	4,507	17.8
82947	Glucose; quantitative, blood (except reagent strip)	21	2,651	16.4	21	4,145	16.3
99243	Office consultation for a new or established patient, which requires these 3 key components: A detailed history; A detailed examination; and Medical decision making of low complexity. Counseling and/or coordination of care with other providers or agencies	22	2,518	15.5	22	3,846	15.2
84460	Transferase; alanine amino (ALT) (SGPT)	23	2,299	14.2	23	3,584	14.1
82962	Glucose, blood by glucose monitoring device(s) cleared by the FDA specifically for home use	24	2,243	13.8	25	3,370	13.3

Table 2.2b. The Top 100 Most Frequently Recorded Procedures among Exenatide Initiators and OADs Initiators in the 9-Month Baseline Period, Impact National Benchmark Database 6/1/2005-7/31/2010

CPT or HCPC Code	Description	Exenatide N = 16,206			OADs N = 25,385		
		Rank	Count	Percent	Rank	Count	Percent
99203	Office or other outpatient visit for the evaluation and management of a new patient, which requires these 3 key components: A detailed history; A detailed examination; Medical decision making of low complexity. Counseling and/or coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of moderate severity. Physicians typically spend 30 minutes face-to-face with the patient and/or family.	25	2,214	13.7	24	3,395	13.4
88305	Level IV - Surgical pathology, gross and microscopic examination Abortion - spontaneous/missed Artery, biopsy Bone marrow, biopsy Bone exostosis Brain/meninges, other than for tumor resection Breast, biopsy, not requiring microscopic evaluation of surgical margins Breast, reduction mammoplasty Bronchus, biopsy Cell block, any source Cervix, biopsy Colon, biopsy Duodenum, biopsy Endocervix, curettings/biopsy Endometrium, curettings/biopsy Esophagus, biopsy Extremity, amputation, traumatic Fallopian tube, biopsy Fallopian tube, ectopic pregnancy Femoral head, fracture Fingers/toes, amputation, non-traumatic Gingiva/oral mucosa, biopsy Heart valve Joint, resection Kidney, biopsy Larynx, biopsy Leiomyoma(s), uterine myomectomy - without uterus Lip, biopsy/wedge resection Lung, transbronchial biopsy Lymph node, biopsy Muscle, biopsy Nasal mucosa, biopsy Nasopharynx/oropharynx, biopsy Nerve, biopsy Odontogenic/dental cyst Omentum, biopsy Ovary with or without tube, non-neoplastic Ovary, biopsy/wedge resection Parathyroid gland Peritoneum, biopsy	26	2,104	13.0	26	3,225	12.7
81002	Urinalysis, by dip stick or tablet reagent for bilirubin, glucose, hemoglobin, ketones, leukocytes, nitrite, pH, protein, specific gravity, urobilinogen, any number of these constituents; non-automated, without microscopy	27	1,995	12.3	28	3,022	11.9
80050	Obstetric panel This panel must include the following: Blood count, complete (CBC), automated and automated differential WBC count (85025 or 85027 and 85004) OR Blood count, complete (CBC), automated (85027) and appropriate manual differential WBC count (85007 or 85009) Hepatitis B surface antigen (HBsAg) (87340) Antibody, rubella (86762) Syphilis test, non-treponemal antibody; qualitative (eg, VDRL, RPR, ART) (86592) Antibody screen, RBC, each serum technique (86850) Blood typing, ABO (86900) AND Blood typing, Rh (D) (86901)	28	1,928	11.9	30	2,931	11.5
84153	Prostate specific antigen (PSA); total	29	1,906	11.8	27	3,054	12.0
93010	Electrocardiogram, routine ECG with at least 12 leads; interpretation and report only	30	1,890	11.7	29	3,012	11.9
99245	Office consultation for a new or established patient, which requires these 3 key components: A comprehensive history; A comprehensive examination; and Medical decision making of high complexity. Counseling and/or coordination of care with other providers	31	1,879	11.6	34	2,707	10.7
84450	Transferase; aspartate amino (AST) (SGOT)	32	1,820	11.2	32	2,810	11.1

Table 2.2b. The Top 100 Most Frequently Recorded Procedures among Exenatide Initiators and OADs Initiators in the 9-Month Baseline Period, Impact National Benchmark Database 6/1/2005-7/31/2010

CPT or HCPC Code	Description	Exenatide N = 16,206			OADs N = 25,385		
		Rank	Count	Percent	Rank	Count	Percent
81001	Urinalysis, by dip stick or tablet reagent for bilirubin, glucose, hemoglobin, ketones, leukocytes, nitrite, pH, protein, specific gravity, urobilinogen, any number of these constituents; automated, with microscopy	33	1,804	11.1	31	2,897	11.4
84439	Thyroxine; free	34	1,740	10.7	39	2,485	9.8
93325	Doppler echocardiography color flow velocity mapping (List separately in addition to codes for echocardiography)	35	1,739	10.7	35	2,671	10.5
93320	Doppler echocardiography, pulsed wave and/or continuous wave with spectral display (List separately in addition to codes for echocardiographic imaging); complete	36	1,730	10.7	36	2,658	10.5
82565	Creatinine; blood	37	1,706	10.5	33	2,765	10.9
80076	Hepatic function panel This panel must include the following: Albumin (82040) Bilirubin, total (82247) Bilirubin, direct (82248) Phosphatase, alkaline (84075) Protein, total (84155) Transferase, alanine amino (ALT) (SGPT) (84460) Transferase, aspartate amino (AST) (SGOT) (84450)	38	1,673	10.3	37	2,580	10.2
93307	Echocardiography, transthoracic, real-time with image documentation (2D) with or without M-mode recording; complete	39	1,642	10.1	38	2,542	10.0
99204	Office or other outpatient visit for the evaluation and management of a new patient, which requires these 3 key components: A comprehensive history; A comprehensive examination; Medical decision making of moderate complexity. Counseling and/or coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of moderate to high severity. Physicians typically spend 45 minutes face-to-face with the patient and/or family.	40	1,629	10.1	41	2,435	9.6
82550	Creatine kinase (CK), (CPK); total	41	1,548	9.6	42	2,352	9.3
99000	Handling and/or conveyance of specimen for transfer from the physician's office to a laboratory	42	1,539	9.5	40	2,457	9.7
99211	Office or other outpatient visit for the evaluation and management of an established patient, that may not require the presence of a physician. Usually, the presenting problem(s) are minimal. Typically, 5 minutes are spent performing or supervising these services.	43	1,505	9.3	43	2,253	8.9
81000	Urinalysis, by dip stick or tablet reagent for bilirubin, glucose, hemoglobin, ketones, leukocytes, nitrite, pH, protein, specific gravity, urobilinogen, any number of these constituents; non-automated, with microscopy	44	1,464	9.0	46	2,217	8.7
78478	Myocardial perfusion study with wall motion, qualitative or quantitative study (List separately in addition to code for primary procedure)	45	1,403	8.7	45	2,217	8.7

Table 2.2b. The Top 100 Most Frequently Recorded Procedures among Exenatide Initiators and OADs Initiators in the 9-Month Baseline Period, Impact National Benchmark Database 6/1/2005-7/31/2010

CPT or HCPC Code	Description	Exenatide N = 16,206			OADs N = 25,385		
		Rank	Count	Percent	Rank	Count	Percent
78465	Myocardial perfusion imaging; tomographic (SPECT), multiple studies (including attenuation correction when performed), at rest and/or stress (exercise and/or pharmacologic) and redistribution and/or rest injection, with or without quantification	46	1,393	8.6	44	2,232	8.8
G0108	Diabetes outpatient self-management training services, individual, per 30 minutes	47	1,383	8.5	57	1,830	7.2
81003	Urinalysis, by dip stick or tablet reagent for bilirubin, glucose, hemoglobin, ketones, leukocytes, nitrite, pH, protein, specific gravity, urobilinogen, any number of these constituents; automated, without microscopy	48	1,366	8.4	47	2,181	8.6
93015	Cardiovascular stress test using maximal or submaximal treadmill or bicycle exercise, continuous electrocardiographic monitoring, and/or pharmacological stress; with physician supervision, with interpretation and report	49	1,316	8.1	52	2,007	7.9
97110	Therapeutic procedure, one or more areas, each 15 minutes; therapeutic exercises to develop strength and endurance, range of motion and flexibility	50	1,304	8.0	51	2,019	8.0
82948	Glucose; blood, reagent strip	51	1,299	8.0	49	2,044	8.1
85027	Blood count; complete (CBC), automated (Hgb, Hct, RBC, WBC and platelet count)	52	1,277	7.9	50	2,037	8.0
78480	Myocardial perfusion study with ejection fraction (List separately in addition to code for primary procedure)	53	1,269	7.8	48	2,076	8.2
92012	Ophthalmological services: medical examination and evaluation, with initiation or continuation of diagnostic and treatment program; intermediate, established patient	54	1,256	7.8	53	1,917	7.6
92015	Determination of refractive state	55	1,231	7.6	58	1,817	7.2
84520	Urea nitrogen; quantitative	56	1,209	7.5	54	1,910	7.5
82270	Blood, occult, by peroxidase activity (eg, guaiac), qualitative; feces, consecutive collected specimens with single determination, for colorectal neoplasm screening (ie, patient was provided 3 cards or single triple card for consecutive collection)	57	1,206	7.4	55	1,870	7.4
99284	Emergency department visit for the evaluation and management of a patient, which requires these 3 key components: A detailed history; A detailed examination; and Medical decision making of moderate complexity. Counseling and/or coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of high severity, and require urgent evaluation by the physician but do not pose an immediate significant threat to life or physiologic function.	58	1,170	7.2	56	1,868	7.4
99283	Emergency department visit for the evaluation and management of a patient, which requires these 3 key components: An expanded problem focused history; An expanded problem focused examination; and Medical decision making of moderate complexity. Counseling and/or coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of moderate severity.	59	1,153	7.1	59	1,788	7.0

Table 2.2b. The Top 100 Most Frequently Recorded Procedures among Exenatide Initiators and OADs Initiators in the 9-Month Baseline Period, Impact National Benchmark Database 6/1/2005-7/31/2010

CPT or HCPC Code	Description	Exenatide N = 16,206			OADs N = 25,385		
		Rank	Count	Percent	Rank	Count	Percent
76092	Screening mammography, bilateral (two view film study of each breast)	60	1,118	6.9	65	1,633	6.4
85610	Prothrombin time;	61	1,113	6.9	60	1,780	7.0
83721	Lipoprotein, direct measurement; LDL cholesterol	62	1,077	6.6	62	1,680	6.6
92250	Fundus photography with interpretation and report	63	1,054	6.5	61	1,682	6.6
97001	Physical therapy evaluation	64	1,040	6.4	66	1,606	6.3
99285	Emergency department visit for the evaluation and management of a patient, which requires these 3 key components within the constraints imposed by the urgency of the patient's clinical condition and/or mental status: A comprehensive history; A comprehensive examination; and Medical decision making of high complexity. Counseling and/or coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of high severity and pose an immediate significant threat to life or physiologic function.	65	1,030	6.4	64	1,634	6.4
84550	Uric acid; blood	66	1,024	6.3	63	1,662	6.5
88142	Cytopathology, cervical or vaginal (any reporting system), collected in preservative fluid, automated thin layer preparation; manual screening under physician supervision	67	1,023	6.3	68	1,581	6.2
71010	Radiologic examination, chest; single view, frontal	68	1,009	6.2	67	1,599	6.3
82248	Bilirubin; direct	69	984	6.1	69	1,546	6.1
77052	Computer-aided detection (computer algorithm analysis of digital image data for lesion detection) with further physician review for interpretation, with or without digitization of film radiographic images; screening mammography (List separately in addition to code for primary procedure)	70	969	6.0	70	1,519	6.0
87086	Culture, bacterial; quantitative colony count, urine	71	944	5.8	74	1,446	5.7
97140	Manual therapy techniques (eg, mobilization/ manipulation, manual lymphatic drainage, manual traction), one or more regions, each 15 minutes	72	938	5.8	76	1,412	5.6
93005	Electrocardiogram, routine ECG with at least 12 leads; tracing only, without interpretation and report	73	937	5.8	73	1,453	5.7
83540	Iron	74	931	5.7	71	1,484	5.8
99202	Office or other outpatient visit for the evaluation and management of a new patient, which requires these 3 key components: An expanded problem focused history; An expanded problem focused examination; Straightforward medical decision making. Counseling and/or coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of low to moderate severity. Physicians typically spend 20 minutes face-to-face with the patient and/or family.	75	926	5.7	78	1,366	5.4

Table 2.2b. The Top 100 Most Frequently Recorded Procedures among Exenatide Initiators and OADs Initiators in the 9-Month Baseline Period, Impact National Benchmark Database 6/1/2005-7/31/2010

CPT or HCPC Code	Description	Exenatide N = 16,206			OADs N = 25,385		
		Rank	Count	Percent	Rank	Count	Percent
92004	Ophthalmological services: medical examination and evaluation with initiation of diagnostic and treatment program; comprehensive, new patient, one or more visits	76	925	5.7	75	1,444	5.7
G0202	Screening mammography, producing direct digital image, bilateral, all views	77	888	5.5	77	1,407	5.5
99232	Subsequent hospital care, per day, for the evaluation and management of a patient, which requires at least 2 of these 3 key components: An expanded problem focused interval history; An expanded problem focused examination; Medical decision making of moderate complexity. Counseling and/or coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the patient is responding inadequately to therapy or has developed a minor complication. Physicians typically spend 25 minutes at the bedside and on the patient's hospital floor or unit.	78	885	5.5	72	1,470	5.8
92135	Scanning computerized ophthalmic diagnostic imaging, posterior segment, (eg, scanning laser) with interpretation and report, unilateral	79	884	5.5	79	1,362	5.4
80051	Electrolyte panel This panel must include the following: Carbon dioxide (82374) Chloride (82435) Potassium (84132) Sodium (84295)	80	844	5.2	80	1,300	5.1
84436	Thyroxine; total	81	829	5.1	81	1,285	5.1
76083	Computer aided detection (computer algorithm analysis of digital image data for lesion detection) with further physician review for interpretation, with or without digitization of film radiographic images; screening mammography (List separately in addition to code for primary procedure)	82	804	5.0	87	1,133	4.5
A7035	Headgear used with positive airway pressure device	83	794	4.9	88	1,127	4.4
20610	Arthrocentesis, aspiration and/or injection; major joint or bursa (eg, shoulder, hip, knee joint, subacromial bursa)	84	792	4.9	83	1,206	4.8
82465	Cholesterol, serum or whole blood, total	85	778	4.8	82	1,240	4.9
92083	Visual field examination, unilateral or bilateral, with interpretation and report; extended examination (eg, Goldmann visual fields with at least 3 isopters plotted and static determination within the central 30 degrees, or quantitative, automated threshold perimetry, Octopus program G-1, 32 or 42, Humphrey visual field analyzer full threshold programs 30-2, 24-2, or 30/60-2)	86	754	4.7	84	1,184	4.7
73630	Radiologic examination, foot; complete, minimum of three views	87	751	4.6	91	1,096	4.3
82607	Cyanocobalamin (Vitamin B-12);	88	738	4.6	89	1,106	4.4

Table 2.2b. The Top 100 Most Frequently Recorded Procedures among Exenatide Initiators and OADs Initiators in the 9-Month Baseline Period, Impact National Benchmark Database 6/1/2005-7/31/2010

CPT or HCPC Code	Description	Exenatide N = 16,206			OADs N = 25,385		
		Rank	Count	Percent	Rank	Count	Percent
99205	Office or other outpatient visit for the evaluation and management of a new patient, which requires these 3 key components: A comprehensive history; A comprehensive examination; Medical decision making of high complexity. Counseling and/or coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of moderate to high severity. Physicians typically spend 60 minutes face-to-face with the patient and/or family.	89	722	4.5	93	1,087	4.3
A7034	Nasal interface (mask or cannula type) used with positive airway pressure device, with or without head strap	90	715	4.4	107	969	3.8
84478	Triglycerides	91	702	4.3	90	1,103	4.3
77057	Screening mammography, bilateral (2-view film study of each breast)	92	692	4.3	99	1,020	4.0
90732	Pneumococcal polysaccharide vaccine, 23-valent, adult or immunosuppressed patient dosage, when administered to individuals 2 years or older, for subcutaneous or intramuscular use	93	691	4.3	92	1,094	4.3
85730	Thromboplastin time, partial (PTT); plasma or whole blood	94	689	4.3	85	1,162	4.6
99242	Office consultation for a new or established patient, which requires these 3 key components: An expanded problem focused history; An expanded problem focused examination; and Straightforward medical decision making. Counseling and/or coordination of care	95	684	4.2	96	1,050	4.1
90806	Individual psychotherapy, insight oriented, behavior modifying and/or supportive, in an office or outpatient facility, approximately 45 to 50 minutes face-to-face with the patient;	96	681	4.2	102	999	3.9
93880	Duplex scan of extracranial arteries; complete bilateral study	97	672	4.1	94	1,082	4.3
A7037	Tubing used with positive airway pressure device	98	669	4.1	116	913	3.6
A9500	Technetium Tc-99m sestamibi, diagnostic, per study dose, up to 40 millicuries	99	664	4.1	98	1,041	4.1
92226	Ophthalmoscopy, extended, with retinal drawing (eg, for retinal detachment, melanoma), with interpretation and report; subsequent	100	662	4.1	95	1,062	4.2

CPT, Current Procedural Terminology; HCPC, Centers for Medicare and Medicaid Services Common Procedure Coding System

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, dipeptidyl peptidase-4 inhibitor, glucagon-like peptide-1 agonists, pramlintide, alpha-glucosidase inhibitors, and insulins. Only a proportion of procedures in the top 100 list were retained in the propensity score model via stepwise selection.

Please note descriptions may be truncated in the data due to SAS limitations.

Table 2.3a. The Top 100 Most Frequently Recorded Drug Class Dispensings among Exenatide Initiators and OADs Initiators in the 9-Month Baseline Period, Life Sciences Research Database 6/1/2005-7/31/2010

Therapeutic Drug Class Description	Exenatide N = 31,301			OADs N = 49,783		
	Rank	Count	%	Rank	Count	%
BLOOD SUGAR DIAGNOSTICS	1	17,446	55.7	1	26,604	53.4
LIPOTROPICS	2	16,351	52.2	2	25,427	51.1
HYPOTENSIVES, ACE INHIBITORS	3	13,085	41.8	3	21,198	42.6
ANALGESICS,NARCOTICS	4	9,806	31.3	4	15,499	31.1
HYPOTENSIVES,ANGIOTENSIN RECEPTOR ANTAGONIST	5	7,615	24.3	5	11,658	23.4
NSAIDS, CYCLOOXYGENASE INHIBITOR - TYPE	6	6,828	21.8	7	10,849	21.8
ANTIHYPERLIPIDEMIC - HMG COA REDUCTASE INHIBITORS	7	6,724	21.5	6	10,952	22.0
DURABLE MEDICAL EQUIPMENT,MISC (GROUP 1)	8	6,584	21.0	9	9,917	19.9
BETA-ADRENERGIC BLOCKING AGENTS	9	6,350	20.3	8	10,130	20.3
PENICILLINS	10	5,829	18.6	10	9,129	18.3
QUINOLONES	11	5,698	18.2	11	8,943	18.0
MACROLIDES	12	5,642	18.0	12	8,778	17.6
SEROTONIN SPECIFIC REUPTAKE INHIBITOR (SSRIS)	13	5,296	16.9	13	7,882	15.8
CALCIUM CHANNEL BLOCKING AGENTS	14	4,744	15.2	14	7,695	15.5
GASTRIC ACID SECRETION REDUCERS	15	4,399	14.1	15	6,626	13.3
THYROID HORMONES	16	4,156	13.3	16	6,378	12.8
LOOP DIURETICS	17	3,870	12.4	17	6,031	12.1
ANTICONVULSANTS	18	3,527	11.3	19	5,483	11.0
THIAZIDE AND RELATED DIURETICS	19	3,520	11.2	18	5,572	11.2
GLUCOCORTICOIDS	20	3,309	10.6	20	5,161	10.4
SKELETAL MUSCLE RELAXANTS	21	3,193	10.2	21	5,008	10.1
ANTI-ANXIETY DRUGS	22	3,178	10.2	22	4,916	9.9
NASAL ANTI-INFLAMMATORY STEROIDS	23	2,865	9.2	24	4,313	8.7
BETA-ADRENERGIC AGENTS	24	2,800	8.9	23	4,406	8.9
ANTIHISTAMINES - 2ND GENERATION	25	2,658	8.5	26	3,989	8.0
CEPHALOSPORINS - 1ST GENERATION	26	2,578	8.2	25	4,004	8.0
SEDATIVE-HYPNOTICS,NON-BARBITURATE	27	2,543	8.1	27	3,839	7.7
ANTIFUNGAL AGENTS	28	2,527	8.1	28	3,835	7.7
TOPICAL ANTI-INFLAMMATORY STEROIDAL	29	2,399	7.7	29	3,764	7.6
POTASSIUM REPLACEMENT	30	2,371	7.6	30	3,708	7.4
TOPICAL ANTIFUNGALS	31	2,323	7.4	31	3,622	7.3
SEROTONIN-NOREPINEPHRINE REUPTAKE-INHIB (SNRIS)	32	2,247	7.2	35	2,940	5.9
PLATELET AGGREGATION INHIBITORS	33	2,048	6.5	32	3,362	6.8
DRUGS TO TREAT IMPOTENCY	34	1,916	6.1	33	3,238	6.5
ABSORBABLE SULFONAMIDES	35	1,828	5.8	34	3,069	6.2

Table 2.3a. The Top 100 Most Frequently Recorded Drug Class Dispensings among Exenatide Initiators and OADs Initiators in the 9-Month Baseline Period, Life Sciences Research Database 6/1/2005-7/31/2010

Therapeutic Drug Class Description	Exenatide N = 31,301			OADs N = 49,783		
	Rank	Count	%	Rank	Count	%
ANGIOTENSIN RECEPTR ANTG./THIAZIDE & RELATED COMB.	36	1,716	5.5	36	2,666	5.4
DIABETIC SUPPLIES	37	1,635	5.2	37	2,591	5.2
ALPHA/BETA-ADRENERGIC BLOCKING AGENTS	38	1,590	5.1	38	2,546	5.1
ANTIHISTAMINES - 1ST GENERATION	39	1,581	5.1	39	2,468	5.0
LAXATIVES AND CATHARTICS	40	1,505	4.8	40	2,379	4.8
NOREPINEPHRINE AND DOPAMINE REUPTAKE INHIB (NDRIS)	41	1,463	4.7	50	1,838	3.7
POTASSIUM SPARING DIURETICS IN COMBINATION	42	1,372	4.4	41	2,175	4.4
TETRACYCLINES	43	1,368	4.4	42	2,120	4.3
ESTROGENIC AGENTS	44	1,336	4.3	46	1,977	4.0
LEUKOTRIENE RECEPTOR ANTAGONISTS	45	1,298	4.1	47	1,907	3.8
ACE INHIBITOR/CALCIUM CHANNEL BLOCKER COMBINATION	46	1,269	4.1	44	2,049	4.1
PROTON-PUMP INHIBITORS	47	1,261	4.0	45	2,022	4.1
VASODILATORS,CORONARY	48	1,254	4.0	43	2,076	4.2
ACE INHIBITOR/THIAZIDE & THIAZIDE-LIKE DIURETIC	49	1,226	3.9	48	1,888	3.8
BETA-ADRENERGICS AND GLUCOCORTICOIDS COMBINATION	50	1,201	3.8	49	1,848	3.7
ANTIVIRALS, GENERAL	51	1,170	3.7	54	1,786	3.6
NARCOTIC ANTITUSSIVE-1ST GENERATION ANTIHISTAMINE	52	1,153	3.7	52	1,814	3.6
NARCOTIC ANTITUSSIVE-EXPECTORANT COMBINATION	53	1,147	3.7	53	1,798	3.6
TRICYCLIC ANTIDEPRESSANTS & REL. NON-SEL. RU-INHIB	54	1,113	3.6	51	1,832	3.7
ANTIHYPERLIP.HMG COA REDUCT INHIB&CHOLEST.AB.INHIB	55	1,049	3.4	55	1,676	3.4
PURINE INHIBITORS	56	1,018	3.3	60	1,412	2.8
OPHTHALMIC ANTIBIOTICS	57	976	3.1	56	1,665	3.3
LINCOSAMIDES	58	965	3.1	57	1,544	3.1
ANTITUSSIVES,NON-NARCOTIC	59	912	2.9	58	1,486	3.0
ORAL ANTICOAGULANTS,COUMARIN TYPE	60	910	2.9	59	1,449	2.9
TOPICAL ANTIBIOTICS	61	865	2.8	64	1,300	2.6
POTASSIUM SPARING DIURETICS	62	858	2.7	67	1,162	2.3
MIOTICS/OTHER INTRAOC. PRESSURE REDUCERS	63	819	2.6	61	1,385	2.8
HYPOTENSIVES,SYMPATHOLYTIC	64	799	2.6	62	1,361	2.7
BENIGN PROSTATIC HYPERTROPHY/MICTURITION AGENTS	65	799	2.6	63	1,319	2.6
DECONGESTANT-EXPECTORANT COMBINATIONS	66	797	2.5	65	1,197	2.4
BONE RESORPTION SUPPRESSION AGENTS	67	724	2.3	69	1,154	2.3
ANTIEMETIC/ANTIVERTIGO AGENTS	68	723	2.3	70	1,133	2.3
CONTRACEPTIVES,ORAL	69	718	2.3	71	1,060	2.1
VITAMIN D PREPARATIONS	70	713	2.3	73	1,036	2.1

Table 2.3a. The Top 100 Most Frequently Recorded Drug Class Dispensings among Exenatide Initiators and OADs Initiators in the 9-Month Baseline Period, Life Sciences Research Database 6/1/2005-7/31/2010

Therapeutic Drug Class Description	Exenatide N = 31,301			OADs N = 49,783		
	Rank	Count	%	Rank	Count	%
CEPHALOSPORINS - 3RD GENERATION	71	676	2.2	72	1,051	2.1
ANAEROBIC ANTIPROTOZOAL-ANTIBACTERIAL AGENTS	72	672	2.1	66	1,191	2.4
NITROFURAN DERIVATIVES	73	639	2.0	75	982	2.0
ANDROGENIC AGENTS	74	630	2.0	83	796	1.6
SEROTONIN-2 ANTAGONIST/REUPTAKE INHIBITORS (SARIS)	75	628	2.0	74	1,014	2.0
ALPHA-ADRENERGIC BLOCKING AGENTS	76	581	1.9	76	977	2.0
NARCOTIC ANTITUSS-1ST GEN. ANTIHISTAMINE-DECONGEST	77	579	1.8	77	927	1.9
INTESTINAL MOTILITY STIMULANTS	78	567	1.8	79	902	1.8
CEPHALOSPORINS - 2ND GENERATION	79	563	1.8	80	884	1.8
URINARY TRACT ANTISPASMODIC/ANTIINCONTINENCE AGENT	80	510	1.6	82	813	1.6
DIGITALIS GLYCOSIDES	81	508	1.6	81	865	1.7
EYE ANTIINFLAMMATORY AGENTS	82	504	1.6	78	904	1.8
ANTIPARKINSONISM DRUGS,OTHER	83	493	1.6	84	743	1.5
2ND GEN ANTIHISTAMINE & DECONGESTANT COMBINATIONS	84	490	1.6	85	743	1.5
VITAMIN B PREPARATIONS	85	459	1.5	90	648	1.3
ANTIMIGRAINE PREPARATIONS	86	438	1.4	92	645	1.3
EYE ANTIBIOTIC-CORTICOID COMBINATIONS	87	434	1.4	89	655	1.3
FOLIC ACID PREPARATIONS	88	420	1.3	87	682	1.4
EYE ANTIHISTAMINES	89	418	1.3	95	614	1.2
NASAL ANTIHISTAMINE	90	417	1.3	94	624	1.3
DENTAL AIDS AND PREPARATIONS	91	414	1.3	91	647	1.3
TOPICAL LOCAL ANESTHETICS	92	404	1.3	97	603	1.2
ANTIMALARIAL DRUGS	93	404	1.3	93	631	1.3
URINARY TRACT ANESTHETIC/ANALGESIC AGNT (AZO-DYE)	94	383	1.2	100	580	1.2
HYPOTENSIVES,MISCELLANEOUS	95	372	1.2	88	656	1.3
ANTI-NARCOLEPSY/ANTI-HYPERKINESIS AGENTS	96	372	1.2	113	442	0.9
PROGESTATIONAL AGENTS	97	370	1.2	101	575	1.2
BILE SALT SEQUESTRANTS	98	361	1.2	105	532	1.1
GENERAL BRONCHODILATOR AGENTS	99	354	1.1	102	560	1.1
ANTIHYPERLIP (HMGCOA) & CALCIUM CHANNEL BLOCKER CMB	100	353	1.1	98	596	1.2

Note: OADs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins

Table 2.3b. The Top 100 Most Frequently Recorded Drug Class Dispensings among Exenatide Initiators and OADs Initiators in the 9-Month Baseline Period, Impact National Benchmark Database 6/1/2005-7/31/2010

Therapeutic Drug Class Description	Exenatide N = 16,206			OADs N = 25,385		
	Rank	Count	%	Rank	Count	%
BLOOD SUGAR DIAGNOSTICS	1	9,702	59.9	1	14,623	57.6
LIPOTROPICS	2	9,551	58.9	2	14,602	57.5
HYPOTENSIVES, ACE INHIBITORS	3	7,221	44.6	3	11,279	44.4
ANALGESICS,NARCOTICS	4	4,558	28.1	4	7,026	27.7
HYPOTENSIVES,ANGIOTENSIN RECEPTOR ANTAGONIST	5	4,075	25.1	5	6,195	24.4
BETA-ADRENERGIC BLOCKING AGENTS	6	3,961	24.4	6	6,181	24.3
DURABLE MEDICAL EQUIPMENT,MISC (GROUP 1)	7	3,809	23.5	7	5,574	22.0
NSAIDS, CYCLOOXYGENASE INHIBITOR - TYPE	8	3,234	20.0	9	5,002	19.7
ANTIHYPERLIPIDEMIC - HMG COA REDUCTASE INHIBITORS	9	3,181	19.6	8	5,226	20.6
PENICILLINS	10	3,099	19.1	10	4,780	18.8
GASTRIC ACID SECRETION REDUCERS	11	3,039	18.8	12	4,456	17.6
MACROLIDES	12	2,953	18.2	11	4,502	17.7
SEROTONIN SPECIFIC REUPTAKE INHIBITOR (SSRIS)	13	2,806	17.3	14	4,198	16.5
QUINOLONES	14	2,704	16.7	13	4,278	16.9
CALCIUM CHANNEL BLOCKING AGENTS	15	2,568	15.8	15	4,012	15.8
THIAZIDE AND RELATED DIURETICS	16	2,176	13.4	16	3,358	13.2
THYROID HORMONES	17	2,067	12.8	17	3,147	12.4
LOOP DIURETICS	18	2,027	12.5	18	3,058	12.0
ANTICONVULSANTS	19	1,736	10.7	19	2,708	10.7
ANTI-ANXIETY DRUGS	20	1,720	10.6	20	2,683	10.6
GLUCOCORTICOIDS	21	1,709	10.5	21	2,665	10.5
BETA-ADRENERGIC AGENTS	22	1,616	10.0	22	2,519	9.9
TOPICAL ANTIFUNGALS	23	1,476	9.1	23	2,308	9.1
TOPICAL ANTI-INFLAMMATORY STEROIDAL	24	1,468	9.1	25	2,232	8.8
NASAL ANTI-INFLAMMATORY STEROIDS	25	1,463	9.0	24	2,251	8.9
SKELETAL MUSCLE RELAXANTS	26	1,369	8.4	27	2,114	8.3
CEPHALOSPORINS - 1ST GENERATION	27	1,303	8.0	26	2,196	8.7
SEDATIVE-HYPNOTICS,NON-BARBITURATE	28	1,208	7.5	29	1,835	7.2
ANTIHISTAMINES - 2ND GENERATION	29	1,204	7.4	28	1,858	7.3
PLATELET AGGREGATION INHIBITORS	30	1,070	6.6	30	1,711	6.7
ANTIFUNGAL AGENTS	31	1,070	6.6	31	1,588	6.3
SEROTONIN-NOREPINEPHRINE REUPTAKE-INHIB (SNRIS)	32	984	6.1	33	1,457	5.7
POTASSIUM REPLACEMENT	33	955	5.9	32	1,504	5.9
DRUGS TO TREAT IMPOTENCY	34	833	5.1	35	1,308	5.2
LAXATIVES AND CATHARTICS	35	821	5.1	34	1,315	5.2

Table 2.3b. The Top 100 Most Frequently Recorded Drug Class Dispensings among Exenatide Initiators and OADs Initiators in the 9-Month Baseline Period, Impact National Benchmark Database 6/1/2005-7/31/2010

Therapeutic Drug Class Description	Exenatide N = 16,206			OADs N = 25,385		
	Rank	Count	%	Rank	Count	%
ALPHA/BETA-ADRENERGIC BLOCKING AGENTS	36	797	4.9	36	1,241	4.9
ABSORBABLE SULFONAMIDES	37	795	4.9	38	1,205	4.7
NOREPINEPHRINE AND DOPAMINE REUPTAKE INHIB (NDRIS)	38	775	4.8	41	1,099	4.3
BETA-ADRENERGICS AND GLUCOCORTICOIDS COMBINATION	39	760	4.7	39	1,144	4.5
VASODILATORS,CORONARY	40	747	4.6	37	1,218	4.8
TETRACYCLINES	41	742	4.6	40	1,128	4.4
NARCOTIC ANTITUSSIVE-EXPECTORANT COMBINATION	42	645	4.0	42	1,007	4.0
PROTON-PUMP INHIBITORS	43	632	3.9	43	971	3.8
TRICYCLIC ANTIDEPRESSANTS & REL. NON-SEL. RU-INHIB	44	609	3.8	44	931	3.7
ORAL ANTICOAGULANTS,COUMARIN TYPE	45	572	3.5	45	913	3.6
POTASSIUM SPARING DIURETICS IN COMBINATION	46	569	3.5	49	852	3.4
OPHTHALMIC ANTIBIOTICS	47	568	3.5	46	912	3.6
LEUKOTRIENE RECEPTOR ANTAGONISTS	48	561	3.5	48	892	3.5
ANGIOTENSIN RECEPTR ANTG./THIAZIDE & RELATED COMB.	49	558	3.4	47	894	3.5
PURINE INHIBITORS	50	541	3.3	53	798	3.1
NARCOTIC ANTITUSSIVE-1ST GENERATION ANTIHISTAMINE	51	529	3.3	50	843	3.3
ESTROGENIC AGENTS	52	524	3.2	55	778	3.1
MIOTICS/OTHER INTRAOC. PRESSURE REDUCERS	53	519	3.2	52	805	3.2
DIABETIC SUPPLIES	54	508	3.1	51	823	3.2
ANTIVIRALS, GENERAL	55	507	3.1	58	746	2.9
ACE INHIBITOR/CALCIUM CHANNEL BLOCKER COMBINATION	56	504	3.1	54	793	3.1
ANTIHISTAMINES - 1ST GENERATION	57	495	3.1	56	768	3.0
BENIGN PROSTATIC HYPERTROPHY/MICTURITION AGENTS	58	485	3.0	57	759	3.0
TOPICAL ANTIBIOTICS	59	482	3.0	60	721	2.8
ANTIEMETIC/ANTIVERTIGO AGENTS	60	467	2.9	59	739	2.9
LINCOSAMIDES	61	458	2.8	61	716	2.8
BONE RESORPTION SUPPRESSION AGENTS	62	456	2.8	62	681	2.7
ANTITUSSIVES,NON-NARCOTIC	63	384	2.4	69	532	2.1
POTASSIUM SPARING DIURETICS	64	381	2.4	64	582	2.3
FOLIC ACID PREPARATIONS	65	344	2.1	66	569	2.2
DIGITALIS GLYCOSIDES	66	330	2.0	71	517	2.0
SEROTONIN-2 ANTAGONIST/REUPTAKE INHIBITORS (SARIS)	67	325	2.0	67	540	2.1
ALPHA-ADRENERGIC BLOCKING AGENTS	68	325	2.0	70	519	2.0
ANTIHYPERLIP.HMG COA REDUCT INHIB&CHOLEST.AB.INHIB	69	325	2.0	68	539	2.1
VITAMIN D PREPARATIONS	70	324	2.0	72	492	1.9

Table 2.3b. The Top 100 Most Frequently Recorded Drug Class Dispensings among Exenatide Initiators and OADs Initiators in the 9-Month Baseline Period, Impact National Benchmark Database 6/1/2005-7/31/2010

Therapeutic Drug Class Description	Exenatide N = 16,206			OADs N = 25,385		
	Rank	Count	%	Rank	Count	%
ACE INHIBITOR/THIAZIDE & THIAZIDE-LIKE DIURETIC	71	315	1.9	65	569	2.2
CONTRACEPTIVES,ORAL	72	303	1.9	75	469	1.8
EYE ANTIINFLAMMATORY AGENTS	73	299	1.8	76	466	1.8
URINARY TRACT ANTISPASMODIC/ANTIINCONTINENCE AGENT	74	299	1.8	79	439	1.7
HYPOTENSIVES,SYMPATHOLYTIC	75	295	1.8	74	471	1.9
ANAEROBIC ANTIPROTOZOAL-ANTIBACTERIAL AGENTS	76	286	1.8	73	481	1.9
ANDROGENIC AGENTS	77	282	1.7	83	397	1.6
NITROFURAN DERIVATIVES	78	277	1.7	82	417	1.6
INTESTINAL MOTILITY STIMULANTS	79	267	1.6	80	432	1.7
ANTIMALARIAL DRUGS	80	266	1.6	84	397	1.6
CEPHALOSPORINS - 2ND GENERATION	81	265	1.6	78	446	1.8
DENTAL AIDS AND PREPARATIONS	82	246	1.5	81	426	1.7
TOPICAL LOCAL ANESTHETICS	83	242	1.5	85	390	1.5
EYE ANTIHISTAMINES	84	241	1.5	86	352	1.4
CEPHALOSPORINS - 3RD GENERATION	85	239	1.5	93	335	1.3
EYE ANTIBIOTIC-CORTICOID COMBINATIONS	86	236	1.5	90	341	1.3
DECONGESTANT-EXPECTORANT COMBINATIONS	87	228	1.4	87	346	1.4
GENERAL BRONCHODILATOR AGENTS	88	227	1.4	89	343	1.4
NARCOTIC ANALGESIC & NON-SALICYLATE ANALGESIC COMB	89	225	1.4	91	338	1.3
ANTIPARKINSONISM DRUGS,OTHER	90	224	1.4	94	319	1.3
2ND GEN ANTIHISTAMINE & DECONGESTANT COMBINATIONS	91	223	1.4	88	346	1.4
UNCLASSIFIED DRUGS	92	201	1.2	101	262	1.0
EAR PREPARATIONS,ANTIBIOTICS	93	200	1.2	92	338	1.3
NASAL ANTIHISTAMINE	94	190	1.2	100	274	1.1
COLCHICINE	95	189	1.2	103	256	1.0
VAGINAL ANTIFUNGALS	96	188	1.2	99	279	1.1
VAGINAL ESTROGEN PREPARATIONS	97	188	1.2	97	305	1.2
VITAMIN B PREPARATIONS	98	187	1.2	116	210	0.8
KERATOLYTICS	99	187	1.2	110	238	0.9
ROSACEA AGENTS, TOPICAL	100	185	1.1	113	233	0.9

Note: OADs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins

Table 3. Proportion of Medical Records Identified and Acquired for Pancreatic Cancer and Thyroid Neoplasm by Cohort, Life Sciences Research Database[1]

	Pancreatic Cancer (N = 61)				Thyroid Cancer (N = 53)				Benign Thyroid Neoplasm (N = 38)			
	Exenatide (N = 11)		OAD (N = 50)		Exenatide (N = 12)		OAD (N = 41)		Exenatide (N = 11)		OAD (N = 27)	
	N	%	N	%	N	%	N	%	N	%	N	%
Identified in Claims Data	11	100	50	100	12	100	41	100	11	100	27	100
Retained after Profile Review (Charts Sought)	11	100	50	100	12	100	41	100	11	100	27	100
Charts Received	8	72.7	36	72.0	9	75.0	35	85.4	11	100	24	88.9

[1] Medical records were sought for all cases of pancreatic or thyroid cancer among patients in the study cohorts in the Life Sciences Research Database.

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, dipeptidyl peptidase-4 inhibitor, glucagon-like peptide-1 agonists, pramlintide, alpha-glucosidase inhibitors, and insulins.

Table 3.1. The Positive Predictive Value of Algorithm-Identified Cases Before and After Algorithm Refinement, Life Sciences Research Database

Algorithm-Identified Pancreatic Cancer	Cases		Positive Predictive Value	95% Confidence Interval
	Chart-Confirmed	Chart-Received		
Pancreatic Cancer				
Identified by Relaxed Algorithm[1]	26	44	0.59	(0.43 - 0.74)
Identified by Restrictive Algorithm	17	26	0.65	(0.44 - 0.83)
Identified by Revised Restrictive Algorithm[2*]	14	16	0.88	(0.62 - 0.98)
Thyroid Cancer (all)				
Identified by Relaxed Algorithm[1]	29	44	0.66	(0.50 - 0.80)
Identified by Restrictive Algorithm[*]	20	21	0.95	(0.76 - 1.00)
Non-Medullary Thyroid Cancer				
Identified by Relaxed Algorithm[1]	26	40	0.65	(0.48 - 0.79)
Identified by Restrictive Algorithm*	20	21	0.95	(0.76 - 1.00)
Medullary Thyroid Cancer				
Identified by Relaxed Algorithm[1*]	3	4	0.75	(0.19 - 0.99)
Identified by Restrictive Algorithm	0	0	-	-
Benign Thyroid Neoplasm				
Identified by Relaxed Algorithm[1]	28	35	0.80	(0.63 - 0.92)
Identified by Restrictive Algorithm*	11	12	0.92	(0.62 - 1.00)

[1] Inclusion of definite cases and probable cases from adjudication

[2] Revised restrictive algorithms with removal of history of selected types of cancers, including malignant neoplasms of the: esophagus, stomach, small intestine (including duodenum), colon, rectum, rectosigmoid junction, anus, liver and intrahepatic bile ducts, gallbladder and extrahepatic bile ducts, other and ill-defined sites within the digestive organs and peritoneum, trachea, bronchus, lung, other and ill-defined sites within the respiratory system and intrathoracic organs, connective and other soft tissue (abdomen), bladder, and other ill-defined sites (abdomen).

[*]Algorithms were used in the data analysis

Table 3.2. Description of Tumor Stage of Chart-Reviewed Outcomes by Cohorts, Life Sciences Research Database

Tumor Stage	Exenatide (N = 36)		OAD (N = 122)	
	N	%	N	%
Pancreatic Cancer	6	100	20	100
Stage I	0	0.0	0	0.0
Stage II	1	16.7	4	20.0
Stage III	2	33.3	2	10.0
Stage VI	1	16.7	8	40.0
Unknown	2	33.3	6	30.0
Thyroid Cancer	6	100	23	100
Stage I	3	50.0	12	52.2
Stage II	0	0.0	1	4.3
Stage III	1	16.7	1	4.3
Stage VI	1	16.7	3	13.0
Unknown	1	16.7	6	26.1
Non-Medullary Thyroid Cancer	6	100	20	100
Stage I	3	50.0	12	60.0
Stage II	0	0.0	1	5.0
Stage III	1	16.7	1	5.0
Stage VI	1	16.7	2	10.0
Unknown	1	16.7	4	20.0
Medullary Thyroid Cancer	0	0.0	3	100
Stage I	0	0.0	0	0.0
Stage II	0	0.0	0	0.0
Stage III	0	0.0	0	0.0
Stage VI	0	0.0	1	33.3
Unknown	0	0.0	2	66.7

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, dipeptidyl peptidase-4 inhibitor, glucagon-like peptide-1 agonists, pramlintide, alpha-glucosidase inhibitors, and insulins.

Table 3.3a. Prevalence of Pancreatic Disease and Diagnostic Procedures During the Follow-Up Period, Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonist Use, Life Sciences Research Database 6/1/2005−7/31/2010

Description	Exenatide		OAD	
	(N = 11,986)	%	(N= 17,603)	%
Pancreatic Diseases				
Abdominal pain	2,889	24.1	4,209	23.9
Other nonspecific abnormal serum enzyme levels	164	1.4	274	1.6
Malignant Neoplasm of Pancreas	17	0.1	27	0.2
Malignant Neoplasm of Head of Pancreas	6	0.1	8	0.0
Malignant Neoplasm of Body of Pancreas	4	0.0	4	0.0
Malignant Neoplasm of Tail of Pancreas	1	0.0	1	0.0
Malignant Neoplasm of Pancreatic Duct	1	0.0	1	0.0
Malignant Neoplasm of Islets of Langerhans	1	0.0	2	0.0
Malignant Neoplasm of Other Spec Sites of Pancreas	4	0.0	6	0.0
Malignant Neoplasm of Pancreas, Part Unspecified	16	0.1	21	0.1
Benign Neoplasm of the Pancreas (Excl)	12	0.1	14	0.1
Pancreatic Diagnostic Procedures				
Lipase	893	7.5	1,107	6.3
Amylase	861	7.2	1,083	6.2
Abdominal ultrasound	1,709	14.3	2,413	13.7
Biopsy of pancreas	3	0.0	2	0.0
Pancreatectomy	7	0.1	7	0.0
Endobronchial Ultrasound	4	0.0	4	0.0
Magnetic Resonance Imaging, abdomen	245	2.0	330	1.9
Magnetic Resonance cholangiopancreatography	2	0.0	2	0.0
Endoscopic retrograde cholangiopancreatography	47	0.4	68	0.4
Other operations on pancreas	3	0.0	6	0.0
X-ray for pancreas	84	0.7	115	0.7
Micro exam of pancreas	0	0.0	0	0.0
Appendectomy/Appendicitis	32	0.3	50	0.3

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins.

Table 3.3b. Prevalence of Pancreatic Diseases and Diagnostic Procedures During the Follow-Up Period, Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonist Use, Impact National Benchmark Databases 6/1/2005−7/31/2010

Description	Exenatide		OAD	
	(N = 6,959)	%	(N= 10,109)	%
Pancreatic Diseases				
Abdominal pain	1,504	21.6	2,181	21.6
Other nonspecific abnormal serum enzyme levels	72	1.0	97	1.0
Malignant Neoplasm of Pancreas	12	0.2	12	0.1
Malignant Neoplasm of Head of Pancreas	5	0.1	6	0.1
Malignant Neoplasm of Body of Pancreas	2	0.0	2	0.0
Malignant Neoplasm of Tail of Pancreas	3	0.0	0	0.0
Malignant Neoplasm of Pancreatic Duct	2	0.0	1	0.0
Malignant Neoplasm of Islets of Langerhans	0	0.0	1	0.0
Malignant Neoplasm of Other Spec Sites of Pancreas	6	0.1	4	0.0
Malignant Neoplasm of Pancreas, Part Unspecified	11	0.2	7	0.1
Benign Neoplasm of the Pancreas (Excl)	2	0.0	5	0.0
Pancreatic Diagnostic Procedures				
Lipase	514	7.4	676	6.7
Amylase	529	7.6	720	7.1
Abdominal ultrasound	1,018	14.6	1,410	13.9
Biopsy of pancreas	1	0.0	0	0.0
Pancreatectomy	3	0.0	5	0.0
Endobronchial Ultrasound	1	0.0	1	0.0
Magnetic Resonance Imaging, abdomen	124	1.8	201	2.0
Magnetic Resonance cholangiopancreatography	0	0.0	3	0.0
Endoscopic retrograde cholangiopancreatography	27	0.4	43	0.4
Other operations on pancreas	2	0.0	4	0.0
X-ray for pancreas	42	0.6	63	0.6
Micro exam of pancreas	0	0.0	0	0.0
Appendectomy/Appendicitis	31	0.4	30	0.3

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins.

Table 3.4a. Prevalence of Thyroid Diseases and Diagnostic Procedures During the Follow-Up Period, Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonist Use, Life Sciences Research Database 6/1/2005−7/31/2010

Description	Exenatide		OAD	
	(N = 11,980)	%	(N= 17,597)	%
Thyroid Diseases				
Malignant Neoplasm of Thyroid Gland	23	0.2	23	0.1
Benign Neoplasm of Thyroid Glands (OC)	17	0.1	27	0.2
Benign Neoplasm of Thyroid Glands (Excl)	49	0.4	68	0.4
Malignant Neoplasm of Thyroid Gland (Excl)	32	0.3	32	0.2
Thyroid Diagnostic Procedures				
Thyrotropin releasing hormone	5,611	46.8	7,569	43.0
T3, T4 testing	4,017	33.5	5,224	29.7
CT, soft tissue neck	171	1.4	287	1.6
Thyroid imaging	991	8.3	1,410	8.0
Ultrasound of head and neck	686	5.7	800	4.5
Biopsy thyroid	43	0.4	41	0.2
Thyroidectomy	51	0.4	64	0.4
Other operations on thyroid	4	0.0	5	0.0
Cancer chemotherapy	54	0.5	108	0.6
Therapeutic rediology	260	2.2	467	2.7
Radioiodine therapy	56	0.5	75	0.4
Calcitonin	16	0.1	17	0.1

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins.

Table 3.4b. Prevalence of Thyroid Diseases and Diagnostic Procedures During the Follow-Up Period, Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonist Use, Impact National Benchmark Databases 6/1/2005−7/31/2010

Description	Exenatide		OAD	
	(N = 6,954)	%	(N = 10,098)	%
Thyroid Diseases				
Malignant Neoplasm of Thyroid Gland	13	0.2	15	0.1
Benign Neoplasm of Thyroid Glands (OC)	8	0.1	18	0.2
Benign Neoplasm of Thyroid Glands (Excl)	28	0.4	53	0.5
Malignant Neoplasm of Thyroid Gland (Excl)	19	0.3	25	0.2
Thyroid Diagnostic Procedures				
Thyrotropin releasing hormone	3,208	46.1	4,388	43.5
T3, T4 testing	1,943	27.9	2,358	23.4
CT, soft tissue neck	110	1.6	136	1.3
Thyroid imaging	41	0.6	70	0.7
Ultrasound of head and neck	372	5.3	421	4.2
Biopsy thyroid	23	0.3	25	0.2
Thyroidectomy	28	0.4	32	0.3
Other operations on thyroid	1	0.0	3	0.0
Cancer chemotherapy	7	0.1	12	0.1
Therapeutic rediology	118	1.7	219	2.2
Radioiodine therapy	59	0.8	76	0.8
Calcitonin	8	0.1	10	0.1

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins.

Table 3.5. Comparison of Algorithm-Defined Cases Included in the Analysis by Chart Abstraction Status, Life Sciences Research Database 6/1/2005−7/31/2010

Chart Status	Algorithm-Identified[1] Cancer Outcome Included in the Analysis			
	Pancreatic Cancer		Thyroid Cancer	
	N	%	N	%
Confirmed Case	2	15.38	5	33.33
Not Confirmed Case	3	23.08	2	13.33
Chart Not Obtained	8	61.54	8	53.33

[1]Included cases met the revised restrictive algorithm for pancreatic cancer cases and the original restrictive algorithm for the thyroid cancer cases. These numbers do not include cases with DPP-4/GLP-1 use during the baseline period or cases occurring before 1 year of follow-up.

Table 4 (Revised). Incidence of Algorithm-identified Pancreatic Cancer Among Exenatide Initiators and Other Antidiabetes Drug Initiators (Overall and by Follow-Up Since Treatment Initiation)----Time-Fixed Analysis (Excluding People with Baseline DPP-4 Inhibitors/GLP-1 Receptor Agonist Use and/or Events and Person-time in the First Year after Drug Initiation)

Variables	Events	Person-years	IR	95% CI	Unadjusted[+]		Adjusted*	
					HR	95% CI	HR	95% CI
Life Sciences Research Database								
Overall[‡]								
Exenatide	7	20,300.2	0.3	(0.1 - 0.7)	1.5	(0.5 - 4.6)	1.4	(0.4 - 4.2)
OADs	6	29,865.6	0.2	(0.1 - 0.4)	Ref.		Ref.	
1 to <2 years								
Exenatide	4	9,691.9	0.4	(0.1 - 1.1)	1.2	(0.3 - 4.9)	1.1	(0.3 - 4.4)
OADs	4	14,033.3	0.3	(0.1 - 0.7)	Ref.		Ref.	
≥2 years to <3 years								
Exenatide	0	6,151.2	0.0	(0.0 - 0.5)	NC		NC	
OADs	1	8,774.6	0.1	(0.0 - 0.6)	Ref.		Ref.	
≥3 years								
Exenatide	3	4,457.1	0.7	(0.1 - 2.0)	5.1	(0.5 - 51.2)	6.0	(0.5 - 66.7)
OADs	1	7,057.7	0.1	(0.0 - 0.8)	Ref.		Ref.	
Impact National Benchmark Database								
Overall[‡]								
Exenatide	3	11,527.9	0.3	(0.1 - 0.8)	0.8	(0.2 - 3.4)	0.8	(0.2 - 3.6)
OADs	5	16,577.4	0.3	(0.1 - 0.7)	Ref.		Ref.	
1 to <2 years								
Exenatide	0	5,654.2	0.0	(0.0 - 0.5)	NC		NC	
OADs	4	8,147.3	0.5	(0.1 - 1.3)	Ref.		Ref.	
≥2 years to <3 years								
Exenatide	3	3,494.1	0.9	(0.2 - 2.5)	NC		NC	
OADs	0	4,923.5	0.0	(0.0 - 0.6)	Ref.		Ref.	
≥3 years								
Exenatide	0	2,379.7	0.0	(0.0 - 1.3)	NC		NC	
OADs	1	3,506.5	0.3	(0.0 - 1.6)	Ref.		Ref.	

Abbreviations: IR=Incidence rate per 1,000 person-years; HR= Hazard ratio; Ref.=Reference; NC= Not calculable.

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins.

[+]The unadjusted models are based on the propensity score matched cohorts, but do not adjust for any other variables.

*Adjusted for imbalanced variables, including cohort initiation in 2006, metformin, sulfonylureas, and/or thiazolidinediones use during the baseline period, number diabetes drug dispensings, days from the start of the initiation period until initiation date, and number of drugs dispensed.

[‡]The duration here is the time since one-year post drug initiation

Table 4a (Revised). Incidence of Algorithm-identified Pancreatic Cancer among Exenatide Initiators and Other Antidiabetes Drug Initiators Stratified By DPP-4 Inhibitor/GLP-1 Receptor Agonist Use in the Baseline Period----Time-Fixed Analysis (Sensitivity Analysis)

Variables	Events‡	Person-years	IR	95% CI	Unadjusted+		Adjusted*	
					HR	95% CI	HR	95% CI
Life Sciences Research Database								
Exenatide [1]	11	35,710.5	0.3	(0.2 - 0.6)	1.2	(0.5 - 2.8)	1.2	(0.5 - 2.8)
OADs Including DPP-4 Inhibitors/GLP-1 Agonists	12	50,754.1	0.2	(0.1 - 0.4)	Ref.		Ref.	
Exenatide [2]	7	20,300.2	0.3	(0.1 - 0.7)	1.5	(0.5 - 4.6)	1.4	(0.4 - 4.2)
OADs Excluding DPP-4 Inhibitors/GLP-1 Agonists	6	29,865.6	0.2	(0.1 - 0.4)	Ref.		Ref.	
Exenatide [2]	7	20,300.2	0.3	(0.1 - 0.7)	0.9	(0.2 - 4.0)	0.9	(0.2 - 4.0)
DPP-4 Initiators/GLP-1 Receptor Agonists	3	10,045.9	0.3	(0.1 - 0.9)	Ref.		Ref.	
Impact National Benchmark Database								
Exenatide [1]	3	17,922.4	0.2	(0.0 - 0.5)	0.4	(0.1 - 1.4)	0.4	(0.1 - 1.5)
OADs Including DPP-4 Inhibitors/GLP-1 Agonists	11	24,591.7	0.4	(0.2 - 0.8)	Ref.		Ref.	
Exenatide [2]	3	11,527.9	0.3	(0.1 - 0.8)	0.8	(0.2 - 3.4)	0.8	(0.2 - 3.6)
OADs Excluding DPP-4 Inhibitors/GLP-1 Agonists	5	16,577.4	0.3	(0.1 - 0.7)	Ref.		Ref.	
Exenatide [2]	3	11,527.9	0.3	(0.1 - 0.8)	0.2	(0.0 - 0.9)	0.2	(0.0 - 0.9)
DPP-4 Initiators/GLP-1 Receptor Agonists	4	3,840.6	1.0	(0.3 - 2.7)	Ref.		Ref.	

Abbreviations: IR=Incidence rate per 1,000 person-years; HR= Hazard ratio; Ref.=Reference. DPP-4/GLP-1=Dipeptidyl peptidase-4 inhibitor/Glucagon-like peptide-1 agonists; NC= Not calculable.

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins.

+The unadjusted models are based on the propensity score matched cohorts, but do not adjust for any other variables.

*Adjusted for imbalanced variables, including cohort initiation in 2006, metformin, sulfonylureas, and/or thiazolidinediones use during the baseline period, number diabetes drug dispensings, days from the start of the initiation period until initiation date, and number of drugs dispensed

‡Assessing events one year after drug initiation

[1] Exenatide compared with OADs including DPP-4 Inhibitors/GLP-1Agonists

[2] Exenatide compared with OADs excluding DPP-4 Inhibitors/GLP-1Agonists and compared with DPP-4 inhibitors/GLP-1 receptor agonists only

Table 4b (Revised). Incidence of Algorithm-identified Pancreatic Cancer Among Exenatide Initiators and Other Antidiabetic Drug Initiators (Overall and by Follow-Up Since Treatment Initiation)----Intent-to-Treat Analysis (Excluding People with Baseline DPP-4 Inhibitor/GLP-1 Receptor Agonist Use and/or Events and Person-time in the First Six Months after Drug Initiation)

Variables	Events	Person-years	IR	95% CI	Unadjusted[+]		Adjusted*	
					HR	95% CI	HR	95% CI
Life Sciences Research Database								
Overall[‡]								
Exenatide	9	26,896.6	0.3	(0.2 - 0.6)	0.9	(0.4 - 2.2)	0.9	(0.4 - 2.1)
OADs	13	39,646.3	0.3	(0.2 - 0.6)	Ref.		Ref.	
>0 to 6 months[§]								
Exenatide	5	7,901.4	0.6	(0.2 - 1.5)	1.1	(0.3 - 3.5)	1.1	(0.3 - 3.4)
OADs	7	12,045.9	0.6	(0.2 - 1.2)	Ref.		Ref.	
>6 months to < 1 year**								
Exenatide	2	6,596.4	0.3	(0.0 - 1.1)	0.4	(0.1 - 2.0)	0.4	(0.1 - 1.9)
OADs	7	9,780.7	0.7	(0.3 - 1.5)	Ref.		Ref.	
1 to < 2 years								
Exenatide	4	9,691.9	0.4	(0.1 - 1.1)	1.2	(0.3 - 4.9)	1.1	(0.3 - 4.4)
OADs	4	14,033.3	0.3	(0.1 - 0.7)	Ref.		Ref.	
2 to < 3 years								
Exenatide	0	6,151.2	0.0	(0.0 - 0.5)	NC		NC	
OADs	1	8,774.6	0.1	(0.0 - 0.6)	Ref.		Ref.	
≥ 3 years								
Exenatide	3	4,457.1	0.7	(0.1 - 2.0)	5.1	(0.5 - 51.2)	6.0	(0.5 - 66.7)
OADs	1	7,057.7	0.1	(0.0 - 0.8)	Ref.		Ref.	
Impact National Benchmark Database								
Overall[‡]								
Exenatide	3	15,339.2	0.2	(0.0 - 0.6)	0.6	(0.1 - 2.2)	0.6	(0.1 - 2.3)
OADs	7	22,166.9	0.3	(0.1 - 0.7)	Ref.		Ref.	
>0 to 6 months[§]								
Exenatide	1	4,631.0	0.2	(0.0 - 1.2)	0.5	(0.0 - 5.3)	0.7	(0.1 - 7.4)
OADs	2	6,960.0	0.3	(0.0 - 1.0)	Ref.		Ref.	
>6 months to < 1 year**								
Exenatide	0	3,811.3	0.0	(0.0 - 0.8)	NC		NC	
OADs	2	5,589.5	0.4	(0.0 - 1.3)	Ref.		Ref.	
1 to < 2 years								
Exenatide	0	5,654.2	0.0	(0.0 - 0.5)	NC		NC	
OADs	4	8,147.3	0.5	(0.1 - 1.3)	Ref.		Ref.	
2 to < 3 years								
Exenatide	3	3,494.1	0.9	(0.2 - 2.5)	NC		NC	
OADs	0	4,923.5	0.0	(0.0 - 0.6)	Ref.		Ref.	

Table 4b (Revised). Incidence of Algorithm-identified Pancreatic Cancer Among Exenatide Initiators and Other Antidiabetic Drug Initiators (Overall and by Follow-Up Since Treatment Initiation)----Intent-to-Treat Analysis (Excluding People with Baseline DPP-4 Inhibitor/GLP-1 Receptor Agonist Use and/or Events and Person-time in the First Six Months after Drug Initiation)

Variables	Events	Person-years	IR	95% CI	Unadjusted[+]		Adjusted*	
					HR	95% CI	HR	95% CI
≥ 3 years								
Exenatide	0	2,379.7	0.0	(0.0 - 1.3)	NC		NC	
OADs	1	3,506.5	0.3	(0.0 - 1.6)	Ref.		Ref.	

Abbreviations: IR=Incidence rate per 1,000 person-years; HR= Hazard ratio; Ref.=Reference; NC= Not calculable.

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins.

[+]The unadjusted models are based on the propensity score matched cohorts, but do not adjust for any other variables.

*Adjusted for imbalanced variables, including cohort initiation in 2006, metformin, sulfonylureas, and/or thiazolidinediones use during the baseline period, number diabetes drug dispensings, days from the start of the initiation period until initiation date, and number of drugs dispensed

[‡]The follow-up excludes events and person-time within six-months post-drug initiation.

[§]Includes events and person-time in the first six months after drug initiation. These events and person-time are not included in the calculation of the "Overall" IRs and HRs.

**Excludes events and person-time in the first six months after drug initiation.

Table 5 (Revised). Incidence of Algorithm-identified Thyroid Cancer among Exenatide Initiators and Other Antidiabetes Drug Initiators (Overall and by Follow-Up Since Treatment Initiation)----Time-Fixed Analysis (Excluding People with Baseline DPP-4 Inhibitors/GLP-1 Receptor Agonist Use and/or Events and Person-time in the First Year after Drug Initiation)

	Events	Person-years	IR	95% CI	Unadjusted+		Adjusted*	
					HR	95% CI	HR	95% CI
Life Sciences Research Database								
Overall‡								
Exenatide	8	20,288.7	0.4	(0.2 - 0.8)	1.8	(0.6 - 5.0)	2.0	(0.7 - 5.6)
OADs	7	29,856.5	0.2	(0.1 - 0.5)	Ref.		Ref.	
1 to <2 years								
Exenatide	3	9,693.2	0.3	(0.1 - 0.9)	1.0	(0.2 - 4.7)	1.1	(0.2 - 5.1)
OADs	4	14,030.0	0.3	(0.1 - 0.7)	Ref.		Ref.	
≥2 years to <3 years								
Exenatide	3	6,146.6	0.5	(0.1 - 1.4)	2.5	(0.4 - 15.6)	2.7	(0.4 - 17.7)
OADs	2	8,770.9	0.2	(0.0 - 0.8)	Ref.		Ref.	
≥3 years								
Exenatide	2	4,449.0	0.4	(0.1 - 1.6)	3.6	(0.3 - 41.3)	3.7	(0.3 - 43.7)
OADs	1	7,055.6	0.1	(0.0 - 0.8)	Ref.		Ref.	
Impact National Benchmark Database								
Overall‡								
Exenatide	8	11,515.5	0.7	(0.3 - 1.4)	1.3	(0.5 - 3.3)	1.3	(0.5 - 3.4)
OADs	9	16,556.1	0.5	(0.2 - 1.0)	Ref.		Ref.	
1 to <2 years								
Exenatide	3	5,648.5	0.5	(0.1 - 1.6)	0.6	(0.2 - 2.4)	0.6	(0.2 - 2.5)
OADs	7	8,141.5	0.9	(0.3 - 1.8)	Ref.		Ref.	
≥2 years to <3 years								
Exenatide	3	3,490.2	0.9	(0.2 - 2.5)	1.9	(0.3 - 11.7)	1.9	(0.3 - 12.0)
OADs	2	4,916.3	0.4	(0.0 - 1.5)	Ref.		Ref.	
≥3 years								
Exenatide	2	2,376.9	0.8	(0.1 - 3.0)	NC		NC	
OADs	0	3,498.3	0.0	(0.0 - 0.9)	Ref.		Ref.	

Abbreviations: IR=Incidence rate per 1,000 person-years; HR= Hazard ratio; Ref.=Reference; NC= Not calculable.

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins.

+The unadjusted models are based on the propensity score matched cohorts, but do not adjust for any other variables.

*Adjusted for imbalanced variables, including South census region, cohort initiation in 2005, metformin, sulfonylureas, and/or thiazolidinediones use during the baseline period, and number of drugs dispensed

‡The duration here is the time since one-year post drug initiation

Table 5a (Revised). Incidence of Algorithm-identified Thyroid Cancer among Exenatide Initiators and Other Antidiabetes Drug Initiators Stratified By DPP-4 Inhibitor/GLP-1 Receptor Agonist Use in the Baseline Period----Time-Fixed Analysis (Sensitivity Analysis)

Variables	Events†	Person-years	IR	95% CI	Unadjusted+		Adjusted*	
					HR	95% CI	HR	95% CI
Life Sciences Research Database								
Exenatide [1]	13	35,691.7	0.4	(0.2 - 0.6)	1.3	(0.6 - 2.8)	1.3	(0.6 - 2.8)
OADs Including DPP-4 Inhibitors/GLP-1 Receptor Agonists	15	50,736.3	0.3	(0.2 - 0.5)	Ref.		Ref.	
Exenatide [2]	8	20,288.7	0.4	(0.2 - 0.8)	1.8	(0.6 - 5.0)	2.0	(0.7 - 5.6)
OADs Excluding DPP-4 Inhibitors/GLP-1 Receptor Agonists	7	29,856.5	0.2	(0.1 - 0.5)	Ref.		Ref.	
Exenatide [2]	8	20,288.7	0.4	(0.2 - 0.8)	0.9	(0.3 - 3.1)	0.9	(0.3 - 3.1)
DPP-4 Initiators/GLP-1 Receptor Agonists	4	10,043.7	0.4	(0.1 - 1.0)	Ref.		Ref.	
Impact National Benchmark Database								
Exenatide [1]	11	17,905.1	0.6	(0.3 - 1.1)	1.0	(0.5 - 2.3)	1.0	(0.5 - 2.3)
OADs Including DPP-4 Inhibitors/GLP-1 Receptor Agonists	14	24,562.8	0.6	(0.3 - 1.0)	Ref.		Ref.	
Exenatide [2]	8	11,515.5	0.7	(0.3 - 1.4)	1.3	(0.5 - 3.3)	1.3	(0.5 - 3.4)
OADs Excluding DPP-4 Inhibitors/GLP-1 Receptor Agonists	9	16,556.1	0.5	(0.2 - 1.0)	Ref.		Ref.	
Exenatide [2]	8	11,515.5	0.7	(0.3 - 1.4)	1.1	(0.2 - 5.3)	1.1	(0.2 - 5.3)
DPP-4 Initiators/GLP-1 Receptor Agonists	2	3,838.1	0.5	(0.1 - 1.9)	Ref.		Ref.	

Abbreviations: IR=Incidence rate per 1,000 person-years; HR= Hazard ratio; Ref.=Reference. DPP-4 Inhibitors/GLP-1 Receptor Agonists=Dipeptidyl peptidase-4

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins.

+The unadjusted models are based on the propensity score matched cohorts, but do not adjust for any other variables.

*Adjusted for imbalanced variables, including South census region, cohort initiation in 2005, metformin, sulfonylureas, and/or thiazolidinediones use during the baseline period, and number of drugs dispensed

†Assessing events one year after drug initiation

[1] Exenatide compared with OADs including DPP-4 inhibitors/GLP-1 agonists

[2] Exenatide compared with OADs excluding DPP-4 inhibitors/GLP-1 agonists

Table 5b (Revised). Incidence of Algorithm-identified Thyroid Cancer among Exenatide Initiators and Other Antidiabetic Drug Initiators (Overall and by by Follow-Up Since Treatment Initiation)----Intent-to-Treat Analysis (Excluding People with Baseline DPP-4 Inhibitor/GLP-1 Receptor Agonist Use and/or Events and Person-time in the First Six Months after Drug Initiation)

Variables	Events	Person-years	IR	95% CI	Unadjusted+		Adjusted*	
					HR	95% CI	HR	95% CI
Life Sciences Research Database								
Overall‡								
Exenatide	13	26,885.2	0.5	(0.3 - 0.8)	2.2	(0.9 - 5.2)	2.3	(1.0 - 5.5)
OADs	9	39,638.4	0.2	(0.1 - 0.4)	Ref.		Ref.	
>0 to 6 months§								
Exenatide	1	7,902.2	0.1	(0.0 - 0.7)	0.3	(0.0 - 2.8)	0.4	(0.0 - 3.6)
OADs	4	12,046.9	0.3	(0.1 - 0.9)	Ref.		Ref.	
>6 months to < 1 year**								
Exenatide	5	6,596.5	0.8	(0.2 - 1.8)	3.6	(0.7 - 19.1)	3.5	(0.7 - 18.5)
OADs	2	9,782.0	0.2	(0.0 - 0.7)	Ref.		Ref.	
1 to < 2 years								
Exenatide	3	9,693.2	0.3	(0.1 - 0.9)	1.0	(0.2 - 4.7)	1.1	(0.2 - 5.1)
OADs	4	14,030.0	0.3	(0.1 - 0.7)	Ref.		Ref.	
2 to < 3 years								
Exenatide	3	6,146.6	0.5	(0.1 - 1.4)	2.5	(0.4 - 15.6)	2.7	(0.4 - 17.7)
OADs	2	8,770.9	0.2	(0.0 - 0.8)	Ref.		Ref.	
3 to < 4 years								
Exenatide	2	4,449.0	0.4	(0.1 - 1.6)	3.6	(0.3 - 41.3)	3.7	(0.3 - 43.7)
OADs	1	7,055.6	0.1	(0.0 - 0.8)	Ref.		Ref.	
Impact National Benchmark Database								
Overall‡								
Exenatide	9	15,324.3	0.6	(0.3 - 1.1)	0.8	(0.4 - 1.9)	0.9	(0.4 - 2.1)
OADs	15	22,143.0	0.7	(0.4 - 1.1)	Ref.		Ref.	
>0 to 6 months§								
Exenatide	6	4,629.3	1.3	(0.5 - 2.8)	1.5	(0.5 - 4.7)	1.4	(0.5 - 4.6)
OADs	6	6,958.3	0.9	(0.3 - 1.9)	Ref.		Ref.	
>6 months to < 1 year**								
Exenatide	1	3,808.8	0.3	(0.0 - 1.5)	0.2	(0.0 - 1.9)	0.3	(0.0 - 2.4)
OADs	6	5,586.9	1.1	(0.4 - 2.3)	Ref.		Ref.	
1 to < 2 years								
Exenatide	3	5,648.5	0.5	(0.1 - 1.6)	0.6	(0.2 - 2.4)	0.6	(0.2 - 2.5)
OADs	7	8,141.5	0.9	(0.3 - 1.8)	Ref.		Ref.	
2 to < 3 years								
Exenatide	3	3,490.2	0.9	(0.2 - 2.5)	1.9	(0.3 - 11.7)	1.9	(0.3 - 12.0)
OADs	2	4,916.3	0.4	(0.0 - 1.5)	Ref.		Ref.	

Table 5b (Revised). Incidence of Algorithm-identified Thyroid Cancer among Exenatide Initiators and Other Antidiabetic Drug Initiators (Overall and by by Follow-Up Since Treatment Initiation)----Intent-to-Treat Analysis (Excluding People with Baseline DPP-4 Inhibitor/GLP-1 Receptor Agonist Use and/or Events and Person-time in the First Six Months after Drug Initiation)

Variables	Events	Person-years	IR	95% CI	Unadjusted[+]		Adjusted*	
					HR	95% CI	HR	95% CI
3 to < 4 years								
Exenatide	2	2,376.9	0.8	(0.1 - 3.0)	NC		NC	
OADs	0	3,498.3	0.0	(0.0 - 0.9)	Ref.		Ref.	

Abbreviations: IR=Incidence rate per 1,000 person-years; HR= Hazard ratio; Ref.=Reference; NC= Not calculable.

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors,

[+]The unadjusted models are based on the propensity score matched cohorts, but do not adjust for any other variables.

*Adjusted for imbalanced variables, including cohort initiation in 2006, metformin, sulfonylureas, and/or thiazolidinediones use during the baseline period,

[‡]The follow-up excludes events and person-time within six-months post-drug initiation.

[§]Includes events and person-time in the first six months after drug initiation. These events and person-time are not included in the calculation of the "Overall" IRs and HRs.

**Excludes events and person-time in the first six months after drug initiation.

Table 6.1a. Incidence of Algorithm-identified Benign Thyroid Neoplasm among Exenatide Initiators and Other Antidiabetes Drugs (OADs) Initiators----Time-Fixed Analysis Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonists Use and/or Events and Person-time in the First Year after Drug Initiation)

Variables	Events	Person-years	IR	95% CI	Unadjusted[+]		Adjusted*	
					HR	95% CI	HR	95% CI
Life Sciences Research Database								
Exenatide	4	20,307.2	0.2	(0.1 - 0.5)	1.6	(0.4 - 6.5)	1.4	(0.3 - 5.7)
OADs	4	29,864.3	0.1	(0.0 - 0.3)	Ref.		Ref.	
Impact National Benchmark Database								
Exenatide	1	11,531.8	0.1	(0.0 - 0.5)	0.8	(0.1 - 8.6)	0.5	(0.0 - 5.7)
OADs	2	16,578.7	0.1	(0.0 - 0.4)	Ref.		Ref.	

Abbreviations: IR=Incidence rate per 1,000 person-years; HR= Hazard ratio

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins.

[+]The unadjusted models are based on the propensity score matched cohorts, but do not adjust for any other variables.

*Adjusted for imbalanced variables, including South census region, cohort initiation in 2005, metformin, sulfonylureas, and/or thiazolidinediones use during the baseline period, and number of drugs dispensed

Table 6.1b. Incidence of Algorithm-identified Medullary Thyroid Cancer among Exenatide Initiators and Other Antidiabetes Drugs (OADs) Initiators ----Time-Fixed Analysis (Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonists Use and/or Events and Person-time in the First Year after Drug Initiation)

Variables	Events	Person-years	IR	95% CI
Life Sciences Research Database				
Exenatide	0	20,312.0	0.0	(0.0 - 0.1)
OADs	2	29,872.6	0.1	(0.0 - 0.2)
Impact National Benchmark Database				
Exenatide	0	11,533.1	0.0	(0.0 - 0.3)
OADs	0	16,586.4	0.0	(0.0 - 0.2)

Abbreviations: IR=Incidence rate per 1,000 person-years; HR= Hazard ratio

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins.

Table 6.1c. Incidence of Algorithm-identified Non-Medullary Thyroid Cancer Among Exenatide Initiators and Other Antidiabetes Drugs (OADs) Initiators----Time-Fixed Analysis (Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonists Use and/or Events and Person-time in the First Year after Drug Initiation)

Variables	Events	Person-years	IR	95% CI
Life Sciences Research Database				
Exenatide	8	20,288.7	0.4	(0.2 - 0.8)
OADs	5	29,859.8	0.2	(0.1 - 0.4)
Impact National Benchmark Database				
Exenatide	8	11,515.5	0.7	(0.3 - 1.4)
OADs	9	16,556.1	0.5	(0.2 - 1.0)

Abbreviations: IR=Incidence rate per 1,000 person-years; HR= Hazard ratio

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins.

Table 6.2a Incidence of Algorithm-identified Pancreatic Cancer Among Patients with Concurrent Use of Exenatide and Insulins and Among Patients with/without Concurrent Use of Comparators and Insulins----Time-Fixed Analysis (Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonists Use and/or Events and Person-time in the First Year after Drug Initiation)

Variables	Number of Patients in the Category	Events	Person-years	IR	95% CI
Life Sciences Research Database					
Concurrent Use of Exenatide and Insulins	2,403	0	4,214.5	0.00	(0.00 - 0.71)
Exenatide without Concurrent Use of Insulins	9,583	7	16,085.7	0.44	(0.17 - 0.90)
Concurrent Use of OADs and Insulins	9,133	4	15,048.7	0.27	(0.07 - 0.68)
OADs without Concurrent Use of Insulins	8,470	2	14,816.8	0.13	(0.02 - 0.49)
Impact National Benchmark Database					
Concurrent Use of Exenatide and Insulins	1,423	0	2,355.6	0.00	(0.00 - 1.27)
Exenatide without Concurrent Use of Insulins	5,536	3	9,172.3	0.33	(0.07 - 0.96)
Concurrent Use of OADs and Insulins	5,333	2	8,705.0	0.23	(0.03 - 0.83)
OADs without Concurrent Use of Insulins	4,776	3	7,872.3	0.38	(0.08 - 1.11)

Abbreviations: IR=Incidence rate per 1,000 person-years

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins.

Table 6.2b Incidence of Algorithm-identified Thyroid Cancer Among Patients with Concurrent Use of Exenatide and Insulins and Among Patients with/without Concurrent Use of Comparators and Insulins ----Time-Fixed Analysis (Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonists Use and/or Events and Person-time in the First Year after Drug Initiation)

Variables	Number of Patients in the Category	Events	Person-years	IR	95% CI
Life Sciences Research Database					
Concurrent Use of Exenatide and Insulins	2,404	1	4,212.5	0.24	(0.01 - 1.32)
Exenatide without Concurrent Use of Insulins	9,582	7	16,076.3	0.44	(0.18 - 0.90)
Concurrent Use of OADs and Insulins	9,134	3	15,045.2	0.20	(0.04 - 0.58)
OADs without Concurrent Use of Insulins	8,471	4	14,811.3	0.27	(0.07 - 0.69)
Impact National Benchmark Database					
Concurrent Use of Exenatide and Insulins	1,422	2	2,354.0	0.85	(0.10 - 3.07)
Exenatide without Concurrent Use of Insulins	5,532	6	9,161.5	0.65	(0.24 - 1.43)
Concurrent Use of OADs and Insulins	5,326	3	8,694.4	0.35	(0.07 - 1.01)
OADs without Concurrent Use of Insulins	4,774	6	7,861.8	0.76	(0.28 - 1.66)

Abbreviations: IR=Incidence rate per 1,000 person-years

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins.

Table 7. Incidence of Algorithm-identified Pancreatic Cancer Among Exenatide Initiators and Other Antidiabetes Drugs Initiators by Cumulative Duration of Exenatide Use---Analysis of Cumulative Duration (Excluding Events in the First Year After Drug Initiation)

Variables	Events	Person-years	IR	95% CI	Unadjusted*		Adjusted+	
					RR	95% CI	RR	95% CI
Life Sciences Research Database								
Non-Use	6	29,750.9	0.2	(0.1 -0.4)	Ref.		Ref.	
0 < 1 years	4	10,383.5	0.4	(0.1 - 1.0)	1.9	(0.5 - 6.8)	1.6	(0.4 - 5.6)
1 to < 2 years	2	6,583.4	0.3	(0.0 - 1.1)	1.5	(0.3 - 7.5)	1.3	(0.3 - 6.4)
≥ 2 years to <3 years	1	2,301.7	0.4	(0.0 - 2.4)	2.2	(0.3 - 17.9)	1.7	(0.2 - 14.8)
≥ 3 years	0	1,031.6	0.0	(0.0 - 2.9)	0.0		0.0	
P-value for trend					0.6		0.8	
Impact National Benchmark Database								
Non-Use	5	16,527.2	0.3	(0.1 - 0.7)	Ref.		Ref.	
0 < 1 years	1	5,313.0	0.2	(0.0 - 1.1)	0.6	(0.1 - 5.3)	0.6	(0.1 - 5.3)
1 to < 2 years	0	4,027.2	0.0	(0.0 - 0.7)	0.0		0.0	
≥ 2 years to <3 years	2	1,485.7	1.4	(0.2 - 4.9)	4.5	(0.9 - 22.9)	4.3	(0.8 - 23.3)
≥ 3 years	0	702.1	0.0	(0.0 - 4.3)	0.0		0.0	
P-value for trend					0.7		0.7	

Abbreviations: IR=Incidence rate per 1,000 person-years; HR= Hazard ratio; Ref.=Reference.

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins.

*The unadjusted models are based on the propensity score matched cohorts, but do not adjust for any other variables.

+Adjusted for time-varying OADs status

Table 8 Incidence of Algorithm-identified Thyroid Cancer Among Exenatide Initiators and Other Antidiabetes Drugs (OADs) Initiators by Cumulative Duration of Exenatide Use---Analysis of Cumulative Duration (Excluding Events in the First Year After Drug Initiation)

Variables	Events	Person-years	IR	95% CI	Unadjusted*		Adjusted+	
					RR	95% CI	RR	95% CI
Life Sciences Research Database								
Non-Use	7	29,742.7	0.2	(0.1 - 0.5)	Ref.		Ref.	
0 < 1 years	4	10,379.2	0.4	(0.1 - 1.0)	1.6	(0.5 - 5.6)	1.7	(0.5 - 5.9)
1 to < 2 years	3	6,577.9	0.5	(0.1 - 1.3)	1.9	(0.5 - 7.5)	1.8	(0.5 - 7.3)
≥ 2 years to <3 years	1	2,300.7	0.4	(0.0 - 2.4)	1.9	(0.2 - 15.0)	1.8	(0.2 - 14.6)
≥ 3 years	0	1,031.0	0.0	(0.0 - 2.9)	0.0		0.0	
P-value for trend					0.5		0.6	
Impact National Benchmark Database								
Non-Use	9	16,511.9	0.6	(0.3 - 1.0)	Ref.		Ref.	
0 < 1 years	5	5,302.8	0.9	(0.3 - 2.2)	1.7	(0.6 - 5.2)	1.6	(0.5 - 4.9)
1 to < 2 years	3	4,020.9	0.8	(0.2 - 2.2)	1.4	(0.4 - 5.1)	1.3	(0.4 - 5.0)
≥ 2 years to <3 years	0	1,489.8	0.0	(0.0 - 2.0)	0.0		0.0	
≥ 3 years	0	702.1	0.0	(0.0 - 4.3)	0.0		0.0	
P-value for trend					0.7		0.6	

Abbreviations: IR=Incidence rate per 1,000 person-years; HR= Hazard ratio; Ref.=Reference.

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins.

*The unadjusted models are based on the propensity score matched cohorts, but do not adjust for any other variables.

+Adjusted for time-varying OADs status

Table 9 Incidence of Algorithm-identified Pancreatic Cancer Among Exenatide Initiators and Other Antidiabetes Drugs (OADs) Initiators by Cumulative Dose of Exenatide Use---Analysis of Cumulative Duration (Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonists Use and/or Events and Person-time in the First Year after Drug Initiation)

Variables	Events	Person-years	IR	95% CI	Unadjusted*		Adjusted+	
					RR	95% CI	RR	95% CI
Life Sciences Research Database								
Non-Use	6	29,750.9	0.2	(0.1 - 0.4)	Ref.		Ref.	
0 - 1,499 mcg	1	5,065.8	0.2	(0.0 - 1.1)	1.0	(0.1 - 8.1)	0.8	(0.1 - 6.9)
1,500 - 5,999 mcg	3	6,209.3	0.5	(0.1 - 1.4)	2.4	(0.6 - 9.6)	1.9	(0.5 - 7.9)
6,000+ mcg	3	9,025.1	0.3	(0.1 - 1.0)	1.7	(0.4 - 6.6)	1.4	(0.3 - 5.7)
P-value for trend					0.3		0.5	
Impact National Benchmark Database								
Non-Use	5	16,527.2	0.3	(0.1 - 0.7)	Ref.		Ref.	
0 - 1,499 mcg	0	2,515.2	0.0	(0.0 - 1.2)	0.0		0.0	
1,500 - 5,999 mcg	1	3,613.2	0.3	(0.0 - 1.5)	0.9	(0.1 - 7.8)	0.9	(0.1 - 8.0)
6,000+ mcg	2	5,399.6	0.4	(0.0 - 1.3)	1.2	(0.2 - 6.3)	1.1	(0.2 - 6.1)
P-value for trend					0.9		0.9	

Abbreviations: IR=Incidence rate per 1,000 person-years; RR= Relative Risk; Ref.=Reference; NC= Not calculable.

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins.

*The unadjusted models are based on the propensity score matched cohorts, but do not adjust for any other variables.

+Adjusted for time-varying OADs status

Table 10 Incidence of Algorithm-identified Thyroid Cancer Among Exenatide Initiators and Other Antidiabetes Drugs (OADs) Initiators by Cumulative Dose of Exenatide Use---Analysis of Cumulative Duration (Excluding People with Baseline DDP-4 Inhibitors/GLP-1 Receptor Agonists Use and/or Events and Person-time in the First Year after Drug Initiation)

Variables	Events	Person-years	IR	95% CI	Unadjusted*		Adjusted+	
					RR	95% CI	RR	95% CI
Life Sciences Research Database								
Non-Use	7	29,742.7	0.2	(0.1 - 0.5)	Ref.		Ref.	
0 - 1,499 mcg	2	5,062.3	0.4	(0.1 - 1.4)	1.7	(0.4 - 8.1)	1.8	(0.4 - 8.7)
1,500 - 5,999 mcg	3	6,209.5	0.5	(0.1 - 1.4)	2.1	(0.5 - 7.9)	2.1	(0.5 - 8.2)
6,000+ mcg	3	9,016.9	0.3	(0.1 - 1.0)	1.4	(0.4 - 5.5)	1.3	(0.3 - 5.3)
P-value for trend					0.4		0.5	
Impact National Benchmark Database								
Non-Use	9	16,511.9	0.5	(0.3 - 1.0)	Ref.		Ref.	
0 - 1,499 mcg	2	2,506.8	0.8	(0.1 - 2.9)	1.5	(0.3 - 6.8)	1.4	(0.3 - 6.4)
1,500 - 5,999 mcg	3	3,610.0	0.8	(0.2 - 2.4)	1.5	(0.4 - 5.6)	1.4	(0.4 - 5.4)
6,000+ mcg	3	5,398.7	0.6	(0.1 - 1.6)	1.0	(0.3 - 3.8)	1.0	(0.3 - 3.7)
P-value for trend					1.0		0.9	

Abbreviations: IR=Incidence rate per 1,000 person-years; HR= Hazard ratio; Ref.=Reference.

Note: OADs=Other antidiabetes drugs include metformin, thiazolidinediones, sulfonylureas, non-sulfonylureas, pramlintide, alpha-glucosidase inhibitors, and insulins.

*The unadjusted models are based on the propensity score matched cohorts, but do not adjust for any other variables.

+Adjusted for time-varying OADs status

8. Figures

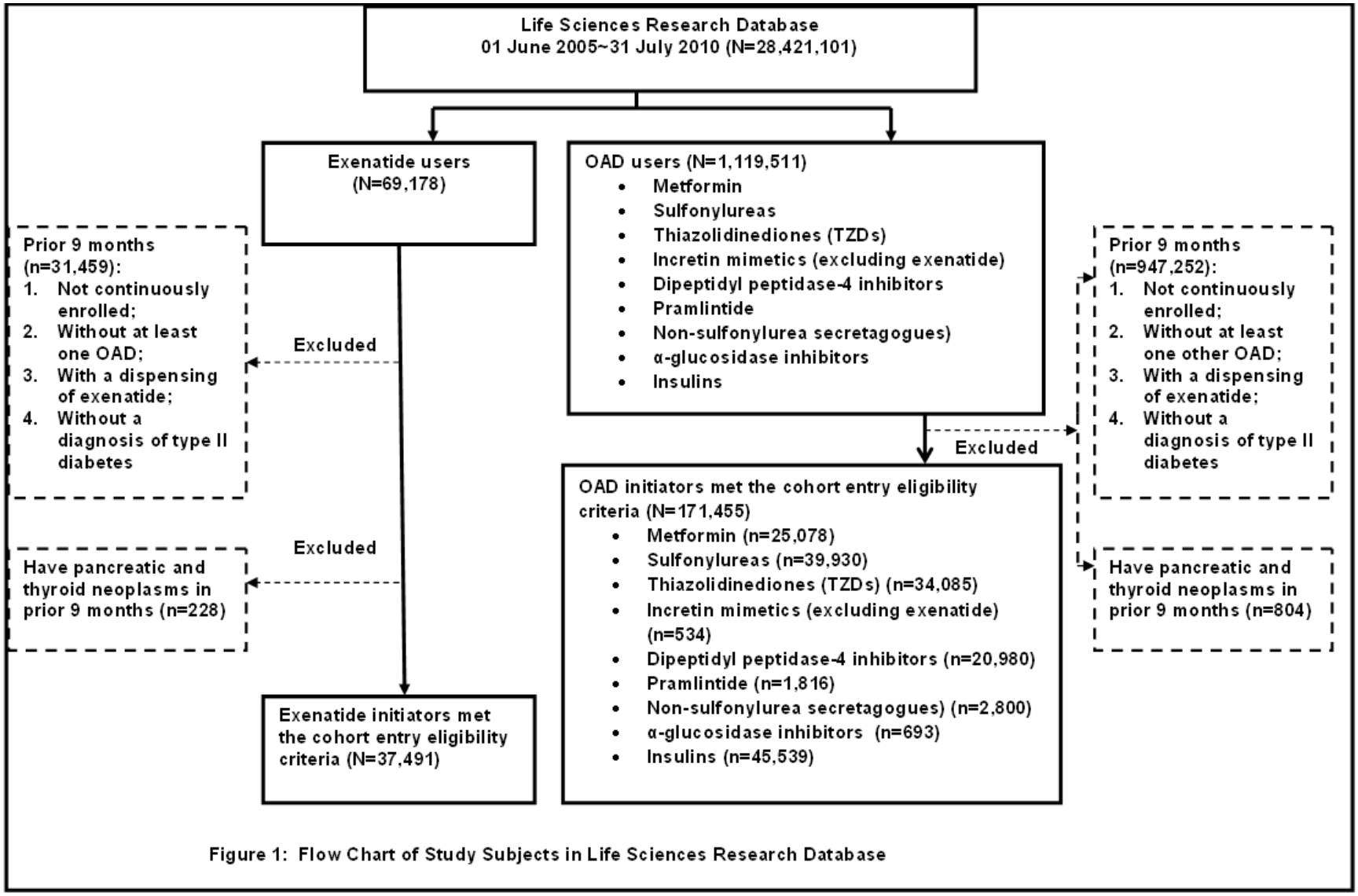


Figure 1: Flow Chart of Study Subjects in Life Sciences Research Database

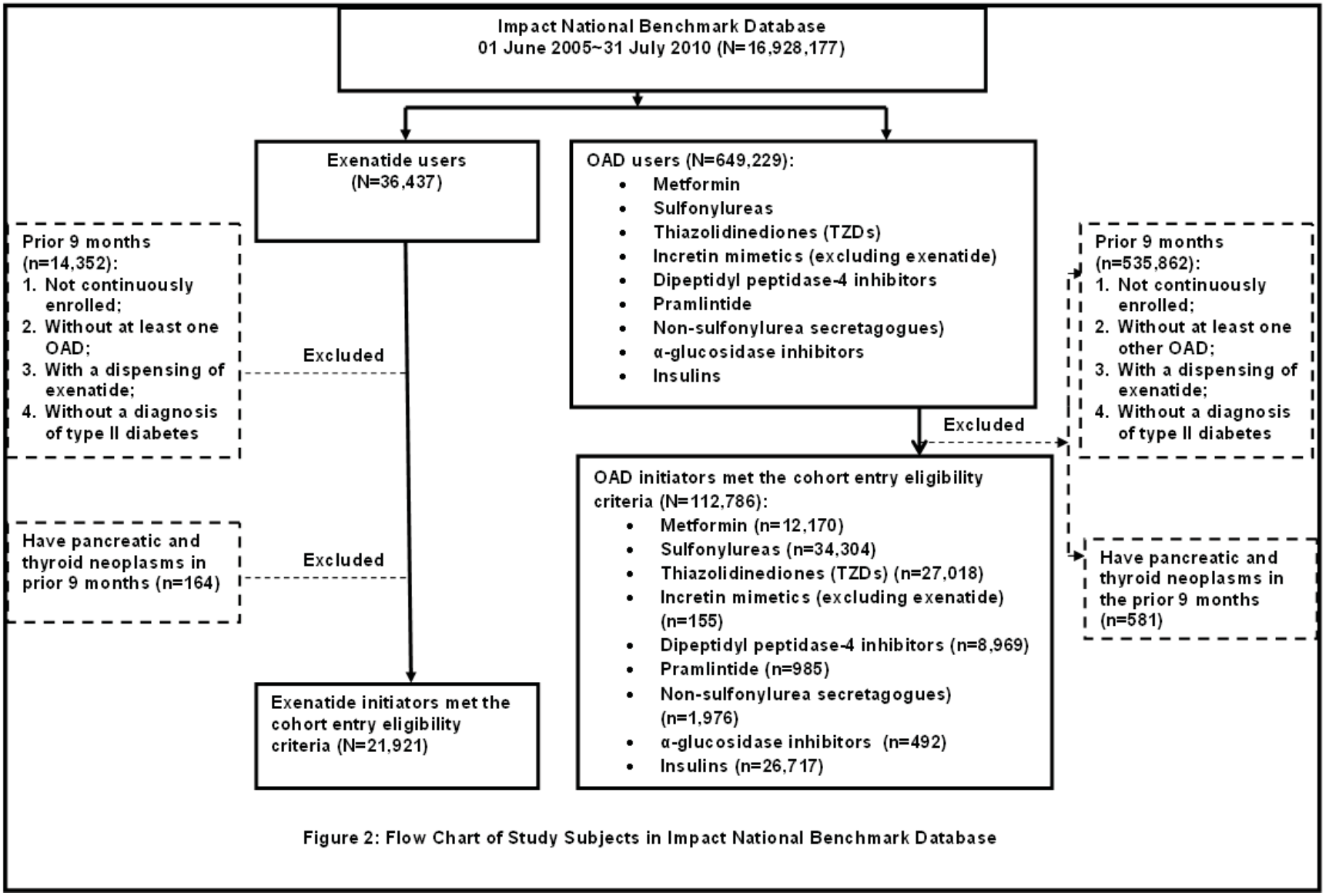


Figure 2: Flow Chart of Study Subjects in Impact National Benchmark Database

Figure 3a. Survival Plot for Time to Algorithm–identified Pancreatic Cancer Initiating Stratified by Drug Cohort – Life Sciences Research Database

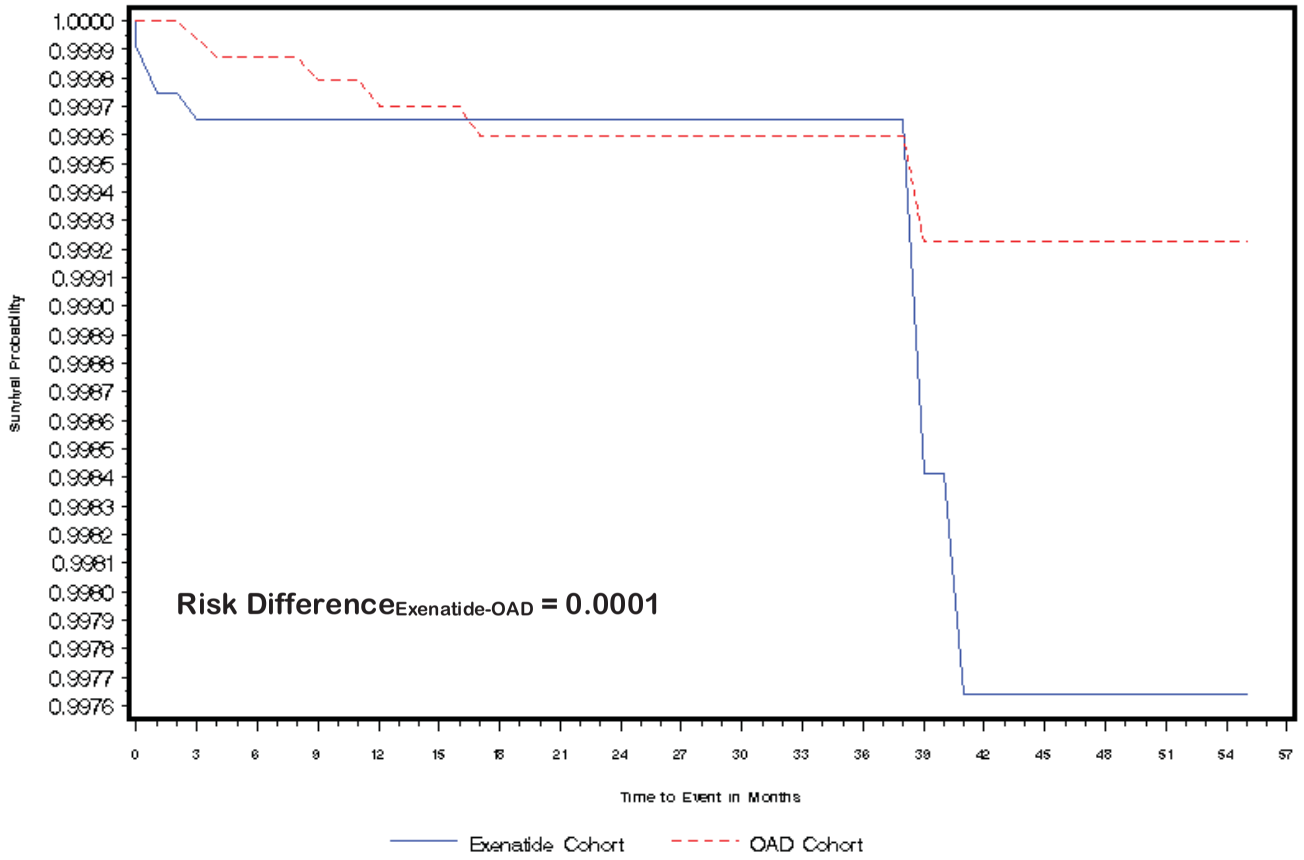


Figure 3b. **Survival Plot for Time to Algorithm–identified Pancreatic Cancer Initiating Stratified by Drug Cohort – Impact Database**

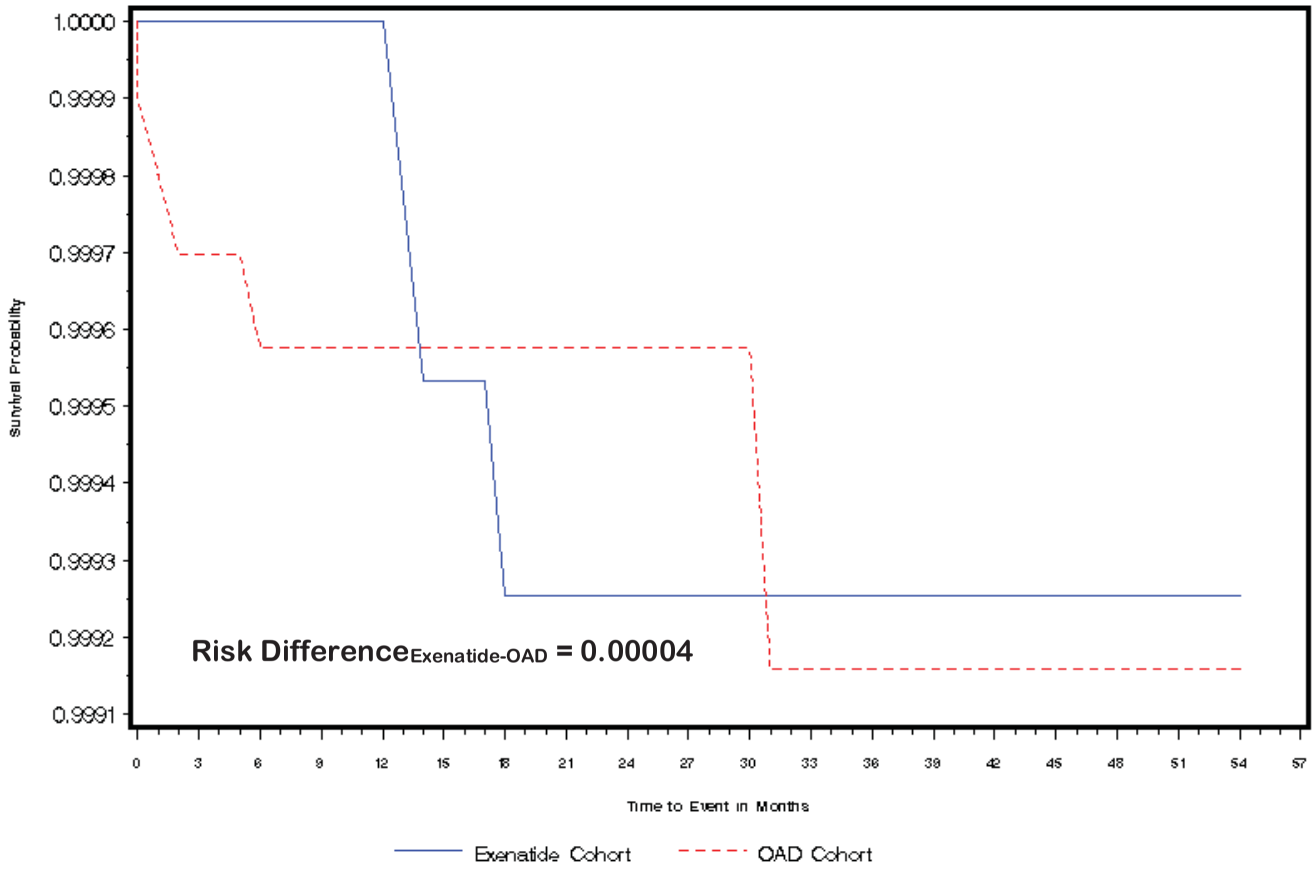


Figure 4a. Survival Plot for Time to Algorithm–identified Thyroid Cancer Initiating Stratified by Drug Cohort – Life Sciences Research Database

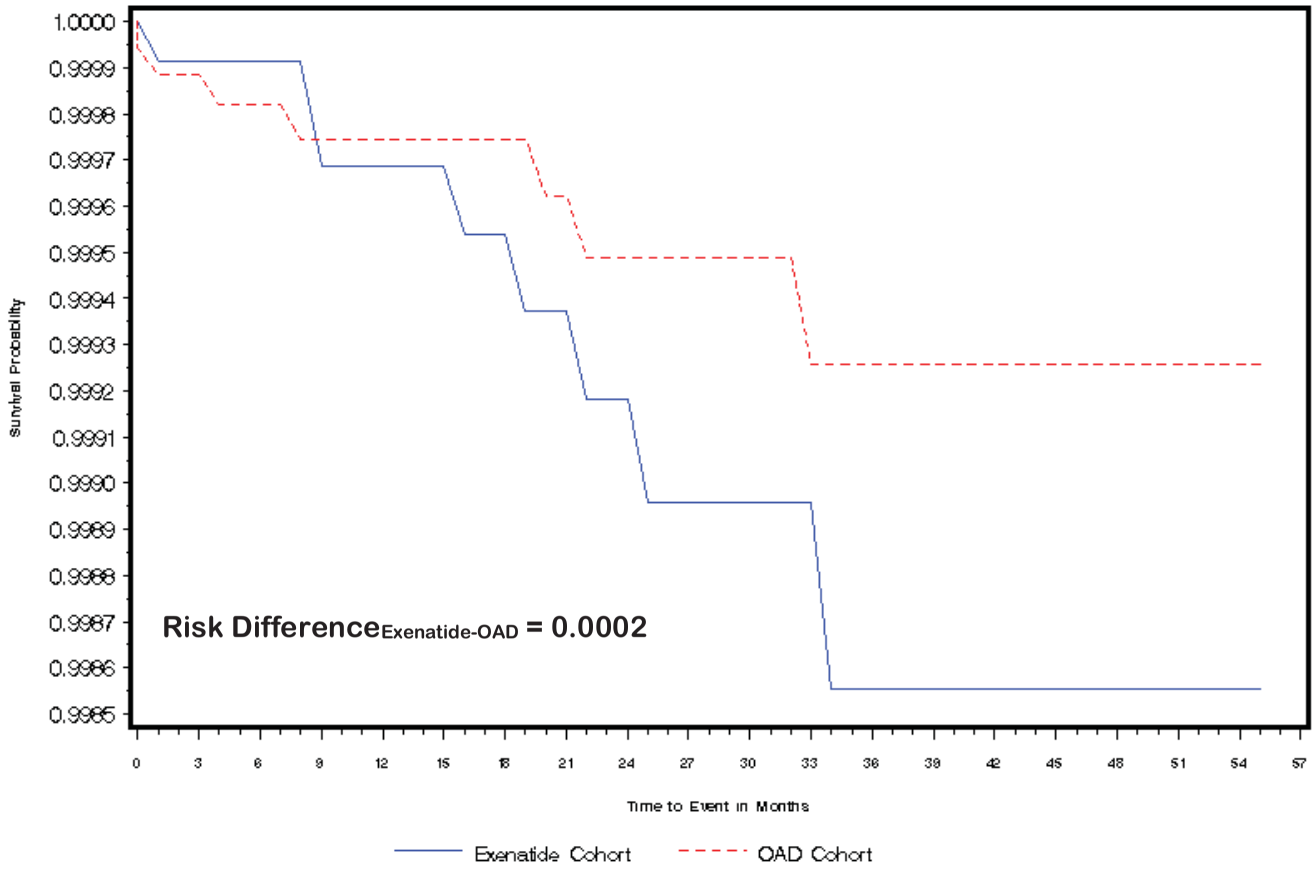


Figure 4b. **Survival Plot for Time to Algorithm–identified Thyroid Cancer Initiating Stratified by Drug Cohort – Impact Database**

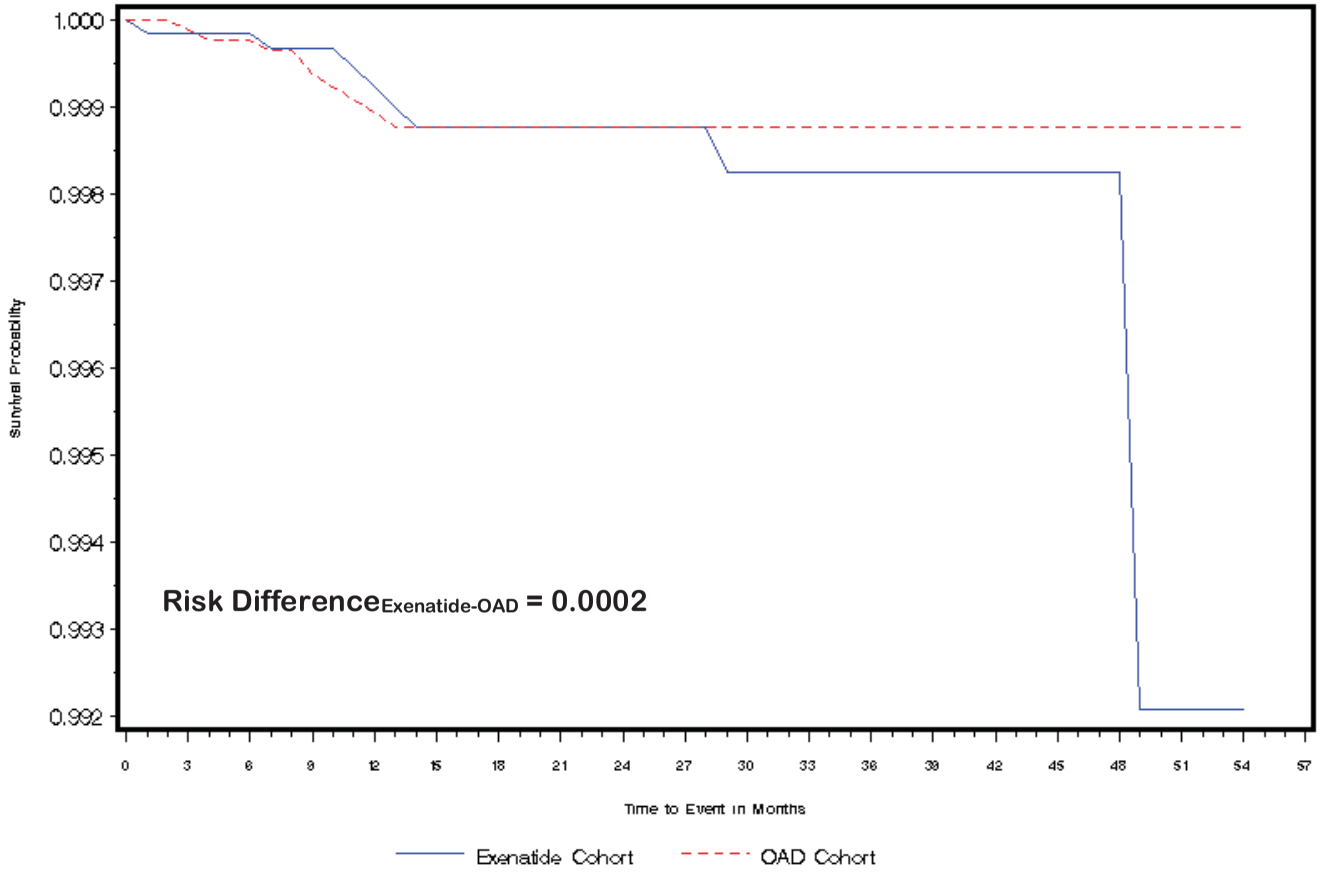
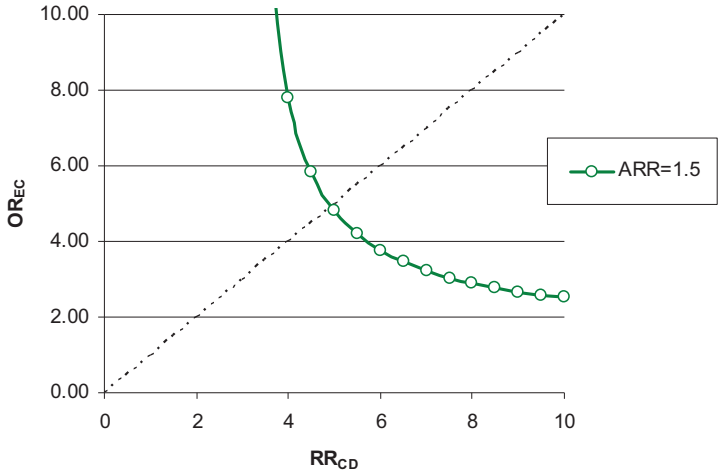
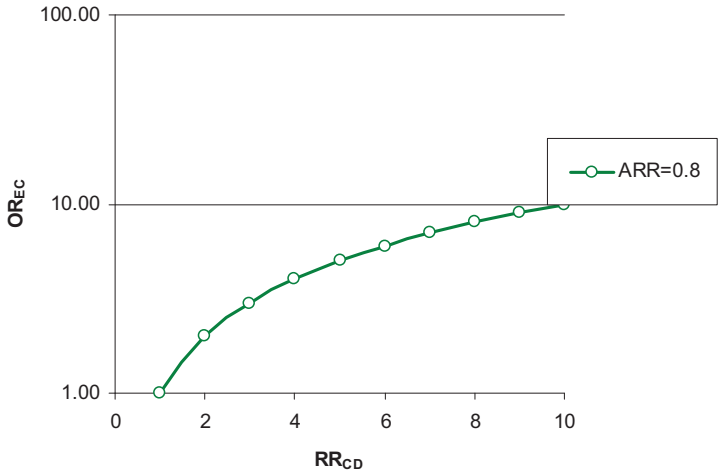


Figure 5a. Evaluation of the Confounding Caused by Smoking Needed to Explain the Apparent Relative Risk of Pancreatic Cancer, Life Sciences Research Database*



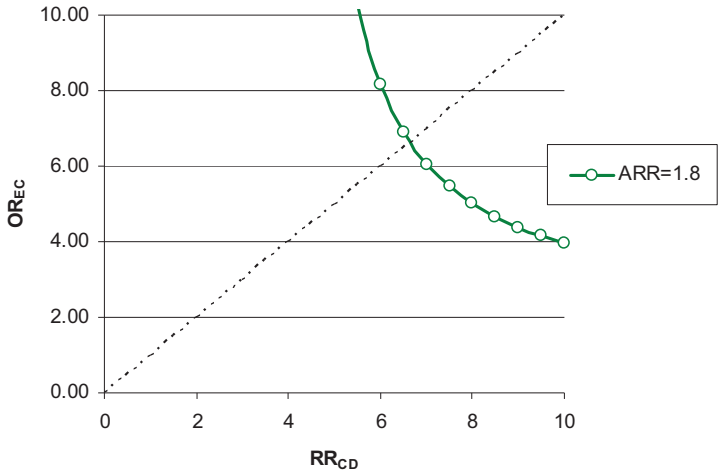
*Exposure prevalence in the Life Sciences Research Database =41%. Assumes the unmeasured confounder is present in 11% of the study population. ARR=1.5 is the observed HR of pancreatic cancer comparing exenatide to other antidiabetes drugs. OR_{EC} is the odds ratio of the association between exenatide exposure and the unmeasured confounder. RR_{CD} is the Relative Risk of the association between the unmeasured confounder and pancreatic cancer.

Figure 5b. Evaluation of the Confounding Caused by Smoking Needed to Explain the Apparent Relative Risk of Pancreatic Cancer, Impact Database*



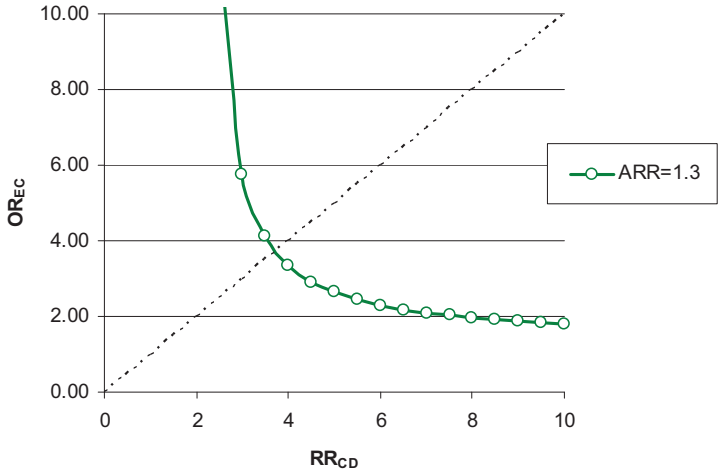
*Exposure prevalence in the Impact database =41%. Assumes the unmeasured confounder is present in 11% of the study population. ARR=0.8 is the observed HR of pancreatic cancer comparing exenatide to other antidiabetes drugs. OR_{EC} is the odds ratio of the association between exenatide exposure and the unmeasured confounder. RR_{CD} is the Relative Risk of the association between the unmeasured confounder and pancreatic cancer. NOTE: This graph is on a logarithmic scale for the purposes of interpretability.

Figure 6a. Evaluation of the Confounding Caused by Smoking Needed to Explain the Apparent Relative Risk of Thyroid Cancer, Life Sciences Research Database*



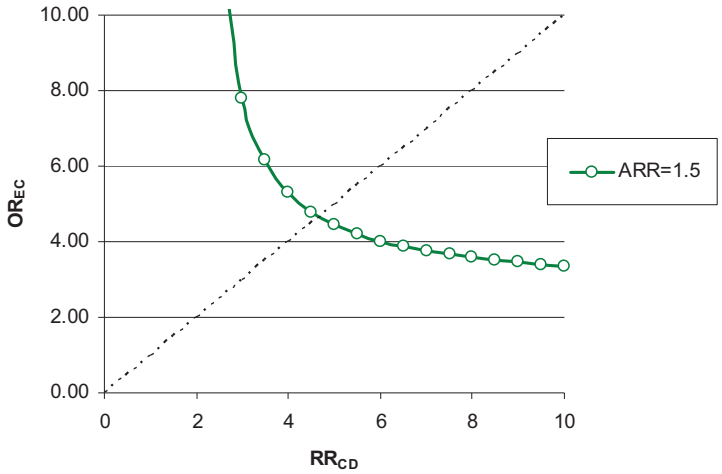
*Exposure prevalence in the Life Sciences Research Database =41%. Assumes the unmeasured confounder is present in 11% of the study population. ARR=1.8 is the observed HR of thyroid cancer comparing exenatide to other antidiabetes drugs. OR_{EC} is the odds ratio of the association between exenatide exposure and the unmeasured confounder. RR_{CD} is the relative risk of the association between the unmeasured confounder and thyroid cancer.

Figure 6b. Evaluation of the Confounding Caused by Smoking Needed to Explain the Apparent Relative Risk of Thyroid Cancer, Impact Database*



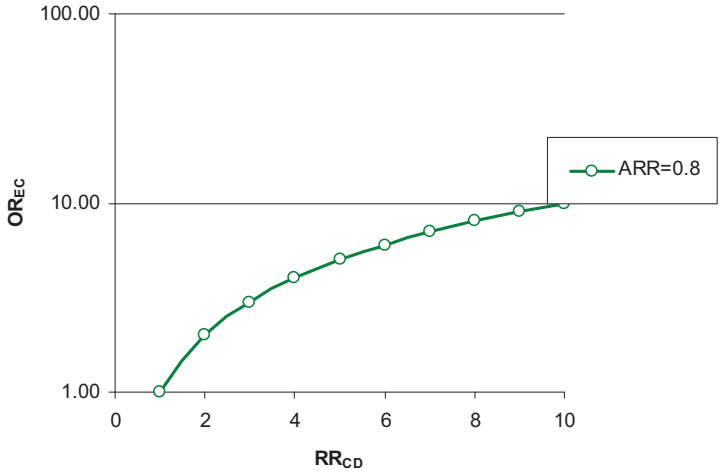
*Exposure prevalence in the Impact database =41%. Assumes the unmeasured confounder is present in 11% of the study population. ARR=1.3 is the observed HR of thyroid cancer comparing exenatide to other antidiabetes drugs. OR_{EC} is the odds ratio of the association between exenatide exposure and the unmeasured confounder. RR_{CD} is the relative risk of the association between the unmeasured confounder and thyroid cancer.

Figure 7a. Evaluation of the Confounding Caused by Obesity Needed to Explain the Apparent Relative Risk of Pancreatic Cancer, Life Sciences Research Database*



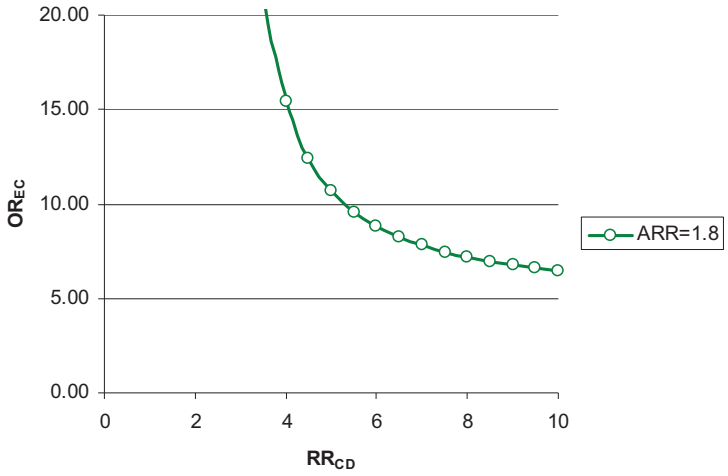
*Exposure prevalence in the Life Sciences Research Database =41%. Assumes the unmeasured confounder is present in 57% of the study population. ARR=1.5 is the observed HR of pancreatic cancer comparing exenatide to other antidiabetes drugs. OR_{EC} is the odds ratio of the association between exenatide exposure and the unmeasured confounder. RR_{CD} is the relative risk of the association between the unmeasured confounder and pancreatic cancer.

Figure 7b. Evaluation of the Confounding Caused by Obesity Needed to Explain the Apparent Relative Risk of Pancreatic Cancer, Impact Database*



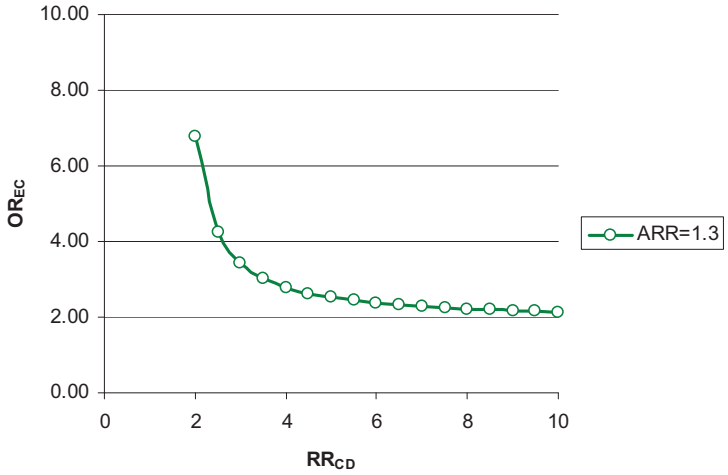
*Exposure prevalence in the Impact database =41%. Assumes the unmeasured confounder is present in 57% of the study population. ARR=0.8 is the observed HR of pancreatic cancer comparing exenatide to other antidiabetes drugs. OR_{EC} is the odds ratio of the association between exenatide exposure and the unmeasured confounder. RR_{CD} is the relative risk of the association between the unmeasured confounder and pancreatic cancer. NOTE: This graph is on a logarithmic scale for the purposes of interpretability.

Figure 8a. Evaluation of the Confounding Caused by Obesity Needed to Explain the Apparent Relative Risk of Thyroid Cancer, Life Sciences Research Database*



*Exposure prevalence in the Life Sciences Research Database =41%. Assumes the unmeasured confounder is present in 57% of the study population. ARR=1.8 is the observed HR of thyroid cancer comparing exenatide to other antidiabetes drugs. OR_{EC} is the odds ratio of the association between exenatide exposure and the unmeasured confounder. RR_{CD} is the relative risk of the association between the unmeasured confounder and thyroid cancer.
NOTE: The Y-axis for this chart goes to 100.00 due to the extreme values of the OR_{EC}.

Figure 8b. Evaluation of the Confounding Caused by Obesity Needed to Explain the Apparent Relative Risk of Thyroid Cancer, Impact Database*



*Exposure prevalence in the Impact database =41%. Assumes the unmeasured confounder is present in 57% of the study population. ARR=1.3 is the observed HR of thyroid cancer comparing exenatide to other antidiabetes drugs. OR_{EC} is the odds ratio of the association between exenatide exposure and the unmeasured confounder. RR_{CD} is the relative risk of the association between the unmeasured confounder and thyroid cancer.

9. Appendices

Appendix I. Other Antidiabetes Drugs (OADs) Excluding Dipeptidyl Peptidase-4 / Glucagon-like Peptide-1 (DPP-4/GLP-1) Receptor Agonist

METFORMIN
METFORMIN HCL
METFORMIN/CAFF/AA7/HRB125/CHOL
METFORMIN/AA COMB.#7/HC#125/CH
SULFONYLUREAS
ACETOHEXAMIDE
TOLBUTAMIDE
CHLORPROPAMIDE
TOLAZAMIDE
GLYBURIDE
GLIPIZIDE
GLIMEPIRIDE
THIAZOLIDINEDIONES
TROGLITAZONE
ROSIGLITAZONE MALEATE
PIOGLITAZONE HCL
AMYLINOMIMETICS
PRAMLINTIDE ACETATE
NONSULFONYLUREA SECRETAGOGUES
REPAGLINIDE
NATEGLINIDE
ALPHA–GLUCOSIDASE INHIBITORS
ACARBOSE
MIGLITOL
INSULINS

Appendix II. Diagnosis Codes for Pancreatic Cancer and Thyroid Neoplasm

The International Classification of Diseases, 9th Revision (ICD–9) diagnosis codes for identification of pancreatic cancer and thyroid neoplasm.

ICD–9	Description
	Pancreatic Cancer
157.X	Malignant neoplasm of pancreas
157.0	Malignant neoplasm of head of pancreas
157.1	Malignant neoplasm of body of pancreas
157.2	Malignant neoplasm of tail of pancreas
157.3	Malignant neoplasm of pancreatic duct
157.4	Malignant neoplasm of islets of Langerhans
157.8	Malignant neoplasm of other specified sites of pancreas
157.9	Malignant neoplasm of pancreas, part unspecified
	Thyroid Neoplasm
193	Malignant neoplasm of thyroid gland
226	Benign neoplasm of thyroid glands

Appendix III. Restrictive Algorithms for Pancreatic Cancer and Thyroid Neoplasm

1. **Case Algorithm for Pancreatic Cancer**
    a. Any in– or out– patient diagnosis codes of pancreatic cancer, and
    b. Without a diagnosis of benign pancreatic neoplasm within 60 days after the diagnosis of pancreatic cancer, and
    c. With **one or more** pancreas surgery, chemotherapy or radiation therapy within 180 days after the diagnosis of pancreatic cancer, ***and***
    d. Without a diagnosis of other cancers (see list below) within 60 days before or after the diagnosis of pancreatic cancer

ICD-9 code	*Cancer*
150.xx	***Malignant neoplasm of esophagus***
151.xx	***Malignant neoplasm of stomach***
152.xx	***Malignant neoplasm of small intestine, including duodenum***
153.xx	***Malignant neoplasm colon***
154.xx	***Malignant neoplasm of rectum, rectosigmoid junction, and anus***
155.xx	***Malignant neoplasm of liver and intrahepatic bile ducts***
156.xx	***Malignant neoplasm of gallbladder and extrahepatic bile ducts***
158.xx	***Malignant neoplasm of retroperitoneum and peritoneum***
159.xx	***Malignant neoplasm of other and ill-defined sites within the digestive organs and peritoneum***
162.xx	***Malignant neoplasm of trachea, bronchus, and lung***
165.xx	***Malignant neoplasm of other and ill-defined sites within the respiratory system and intrathoracic organs***
171.5	***Malignant neoplasm of connective and other soft tissue (Abdomen)***
188.xx	***Malignant neoplasm of bladder***
195.2	***Malignant neoplasm of other and ill-defined sites (Abdomen)***

2. **Case Algorithm for Thyroid Cancer**
    a. Any in– or out– patient diagnosis codes of thyroid cancer, and
    b. Without a diagnosis of benign thyroid neoplasm within 60 days after the diagnosis of thyroid cancer, and
    c. With **one or more** of thyroid surgery, chemotherapy, radioiodine therapy or radiation therapy within 180 days after the diagnosis of thyroid cancer

3. **Case Algorithm for Medullary Thyroid Cancer (MTC)**
    a. Any in– or out– patient diagnosis codes of thyroid cancer, and
    b. Without a diagnosis of benign thyroid neoplasm within 60 days after the diagnosis of thyroid cancer, and
    c. With **2 or more** of thyroid surgery, chemotherapy, radioiodine therapy or radiation therapy **plus** thyroid hormone replacement therapy within 180 days after the diagnosis of thyroid cancer, and
    d. With one or more claims evidence of **serum calcitonin** levels within 180 days after thyroid surgery or thyroid cancer diagnosis

    NOTE: A relaxed algorithm was used in the final analysis of MTC. That algorithm included either **3.a+3.b +3.d or 3.a+3.c +3.d.**

4. **Case Algorithm for Benign Thyroid Neoplasm**
    a. Any in– or out– patient diagnosis codes of benign thyroid neoplasm, and

b. Without a diagnosis of thyroid cancer within 60 days after the diagnosis of benign thyroid neoplasm, and
c. With biopsy claims within 90 days before the diagnosis of benign thyroid neoplasm

Please note that the date of diagnosis above refers to the date of first claim for the diagnosis.

Appendix IV. Adjudication Forms

Pancreatic Cancer Adjudication Form (Example)

Assessed Pancreatic Cancer Category	Presenting Features (1)			Lab Tests (2)			Image Evidence (3)		Diagnostic Tests (4)		Received Chemotherapy or Radiotherapy (5)
	Abdominal Pain	**Obstructive Jaundice**	**Weight Loss or Anorexia**	**IgG4 level**	**Bilirubin Levels**	**Maximum (pre-treatment when possible) Serum CA 19-9 Level**	**Lesion Detected in Pancreas (CT/MRI, PET/CT, ERCP/MRCP, EUS)**	**Comments**	**Pancreas Cytology**	**Pancreas Histology**	
Criteria Categories (Section positive if at least one criteria met for each section)	Yes, No, Not Reported	Yes, No, Not Reported	Yes, No, Not reported	Positive (IgG4 level ≥2 times the upper limit of normal), Negative, Not reported	Elevated, Not elevated (as per normal range in record), Not reported	<37 U/mL, 37-130 U/Ml, >130 U/mL, Not reported	Mass present, Mass absent, Indeterminate, Not reported		Malignant, Suspicious, Atypical cells, Undetermined, Benign, Not reported	Malignant, Suspicious, Atypical cells, Undetermined, Benign, Not reported	Chemotherapy, Radiotherapy Not reported
Definite: Meet (4)									Adenocarcinoma	Adenocarcinoma	
Probable: Meet at least (2+3) or (4)				Negative		>130 U/Ml	Pancreatic mass on imaging		Suspicious for Adenocarcinoma	Suspicious for Adenocarcinoma	
Possible: Meet at least (1+2+3) or (4) or (5) if primary data not available	Yes	Yes	Yes	Negative	Elevated	>37 U/Ml	Pancreatic mass on imaging		Atypical cells	Atypical cells	Chemotherapy; or Radiotherapy
Non-diagnostic: Meet (4) or (3)							No pancreatic mass on imaging		Benign or indeterminate	Benign or indeterminate	
Treating Physician Diagnosed Patient with Pancreatic Cancer	**If insufficient evidence of a diagnosis then check 'no'**						Yes			No	
Diagnosis Information	**Date of confirmed diagnosis: (Date of biopsy or if diagnosis not definite, date criteria fully recorded)**						**Recorded Tumor Stage :**				
							Calculated Tumor Stage (AJCC 7th ed TNM): 0 I II III IV Not Enough information				

Thyroid Cancer Adjudication Form (Example)

Assessed Thyroid Cancer Category (prioritize histology >cytology >other; Prioritize higher certainty over lower certainty)	**Lab Tests**	**Image Evidence**	**Diagnostic Tests**		Treatment
	Basal Serum Calcitonin Level	**Detected lesion in thyroid (X-ray, PET, CT/MRI Scan and Ultrasound)**	**Cytology**	**Histology from Surgery or Autopsy Report**	Radioiodine treatment after thyroidectomy
Criteria Categories	<30, 30-50, >50-100, >100, Not reported		Malignant, Suspicious, Undetermined, Benign, Not reported	Malignant, Benign, Not reported	Yes, No, Not reported
Definite: Meet any criteria of the following columns ☐	>100 ng/L	DxWBS after thyroidectomy	Malignant	Malignant	Yes/No
Probable: Meet any criteria of the following columns ☐	>50-100 ng/L	Thyroid nodule with only local lymphadenopathy on US, CT, or MRI Thyroid nodule with ipsilateral vocal cord paralysis	Suspicious	Not reported	Yes
Possible: Meet any criteria of the following columns ☐	30-50 ng/L	Focal PET positive thyroid nodule without regional lymphadenopathy, “cold” thyroid nodule on thyroid scan	Atypia of undetermined significance, follicular lesion of undetermined significance, follicular or hurthle cell neoplasm	Not reported	No, or Not reported
Non-Malignant or Non-Diagnostic: Meet any criteria of the following columns ☐	<30	”Hot” thyroid nodule on thyroid scan	Benign or undetermined	Benign or not reported	No, or Not reported
Treating Physician Diagnosed Patient with Thyroid Cancer	If insufficient evidence of a diagnosis then check ‘no’		Yes ☐	No ☐	
Diagnosis Information	Date of confirmed diagnosis: _____		**Tumor Stage (7th ed TNM):** ☐ I ☐ II ☐ III ☐ IV ☐ Not Reported		
Subgroups of Thyroid Neoplasm	☐ Papillary ☐ Follicular ☐ Medullary ☐ Anaplastic ☐ Benign Thyroid Neoplasm				

Benign Thyroid Neoplasm Adjudication Form (Example)

Assessed Benign Thyroid Neoplasm Category (prioritize histology >cytology >other; Prioritize higher certainty over lower certainty)	Presenting Features	Lab Tests		Diagnostic Tests			Treatment
	Neck lump or Nodule	Basal Serum Calcitonin Level	Abnormal Thyroid Hormone (TSH, T3, T4)	Positive Image evidence with a detected lesion in thyroid (X-ray, PET, CT/MRI Scan and Ultrasound)	Cytology	Histology from Surgery or Autopsy Report	
Definite: ☐				"hot" thyroid nodule on thyroid scan	Benign	Benign	
Probable: ☐	Palpable thyroid nodule			PET negative thyroid nodule, "cold thyroid nodule", Thyroid nodule without lymphadenopathy on CT/US/MRI	Non-diagnostic, Atypia of Undetermined Significance, Follicular lesion of Undetermined Significance, Follicular or Hurthle cell Neoplasm		Thyroidectomy without histologic diagnosis
Possible: ☐					Suspicious		
Non-Benign or Non-Diagnostic: ☐		>100 ng/L		DxWBS after thyroidectomy, Thyroid nodule with only local lymphadenopathy on US, CT, or MRI Thyroid nodule with ipsilateral vocal cord paralysis	Malignant	Malignant	
Treating Physician Diagnosed Patient with Benign Thyroid Neoplasm	If insufficient evidence of a diagnosis then check 'no'			Yes ☐		No ☐	
Diagnosis Information	Date of confirmed diagnosis: _____				**Tumor Stage:** ☐ I ☐ II ☐ III ☐ IV ☐ Not Reported		
Subgroups of Thyroid Neoplasm		☐ Papillary ☐ Follicular ☐ Medullary ☐ Anaplastic ☐ Benign Thyroid Neoplasm ____					