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Trends in the Prevalence and Treatment of Diabetic Macular Edema and Vision-Threatening Diabetic Retinopathy Among Commercially Insured Adults Aged <65 Years

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Abstract

Objective: Examine the ten-year trend in the prevalence and treatment of diabetic macular edema (DME) and vision-threatening diabetic retinopathy (VTDR) among commercially insured adults with diabetes.

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Prior Publication: An abstract based on this analysis was presented virtually as a poster at the 81st American Diabetes Association Scientific Sessions (2021).

Research Design and Methods: We analyzed the ten-year trend (2009–2018) in healthcare claims for adults 18–64 years using the IBM® MarketScan® Database, a national convenience sample of employer-sponsored health insurance. We included patients continuously enrolled in commercial fee-for-service health insurance for 24 months who had a diabetes ICD-9/10-CM code on 1 inpatient or 2 different day outpatient claims in the index year or previous calendar year. We used diagnosis and procedure codes to calculate the annual prevalence of patients with 1 claim for: 1) *any DME*, 2) either *DME/VTDR*, and 3) anti-vascular endothelial growth factor injections [anti-VEGF] and laser photocoagulation treatment, stratified by *any DME*, *VTDR with DME*, and *VTDR without DME*. We calculated Average Annual Percent Change (AAPC).

Results: From 2009–2018, there was an increase in the annual prevalence of patients with *DME/VTDR* (2.1% to 3.4%; AAPC=7.5%; $p<0.001$) and *any DME* (0.7% to 2.6%; AAPC=19.8%; $p<0.001$). There were sex differences in the annual prevalence of *DME/VTDR* and *any DME*, with males having a higher prevalence than females. Annual claims for anti-VEGF increased among those with *any DME* (327%) and *VTDR with DME* (206%); laser photocoagulation decreased among patients with *any DME* (–68%), *VTDR with DME* (–54%), and *VTDR without DME* (–62%).

Conclusions: Annual claims for *DME/VTDR* and anti-VEGF injections increased while laser photocoagulation decreased among commercially insured adults with diabetes.

Twitter summary:

Vision-threatening diabetes-related eye disease among commercially insured adults 18–64 years with diabetes has increased, along with annual claims for anti-vascular endothelial growth factor injections.

Over 37 million adults aged 18 years in the United States have diabetes (1), putting them at risk for serious complications like diabetic retinopathy (DR), the leading cause of incident blindness among US adults 20–74 years (2). DR is a condition that occurs when prolonged exposure to high blood glucose damages blood vessels in the retina of the eye. Risk of DR is primarily influenced by diabetes duration and long-term glycemic control (3–7). DR is estimated to affect 28.5% of US adults 40 years with diabetes (8). Vision-threatening DR (VTDR) includes severe non-proliferative DR and proliferative DR. Diabetic macular edema (DME), which can be present alone or with any stage of DR, is a vision-threatening condition that occurs when blood vessels in the retina leak fluid into the macula. Nationally representative data show that VTDR and DME affect 4.4%, and 3.8%, respectively, of US adults 40 years with diabetes (3,8).

Studies have documented an increase in diabetes prevalence among US adults in the last two decades (9,10). Data from the National Health and Nutrition Examination Survey (NHANES) show that the prevalence of diabetes among US adults 18 years increased from 9.8% (95% CI: 8.6%–11.1%) in 1999–2000 to 14.3% (95% CI: 12.9%–15.8%) in 2017–2018 (10). Additionally, the prevalence of HbA1c<7% among US adults 20 years with diabetes decreased from 57.4% (95% CI: 52.9%–61.8%) in 2007–2010 to 50.5% (95% CI: 45.8%–55.3%) in 2015–2018 (11). These recent trends in the prevalence of diabetes and glucose control merit the examination of trends in DR and DME among adults with diabetes to help inform prevention and treatment interventions.

Early detection and timely treatment of diabetes-related eye diseases can reduce the risk of permanent vision loss. Without treatment, a person who develops proliferative DR has a 50% chance of becoming blind within 5 years (12,13). The last twenty years have seen the emergence of new treatments, particularly for DME, that show superior effectiveness in reducing vision loss. For decades, laser photocoagulation was the mainstay of treatment for VTDR and DME. Specifically, the preferred treatment for proliferative DR is panretinal laser photocoagulation (i.e., scatter laser surgery) and the standard of care for non-center-involved DME was focal laser photocoagulation surgery (5,14,15). In the early 2000s, ophthalmologists began treating center-involved DME using intravitreal injections of anti-vascular endothelial growth factor (VEGF) agents (ranibizumab, bevacizumab, and later aflibercept). A meta-analysis of randomized clinical trials of the efficacy of these three anti-VEGF agents in treating moderate vision loss among patients with DME found they were all superior in improving vision after one year compared to laser photocoagulation treatment (16). Studies have also demonstrated that intravitreal injections of anti-VEGF therapies can be alternatives to panretinal laser photocoagulation for proliferative DR (17,18).

Previous studies on the prevalence of DR and DME in the United States are limited by older data. The only nationally representative, objectively measured data on the prevalence of DR and DME among adults ≥ 40 years are from NHANES, which last fielded this information from 2005–2008 (3,8). Few studies have examined recent trends in the prevalence and treatment of diabetes-related eye diseases. Previously, we described an increase from 2009–2018 in the annual prevalence of Medicare Part B fee-for-service beneficiaries ≥ 65 years who had a claim for DME or VTDR (from 2.8% to 4.3%) as well as significant changes in the use of different treatment modalities during this period (19). However, similar studies of persons aged <65 years have not been conducted. It is important to also understand these trends in patients with diabetes <65 years, as this age group is in their prime working years and has experienced greater growth in the prevalence of diabetes from 1999–2002 to 2015–2018 (10). In this paper, we examine the ten-year trend (2009–2018) in the annual prevalence of commercially insured adults 18–64 years with diabetes who have payment claims for DME or VTDR, the annual prevalence of treatment, and differences in prevalence of DME or VTDR by age and sex groups.

Research Design and Methods

We analyzed annual trends in healthcare claims from 2009–2018 for adults 18–64 years using the IBM[®] MarketScan[®] Database, a national convenience sample of employer-sponsored health insurance beneficiaries (20). Patients were retained in the analytic sample for each index year if they were continuously enrolled in commercial non-capitated (fee-for-service) health insurance for 24 months, consisting of the index year and the previous calendar year. The analytic sample for each year was further restricted to patients with diabetes (all types), defined using the Chronic Conditions Data Warehouse algorithm as those who had an International Classification of Diseases 9th Revision (ICD-9-CM) or 10th Revision (ICD-10-CM) diabetes diagnosis code on ≥ 1 inpatient or ≥ 2 different day outpatient claims in the index year or previous calendar year (21). In each index year, we determined the annual prevalence of patients with diabetes who had ≥ 1 claim for diabetic macular edema or vision-threatening diabetic retinopathy (hereafter *DME/VTDR*),

defined using ICD-9-CM and ICD-10-CM diagnosis codes (Supplemental Table S1). Annual prevalence of *DME/VTDR* was calculated as the number of patients with 1 claim with a diagnosis of *DME/VTDR* in the index year divided by the number of patients with diabetes in that year. Due to the emergence of new therapies for DME, we also separately calculate the annual prevalence of patients with diabetes with 1 claim for any DME (hereafter *any DME*), with or without any stage of DR, using ICD diagnosis codes (Supplemental Table S2). Lastly, we present the annual prevalence of patients with diabetes with 1 claim for non-vision-threatening diabetes-related eye diseases, defined using ICD diagnosis codes (Supplemental Table S3) as background DR, non-proliferative DR (not otherwise specified), unspecified DR without macular edema, mild non-proliferative DR (without DME), moderate non-proliferative DR (without DME), diabetes with ophthalmic manifestations, and other diabetic ophthalmic complications. The annual prevalence of these three categories of disease is presented overall and stratified by sex, age groups (18–44, 45–54, and 55–64 years), and cross-stratified by age group and sex.

We also examined trends in the annual prevalence of four types of treatment: anti-vascular endothelial growth factor (anti-VEGF) injections, laser photocoagulation, retinal detachment repair, and vitrectomy. Patients were defined as having each of these treatment types if they had 1 claim in the index year with the Current Procedural Terminology (CPT) codes or Healthcare Common Procedure Coding System (HCPCS) codes for these procedures (Supplemental Table S4). The annual prevalence for each of the four treatment types is presented for three groups of patients: those with *any DME*, *VTDR with DME*, and *VTDR without DME* (Supplemental Tables S5–7). All prevalence figures were standardized using the direct method to the age and sex distribution of the analytic sample in 2009 in order to account for differences in the age and sex composition of the study population when assessing trends over time. Analyses were performed using Stata 16 (StataCorp LLC, College Station, TX) and SAS 9.4 (SAS Institute Inc., Cary, NC). To assess trends in the annual prevalence of *DME/VTDR*, *any DME*, non-vision-threatening diabetes-related eye diseases, and the four treatment types, we used the Joinpoint Regression Program version 4.8.0.1 (National Cancer Institute). This software uses permutation tests to find points where the trend changes significantly and calculates the annual percentage change (APC) for each segment of the trend, as well as the average annual percent change (AAPC), which is a summary measure of the trend over the entire time period. Lastly, differences by age and sex in the annual prevalence of *DME/VTDR*, *any DME*, and non-vision-threatening diabetes-related eye disease were tested for statistical significance using the Wald test (Supplemental Tables S8–10). Confidence intervals for the statistics presented in all figures are shown in Supplemental Tables S11–14. This research was considered exempt from institutional review board review under 45 Code of Federal Regulations 46.101[b][5], which covers Department of Health and Human Services research and demonstration projects that are designed to study, evaluate, or examine public benefit or service programs. Findings of this study are reported in accordance with Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.

Results

From 2009–2018, among commercially insured adults aged 18–64 years, approximately one in fifteen patients had diabetes (range: 6.83% [95% confidence interval, CI: 6.82, 6.85] in 2013 to 7.51% [CI: 7.49, 7.53] in 2017) [Supplemental Table S15]. The size of the patient population with diabetes was 1.12 million in 2009 and 779,212 in 2018. The age and sex distribution of the population remained stable over the ten-year period, with approximately half of the patients being female and half aged 55–64 years.

The annual prevalence of patients with diabetes who had *DME/VTDR* increased significantly from 2.07% [CI: 2.05, 2.10] in 2009 to 3.38% [CI: 3.33, 3.42] in 2018 (AAPC=7.5%; $p<0.001$) [Figure 1]. An inflection point in the trend was found at 2011, with the annual prevalence decreasing non-significantly from 2009–2011 (APC=-4.2%; $p=0.60$) and then increasing significantly from 2011–2018 (APC=9.6%; $p<0.001$). The prevalence of *DME/VTDR* was significantly higher among males compared with females from 2010–2018 (all $p < 0.01$; Figure 1, Supplemental Table S8). Beginning in 2010, the prevalence of *DME/VTDR* was highest among males and females aged 55–64 years and males 45–54 years, compared to the other age and sex groups (all $p < 0.05$; Figure 1).

Similarly, the annual prevalence of patients with diabetes who had *any DME* increased significantly from 0.67% [CI: 0.65, 0.68] in 2009 to 2.60% [CI: 2.57, 2.64] in 2018 (AAPC=19.8%; $p<0.001$) [Figure 2]. From 2010–2018, the prevalence of *any DME* was significantly higher among males compared with females (all $p<0.01$; Figure 2) and the prevalence was highest among males and females aged 55–64 years and males 45–54 years (all $p < 0.01$; Figure 2, Supplemental Table S9). Conversely, from 2009–2018 the annual prevalence of non-vision-threatening diabetes-related eye diseases among patients with diabetes decreased significantly from 8.93% [CI: 8.88, 8.99] in 2009 to 5.96% [CI: 5.91, 6.01] in 2018 (AAPC=-4.9%; $p<0.001$) [Figure 3]. An inflection point in the trend was detected at 2014, with the annual prevalence decreasing non-significantly from 2009–2014 (APC=-0.9%; $p=0.60$) and then decreasing significantly from 2014–2018 (APC=-9.6%; $p<0.001$). From 2009–2018, the prevalence of non-vision-threatening diabetes-related eye disease was significantly higher among males compared with females (all $p<0.01$; Figure 3) and the prevalence was highest among males and females aged 55–64 years and males 45–54 years (all $p < 0.01$; Figure 3, Supplemental Table S10).

From 2009–2018, the annual prevalence of having laser photocoagulation decreased significantly among all three groups: those with *any DME* (51.32% [CI: 49.80, 52.83] to 16.56% [CI: 15.96, 17.18]; AAPC=-11.7%; $p<0.001$), *VTDR with DME* (68.31% [CI: 66.71, 69.87] to 31.45% [CI: 30.52, 32.39]; AAPC=-8.0%; $p<0.001$), and *VTDR without DME* (33.03% [CI: 32.30, 33.77] to 12.7% [CI: 11.89, 13.57]; AAPC=-9.2%; $p<0.001$) [Figure 4]. During this period the annual prevalence of having anti-VEGF injections increased significantly among those with *any DME* (7.95% [CI: 7.16, 8.81] to 33.74% [CI: 32.97, 34.52]; AAPC=6.3%; $p<0.001$) and *VTDR with DME* (18.66% [CI: 17.37, 20.02] to 57.32% [CI: 56.32, 58.31]; AAPC= 5.6%; $p<0.001$). Among those with *VTDR with DME*, joinpoint regression detected two distinct trend lines, with the annual anti-VEGF prevalence increasing significantly and steeply from 2009–2012 (APC=26.8%; $p<0.001$)

and still increasing but less steeply from 2012–2018 (APC= 3.1%; $p<0.001$). By 2018, over half of patients with *VTDR with DME* received treatment using anti-VEGF injections. Over the ten-year period, among those with *VTDR without DME* there was a trend of increasing annual prevalence of having received anti-VEGF injections, but this increase was not significant (APC=7.0%; $p=0.1$).

Vitrectomy and retinal detachment repair were expectedly less common procedures overall, which were most frequently performed among patients with *VTDR with DME* (range in annual prevalence across the ten-year period: 7.04% [CI: 6.54, 7.58] in 2018 to 13.78% [CI: 12.62, 15.02] in 2010 and 5.00% [CI: 4.57, 5.47] in 2018 to 6.89% [CI: 6.05, 7.84] in 2010, respectively). From 2009–2018, the annual prevalence of having a vitrectomy significantly decreased among patients with *VTDR with DME* (12.94% [CI: 11.84, 14.13] to 7.04% [CI: 6.54, 7.58]; AAPC= -7.1% ; $p<0.001$) and *VTDR without DME* (9.33% [CI: 8.89, 9.79] to 4.16% [CI: 3.68, 4.70]; AAPC= -7.9% ; $p<0.001$). Annual prevalence of retinal detachment repair declined only among patients with *VTDR without DME*.

Conclusions

From 2009–2018, we found a 62% increase in the annual prevalence of commercially-insured adults with diabetes who had a claim for DME or VTDR. We found significant age and sex differences from 2010–2018, with the annual prevalence of having a claim for *DME/VTDR* higher among males than females and highest among males and females aged 55–64 years and males 45–54 years compared to the other age and sex groups. There were marked changes during this time period in the use of different treatment modalities for DME and VTDR, including a substantial increase in the annual prevalence of having a claim for anti-VEGF injections, particularly among those with *any DME* and those with *VTDR with DME* (a 327% and 206% increase, respectively). Among all three groups of patients—those with *any DME*, *VTDR with DME*, and *VTDR without DME*—there was a similarly pronounced decline (68%, 54%, and 62%, respectively) in the annual prevalence of having a claim for laser photocoagulation.

To our knowledge, there are no comparable published data on trends in the prevalence of DR and DME among adults <65 years. Our prevalence estimates are similar to those published using the 2005–2008 NHANES data, which showed that VTDR and DME affect 4.4%, and 3.8%, respectively, of US adults 40 years with diabetes (3,8). Using identical case definitions as the present study, we published a study describing very similar trends from 2009–2018 in the annual prevalence of Medicare Part B fee-for-service beneficiaries 65 years who had a claim for *DME/VTDR* (from 2.8% to 4.3%) or *any DME* (1.0% to 3.3%) (19). The reasons for the trends we observed that show an increase in annual claims for vision-threatening diabetes-related eye disease are unknown. Diabetes duration and long-term glycemic control are primary risk factors for DR and DME (3–7). The significant decrease in age at diagnosis of type 2 diabetes seen in the 1990s in the US could have contributed to our observed trends in complications, as people are living longer with diabetes (22). Another contributing factor might be the documented trends showing continued poor glycemic control among adults with diabetes during this period (10,11). A study using MarketScan data with linked claims and electronic health records, found

that from 2012–2019, there was a decrease in the percentage of adults 18 years with diabetes who achieved a HbA1c<7% (23). However, we cannot discount the possibility that improvements in screening, imaging technology, diagnosis, or medical coding over the last decade may have influenced these trends.

We document statistically significant differences in the prevalence of annual claims for *DME/VTDR*, *any DME*, and non-vision-threatening diabetes diabetes-related eye disease by sex, with males having a higher prevalence than females; however, these differences by sex are small and may not be clinically meaningful. Several US examination-based population studies have stratified the prevalence of diabetes-related eye disease by sex; however, the older age and small sample size of some of these studies makes a direct comparison with our study results difficult (24–28). A study using data from the New Jersey 725 and the Wisconsin Epidemiologic Study of Diabetic Retinopathy examined the prevalence of DR among adults with type 1 diabetes and found that males were more likely to have VTDR than females (relative risk: 1.17; 95% CI: 1.01–1.36) (24). The Chinese American Eye Study found that males had a higher prevalence than females of moderate DR (15.0% vs. 9.2%; $p=0.02$) and proliferative DR (3.6% vs. 1.4%; $p=0.049$), even after adjusting for age (25). A retrospective study in Puerto Rico examined eye clinic health records collected through a screening program for patients with diabetes and found that DR was more common in males (47.2%) than females (33.7%; $p=0.004$) (26). Other population-based studies have found no difference by sex in the prevalence of any DR (27) and proliferative DR (28). The most recent nationally representative NHANES data showed that among adults 40 years with diabetes, the prevalence of DR was higher in males (31.6%, 95% CI: 26.8–36.8) than females (25.7%, 95% CI: 21.7–30.1; $p=0.04$) [adjusted odds ratio: 2.07; 95% CI: 1.39–3.10] (8). However, there was no difference in the prevalence of VTDR among males (4.2%; 95% CI: 2.8–6.1) compared to females (4.7%; 95% CI: 3.2–6.9; $p=0.67$) [adjusted odds ratio: 1.79; 95% CI: 0.67–4.80] (8); the same was true for the prevalence of DME (3).

A previously published analysis by Benoit et al. using the IBM® MarketScan® Database of healthcare claims documented sex differences in DR that were similar to our findings (29). This study examined claims for DR, VTDR, and eye examinations among a cohort of patients with type 1 and type 2 diabetes who were continuously enrolled in health insurance from 2010–2014. They found that among patients with type 2 diabetes, the 5-year period prevalence of DR and VTDR was 24.4% and 8.3%, respectively, and that males had a higher prevalence than females of both DR (27.3% vs. 21.7%; $p<0.0001$) and VTDR (9.3% vs. 7.3%; $p<0.0001$). Among patients with type 1 diabetes, the 5-year period prevalence of DR and VTDR was 54.0% and 24.3%, respectively, and in this population, males also had a higher prevalence than females of both DR (56.1% vs. 51.8%; $p<0.0001$) and VTDR (25.4% vs. 23.2%; $p<0.01$).

Reasons for the observed differences in the prevalence of *DME/VTDR* and *any DME* by sex are unknown. A higher prevalence among men of risk factors such as hypertension could be a contributing factor (30). It is recommended that individuals with diabetes receive annual or biennial dilated eye examinations, as early detection and timely treatment of DR are vital for preventing disease progression and preserving vision (31–34). Benoit et al. found that among patients with type 2 diabetes, 14.7% of males and 15.8% of females

met the American Diabetes Association recommendations for annual or biennial eye exams; among those with type 1 diabetes this prevalence was 24.3% among males and 28.4% among females (29). Another study used 2007–2015 data from a nationwide commercial claims database to determine the rate of eye examinations and diabetes-related eye disease in the first 5 years after diagnosis of type 2 diabetes among adults (35). They found that males had lower odds of receiving an annual eye examination (odds ratio: 0.84; $p < 0.01$) and higher odds of developing diabetic retinopathy within 5 years (odds ratio: 1.17; $p < 0.01$) than females. If males with diabetes meet guidelines for routine eye exams at a lower rate than females, this could translate to males' eye disease being diagnosed at a more advanced stage, which could contribute to the sex differences we observed in the prevalence of annual claims for *DME/VTDR* and *any DME*. An important risk factor for the development of diabetic retinopathy is glycemic control. However, pooled data from the 2007–2010 NHANES showed no difference in having poor glycemic control by sex (36), and a study using 2007–2012 NHANES data found no differences by sex in meeting individualized HbA1c targets (37).

We observed a precipitous rise in the annual prevalence of having a claim for anti-VEGF injections from 2009–2018, a time period during which physicians began to replace laser photocoagulation treatment in response to studies documenting superior efficacy of anti-VEGF injections for DME (16). In 2012, the Food and Drug Administration approved the anti-VEGF drug ranibizumab for DME treatment, and later approved aflibercept for DME treatment (2014) and ranibizumab and aflibercept for the treatment of DR in patients with DME (2015). Other US studies have documented similar increases in the use of anti-VEGF treatment for DME during this time period. Recently published data using claims for Medicare Part B fee-for-service beneficiaries ≥ 65 years with diabetes showed an increase from 2009–2018 in the annual prevalence of anti-VEGF treatment, particularly among patients with any DME (15.7% to 35.2%) or VTDR with DME (20.2% to 47.6%); this coincided with a decrease in the annual prevalence of laser photocoagulation among those with any DME (45.5% to 12.5%), VTDR with DME (54.0% to 20.3%), and VTDR without DME (22.5% to 5.8%) (19).

An earlier study using a nationally representative sample of Medicare beneficiaries found that the use of laser photocoagulation for patients with DME decreased from 43% of patients receiving laser photocoagulation in 2000 to only 30% of patients in 2004, compared to an increase in receipt of intravitreal injection from 1% to 13% of patients in this time period (38). Another study using administrative claims for patients with DME and either commercial health insurance or government insurance (Medicaid, Medicare, and Medicare Advantage) found that the prevalence of receiving anti-VEGF treatments increased from 5.0% of patients in 2009 to 27.1% in 2014, and that anti-VEGF treatments, as a proportion of all DME treatments, increased from 11.6% in 2009 to 61.9% in 2014 (compared to a decrease in focal laser procedures from 75.3% of all DME treatments in 2009 to 24.0% in 2014) (39). One study combined healthcare claims data from commercial health insurance and Medicare Advantage for adults ≥ 18 years and found that the annual use of anti-VEGF treatment, measured as the number of injections per 1,000 patients with diabetes-related retinal disease, increased from 2006 to 2015, and this trend was particularly pronounced for bevacizumab which increased from 2.4 injections/1,000 patients with DR in 2009 to

13.6 injections/1,000 patients in 2015 (40). An interesting finding of this research was that female patients received 57.1% of the administered anti-VEGF injections and male patients received 42.9%, documenting important differences in treatment by sex which could have implications for progression and severity of eye disease.

This analysis is subject to several limitations. While the MarketScan database of administrative claims provides a robust sample size with patients from all US states, the data are a national convenience sample of individuals who are commercially insured through their employers; therefore, our findings are not generalizable to all US adults <65 years. Second, the trends described in this analysis are based on the annual prevalence of having a healthcare claim for diabetes-related eye disease and can be influenced by changes in coding and treatment practices. Our estimates are likely an underestimate, as they are less accurate than those based on the measured presence of eye disease in examination-based studies. Third, our study period overlapped with the 2015 transition from ICD-9-CM to ICD-10-CM diagnosis coding, and we cannot discount the possibility that these coding changes influenced the observed trends. ICD-10-CM codes provide significantly more granular detail on the nature of the diabetes-related eye disease, including laterality information. This could have affected our prevalence estimates in either direction, resulting in under- or over-reporting of DME/VTDR prevalence. Fourth, our analytic sample size declined from 16.1 to 10.6 million patients from 2009 to 2018, due to loss of data in the MarketScan database from a participating insurance provider. Lastly, the data allowed for a description of important differences in diabetes-related eye disease by sex; however, we were not able to explore disparities by other important factors such as race, ethnicity, and income due to the absence of this information in MarketScan.

In summary, from 2009–2018 we observed a significant increase in the annual prevalence of having a healthcare claim for vision-threatening diabetes-related eye disease among commercially insured adults aged 18–64 years with diabetes. We also documented important differences in disease prevalence by sex, with males having a higher prevalence, and marked changes over this decade in the use of different treatment modalities, with anti-VEGF surpassing laser photocoagulation as the most used treatment for DME/VTDR. Future research could explore causes of the observed differences in eye disease by sex, as well as the barriers to eye care and treatment, in order to inform prevention interventions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Disclaimer:

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

References

1. Centers for Disease Control and Prevention. National Diabetes Statistics Report website. <https://www.cdc.gov/diabetes/data/statistics-report/index.html>. Accessed [September 1, 2022].
2. Klein R, Klein BEK. Vision disorders in diabetes [Chapter 14]. In: Diabetes in America [Internet]. 2nd ed. Bethesda, MD: National Institutes of Health; 1995. p. 293–338. Available from: <https://www.niddk.nih.gov/about-niddk/strategic-plans-reports/diabetes-in-america-2nd-edition>
3. Varma R, Bressler NM, Doan QV, Gleeson M, Danese M, Bower JK, et al. Prevalence of and risk factors for diabetic macular edema in the United States. *JAMA Ophthalmol*. 2014;132(11):1334–40. [PubMed: 25125075]
4. Lachin JM, White NH, Hainsworth DP, Sun W, Cleary PA. Effect of intensive diabetes therapy on the progression of diabetic retinopathy in patients with type 1 diabetes: 18 years of follow-up in the DCCT/EDIC. *Diabetes*. 2015;64(2):631–42. [PubMed: 25204977]
5. Jampol LM, Glassman AR, Sun J. Evaluation and Care of Patients with Diabetic Retinopathy. *N Engl J Med*. 2020;382(17):1629–37. [PubMed: 32320570]
6. Mohamed Q, Gillies MC. Management of diabetic retinopathy: a systematic review. *JAMA*. 2007;298(8):902–16. [PubMed: 17712074]
7. Varma R, Choudhury F, Klein R, Chung J, Torres M, Azen SP. Four-year incidence and progression of diabetic retinopathy and macular edema: the Los Angeles Latino Eye Study. *Am J Ophthalmol*. 2010;149(5):752–61. [PubMed: 20149342]
8. Zhang X, Saaddine JB, Chou C-F, Cotch MF, Cheng YJ, Geiss LS, et al. Prevalence of Diabetic Retinopathy in the United States, 2005–2008. *JAMA*. 2010;304(6):649–56. [PubMed: 20699456]
9. Menke A, Casagrande S, Geiss L, Cowie CC. Prevalence of and Trends in Diabetes Among Adults in the United States, 1988–2012. *JAMA*. 2015;314(10):1021–9. [PubMed: 26348752]
10. Wang L, Li X, Wang Z, Bancks MP, Carnethon MR, Greenland P, et al. Trends in Prevalence of Diabetes and Control of Risk Factors in Diabetes Among US Adults, 1999–2018. 2021;326(8):704–16.
11. Fang M, Wang D, Coresh J, Selvin E. Trends in Diabetes Treatment and Control in U.S. Adults, 1999–2018. *N Engl J Med*. 2021;384(23):2219–28. [PubMed: 34107181]
12. Ferris FL, Davis MD, Aiello LM. Treatment of diabetic retinopathy. *N Engl J Med*. 1999;341(9):667–78. [PubMed: 10460819]
13. Caird FI, Burditt AF, Draper G. Diabetic retinopathy: a further study of prognosis for vision. *Diabetes*. 1968;17(3):121–3. [PubMed: 5638572]
14. Bressler NM, Beck RW, Ferris FL. Panretinal photocoagulation for proliferative diabetic retinopathy. *N Engl J Med*. 2011;365(16):1520–6. [PubMed: 22010918]
15. Flaxel CJ, Bailey ST, Fawzi A, Lim JI, Adelman RA, Vemulakonda GA, et al. American Academy of Ophthalmology. Diabetic Retinopathy Preferred Practice Pattern 2019 [Internet]. Garratt S, editor. San Francisco, CA; Available from: <https://www.aao.org/preferred-practice-pattern/diabetic-retinopathy-ppp>
16. Virgili G, Parravano M, Evans JR, Gordon I. Anti-vascular endothelial growth factor for diabetic macular oedema: a network meta-analysis. *Cochrane Database Syst Rev*. 2017;6(6):CD007419.
17. Sivaprasad S, Prevost AT, Vasconcelos JC, Riddell A, Murphy C, Kelly J, et al. Clinical efficacy of intravitreal aflibercept versus panretinal photocoagulation for best corrected visual acuity in patients with proliferative diabetic retinopathy at 52 weeks (CLARITY): a multicentre, single-blinded, randomised, controlled, phase 2b, n. *Lancet*. 2017;389(10085):2193–203. [PubMed: 28494920]
18. Writing Committee for the Diabetic Retinopathy Clinical Research Network, Gross JG, Glassman AR, Jampol LM, Inusah S, Aiello LP, et al. Panretinal Photocoagulation vs Intravitreal Ranibizumab for Proliferative Diabetic Retinopathy: A Randomized Clinical Trial. *JAMA*. 2015;314(20):2137–46. [PubMed: 26565927]
19. Lundeen EA, Andes LJ, Rein DB, Wittenborn JS, Erdem E, Gu Q, et al. Trends in Prevalence and Treatment of Diabetic Macular Edema and Vision-Threatening Diabetic Retinopathy Among Medicare Part B Fee-for-Service Beneficiaries. *JAMA Ophthalmol*. 2022;140(4):345–53. [PubMed: 35238912]

20. Watson Health. IBM MarketScan Research Databases for Life Sciences Researchers. Accessed August 15, 2022 at: <https://www.ibm.com/downloads/cas/OWZWJ0QO>.
21. Chronic Conditions Data Warehouse Condition Categories [Internet]. Available from: <https://www2.ccwdata.org/web/guest/condition-categories>
22. Koopman RJ, Mainous AG, Diaz VA, Geesey ME. Changes in age at diagnosis of type 2 diabetes mellitus in the United States, 1988 to 2000. *Ann Fam Med*. 2005;3(1):60–3. [PubMed: 15671192]
23. Boye KS, Lage MJ, Shinde S, Thieu V, Bae JP. Trends in HbA1c and Body Mass Index Among Individuals with Type 2 Diabetes: Evidence from a US Database 2012–2019. *Diabetes Ther*. 2021;12(7):2077–87. [PubMed: 34076849]
24. Roy MS, Klein R, O'Colmain BJ, Klein BEK, Moss SE, Kempen JH. The prevalence of diabetic retinopathy among adult type 1 diabetic persons in the United States. *Arch Ophthalmol*. 2004;122(4):546–51. [PubMed: 15078673]
25. Varma R, Wen G, Jiang X, Hsu C, Torres M, Klein R, et al. Prevalence of diabetic retinopathy in adult Chinese American individuals: The Chinese American eye study. *JAMA Ophthalmol*. 2016;134(5):563–9. [PubMed: 27055063]
26. Rodriguez NM, Aguilar S. Prevalence of Diabetic Retinopathy in a Clinic Population from Puerto Rico. *Optom Vis Sci*. 2016;93(7):750–3. [PubMed: 27046091]
27. Varma R, Torres M, Peña F, Klein R, Azen SP. Prevalence of diabetic retinopathy in adult Latinos: the Los Angeles Latino eye study. *Ophthalmology*. 2004;111(7):1298–306. [PubMed: 15234129]
28. Klein R, Klein BE, Moss SE. Epidemiology of proliferative diabetic retinopathy. *Diabetes Care*. 1992;15(12):1875–91. [PubMed: 1464243]
29. Benoit SR, Swenor B, Geiss LS, Gregg EW, Saaddine JB. Eye Care Utilization Among Insured People With Diabetes in the U.S., 2010–2014. *Diabetes Care*. 2019;42(3):427–33. [PubMed: 30679304]
30. Ostchega Y, Fryar CD, Nwankwo T, Nguyen DT. Hypertension prevalence among adults aged 18 and over: United States, 2017–2018. NCHS Data Brief, no 364. Hyattsville, MD: National Center for Health Statistics. 2020.
31. American Optometric Association. Evidence-Based Clinical Practice Guideline. Eye Care of the Patient with Diabetes Mellitus [Internet]. Available from: <https://aoa.uberflip.com/i/374890-evidence-based-clinical-practice-guideline-diabetes-mellitus>
32. American Academy of Ophthalmology. Top Five Steps to Help Prevent Diabetic Eye Diseases [Internet]. Available from: <https://www.aao.org/eye-health/tips-prevention/top-five-diabetes-steps>
33. American Diabetes Association. Microvascular complications and foot care. *Diabetes Care*. 2017;40(Suppl. 1):S88–98. [PubMed: 27979897]
34. Fong DS, Gottlieb J, Ferris FL. Understanding the value of diabetic retinopathy screening. *Arch Ophthalmol*. 2001;119(5):758–60. [PubMed: 11346406]
35. Gange WS, Xu BY, Lung K, Toy BC, Seabury SA. Rates of Eye Care and Diabetic Eye Disease among Insured Patients with Newly Diagnosed Type 2 Diabetes. *Ophthalmol Retin*. 2021;2(2):160–8.
36. Ali MK, Bullard KM, Imperatore G, Barker L, Gregg EW. Characteristics associated with poor glycemic control among adults with self-reported diagnosed diabetes--National Health and Nutrition Examination Survey, United States, 2007–2010. *MMWR Suppl*. 2012;61(2):32–7. [PubMed: 22695461]
37. Ali MK, Bullard KM, Gregg EW, Rio C Del. A cascade of care for diabetes in the United States: visualizing the gaps. *Ann Intern Med*. 2014;161(10):681–9. [PubMed: 25402511]
38. Shea AM, Curtis LH, Hammill BG, Kowalski JW, Ravelo A, Lee PP, et al. Resource use and costs associated with diabetic macular edema in elderly persons. *Arch Ophthalmol*. 2008;126(12):1748–54. [PubMed: 19064859]
39. Moulin TA, Boakye EA, Wirth LS, Chen J, Burroughs TE, Vollman DE. Yearly Treatment Patterns for Patients with Recently Diagnosed Diabetic Macular Edema. *Ophthalmol Retin*. 2019;3(4):362–70.
40. Parikh R, Ross JS, Sangaralingham LR, Adelman RA, Shah ND, Barkmeier AJ. Trends of Anti-Vascular Endothelial Growth Factor Use in Ophthalmology Among Privately Insured and Medicare Advantage Patients. *Ophthalmology*. 2017;124(3):352–8. [PubMed: 27890437]

Article Highlights:

- Diabetic retinopathy is a diabetes complication that can threaten vision.
- Using commercial health insurance claims, we examined the trend (2009–2018) in prevalence and treatment of diabetic macular edema (DME) and vision-threatening diabetic retinopathy (VTDR) among adults 18–64 years with diabetes.
- The annual prevalence of having DME or VTDR increased (2.1% to 3.4%; $p < 0.001$). Annual claims for anti-vascular endothelial growth factor injections increased by 327% among those with *any DME* and 206% among those with *VTDR with DME*.
- Vision-threatening diabetes-related eye disease among adults with diabetes has increased, highlighting the importance of clinical prevention interventions.

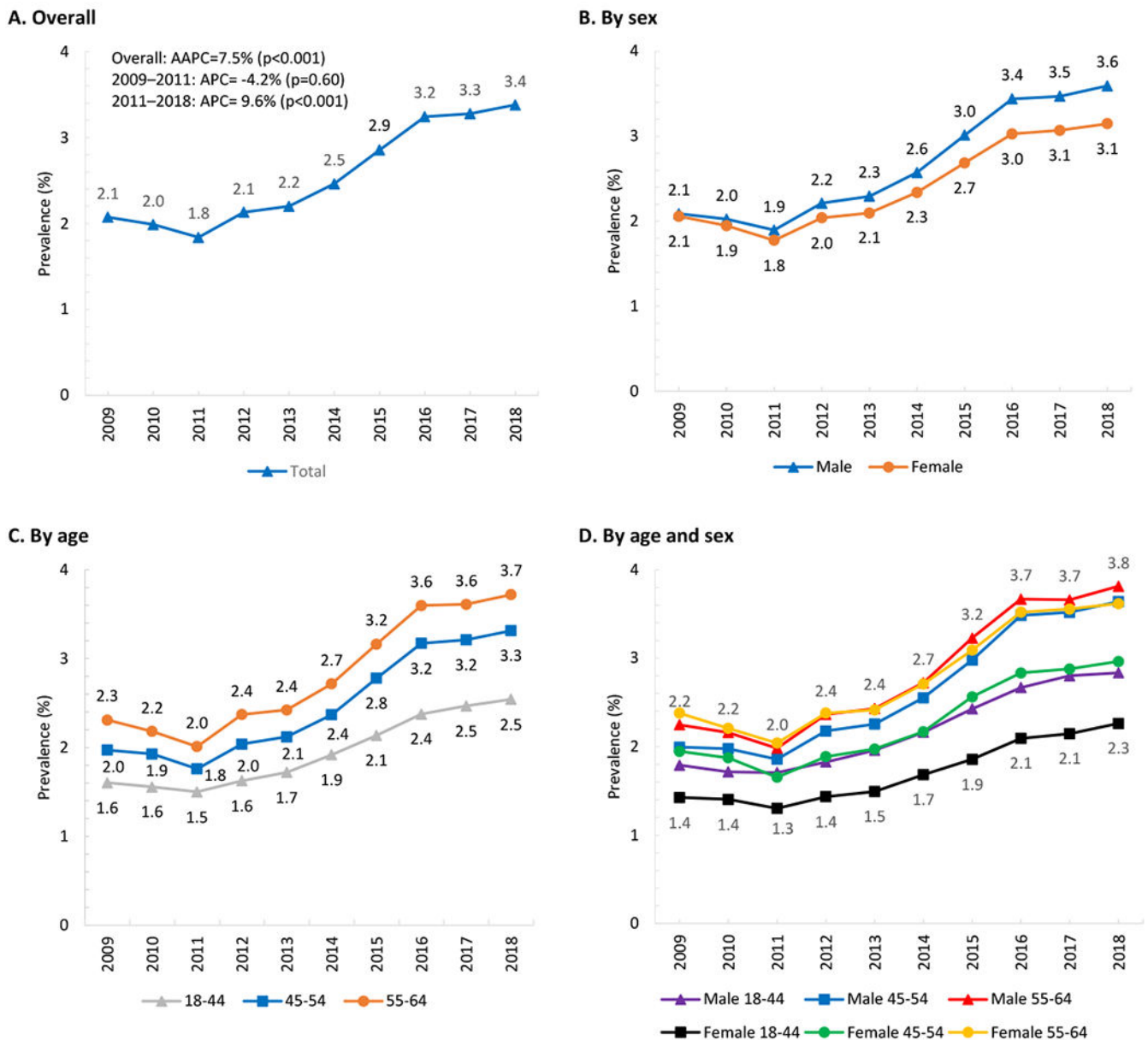
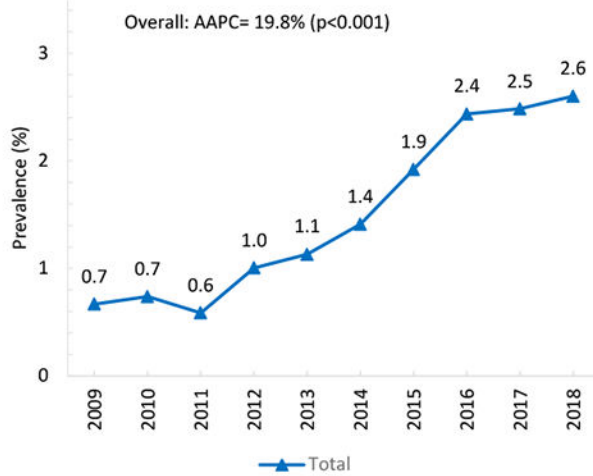


Figure 1, Panels A-D. Annual prevalence of having 1 claim for diabetic macular edema or vision-threatening diabetic retinopathy (DME/VTDR) among adults 18–64 years of age with diabetes, IBM® MarketScan® Database (2009–2018)

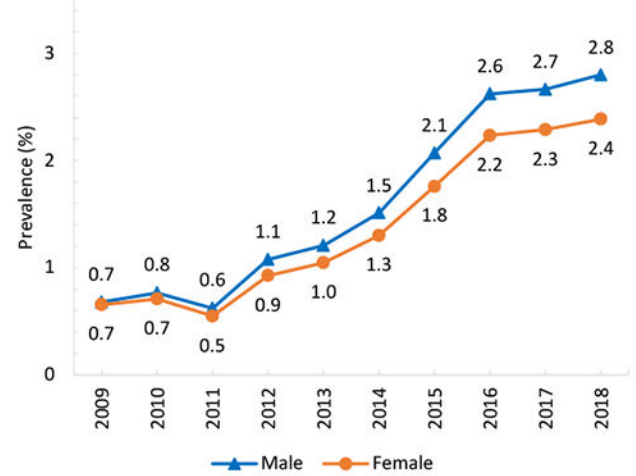
Abbreviations: APC (Annual Percent Change), AAPC (Average Annual Percent Change).

Diabetic macular edema or vision-threatening diabetic retinopathy (DME/VTDR) was defined as diabetic macular edema, severe non-proliferative diabetic retinopathy (with or without diabetic macular edema), or proliferative diabetic retinopathy (with or without diabetic macular edema).

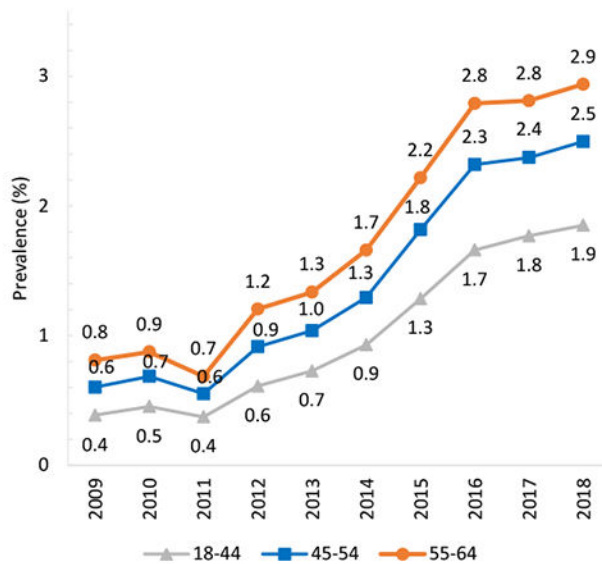
A. Overall



B. By sex



C. By age



D. By age and sex

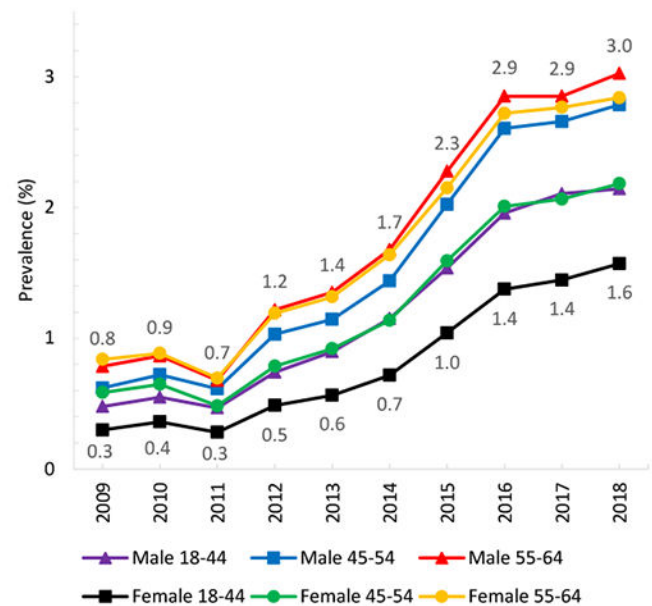


Figure 2, Panels A-D. Annual prevalence of having 1 claim for any diabetic macular edema (any DME) among adults 18–64 years of age with diabetes, IBM[®] MarketScan[®] Database (2009–2018).

Abbreviation: AAPC (Average Annual Percent Change). Any diabetic macular edema (any DME) was characterized as any diagnosis of diabetic macular edema, by itself or with any stage of diabetic retinopathy.

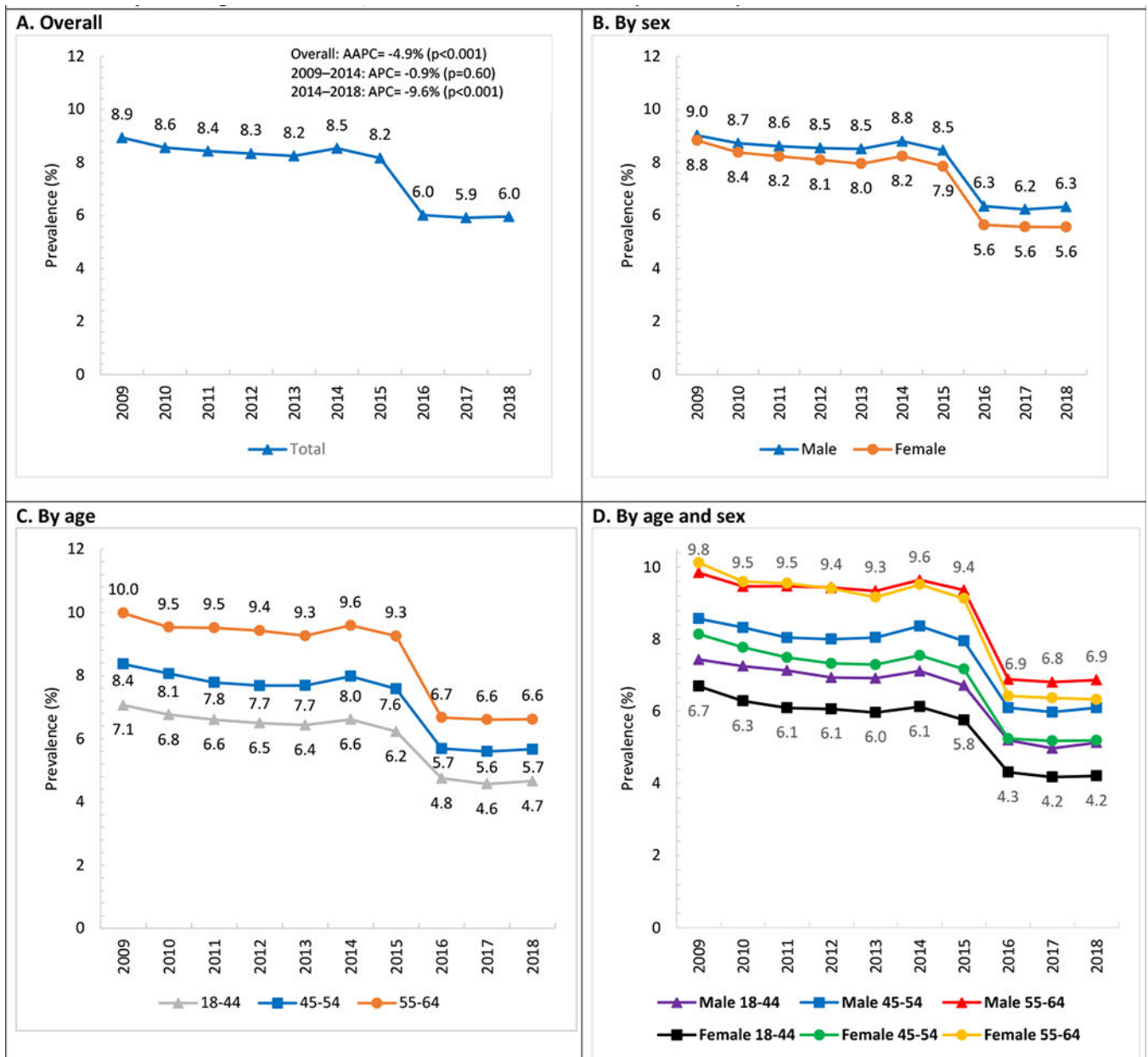
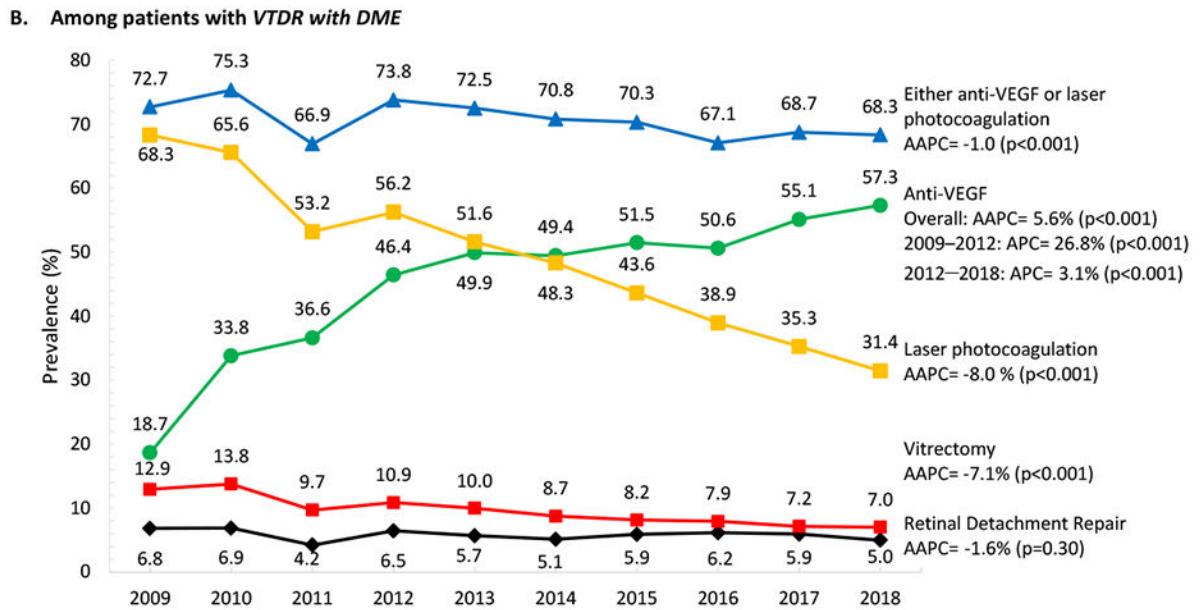
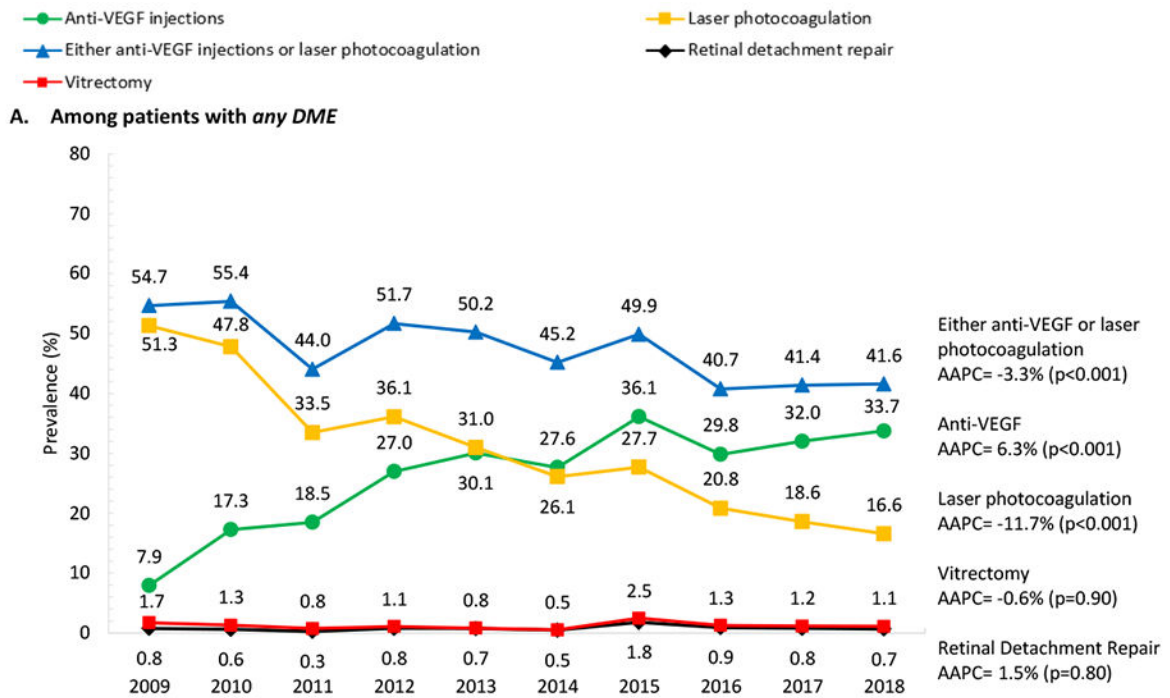


Figure 3, Panels A-D. Annual prevalence of having 1 claim for non-vision-threatening diabetes-related eye disease among adults 18-64 years of age with diabetes, IBM® MarketScan® Database (2009-2018)

Abbreviation: APC (Annual Percent Change), AAPC (Average Annual Percent Change).

Non-vision-threatening diabetes-related eye disease was characterized as background diabetic retinopathy, non-proliferative diabetic retinopathy (not otherwise specified), unspecified diabetic retinopathy without macular edema, mild non-proliferative diabetic retinopathy (without diabetic macular edema), moderate non-proliferative diabetic retinopathy (without diabetic macular edema), diabetes with ophthalmic manifestations, or other diabetic ophthalmic complication.



C. Among patients with VTDR without DME

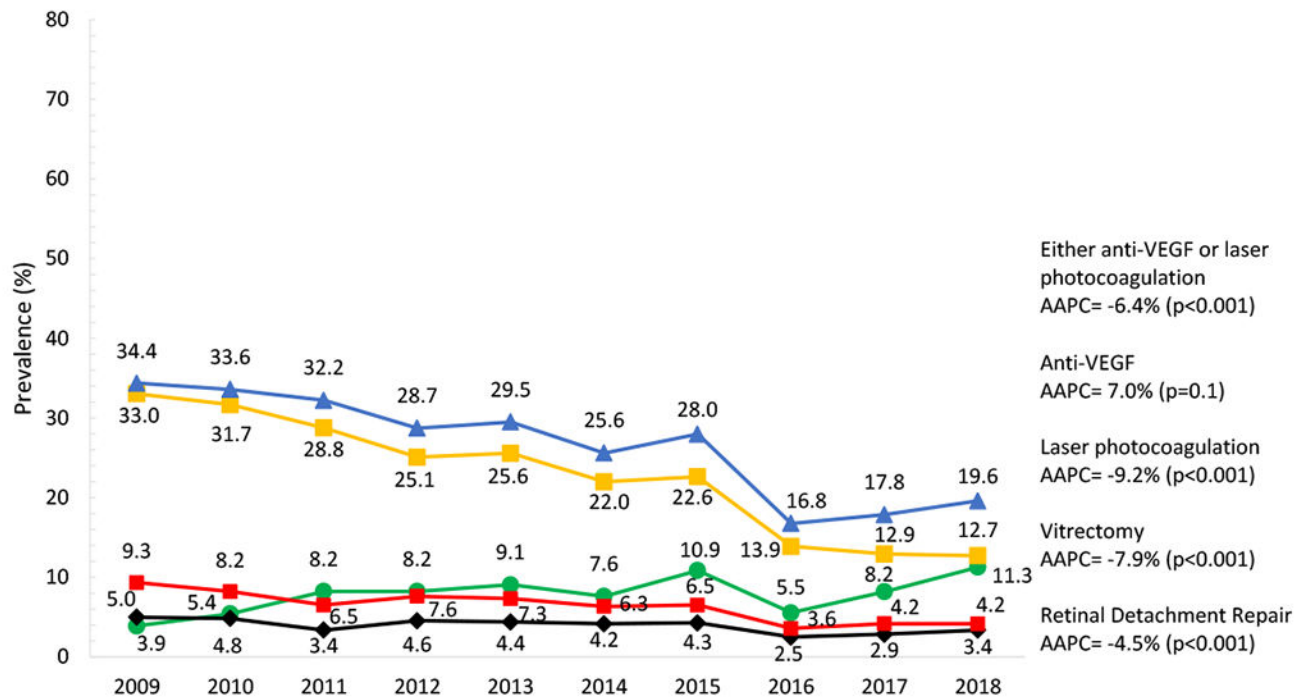


Figure 4, Panels A-C. Annual prevalence of having 1 claim for treatment among adults 18–64 years with diabetes, IBM® MarketScan® Database (2009–2018).

Abbreviations: APC (Annual Percent Change), AAPC (Average Annual Percent Change), DME (diabetic macular edema), VEGF (vascular endothelial growth factor), VTDR (vision-threatening diabetic retinopathy). Vision-threatening diabetic retinopathy was defined as severe non-proliferative diabetic retinopathy or proliferative diabetic retinopathy.