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

Elizabeth A. Lundeen, Minchul Kim, David B. Rein, John S. Wittenborn, Jinan Saaddine, Joshua R. Ehrlich, and Christopher S. Holliday
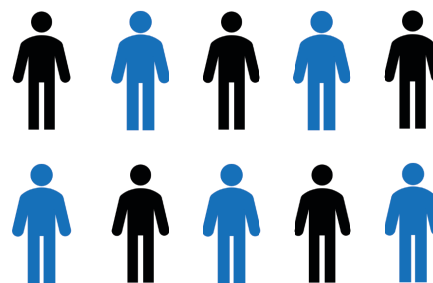
Trends in Vision-Threatening Diabetes-Related Eye Disease

Annual prevalence of having one or more claims for diabetic macular edema or vision-threatening diabetic retinopathy among adults 18–64 years of age with diabetes, IBM MarketScan Database (2009–2018)
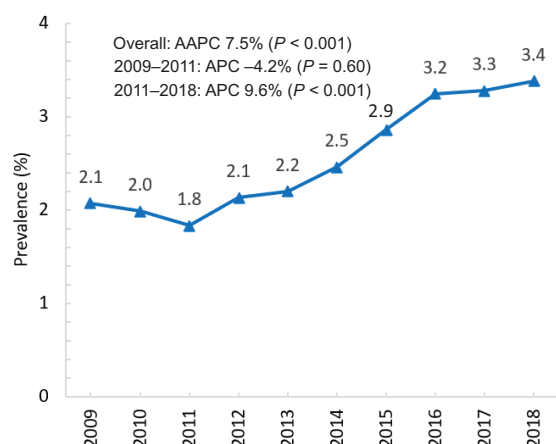
By 2018, more than half of patients who had vision-threatening diabetic retinopathy with diabetic macular edema received treatment using anti-vascular endothelial growth factor injections.

Overall: AAPC 7.5% ($P < 0.001$)
2009–2011: APC −4.2% ($P = 0.60$)
2011–2018: APC 9.6% ($P < 0.001$)

AAPC, average annual percent change; APC, annual percent change.

ARTICLE HIGHLIGHTS

- Diabetic retinopathy is a diabetes complication that can threaten vision.
- Using commercial health insurance claims, we examined the trends (2009–2018) in prevalence and treatment of diabetic macular edema (DME) and vision-threatening diabetic retinopathy (VTDR) among adults aged 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 antivascular 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.

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

Elizabeth A. Lundeen,[1] Minchul Kim,[2] David B. Rein,[3] John S. Wittenborn,[3] Jinan Saaddine,[1] Joshua R. Ehrlich,[4] and Christopher S. Holliday[1]

OBJECTIVE

Examine the 10-year trend in the prevalence and treatment of diabetic macular edema (DME) and vision-threatening diabetic retinopathy (VTDR) among commercially insured adults with diabetes.

RESEARCH DESIGN AND METHODS

We analyzed the 10-year trend (2009–2018) in health care claims for adults aged 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 one or more inpatient or two or more 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 one or more claims for *1*) any DME, *2*) either DME or VTDR, and *3*) antivascular endothelial growth factor (anti-VEGF) injections and laser photocoagulation treatment, stratified by any DME, VTDR with DME, and VTDR without DME. We calculated the average annual percent change (AAPC).

RESULTS

From 2009 to 2018, there was an increase in the annual prevalence of patients with DME or 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 or VTDR and any DME, with men having a higher prevalence than women. Annual claims for anti-VEGF injections increased among patients 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 or VTDR and anti-VEGF injections increased whereas those for laser photocoagulation decreased among commercially insured adults with diabetes.

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More than 37 million adults aged ≥18 years in the U.S. have diabetes (1), putting them at risk for serious complications like diabetic retinopathy (DR), the leading

cause of incident blindness among U.S. adults aged 20–74 years (2). DR occurs when prolonged exposure to high blood glucose levels damages blood vessels in the retina. Risk of DR is primarily influenced by diabetes duration and long-term glycemic control (3–7). DR is estimated to affect 28.5% of U.S. adults aged ≥40 years who have diabetes (8). Vision-threatening DR (VTDR) includes severe nonproliferative 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 U.S. adults aged ≥40 years who have diabetes (3,8).

Studies have documented an increase in diabetes prevalence among U.S. adults in the past two decades (9,10). Data from the National Health and Nutrition Examination Survey (NHANES) show that the prevalence of diabetes among U.S. adults aged ≥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 HbA_{1c} <7% among US adults aged ≥20 years who have 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 past 20 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 antivascular endothelial growth factor (anti-VEGF) agents (namely, 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 1 year compared with 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 aged ≥40 years are from NHANES, which last fielded this information from 2005 to 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 to 2018 in the annual prevalence of Medicare Part B fee-for-service beneficiaries aged ≥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, to our knowledge, similar studies of people aged <65 years have not been conducted. It is important to also understand these trends in patients with diabetes aged <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 article, we examine the 10-year trend (2009–2018) in the annual prevalence of commercially insured adults aged 18–64 years who have diabetes and 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 health care claims from 2009 to 2018 for adults aged 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 noncapitated (i.e., 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 one or more inpatient or two or more 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 one or more claims for DME or VTDR (hereafter, DME/VTDR), defined using ICD-9-CM and ICD-10-CM diagnosis codes (Supplementary Table 1). Annual prevalence of DME/VTDR was calculated as the number of patients with one or more claims with a diagnosis of DME/VTDR in the index year divided by the number of patients with diabetes in that year. Because of the emergence of new therapies for DME, we also separately calculated the annual prevalence of patients with diabetes with one or more claims for any DME (hereafter, any DME), with or without any stage of DR, using ICD diagnosis codes (Supplementary Table 2). Last, we present the annual prevalence of patients with diabetes with one or more claims for non–vision-threatening diabetes-related eye diseases, defined using ICD diagnosis codes (Supplementary Table 3) as background DR, nonproliferative DR (not otherwise specified), unspecified DR without macular edema, mild nonproliferative DR (without DME), moderate nonproliferative DR (without DME), diabetes with ophthalmic manifestations, and other diabetic ophthalmic complications. The annual prevalence of these three categories of disease (i.e., DME/VTDR, any DME, and diabetes with non–vision-threatening diabetes-related eye diseases) is presented overall, stratified by sex and 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-VEGF injections, laser photocoagulation, retinal detachment repair, and vitrectomy. Patients were defined as having ach of these treatment types if they had one or more claims in the index year with the Current Procedural Terminology codes or Healthcare Common Procedure Coding System codes for these procedures (Supplementary Table 4). 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 (Supplementary Tables 5–7). All prevalence figures were standardized using the direct method to the age and sex distribution of the analytic sample in 2009 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, College Station, TX) and SAS 9.4 (SAS Institute, 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 period. Last, 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 (Supplementary Tables 8–10). Confidence intervals for the statistics presented in all figures are shown in Supplementary Tables 11–14.

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 to 2018, among commercially insured adults aged 18–64 years, approximately 1 in 15 patients had diabetes (range: 6.83% [95% CI 6.82–6.85] in 2013 to 7.51% [95% CI 7.49–7.53] in 2017) (Supplementary Table 15). 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 10-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% (95% CI 2.05–2.10) in 2009 to 3.38% (95% CI 3.33–3.42) in 2018 (AAPC 7.5%; $P < 0.001$) (Fig. 1). An inflection point in the trend was found at 2011, with the annual prevalence decreasing nonsignificantly from 2009 to 2011 (APC −4.2%; $P = 0.60$) and then increasing significantly from 2011 to 2018 (APC 9.6%; $P < 0.001$). The prevalence of DME/VTDR was significantly higher among men compared with women from 2010 to 2018 (all $P \le 0.01$ (Fig. 1, Supplementary Table 8). Beginning in 2010, the prevalence of DME/VTDR was highest among men and women aged 55–64 years and men 45–54 years, compared with the other age and sex groups (all $P \le 0.05$) (Fig. 1).

Similarly, the annual prevalence of patients with diabetes who had any DME increased significantly from 0.67% (95% CI 0.65–0.68) in 2009 to 2.60% (95% CI 2.57–2.64) in 2018 (AAPC 19.8%; $P < 0.001$) (Fig. 2). From 2010 to 2018, the prevalence of any DME was significantly higher among men compared with women (all $P < 0.01$) (Fig. 2), and the prevalence was highest among men and women aged 55–64 years and men aged 45–54 years (all $P \le 0.01$) (Fig. 2, Supplementary Table 9). Conversely, from 2009 to 2018, the annual prevalence of non–vision-threatening diabetes-related eye diseases among patients with diabetes decreased significantly from 8.93% (95% CI 8.88–8.99) in 2009 to 5.96% (95% CI 5.91–6.01) in 2018 (AAPC −4.9%; $P < 0.001$) (Fig. 3). An inflection point in the trend was detected at 2014, with the annual prevalence decreasing nonsignificantly from 2009 to 2014 (APC −0.9%; $P = 0.60$) and then decreasing significantly from 2014 to 2018 (APC −9.6%; $P < 0.001$). From 2009 to 2018, the prevalence of non–vision-threatening diabetes-related eye disease was significantly higher among men compared with women (all $P < 0.01$) (Fig. 3), and the prevalence was highest among men and women aged 55–64 years and men aged 45–54 years (all $P \le 0.01$) (Fig. 3, Supplementary Table 10).
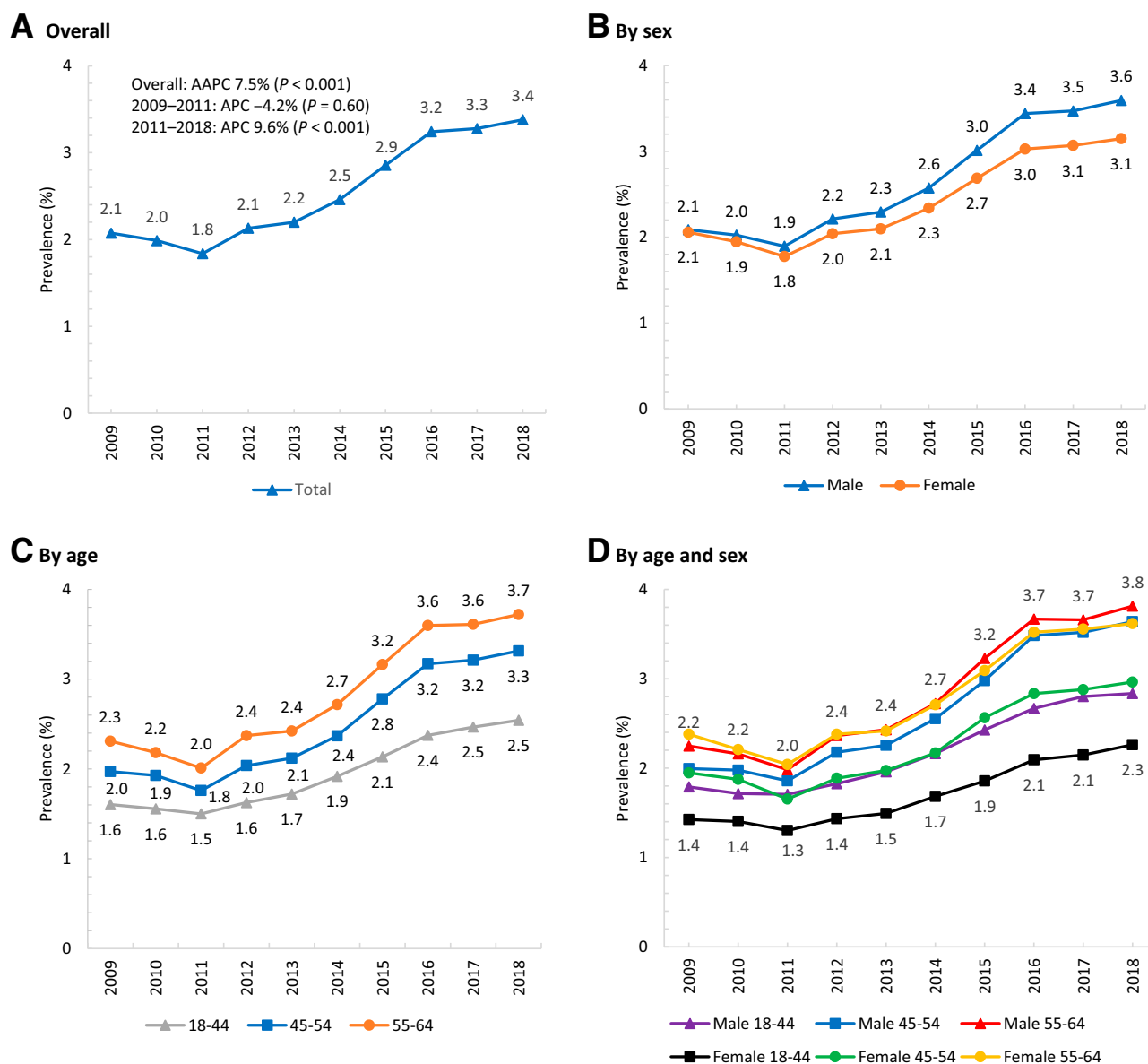
From 2009 to 2018, the annual prevalence of having laser photocoagulation decreased significantly among all three groups: those with any DME (51.32% [95% CI 49.80–52.83] to 16.56% [95% CI 15.96–17.18]; AAPC −11.7%; $P < 0.001$);

VTDR with DME (68.31% [95% CI 66.71–69.87] to 31.45% [95% CI 30.52–32.39]; AAPC −8.0%; $P < 0.001$); and VTDR without DME (33.03% [95% CI 32.30–33.77] to 12.7% [95% CI 11.89–13.57]; AAPC −9.2%; $P < 0.001$) (Fig. 4). During this period, the annual prevalence of having anti-VEGF injections increased significantly among those with any DME (7.95% [95% CI 7.16–8.81] to 33.74% [95% CI 32.97–34.52]; AAPC 6.3%; $P < 0.001$) and those having VTDR with DME (18.66% [95% CI 17.37–20.02] to 57.32% [95% 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 to 2012 (APC 26.8%; $P < 0.001$) and still increasing, but less steeply, from 2012 to 2018 (APC 3.1%; $P < 0.001$). By 2018, more than half of patients with VTDR with DME received treatment using anti-VEGF injections. Over the 10-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 less common procedures overall, as expected, and were most frequently performed among patients with VTDR with DME (range in annual prevalence across the 10-year period: from 7.04% [95% CI 6.54–7.58] in 2018 to 13.78% [95% CI 12.62–15.02] in 2010; and from 5.00% [95% CI 4.57–5.47] in 2018 to 6.89% [95% CI 6.05–7.84] in 2010, respectively). From 2009 to 2018, the annual prevalence of having a vitrectomy significantly decreased among patients with VTDR with DME (from 12.94% [95% CI 11.84–14.13] to 7.04% [95% CI 6.54–7.58]; AAPC −7.1%; $P < 0.001$) and those with VTDR without DME (9.33% [95% CI 8.89–9.79] to 4.16% [95% 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 to 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 to 2018, with the annual prevalence

A Overall

Overall: AAPC 7.5% ($P < 0.001$)
2009–2011: APC –4.2% ($P = 0.60$)
2011–2018: APC 9.6% ($P < 0.001$)
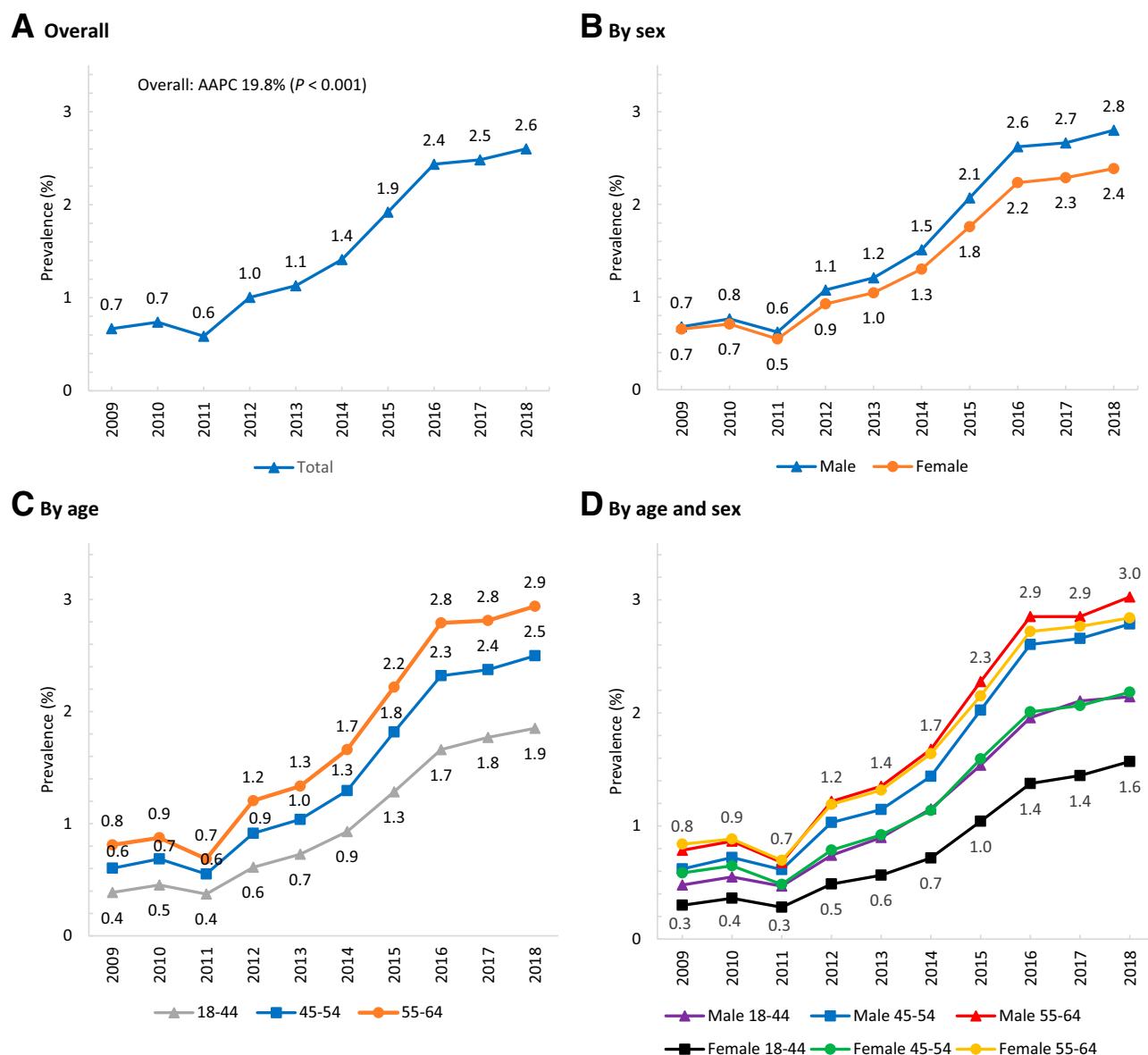
B By sex

C By age

D By age and sex

Figure 1—Annual prevalence of having one or more claims for DME/VTDR among adults 18–64 years of age with diabetes, according to the IBM MarketScan Database (2009–2018) (20). DME or VTDR was defined as DME, severe nonproliferative DR (with or without DME), or proliferative DR (with or without DME).

of having a claim for DME/VTDR higher among men than women and highest among men and women aged 55–64 years and men aged 45–54 years compared with the other age and sex groups. There were marked changes during this time 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 aged <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 U.S. adults aged ≥40 years who have diabetes (3,8). Using identical case definitions as the present study, we published a study describing very similar trends from 2009 to 2018 in the annual prevalence of Medicare

Part B fee-for-service beneficiaries aged ≥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 U.S. 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

A Overall

Overall: AAPC 19.8% (*P* < 0.001)

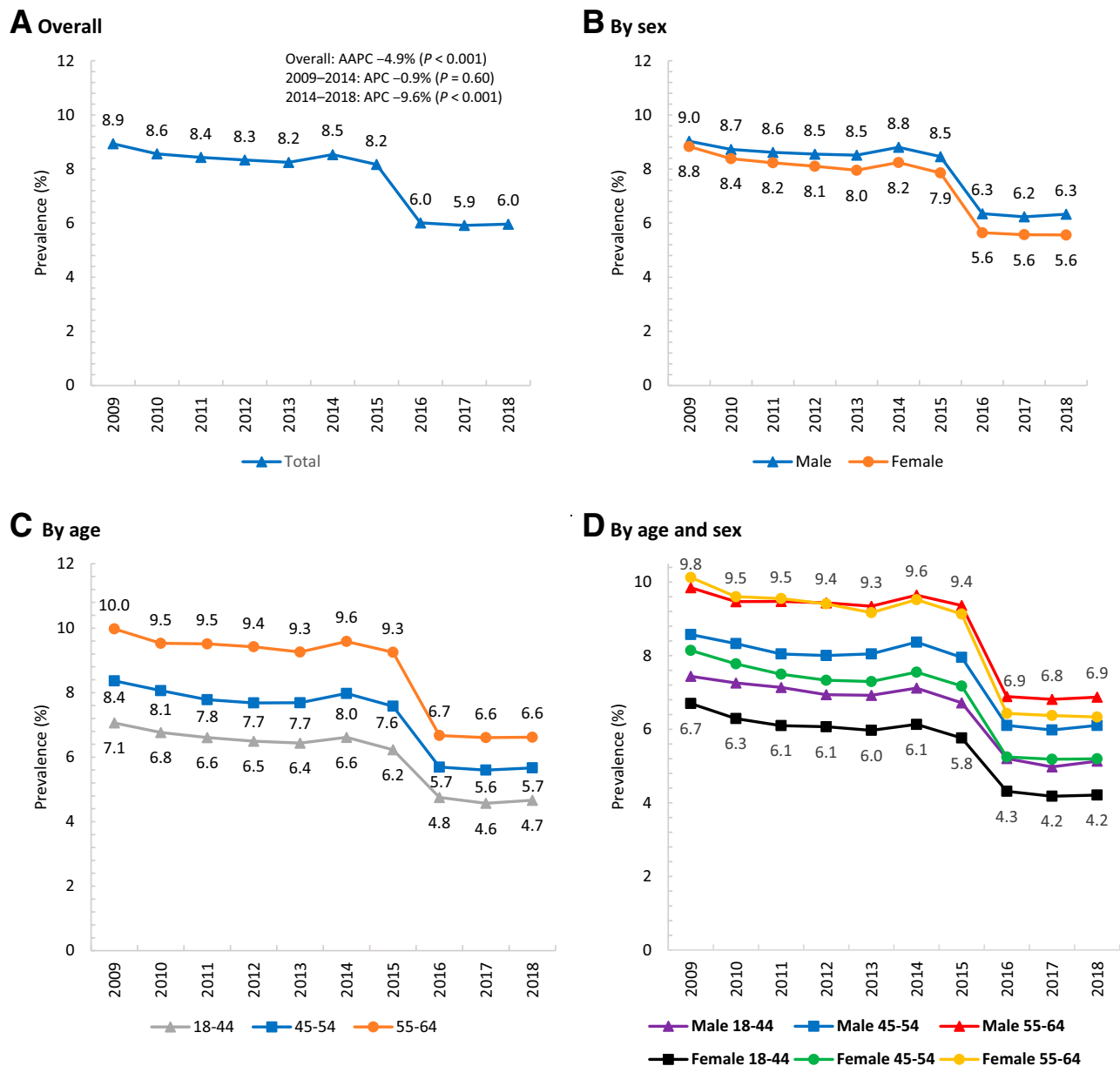## B By sex

C By age

D By age and sex

Figure 2—Annual prevalence of having one or more claims for any DME among adults 18–64 years of age with diabetes, according to the IBM MarketScan Database (2009–2018) (20). Any DME was characterized as any diagnosis of DME, by itself or with any stage of DR.

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 to 2019, there was a decrease in the percentage of adults aged ≥18 years with diabetes who achieved a HbA$_{1c}$ <7% (23). However, we cannot discount the possibility that improvements in screening, imaging technology, diagnosis, or medical coding over the past decade may have influenced these trends.

We documented statistically significant differences in the prevalence of annual claims for DME/VTDR, any DME, and non–vision-threatening diabetes-related eye disease by sex, with men

having a higher prevalence than women; however, these differences by sex are small and may not be clinically meaningful. Several U.S. 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 make a direct comparison with our study results difficult (24–28). A study using data from the New Jersey 725 study and the Wisconsin Epidemiologic Study of Diabetic Retinopathy examined the prevalence of DR among adults with type 1 diabetes and found that men were more likely to have VTDR than women (relative risk 1.17; 95% CI 1.01–1.36) (24). The Chinese American

Eye Study found that men had a higher prevalence than women of moderate DR (15.0% vs. 9.2%, respectively; *P* = 0.02) and proliferative DR (3.6% vs. 1.4%, respectively; *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 men (47.2%) than women (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 aged ≥40 years with diabetes, the

A Overall

Overall: AAPC −4.9% (*P* < 0.001)
2009–2014: APC −0.9% (*P* = 0.60)
2014–2018: APC −9.6% (*P* < 0.001)

8.9 8.6 8.4 8.3 8.2 8.5 8.2 6.0 5.9 6.0

── Total

B By sex

9.0 8.7 8.6 8.5 8.5 8.8 8.5 6.3 6.2 6.3
8.8 8.4 8.2 8.1 8.0 8.2 7.9 5.6 5.6 5.6

── Male   ── Female

C By age

10.0 9.5 9.5 9.4 9.3 9.6 9.3 6.7 6.6 6.6
8.4 8.1 7.8 7.7 7.7 8.0 7.6 5.7 5.6 5.7
7.1 6.8 6.6 6.5 6.4 6.6 6.2 4.8 4.6 4.7

── 18-44   ── 45-54   ── 55-64

D By age and sex

9.8 9.5 9.5 9.4 9.3 9.6 9.4 6.9 6.8 6.9
6.7 6.3 6.1 6.1 6.0 6.1 5.8 4.3 4.2 4.2

── **Male 18-44**   ── **Male 45-54**   ── **Male 55-64**
── **Female 18-44**   ── **Female 45-54**   ── **Female 55-64**

Figure 3—Annual prevalence of having one or more claims for non–vision-threatening diabetes-related eye disease among adults 18–64 years of age with diabetes, according to the IBM MarketScan Database (2009–2018) (20). Non–vision-threatening diabetes-related eye disease was characterized as background DR, nonproliferative DR (not otherwise specified), unspecified DR without macular edema, mild nonproliferative DR (without DME), moderate nonproliferative DR (without DME), diabetes with ophthalmic manifestations, or other diabetic ophthalmic complication.

prevalence of DR was higher in men (31.6%; 95% CI 26.8–36.8) than women (25.7% [95% CI 21.7–30.1], *P* = 0.04; adjusted odds ratio [OR] 2.07 [95% CI 1.39–3.10]) (8). However, there was no difference in the prevalence of VTDR among men (4.2%; 95% CI 2.8–6.1) compared with women (4.7% [95% CI 3.2–6.9], *P* = 0.67; adjusted OR 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. (29), using the IBM MarketScan Database of health care claims,

documented sex differences in DR that were similar to our findings. They 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 to 2014. Benoit et al. (29) 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 men had a higher prevalence than women of both DR (27.3% vs. 21.7%; *P* < 0.0001) and VTDR (9.3% vs. 7.3%; *P* < 0.0001). Among
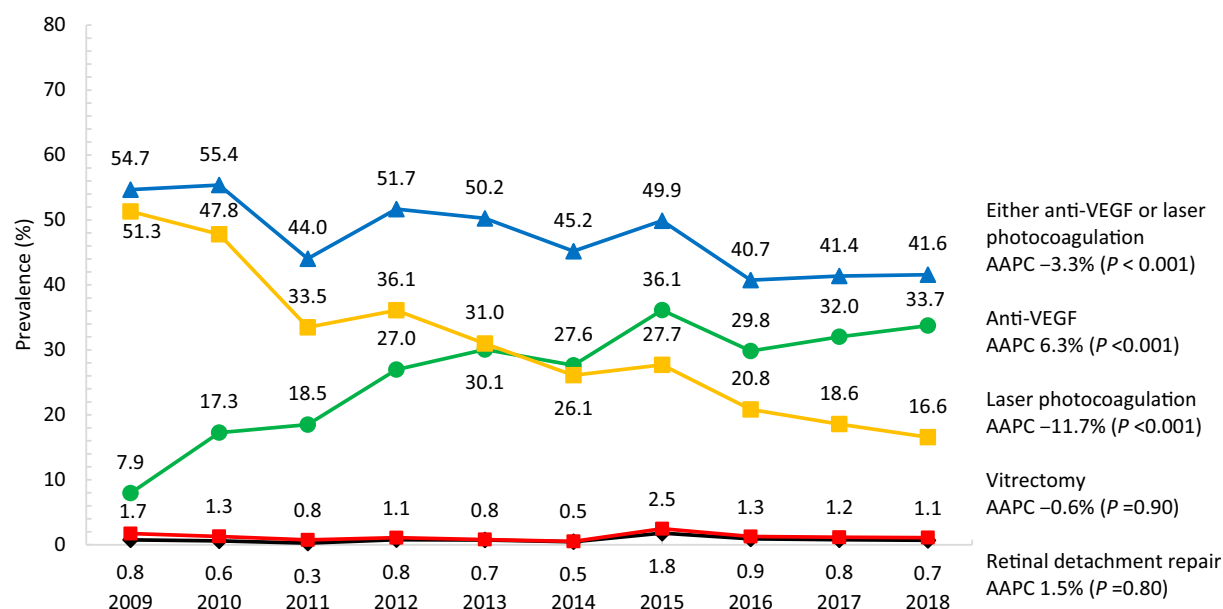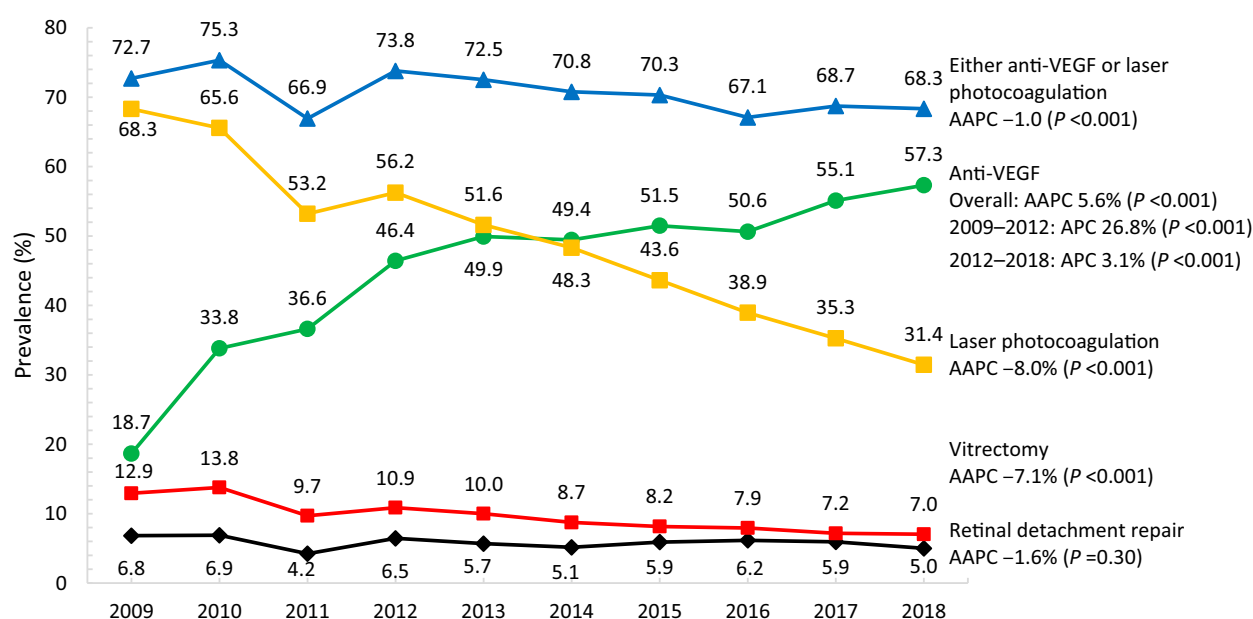
patients with type 1 diabetes, the 5-year period prevalence of DR and VTDR was 54.0% and 24.3%, respectively, and in this population, men also had a higher prevalence than women of both DR (56.1% vs. 51.8%; *P* < 0.0001) and VTDR (25.4% vs. 23.2%; *P* < 0.01).

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

Legend

- ● Anti-VEGF injections
- ▲ Either anti-VEGF injections or laser photocoagulation
- ■ Vitrectomy
- ■ Laser photocoagulation
- ◆ Retinal detachment repair

A Among patients with any DME

Either anti-VEGF or laser photocoagulation
AAPC −3.3% ($P < 0.001$)

Anti-VEGF
AAPC 6.3% ($P < 0.001$)

Laser photocoagulation
AAPC −11.7% ($P < 0.001$)

Vitrectomy
AAPC −0.6% ($P = 0.90$)

Retinal detachment repair
AAPC 1.5% ($P = 0.80$)

B Among patients with VTDR with DME

Either anti-VEGF or laser photocoagulation
AAPC −1.0 ($P < 0.001$)

Anti-VEGF
Overall: AAPC 5.6% ($P < 0.001$)
2009–2012: APC 26.8% ($P < 0.001$)
2012–2018: APC 3.1% ($P < 0.001$)

Laser photocoagulation
AAPC −8.0% ($P < 0.001$)

Vitrectomy
AAPC −7.1% ($P < 0.001$)

Retinal detachment repair
AAPC −1.6% ($P = 0.30$)

Figure 4—Annual prevalence of having one or more claims for treatment among adults 18–64 years with diabetes, according to the IBM Market-Scan Database (2009–2018) (20). VTDR was defined as severe nonproliferative DR or proliferative DR.

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. (29) found that among patients with type 2 diabetes, 14.7% of men and 15.8% of women met the American Diabetes Association recommendations for annual or biennial eye examinations; among those with type 1 diabetes this prevalence was 24.3% among men and 28.4% among women. 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). The authors found that men had lower odds of receiving an annual eye examination (OR 0.84; $P < 0.01$) and higher odds of
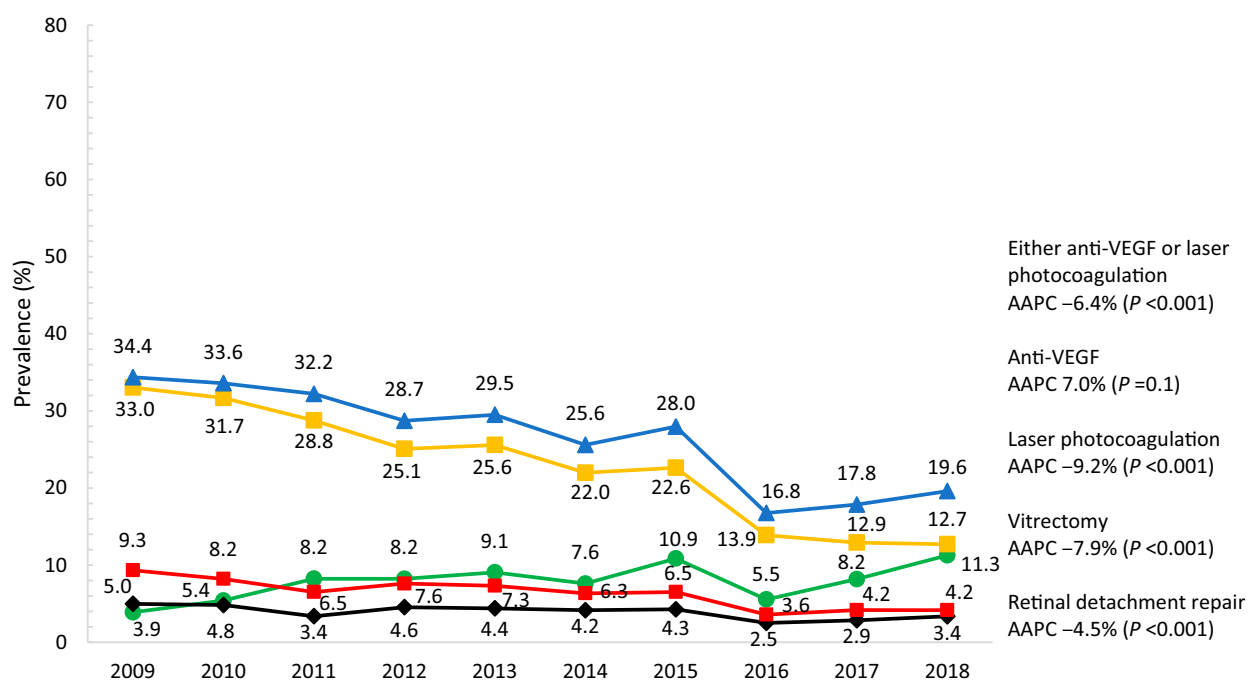
C Among patients with VTDR without DME

Figure 4—*Continued.*

developing DR within 5 years (OR 1.17; $P < 0.01$) than women. If men with diabetes meet guidelines for routine eye examinations at a lower rate than women, this could translate to men's 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 DR 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 HbA$_{1c}$ targets (37).

We observed a precipitous increase in the annual prevalence of having a claim for anti-VEGF injections from 2009 to 2018, a period during which physicians began to replace laser photocoagulation treatment with the injections 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 (38), and later approved aflibercept for DME treatment in 2014 (39) and ranibizumab and aflibercept for the treatment of DR in patients with DME in 2015 (40,41). Other U.S.

studies have documented similar increases in the use of anti-VEGF treatment for DME during this period. Recently published data using claims for Medicare Part B fee-for-service beneficiaries aged ≥65 years with diabetes showed an increase from 2009 to 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 increase 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 with an increase in receipt of intravitreal injection from 1% to 13% of patients in this period (42). Another study using administrative claims for patients with DME and either commercial health insurance or government insurance (i.e., 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 with a decrease in focal laser procedures from 75.3% of all DME treatments in 2009 to 24.0% in 2014) (43). One study combined health care claims data from commercial health insurance and Medicare Advantage for adults aged ≥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, the use of which increased from 2.4 injections/1,000 patients with DR in 2009 to 13.6 injections/1,000 patients in 2015 (44). 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 that could have implications for progression and severity of eye disease.

This analysis is subject to several limitations. Although the MarketScan database of administrative claims provides a robust sample size with patients from all U.S. 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 U.S. adults aged <65 years. Second, the trends described in this analysis are based on the annual prevalence of having a health care 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 substantially 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 overreporting of DME/VTDR prevalence. Fourth, our analytic sample size declined from 16.1 million to 10.6 million patients from 2009 to 2018, due to loss of data in the MarketScan database from a participating insurance provider. Last, 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 because of the absence of this information in MarketScan.

In summary, from 2009 to 2018, we observed a significant increase in the annual prevalence of having a health care 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 men 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, to inform prevention interventions.

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