

## Online-Only Supplementary material

*Poirrier J-E, et al. Herpes Zoster Incidence and Burden in Adults with Type 2*

*Diabetes Mellitus in the United States: A Retrospective Database Analysis*

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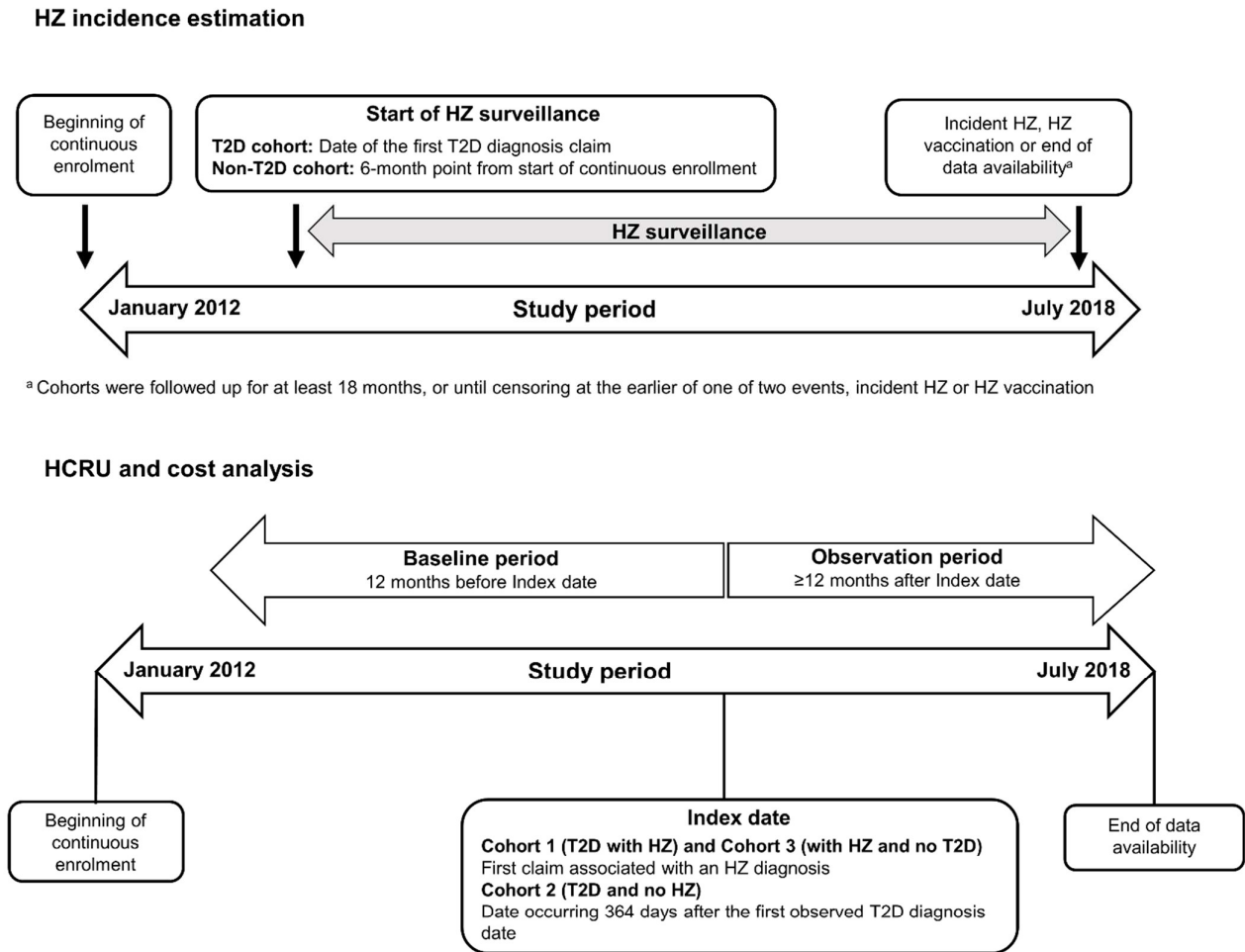
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**Supplementary Table 1. Inclusion and exclusion criteria**

Cohorts	Inclusion criteria	Exclusion criteria
Patients with T2D and HZ (cohort 1)	<ul style="list-style-type: none"> <li>▪ Primary or secondary diagnosis of HZ (ICD-9-CM diagnosis code 053.xx; ICD-10-CM diagnosis code B02.xx)</li> <li>▪ At least 12 months of continuous health plan enrollment before the HZ index date</li> <li>▪ At least 12 months of continuous health plan enrollment after the HZ index date</li> <li>▪ ≥18 years on HZ index date</li> <li>▪ At least one inpatient or two outpatient (≥30 days apart) primary or secondary diagnoses of T2D (ICD-9-CM codes 250.x0 and 250.x2; or ICD-10-CM code E11.xx) during the 12 months before the HZ index date</li> </ul>	<ul style="list-style-type: none"> <li>▪ First observed HZ diagnosis is postherpetic trigeminal neuralgia (ICD-9-CM, 053.12; ICD-10-CM, B02.22) or postherpetic polyneuropathy (ICD-9-CM, 053.13; ICD-10-CM, B02.23)</li> <li>▪ HZ vaccination during the study period</li> </ul>
Patients with T2D and no HZ (cohort 2)	<ul style="list-style-type: none"> <li>▪ At least one inpatient or two outpatient (≥30 days apart) primary or secondary diagnoses of T2D (ICD-9-CM codes 250.x0 and 250.x2; or ICD-10-CM code E11.xx)</li> <li>▪ ≥18 years on their first observed T2D diagnosis date</li> <li>▪ At least 24 months of continuous health plan enrollment after the first observed type 2 diabetes diagnosis date (12-month baseline period and a 12-month follow-up period)</li> </ul>	<ul style="list-style-type: none"> <li>▪ Diagnosis of HZ (ICD-9-CM diagnosis code 053.xx; ICD-10-CM diagnosis code B02.xx) at any time during the study period</li> <li>▪ HZ vaccination during the study period</li> </ul>
Patients with HZ and no T2D (cohort 3)	<ul style="list-style-type: none"> <li>▪ Primary or secondary diagnosis of HZ (ICD-9-CM diagnosis code 053.xx; ICD-10-CM diagnosis code B02.xx).</li> <li>▪ At least 12 months of continuous health plan enrollment before the HZ index date</li> <li>▪ At least 12 months of continuous health plan enrollment after the HZ index date</li> <li>▪ ≥ 18 years on their HZ index date</li> <li>▪ No diagnosis of T2D (during the 12 months before the HZ index date)</li> </ul>	<ul style="list-style-type: none"> <li>▪ First observed HZ diagnosis is postherpetic trigeminal neuralgia (ICD-9-CM, 053.12; ICD-10-CM, B02.22) or postherpetic polyneuropathy (ICD-9-CM, 053.13; ICD-10-CM, B02.23)</li> <li>▪ HZ vaccination during the study period</li> </ul>

HZ, herpes zoster; T2D, type 2 diabetes

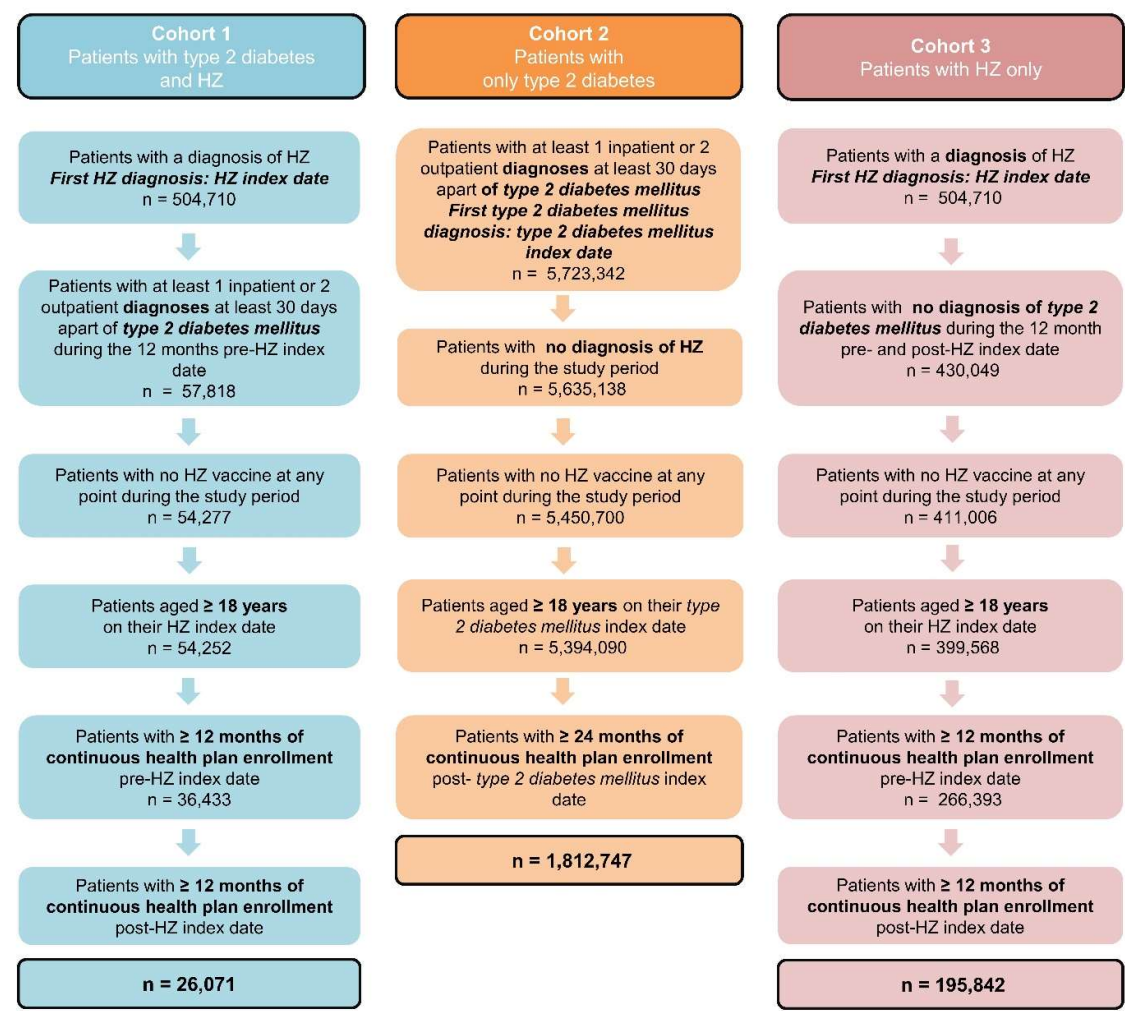
# **Supplementary Figure 1. Study schematics for incidence estimations and for HCRU and cost analysis**



For patients with HZ (cohorts 1 and 3), the index date was defined as the HZ index date; the baseline period was defined as the 12-month period before the HZ index date; the follow-up period was defined as the 12-month period after the HZ index date. For patients with type 2 diabetes without HZ (cohort 2), the index date was defined as the date occurring 364 days after the first observed type 2 diabetes diagnosis date; the baseline period was defined as the 12-month period before the corresponding index date for this population.

HCRU, Healthcare resource use; HZ, herpes zoster; T2D, type 2 diabetes

Supplementary Figure 2. Patient selection for the HCRU and cost analysis



HCRU, healthcare resource use; HZ, herpes zoster; n, number

**Supplementary Table 2. Baseline demographics before and after propensity matching.**

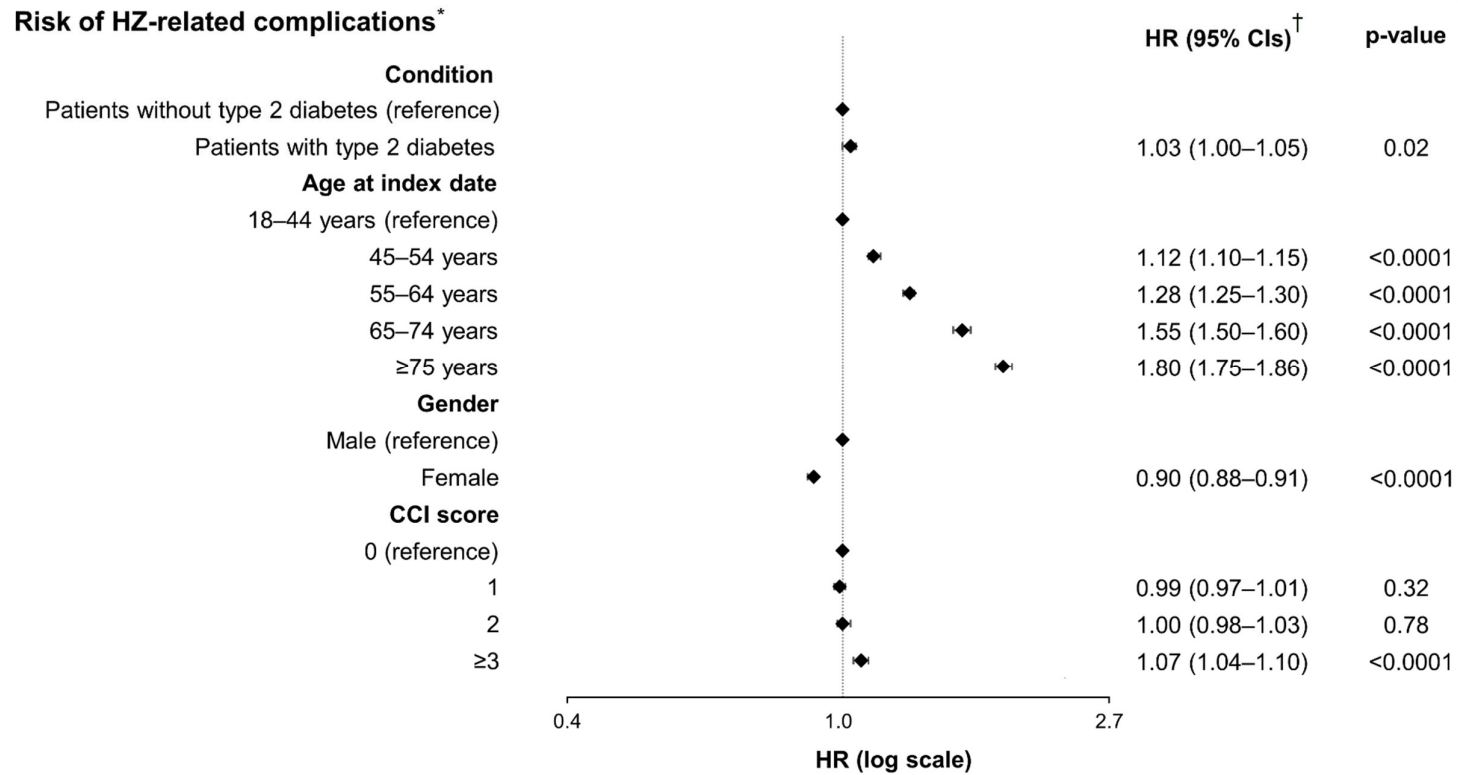
	Pre-matching			Post- matching		
	Cohort 1	Cohort 2	Cohort 3	Cohort 1	Cohort 2	Cohort 3
	With T2D and HZ* (N = 26,071)	With T2D and no HZ (N = 1,812,747)	With HZ and no T2D (N = 195,842)	With T2D and HZ* (N= 26,070/26,071)	With T2D and no HZ (N = 26,070)	With HZ and no T2D (N = 26,071)
<b>Demographics</b>						
<b>Age at index date, years, mean <math>\pm</math> SD</b>	62.2 $\pm$ 12.9	56.2 $\pm$ 14.0	51.6 $\pm$ 15.6	62.2 $\pm$ 12.9	62.1 $\pm$ 13.0	61.8 $\pm$ 13.8
<50, n (%)	3,745 (14.4)	530,497 (29.3)	83,110 (42.4)	3,745 (14.4)	3,760 (14.4)	3,957 (15.2)
50–54, n (%)	3,081 (11.8)	273,873 (15.1)	27,417 (14.0)	3,081 (11.8)	3,014 (11.6)	2,903 (11.1)
55–59, n (%)	4,824 (18.5)	321,031 (17.7)	31,392 (16.0)	4,824 (18.5)	4,786 (18.4)	5,366 (20.6)
60–64, n (%)	5,012 (19.2)	263,407 (14.5)	23,336 (11.9)	5,011 (19.2)	5,047 (19.4)	4,463 (17.1)
65–69, n (%)	2,059 (7.9)	121,869 (6.7)	7,390 (3.8)	2,059 (7.9)	2,300 (8.8)	2,189 (8.4)
70–74, n (%)	2,364 (9.1)	106,515 (5.9)	6,834 (3.5)	2,364 (9.1)	2,251 (8.6)	2,240 (8.6)
75–79, n (%)	2,003 (7.7)	82,990 (4.6)	5,746 (2.9)	2,003 (7.7)	1,957 (7.5)	1,968 (7.6)
$\geq 80$ , n (%)	2,983 (11.4)	112,565 (6.2)	10,617 (5.4)	2,983 (11.4)	2,955 (11.3)	2,985 (11.5)
<b>Female, n (%)</b>	15,149 (58.1)	921,745 (50.9)	125,270 (64.0)	15,148 (58.1)	15,150 (58.1)	15,103 (57.9)
<b>Geographic region, n (%)</b>						
Northeast	4,115 (15.8)	317,180 (17.5)	34,274 (17.5)	4,115 (15.8)	5,527 (21.2)	4,926 (18.9)
North Central	6,188 (23.7)	387,618 (21.4)	40,734 (20.8)	6,188 (23.7)	6,207 (23.8)	5,760 (22.1)
South	9,839 (37.7)	659,689 (36.4)	76,231 (38.9)	9,839 (37.7)	8,432 (32.3)	8,974 (34.4)
West	2,353 (9.0)	181,202 (10.0)	27,029 (13.8)	2,353 (9.0)	2,316 (8.9)	2,837 (10.9)
Unknown	3,576 (13.7)	267,058 (14.7)	17,574 (9.0)	3,575 (13.7)	3,588 (13.8)	3,574 (13.7)
<b>Insurance type, n (%)</b>						
Commercial/Medicare	22,551 (86.5)	1,550,394 (85.5)	178,857 (91.3)	22,551 (86.5)	22,539 (86.5)	22,553 (86.5)
Medicaid	3,520 (13.5)	262,353 (14.5)	16,985 (8.7)	3,519 (13.5)	3,531 (13.5)	3,518 (13.5)
<b>All-cause healthcare service costs in 12-months prior to index date (in 2018 U.S. \$), mean <math>\pm</math> SD (median).</b>	\$20,305 $\pm$ 53,023 (5,361)	\$9,725 $\pm$ 36,168 (1752)	\$9,154 $\pm$ 33,042 (2019)	\$20,305 $\pm$ 53,023 (5,361)	\$16,538 $\pm$ 44,248 (4,672)	\$17,926 $\pm$ 47,595 (4,796)
<b>CCI, mean <math>\pm</math> SD</b>	2.8 $\pm$ 2.5	2.0 $\pm$ 2.2	1.1 $\pm$ 1.8	2.8 $\pm$ 2.5	2.7 $\pm$ 2.4	2.7 $\pm$ 2.5
<b>CCI conditions, n (%)</b>						
Myocardial infarction	1,192 (4.6)	50,394 (2.8)	2,083 (1.1)	1,192 (4.6)	1,177 (4.5)	917 (3.5)
Congestive heart failure	2,911 (11.2)	114,203 (6.3)	4,413 (2.3)	2,911 (11.2)	3,084 (11.8)	1,877 (7.2)
Peripheral vascular disease	2,844 (10.9)	133,236 (7.4)	5,714 (2.9)	2,844 (10.9)	3,191 (12.2)	2,316 (8.9)

Cerebrovascular disease	2,962 (11.4)	133,780 (7.4)	7,266 (3.7)	2,962 (11.4)	3,163 (12.1)	2,708 (10.4)
Dementia	358 (1.4)	15,770 (0.9)	802 (0.4)	358 (1.4)	343 (1.3)	326 (1.3)
Chronic pulmonary disease	6,330 (24.3)	304,722 (16.8)	26,043 (13.3)	6,330 (24.3)	5,323 (20.4)	7,037 (27.0)
Rheumatic disease	1,125 (4.3)	42,237 (2.3)	5,824 (3.0)	1,125 (4.3)	767 (2.9)	1,576 (6.1)
Ulcer disease	322 (1.2)	16,495 (0.9)	1,293 (0.7)	322 (1.2)	296 (1.1)	420 (1.6)
Mild liver disease	1,313 (5.0)	81,936 (4.5)	3,190 (1.6)	1,313 (5.0)	1,455 (5.6)	1,036 (4.0)
Moderate-to-severe liver disease	1,936 (7.4)	118,734 (6.6)	6,988 (3.6)	1,936 (7.4)	2,421 (9.3)	2,485 (9.5)
Diabetes with complications	11,760 (45.1)	427,445 (23.6)	–	11,759 (45.1)	13,146 (50.4)	-
Hemiplegia or paraplegia	294 (1.1)	14,683 (0.8)	751 (0.4)	294 (1.1)	268 (1.0)	267 (1.0)
Renal disease	3,739 (14.3)	139,581 (7.7)	5,136 (2.6)	3,739 (14.3)	2,822 (10.8)	2,088 (8.0)
Cancer- non metastatic	2,269 (8.7)	111,121 (6.1)	10,049 (5.1)	2,269 (8.7)	2,454 (9.4)	3,709 (14.2)
Cancer- metastatic	350 (1.3)	13,414 (0.7)	1,731 (0.9)	350 (1.3)	283 (1.1)	760 (2.9)
HIV/AIDS	152 (0.6)	6,525 (0.4)	1,229 (0.6)	152 (0.6)	55 (0.2)	441 (1.7)
Depression	4,248 (16.3)	227,681 (12.6)	20,403 (10.4)	4,248 (16.3)	3,668 (14.1)	4,820 (18.5)
Hypertension	21,161 (81.2)	1,210,914 (66.8)	58,204 (29.7)	21,161 (81.2)	20,613 (79.1)	16,302 (62.5)
Skin Ulcers	2,900 (11.1)	155,896 (8.6)	8,368 (4.3)	2,900 (11.1)	3,529 (13.5)	2,641 (10.1)
<b>DCSI, mean <math>\pm</math> SD (median)</b>	<b>2.6 <math>\pm</math> 2.3 (2.0)</b>	<b>1.4 <math>\pm</math> 1.9 (0.0)</b>	<b>–</b>	<b>2.6 <math>\pm</math> 2.3 (2.0)</b>	<b>2.1 <math>\pm</math> 2.2 (1.0)</b>	<b>–</b>
<b>Diabetes medications, n (%)</b>						
Metformin	14,022 (53.8)	639,565 (35.3)	–	14,022 (53.8)	13,438 (51.5)	–
Sulfonylureas	6,949 (26.7)	302,338 (16.7)	–	6,949 (26.7)	7,428 (28.5)	–
Meglitinides	302 (1.2)	11,197 (0.6)	–	302 (1.2)	345 (1.3)	–
Thiazolidinediones	1,261 (4.8)	53,353 (2.9)	–	1,261 (4.8)	1,285 (4.9)	–
GLP-1 receptor agonists	2,004 (7.7)	77,699 (4.3)	–	2,004 (7.7)	1,948 (7.5)	–
DPP-4 inhibitors	2,740 (10.5)	103,773 (5.7)	–	2,740 (10.5)	2,725 (10.5)	–
SGLT-2 inhibitors	1,861 (7.1)	36,959 (2.0)	–	1,861 (7.1)	885 (3.4)	–
Insulin	7,542 (28.9)	295,158 (16.3)	–	7,542 (28.9)	7,605 (29.2)	–
Combination agents	1,766 (6.8)	79,280 (4.4)	–	1,766 (6.8)	1,806 (6.9)	–

\* For comparisons between T2D cohorts with and without HZ (cohort 1 and 2), cohort 1 included 26,070 patients; for comparisons between patients with HZ with and without T2D (cohort 1 and 3), cohort 1 included 26,071 patients.

CCI, modified Charlson-Quan comorbidity index; DCSI, diabetes complication severity index; DPP-4, dipeptidyl-peptidase-4; GLP-1, glucagon-like peptide-1; SGLT-2, sodium-glucose cotransporter-2; HCRU, healthcare resource use; HZ, herpes zoster; SD, standard deviation; T2D, type 2 diabetes

### Supplementary Figure 3. Risk of HZ-related complications



\* Risk of HZ complications was evaluated across all patients with HZ (N = 221,913); comprising patients with HZ without T2D (n = 195,842) and patients with HZ and T2D (n = 26,071).

† Hazard ratios (HRs) with 95% CIs and p-values were calculated using multivariable Cox regression analysis, with adjustment for cohort (condition), age, gender, and baseline CCI score (excluding scoring for T2D related conditions).

CCI, modified Charlson-Quan comorbidity index; HZ, herpes zoster; T2D, type 2 diabetes

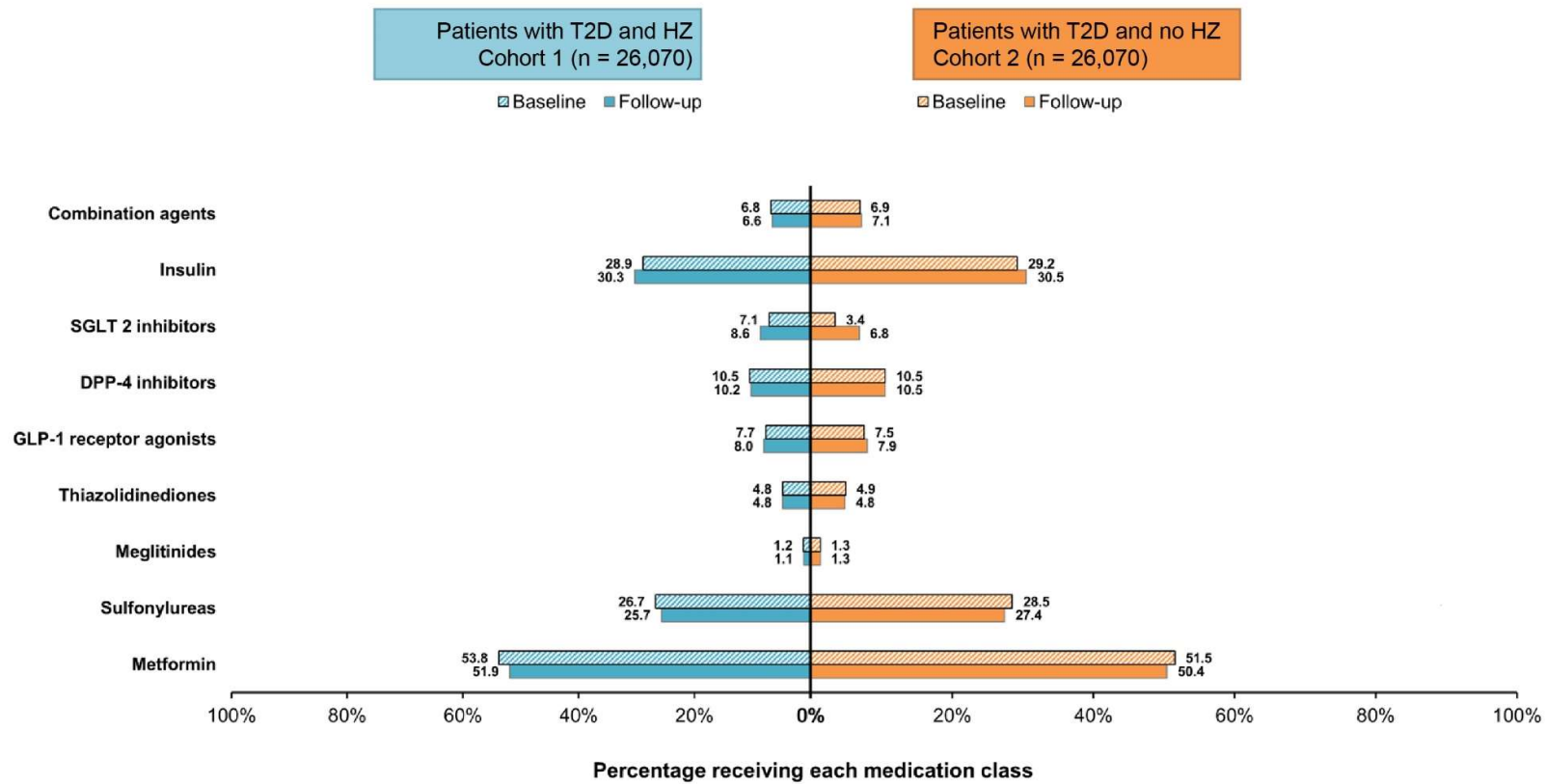
**Supplementary Table 3. HZ-related complications in the matched cohorts  
(patients with and without T2D)**

	Cohort 1	Cohort 3
	With T2D and HZ (N = 26,071)	With HZ and no T2D (N = 26,071)
Patients with any HZ-related complication, n (%)	8,062 (30.9)	7,798 (29.9)
PHN	6,462 (24.8)	6,271 (24.1)
Ophthalmic complications	1,554 (5.9)	1,558 (6.0)
Cutaneous complications	878 (3.4)	782 (3.0)
Neurological complications (excluding PHN)	190 (0.7)	207 (0.8)

HZ, herpes zoster; PHN, postherpetic neuralgia; T2D, type 2 diabetes



**Supplementary Figure 4. Comparison of diabetes medication classes received in the baseline and follow-up periods in matched cohorts 1 and 2**



DPP-4, dipeptidyl-peptidase-4; GLP-1, glucagon-like peptide-12; SGLT-2, sodium-glucose cotransporter-2; HZ, herpes zoster; T2D, type 2 diabetes

**Supplementary Table 4. Healthcare resource use in matched cohorts by place of service in the 12-month follow-up period**

	<b>Cohort 1</b>	<b>Cohort 2</b>	<b>Cohort 3</b>
	<b>With T2D and HZ (N = 26,070)</b>	<b>With T2D and no HZ (N = 26,070)</b>	<b>With HZ and no T2D (N = 26,071)</b>
<b>First month</b>			
<b>Inpatient stays, %</b>	4.9%	2.1%	4.0%
<b>ED visits, %</b>	19.6%	4.9%	17.4%
<b>Outpatient hospital visits, %</b>	34.2%	22.7%	32.0%
<b>Outpatient office visits, %</b>	89.2%	60.4%	88.2%
<b>Pharmacy visits, %</b>	96.2%	83.7%	94.9%
<b>Other, %</b>	40.6%	32.2%	33.2%
<b>First quarter</b>			
<b>Inpatient stays, %</b>	8.7%	5.7%	6.7%
<b>ED visits, %</b>	26.0%	11.8%	22.6%
<b>Outpatient hospital visits, %</b>	51.0%	43.1%	47.6%
<b>Outpatient office visits, %</b>	94.4%	85.5%	93.1%
<b>Pharmacy visits, %</b>	98.0%	95.2%	97.3%
<b>Other, %</b>	59.4%	55.2%	47.8%
<b>First 12 months</b>			
<b>Inpatient stays, %</b>	20.7%	17.6%	16.1%
<b>ED visits, %</b>	44.0%	31.7%	38.2%
<b>Outpatient hospital visits, %</b>	77.3%	72.8%	74.6%
<b>Outpatient office visits, %</b>	98.0%	96.8%	97.3%
<b>Pharmacy visits, %</b>	98.6%	97.8%	98.3%
<b>Other, %</b>	81.1%	78.9%	72.6%

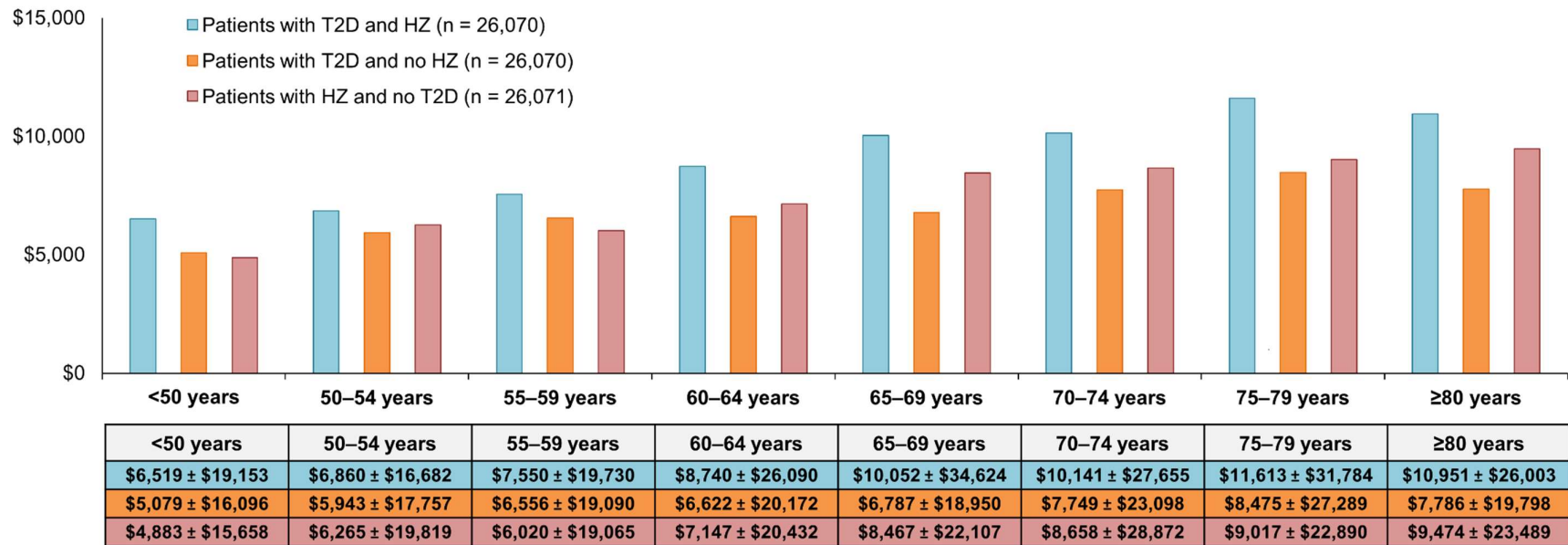
ED, emergency department; HZ, herpes zoster; T2D, type 2 diabetes

**Supplementary Table 5. Longitudinal healthcare costs in patient cohorts (2018 U.S. \$).**

	Cohort 1	Cohort 2	Incremental Cost Difference	Cohort 1	Cohort 3	Incremental Cost Difference
	With T2D and HZ (N = 26,070)	With T2D and no HZ (N = 26,070)		With T2D and HZ (N = 26,071)	With HZ and no T2D (N = 26,071)	
<b>All-cause healthcare service costs mean ± SD (median)</b>						
Month 1 Post-Index Date	3,497 ± 11,772 (921)	2,265 ± 8,903 (570)	\$1,231	3,497 ± 11,772 (921)	2,961 ± 11,104 (613)	\$536
Quarter 1 Post-Index Date	8,683 ± 24,702 (2,768)	6,815 ± 20,036 (2,299)	\$1,868	8,683 ± 24,702 (2,768)	7,122 ± 21,091 (1,673)	\$1,561
Year 1 Post-Index Date	32,061 ± 76,683 (12,547)	26,845 ± 59,362 (11,261)	\$5,216	32,061 ± 76,683 (12,547)	25,262 ± 62,608 (7,570)	\$6,799
<b>HZ-related healthcare service costs mean ± SD (median)</b>						
Month 1 Post-Index Date	–	–	–	1,622 ± 6,100 (490)	1,317 ± 6,064 (296)	\$306
Quarter 1 Post-Index Date	–	–	–	3,004 ± 7,598 (1,304)	2,304 ± 7,962 (565)	\$700
Year 1 Post-Index Date	–	–	–	9,077 ± 23,040 (4,552)	6,351 ± 18,132 (1,517)	\$2,726

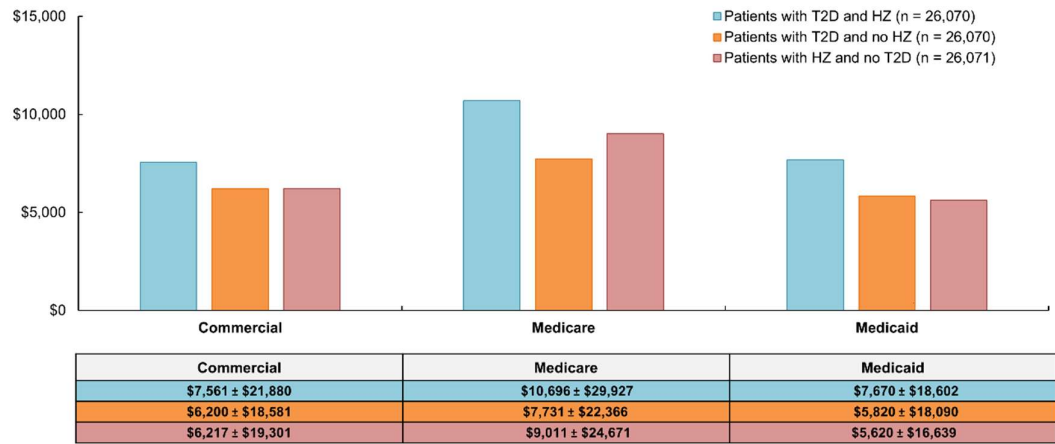
HZ, herpes zoster; T2D, type 2 diabetes

**Supplementary Figure 5. All-cause healthcare costs in first quarter post-index date for patients in matched cohorts in different age-strata**



HZ, herpes zoster; T2D, type 2 diabetes

**Supplementary Figure 6. All-cause healthcare costs in first quarter post-index date for patients in matched cohorts in different payment plans**



HZ, herpes zoster; T2D, type 2 diabetes