

# Supplementary Material

## The Impact of Routine Vaccinations on Alzheimer’s Disease Risk in Persons 65 Years and Older: A Claims-Based Cohort Study using Propensity Score Matching

**Supplementary Table 1.** Definitions of Variables, Study Dates, and Study Periods

Variable, Date, or Period	Definition
<b>Period</b>	
Look-back period	September 1, 2009, through August 31, 2011 Exceptions: <ul style="list-style-type: none"> <li>● For the HZ vaccination subanalysis with the completed Shingrix (2 doses) vaccination without any Zostavax vaccination, the analysis was performed using a look back period of September 1, 2009- August 31, 2017 and the follow up period of September 1, 2017- August 31, 2019.</li> <li>● For the HZ vaccination subanalysis with the one or more doses of Shingrix vaccination without any Zostavax vaccination, the analysis was performed using a look back period of September 1, 2009- August 31, 2017 and the follow up period of September 1, 2017- August 31, 2019.</li> <li>● For the pneumococcal vaccination subanalysis with one or more doses of PCV-13 vaccination without any PPSV-23vaccination, the analysis was performed using a look back period of September 1, 2009- August 31, 2014 and the follow up period of September 1, 2014- August 31, 2019.</li> </ul>
Follow-up period	September 1, 2011, through August 31, 2019 Exceptions: <ul style="list-style-type: none"> <li>● For the HZ vaccination subanalysis with the completed Shingrix (2 doses) vaccination without any Zostavax vaccination, the analysis was performed using a look back period of September 1, 2009- August 31, 2017 and the follow up period of September 1, 2017- August 31, 2019.</li> <li>● For the HZ vaccination subanalysis with the one or more doses of Shingrix vaccination without any Zostavax vaccination, the analysis was performed using a look back period of September 1, 2009- August 31, 2017 and the follow up period of September 1, 2017- August 31, 2019.</li> <li>● For the pneumococcal vaccination subanalysis with one or more doses of PCV-13 vaccination without any PPSV-23vaccination, the analysis was performed using a look back period of September 1, 2009- August 31, 2014 and the follow up period of September 1, 2014- August 31, 2019.</li> </ul>

Follow-up duration for each patient	<p>For unvaccinated patients: Number of months from the start of the follow-up period to the date of the first AD-related record, death, censoring (i.e., patient’s last record during the follow-up period), or end of the study period.</p> <p>For vaccinated patients: Number of months from the date in which exposure definition for the given analysis was satisfied to the date of the first AD-related record, death, censoring (i.e., patient’s last record during the follow-up period), or end of the study period.</p>
<b>Outcome and Exclusions</b>	
Alzheimer’s Disease (AD) Medications	<p>Donepezil, galantamine, rivastigmine, memantine</p> <p>Used in the look-back period in order to exclude patients with preexisting cognitive impairment, and in the follow-up period to identify patients with AD.</p>
Outcome Diagnosis Codes for Exclusion	<p><u>ICD-9 codes</u>: 046.1x, 046.3, 290.x, 291.1, 291.2, 294.x, 294.1x, 294.2x, 331.x, 332.x, 333.0, 333.4, 438.0, 780.93, 797</p> <p><u>ICD-10 codes</u>: A81.0x, A81.2, F01.x, F02.x, F03.x, F04, F05, F10.26, F10.27, F10.96, F10.97, G10, G20, G21.1x, G21.2, G21.3, G21.4, G21.8, G21.9, G23.x, G30.x, G31.0x, G31.1, G31.2, G31.83, G31.84, G31.85, G31.89, G31.9, G91.x, G93.7, G94, I69.91, R41.2, R41.3, R41.81</p> <p>Used in the look-back period to exclude patients with dementia, mild cognitive impairment, or encephalopathy.</p>
Diagnosis Codes for Incident AD Case-Detection Algorithm	<p><u>ICD-9 codes</u>: 290.0, 290.1x, 290.2x, 290.3, 294.2x, 331.0, 331.2, 331.9</p> <p><u>ICD-10 codes</u>: F03.9x, G30.x, G31.1, G31.9</p> <p>Used in the follow-up period to identify the outcome. Includes AD, dementia of unspecified cause, and “senile” dementia.</p>
<b>Outcome Diagnosis Codes for Sensitivity Analyses</b>	
Incident AD <i>without</i> Unspecified or “Senile” Dementias	<p><u>ICD-9 codes</u><sup>a</sup>: 331.0</p> <p><u>ICD-10 codes</u><sup>a</sup>: G30.x</p> <p><sup>a</sup>Schliep KC, Ju S, Foster NL, Smith KR, Varner MW, Ostbye T, Tschanz JT (2021) How good are medical and death records for identifying dementia? <i>Alzheimers Dement</i> <b>18</b>, 1812-1823.</p>
Incident Alzheimer Disease and Related Dementias (ADRD)	<p><u>ICD-9 codes</u><sup>a</sup>: 290.0, 290.10, 290.11, 290.12, 290.13, 290.20, 290.21, 290.3, 290.40, 290.41, 290.42, 290.43, 294.0, 294.10, 294.11, 294.20, 294.21, 294.8, 331.0, 331.11, 331.19, 331.2, 331.7, 797</p> <p><u>ICD-10 codes</u><sup>b</sup>: F01.50, F01.51, F02.80, F02.81, F03.90, F03.91, G30.0, G30.1, G30.8, G30.9, G31.01, G31.09, G31.1, R41.81</p> <p><sup>a</sup>Lee E, Gatz M, Tseng C, Schneider LS, Pawluczyk S, Wu AH, Deapen D (2019) Evaluation of Medicare Claims Data as a Tool to Identify Dementia. <i>J Alzheimers Dis</i> <b>67</b>, 769-778.</p> <p><sup>b</sup>Moura L, Festa N, Price M, Volya M, Benson NM, Zafar S, Weiss M, Blacker D, Normand SL, Newhouse JP, Hsu J (2021) Identifying Medicare Beneficiaries with Dementia. <i>J Am Geriatr Soc</i> <b>69</b>, 2240-2251.</p>

<b>Vaccinations</b>	
Tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap); Tetanus toxoid and reduced diphtheria toxoid (Td); Tetanus toxoid (TT) vaccination	<u>Drug names:</u> Boostrix Tdap, Adacel, Tetanus Diphtheria Toxoids, Decavac, Tetanus Toxoids adsorbed, Tenivac, Tetanus-Diphtheria-Devac, Tdvax, Tetanus Toxoid (Fluid), Tetanus Toxoid (Adsorbed)
Herpes Zoster vaccination	<u>Drug names:</u> Zoster vaccine LIVE/PF, Varicella-Zoster GE/AS01B/PF, Zoster vaccine LIVE/PF, Varicella-Zoster GE VAC
Pneumococcal vaccination	<u>Drug names:</u> Pneumoc 13-val CONJ-DIP CRM/PF, Pneumococcal 23-val P-SAC Vac
Influenza vaccination	<u>Drug names:</u> Afluria, Agriflu, Fluad, Fluarix, Flublok, Flucelvax, Flulaval, Fluzone, Flushield, Fluvirin, Fluogen, Flu-Imune <u>CPT codes:</u> 90630, 90653-90659, 90661, 90662, 90663, 90664, 90673, 90674, 90682, 90685-90689, 90694, 90724, 90756 <u>Healthcare Common Procedure Coding System (HCPCS) codes:</u> Q2034, Q2035, Q2036, Q2037, Q2038, Q2039, G0008
<b>Covariates – measured during the look-back period (except for age, which was measured at the index date)</b>	
Age	Age in years at the index date of the follow-up period
Sex	Female, male, unknown
Race	Asian, Black, Hispanic, White, unknown Optum’s CDM places people identifying as Pacific Islander within the “Asian” race/ethnicity category, and does not identify Native Americans as a separate racial/ethnic category.
Geographic region	A patient's geographic region is classified based on the primary beneficiary’s state residence in Optum’s CDM. States were grouped into the following regions: <ul style="list-style-type: none"> <li>• Northeast (CT, ME, MA, NH, RI, VT, NJ, NY, PA)</li> <li>• North Central (IL, IN, MI, OH, WI, IA, KS, MN, MO, NE, ND, SD)</li> <li>• South (DC, DE, FL, GA, MD, NC, SC, VA, WV, AL, KY, MS, TN, AR, LA, OK, TX)</li> <li>• West (AZ, CO, ID, MT, NV, NM, UT, WY, AK, CA, HI, OR, WA)</li> <li>• Unknown</li> </ul>
Number of healthcare encounters	The number of outpatient and inpatient healthcare encounters during the look-back period. For patients with an inpatient admission (i.e., hospitalization), the admission was counted as one health care encounter, regardless of the length of stay. In order to exclude pharmacy records, we only counted outpatient records with at least one ICD code as a healthcare encounter.
Number of routine “well visit” examinations	<u>CPT codes:</u> 99386, 99387, 99396, 99397 <u>HCPCS codes:</u> G0402, G0438, G0439, G0444, S0610, S0612, S0613, G0101, G0091 <u>ICD-9 codes:</u> V70.0, V72.31 <u>ICD-10 codes:</u> Z00.00, Z00.01, Z01.411, Z01.419

Asthma	<u>ICD-9 codes:</u> 493.x; <u>ICD-10 codes:</u> J45.x
Atrial fibrillation of flutter	<u>ICD-9 codes:</u> 427.3x; <u>ICD-10 codes:</u> I48.x
Vitamin B12 deficiency	<u>ICD-9 codes:</u> 266.2, 281.1 <u>ICD-10 codes:</u> E53.8, D51.x
Congestive heart failure (CHF)	<u>ICD-9 codes:</u> 398.91, 402.11, 402.91, 404.11, 404.13, 404.91, 404.93, 428.x; <u>ICD-10 codes:</u> I09.81, I11.0, I13.0, I13.2, I50.x
Chronic obstructive pulmonary disease (COPD)	<u>ICD-9 codes:</u> 491.x, 492.x, 496; <u>ICD-10 codes:</u> J41.x, J42, J43.2, J43.8, J43.9, J44.x
Hyperlipidemia	<u>ICD-9 codes:</u> 272.0, 272.1, 272.2, 272.4; <u>ICD-10 codes:</u> E78.0-E78.2, E78.4-E78.5
Hypertension	<u>ICD-9 codes:</u> 401.x <u>ICD-10 codes:</u> I10
Ischemic heart disease (IHD)	<u>ICD-9 codes:</u> 410.x, 411.x, 412.x, 413.x, 414.x, V45.81, V45.82; <u>ICD-10 codes:</u> I20.x, 121.x, 122.x, 123.x, 124.x, I25.x
Obesity	<u>ICD-9 codes:</u> 278.00, 278.01, 278.03, V85.3x, V85.4x; <u>ICD-10 codes:</u> E66.01, E66.09, E66.1, E66.2, E66.8, E66.9, Z68.3x, Z68.4x <u>BMI:</u> Last BMI during the look-back period is $\geq 30$ kg/m <sup>2</sup>
Traumatic brain injury (TBI)	<u>ICD-9 codes:</u> 800.x-804.x, 850.x-854.x, 905.0, 907.0, 959.01, V15.52; <u>ICD-10 codes:</u> S01.90x, S02.x, S04.x, S06.x, S07.x, S09.8x, S09.9x, Z87.820
Type II diabetes	<u>ICD-9 codes:</u> 250.x0, 250.x2, 357.2, 362.0x, 366.41; <u>ICD-10 codes:</u> E11.x, E08.42, E09.42, E13.42, E08.36, E09.36, E13.36  If patients had at least two outpatient occurrences on different days within the same 24-month period or one inpatient occurrence during the look-back period, then it was determined that they had type II diabetes.
Stroke	<u>ICD-9 codes:</u> 430, 431, 433.x1, 434.x1, 438.x; <u>ICD-10 codes:</u> I61.x, I63.3x, I63.4x, I63.5x, I63.6, I63.8, I63.9, I66.x, I69.1x, I69.2x, I69.3x, I69.8x, I69.9x
Alcohol-related disorder	<u>ICD-9 codes:</u> 303.9x, 305.0x; <u>ICD-10 codes:</u> F10.x  Includes both alcohol dependence and alcohol use disorder.

Anxiety disorder	<p><u>ICD-9 codes:</u> 309.81, 300.00, 300.01, 300.02, 300.23, 300.3; <u>ICD-10 codes:</u> F40.1x, F41.0, F41.1, F41.9, F42, F43.1x</p> <p>A composite variable which includes post-traumatic stress disorder, panic disorder, obsessive compulsive disorder, social phobia, generalized anxiety disorder, and anxiety disorder not otherwise specified. If patients had two or more outpatient occurrences on different days within the same 12-month period or one inpatient occurrence during the look-back period, then it was determined that they had an anxiety disorder.</p>
Depression	<p><u>ICD-9 codes:</u> 296.2x, 296.3x, 311; <u>ICD-10 codes:</u> F32.0-F32.5, F32.9, F33.0-F33.3, F33.4x, F33.9</p> <p>If patients had two or more outpatient occurrences on different days within the same 12-month period or one inpatient occurrence during the look-back period, then it was determined that they had depression.</p>
Substance use disorder	<p><u>ICD-9 codes:</u> 304.0x, 304.1x, 304.2x, 304.3x, 304.4x, 304.5x, 304.6x, 304.7x, 304.8x, 304.9x, 305.2x, 305.3x, 305.4x, 305.5x, 305.6x, 305.7x, 305.9x <u>ICD-10 codes:</u> F11.x, F12.x, F13.x, F14.x, F15.x, F16.x, F18.x, F19.x</p> <p>A composite variable of substance use disorders which includes: opioids; cannabis; sedatives, hypnotics, or anxiolytics; cocaine; amphetamines or other stimulants; hallucinogens; inhalants; and/or other psychoactive substances, including polysubstance use. Excludes alcohol and tobacco related disorders.</p>
Tobacco use (including current or former use)	<p><u>ICD-9 codes:</u> V15.82, 305.1; <u>ICD-10 codes:</u> Z87.891, Z72.0, F17.20x, F17.21x <u>CPT codes:</u> 99406, 99407 <u>HCPCS codes:</u> G0436, G0437</p>
Medications (includes multiple variables)	<p>A variable was created for each of the following medication classes, based on the American Hospital Formulary Service (AHFS) Pharmacologic-Therapeutic Classification system.</p> <ul style="list-style-type: none"> <li>● <b>Anticholinergics</b> - AHFS codes: 12:08, 28:36.08, 04:04</li> <li>● <b>Antihypertensives</b> - AHFS codes: 24:08</li> <li>● <b>Antivirals</b> - AHFS codes: 08:18</li> <li>● <b>Glucocorticoids</b> - AHFS codes: 68:04</li> <li>● <b>Metformin</b> - AHFS codes: 68:20.04</li> <li>● <b>NSAIDs</b> - AHFS codes: 28:08.04</li> <li>● <b>Statins</b> - AHFS codes: 24:06.08</li> <li>● <b>Sulfonylureas</b> - AHFS codes: 68:20.20</li> </ul> <p>Sustained use: If patients had a medication class recorded for <math>\geq 2</math> pharmacy claim records within any 6-month period during the look-back period, then the medication class variable was coded as “yes”.</p>

Table adapted from Bukhbinder et al. (2022). Reprinted from *Journal of Alzheimer's Disease*, vol. 88, no. 3, Bukhbinder AS, Ling Y, Hasan O, Jiang X, Kim Y, Phelps KN, Schmandt RE, Amran A, Coburn R, Ramesh S, Xiao Q, Schulz PE, Risk of Alzheimer's disease following influenza vaccination: a claims-based cohort study using propensity score matching, pp. 1061-1074, 2022, with permission from IOS Press. The publication is available at IOS Press through <http://dx.doi.org/10.3233/JAD-220361>.

**Supplementary Table 2.** Baseline Characteristics of Patients with and without HZ and Pneumococcal during the Follow-up Period before and after PSM

A) Herpes Zoster

	Panel 1: before propensity score matching			Panel 2: after propensity score matching		
	No HZ vaccination during follow-up (n=1,439,574)	≥1 HZ vaccinations during follow-up (n=212,417)	SMD	No HZ vaccinations during follow-up (n = 198,847)	≥1 HZ vaccinations during follow-up (n = 198,847)	SMD
Age, y, mean (SD)	73.1 (5.6)	72.2 (5.1)	0.1954	72.1 (5.3)	72.2 (5.1)	-0.0166
Sex						
<i>Unknown</i>	224 (0.02%)	1 (0.00%)	0.0168	NA	NA	NA
<i>Female</i>	799,870 (55.56%)	125,710 (59.18%)	-0.0732	117,732 (59.21%)	117,673 (59.18%)	0.0006
<i>Male</i>	639,480 (44.42%)	86,706 (40.81%)	0.0729	81,115 (40.79%)	81,174 (40.82%)	-0.0006
Race						
<i>Unknown</i>	106,971 (7.43%)	13,448 (6.33%)	0.0435	NA	NA	NA
<i>Asian</i>	38,970 (2.71%)	7,663 (3.61%)	-0.0537	6,032 (3.03%)	7,657 (3.85%)	-0.0448
<i>Black</i>	130,730 (9.08%)	16,119 (7.30%)	0.054	17,140 (8.62%)	16,115 (8.10%)	0.0186
<i>Hispanic</i>	125,386 (8.71%)	17,792 (7.59%)	0.0119	18,424 (9.27%)	17,777 (8.94%)	0.0113
<i>White</i>	1,037,517 (72.07%)	157,395 (74.10%)	-0.0547	157,251 (79.08%)	157,298 (79.11%)	-0.0006
Geographic region						
<i>Unknown</i>	970 (0.07%)	134 (0.06%)	0.0017	NA	NA	NA
<i>Northeast</i>	132,464 (9.20%)	17,157 (7.86%)	0.04	16,842 (8.47%)	16,284 (8.19%)	0.0102
<i>North central</i>	333,904 (23.19%)	39,678 (18.67%)	0.1112	37,131 (18.67%)	37,931 (19.08%)	-0.0109
<i>South</i>	529,005 (36.75%)	80,001 (37.66%)	-0.0189	77,587 (39.02%)	75,907 (38.17%)	0.0174
<i>West</i>	443,231 (30.79%)	75,447 (35.52%)	-0.1157	67,287 (33.84%)	68,725 (34.56%)	-0.0152
No. of health care encounters <sup>a</sup> , mean (SD)	24.8 (26.4)	24.2 (22.2)	0.0235	23.7 (24.8)	24.6 (22.4)	-0.0379
No. of routine annual check-ups ("well visits")	0.6 (1.0)	0.8 (1.1)	-0.1913	0.8 (1.1)	0.8 (1.1)	-0.0146
Comorbidities						
Asthma	111,985 (7.78%)	16,874 (7.94%)	-0.0061	14,549 (7.32%)	15,894 (7.99%)	-0.0254
Atrial fibrillation or flutter	145,551 (10.11%)	15,889 (7.48%)	0.093	13,915 (7.00%)	15,061 (7.57%)	-0.0222
B12 deficiency	50,107 (3.48%)	6,524 (3.07%)	0.023	5,677 (2.85%)	6,198 (3.12%)	-0.0154
Congestive heart failure	133,887 (9.30%)	12,078 (5.69%)	0.1376	10,316 (5.19%)	11,459 (5.76%)	-0.0253

COPD	210,447 (14.62%)	23,364 (11.00%)	0.1085	20,594 (10.36%)	22,142 (11.14%)	-0.0251
Hyperlipidemia	1,000,913 (69.53%)	157,595 (74.19%)	-0.1038	147,241 (74.05%)	148,149 (74.50%)	-0.0104
Hypertension	1,032,079 (71.69%)	148,825 (70.06%)	0.0359	138,774 (69.79%)	140,112 (70.46%)	-0.0147
Ischemic heart disease	335,372 (23.30%)	40,665 (19.14%)	0.1017	36,438 (18.32%)	38,485 (19.35%)	-0.0263
Obesity	109,027 (7.57%)	16,217 (7.63%)	-0.0023	14,033 (7.06%)	15,261 (7.67%)	-0.0236
Traumatic brain injury	6,523 (0.45%)	855 (0.40%)	0.0078	729 (0.37%)	817 (0.41%)	-0.0071
Type II diabetes	366,861 (25.48%)	48,597 (22.88%)	0.0609	43,953 (22.10%)	45,826 (23.05%)	-0.0225
Stroke	50,536 (3.51%)	5,195 (2.45%)	0.0627	4,266 (2.15%)	4,936 (2.48%)	-0.0224
Alcohol use disorder	13,452 (0.93%)	1,486 (0.70%)	0.0261	1,259 (0.63%)	1,385 (0.70%)	-0.0078
Anxiety disorder <sup>b</sup>	153,382 (10.65%)	20,294 (9.55%)	0.0365	17,661 (8.88%)	19,160 (9.64%)	-0.026
Depression	103,315 (7.18%)	12,802 (6.02%)	0.0463	10,940 (5.50%)	12,135 (6.10%)	-0.0257
Substance use disorder <sup>c</sup>	10,463 (0.73%)	1,488 (0.70%)	0.0031	1,297 (0.65%)	1,393 (0.70%)	-0.0059
Tobacco use	139,041 (9.66%)	17,020 (8.01%)	0.058	14,941 (7.51%)	16,035 (8.06%)	-0.0205
Medications (sustained use) <sup>d</sup>						
Anticholinergics	80,970 (5.62%)	10,714 (5.04%)	0.0258	9,518 (4.79%)	10,204 (5.13%)	-0.0159
Antihypertensives	38,944 (2.71%)	4,579 (2.16%)	0.0357	3,870 (1.95%)	4,355 (2.19%)	-0.0171
Antivirals	19,262 (1.34%)	3,796 (1.79%)	-0.0362	3,316 (1.67%)	3,608 (1.81%)	-0.0112
Glucocorticoids	125,374 (8.71%)	18,641 (8.78%)	-0.0024	16,626 (8.36%)	17,814 (8.96%)	-0.0212
Metformin	151,572 (10.53%)	24,000 (11.30%)	-0.0247	21,643 (10.88%)	22,629 (11.38%)	-0.0158
NSAIDs	180,751 (12.56%)	32,965 (15.52%)	-0.0854	27,395 (13.78%)	31,237 (15.71%)	-0.0545
Statins	575,605 (39.98%)	103,024 (48.50%)	-0.1721	95,546 (48.05%)	96,970 (48.77%)	-0.0143
Sulfonylureas	114,281 (7.94%)	15,208 (7.16%)	0.0295	13,621 (6.85%)	14,443 (7.26%)	-0.0161
Vaccination records						
Influenza vaccination	77,720 (5.40%)	19,209 (9.04%)	-0.1411	16,447 (8.29%)	18,322 (9.21%)	-0.0328
Tdap/Td vaccination	6,544 (0.45%)	1,597 (0.75%)	-0.0384	1,200 (0.60%)	1,514 (0.76%)	-0.0192
Pneumococcal vaccination	9,334 (0.65%)	2,259 (1.06%)	-0.0451	1,812 (0.91%)	2,126 (1.07%)	-0.0159

B) Pneumococcal

	<b>Panel 1: before propensity score matching</b>			<b>Panel 2: after propensity score matching</b>		
	<b>No Pneumococcal vaccinations during follow-up (n=1,365,487)</b>	<b>≥1 Pneumococcal vaccinations during follow-up (n=286,504)</b>	<b>SMD</b>	<b>No Pneumococcal vaccinations during follow-up (n = 270,835)</b>	<b>≥1 Pneumococcal vaccinations during follow-up (n = 270,835)</b>	<b>SMD</b>
Age, y, mean (SD)	73.2 (5.8)	72.1 (5.1)	0.196	72.2 (5.3)	72.2 (5.1)	0.0073
<b>Sex</b>						
<i>Unknown</i>	200 (0.01%)	25 (0.00%)	0.0067	NA	NA	NA
<i>Female</i>	759,350 (55.61%)	166,230 (58.02%)	-0.0487	156,702 (57.86%)	156,696 (57.85%)	0
<i>Male</i>	605,937 (44.38%)	120,249 (41.97%)	0.0485	114,133 (42.14%)	114,139 (42.14%)	0
<b>Race</b>						
<i>Unknown</i>	104,935 (7.68%)	15,484 (5.40%)	0.0923	NA	NA	NA
<i>Asian</i>	39,028 (2.86%)	7,605 (2.65%)	0.0124	7,132 (2.63%)	7,601 (2.81%)	-0.0106
<i>Black</i>	119,112 (8.72%)	27,737 (9.68%)	-0.0332	24,587 (9.08%)	27,732 (10.24%)	-0.0393
<i>Hispanic</i>	121,713 (8.91%)	21,465 (7.49%)	0.0518	22,821 (8.43%)	21,443 (7.92%)	0.0186
<i>White</i>	980,699 (71.82%)	214,213 (74.77%)	-0.0667	216,295 (79.86%)	214,059 (79.04%)	0.0204
<b>Geographic region</b>						
<i>Unknown</i>	944 (0.07%)	160 (0.06%)	0.0053	NA	NA	NA
<i>Northeast</i>	129,484 (9.48%)	20,137 (7.03%)	0.0893	23,786 (8.78%)	18,813 (6.95%)	0.0668
<i>North central</i>	304,786 (22.32%)	68,796 (24.01%)	-0.0401	65,319 (24.12%)	65,523 (24.19%)	-0.0018
<i>South</i>	487,025 (35.66%)	121,981 (42.58%)	-0.1419	105,322 (38.89%)	116,455 (43.00%)	-0.0837
<i>West</i>	443,248 (32.46%)	75,430 (26.33%)	0.1349	76,408 (28.21%)	70,044 (25.86%)	0.0529
No. of health care encounters <sup>a</sup> , mean (SD)	25.1 (26.7)	23.1 (21.2)	0.082	22.4 (22.1)	23.2 (21.8)	-0.0355
No. of routine annual check-ups ("well visits")	0.6 (1.0)	0.7 (1.0)	-0.0697	0.6 (1.0)	0.7 (1.0)	-0.0176
<b>Comorbidities</b>						
Asthma	106,584 (7.81%)	22,275 (7.77%)	0.0011	19,707 (7.28%)	21,139 (7.81%)	-0.02
Atrial fibrillation or flutter	140,382 (10.28%)	21058 (7.35%)	0.1035	18,596 (6.87%)	20,059 (7.41%)	-0.021
B12 deficiency	47,173 (3.45%)	9,458 (3.30%)	0.0085	8,348 (3.08%)	9,007 (3.33%)	-0.0138
Congestive heart failure	129,667 (9.50%)	16,298 (5.69%)	0.1441	13,733 (5.07%)	15,592 (5.76%)	-0.0303
COPD	200,649 (14.69%)	33,162 (11.57%)	0.0924	29,754 (10.99%)	31,597 (11.67%)	-0.0215
Hyperlipidemia	947,596 (69.40%)	210,912 (73.62%)	-0.0936	198,349 (73.24%)	199,725 (77.74%)	-0.0115



Hypertension	977,744 (71.60%)	203,160 (70.91%)	0.0153	191,676 (70.77%)	192,635 (71.13%)	-0.0078
Ischemic heart disease	319,594 (23.41%)	56,443 (19.70%)	0.0902	51,752 (19.11%)	53,729 (19.84%)	-0.0184
Obesity	104,143 (7.63%)	21,101 (7.36%)	0.0099	18,559 (6.85%)	20,061 (7.41%)	-0.0216
Traumatic brain injury	6,342 (0.46%)	1,036 (0.36%)	0.016	872 (0.32%)	985 (0.36%)	-0.0071
Type II diabetes	348,030 (25.49%)	67,428 (23.53%)	0.0454	61,213 (22.60%)	64,169 (23.69%)	-0.0259
Stroke	48,878 (3.58%)	6,853 (2.39%)	0.0698	6,056 (2.24%)	6,526 (2.41%)	-0.0115
Alcohol use disorder	13,031 (0.95%)	1,907 (0.67%)	0.0322	1,689 (0.62%)	1,803 (0.67%)	-0.0053
Anxiety disorder <sup>b</sup>	146,460 (10.73%)	27,216 (9.50%)	0.0407	24,132 (8.91%)	25,793 (9.52%)	-0.0212
Depression	102,024 (7.19%)	14,093 (6.05%)	0.0456	15,131 (5.59%)	16,332 (6.03%)	-0.019
Substance use disorder <sup>c</sup>	10,621 (0.78%)	1,330 (0.46%)	0.0399	1,190 (0.44%)	1,267 (0.47%)	-0.0042
Tobacco use	130,406 (9.55%)	25,655 (8.95%)	0.0206	23,106 (8.53%)	24,416 (9.01%)	-0.0171
Medications (sustained use) <sup>d</sup>						
Anticholinergics	77,410 (5.67%)	14,274 (4.98%)	0.0306	13,097 (4.84%)	13,692 (5.06%)	-0.0101
Antihypertensives	37,195 (2.72%)	6,328 (2.21%)	0.0359	5,569 (2.06%)	6,126 (2.26%)	-0.0142
Antivirals	18,834 (1.38%)	4,224 (1.47%)	-0.008	3,648 (1.35%)	4,059 (1.50%)	-0.0128
Glucocorticoids	117,760 (8.62%)	26,255 (9.16%)	-0.019	23,577 (8.71%)	25,265 (9.33%)	-0.0218
Metformin	413,898 (10.54%)	31,674 (11.06%)	-0.0167	28,643 (10.58%)	30,278 (11.18%)	-0.0194
NSAIDs	172,690 (12.65%)	41,026 (14.32%)	-0.049	35,372 (13.19%)	39,450 (14.57%)	-0.0397
Statins	553,022 (40.50%)	125,607 (43.84%)	-0.0677	118,577 (43.78%)	119,957 (44.29%)	-0.0103
Sulfonylureas	108,885 (7.97%)	20,604 (7.19%)	0.0296	18,616 (6.87%)	19,756 (7.29%)	-0.0164
Vaccination records						
Influenza vaccines	66,136 (4.84%)	30,793 (10.75%)	-0.2216	28,381 (10.48%)	29,226 (10.79%)	-0.0101
Tdap/Td vaccines	5,728 (0.42%)	2,413 (0.84%)	-0.0534	2,092 (0.77%)	2,274 (0.84%)	-0.0075
HZ vaccines	16,815 (1.23%)	5,829 (2.03%)	-0.0534	5,079 (1.88%)	5,459 (2.02%)	-0.0075

Variable definitions are provided in Supplementary Table 1. Categorical variables are shown as frequency and percentage, and continuous variables as mean and standard deviation. Because patients with unknown geographic region, race, and sex are excluded prior to performing the propensity score matching (PSM), those rows after PSM are labeled as NA. <sup>a</sup>Number of outpatient or inpatient healthcare encounters during the look-back period. <sup>b</sup>“Anxiety disorder” is a composite variable of post-traumatic stress disorder, panic disorder, anxiety disorder not otherwise specified, obsessive compulsive disorder, social phobia, and generalized anxiety disorder. <sup>c</sup>“Substance use disorder” is a composite variable of substance use disorders involving any of the following: opioids; cannabis; sedatives, hypnotics, or anxiolytics; cocaine; amphetamines or other stimulants; hallucinogens; inhalants; and/or other psychoactive substances, including polysubstance use. <sup>d</sup>“Sustained use” is defined as  $\geq 2$  prescription claims in any 6-month period during the look-back period. COPD, chronic obstructive pulmonary disease; HZ, Herpes zoster; NSAIDs, nonsteroidal anti-inflammatory drugs; SD, standard deviation; SMD, standardized mean difference; Tdap, Tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis; Td, Tetanus toxoid and reduced diphtheria toxoid.

Table adapted from Bukhbinder et al. (2022). Reprinted from *Journal of Alzheimer's Disease*, vol. 88, no. 3, Bukhbinder AS, Ling Y, Hasan O, Jiang X, Kim Y, Phelps KN, Schmandt RE, Amran A, Coburn R, Ramesh S, Xiao Q, Schulz PE, Risk of Alzheimer's disease following influenza vaccination: a claims-based cohort study using propensity score matching, pp. 1061-1074, 2022, with permission from IOS Press. The publication is available at IOS Press through <http://dx.doi.org/10.3233/JAD-220361>.

**Supplementary Table 3.** Distributions of Follow-up Duration in Months

<b>Exposure Definition</b>	<b>Vaccinated group (Median, (25%, 75%))</b>	<b>Unvaccinated group (Median, (25%, 75%))</b>
<i>Tdap, Td, and/or TT Vaccination versus Unvaccinated</i>		
≥ 1 Tdap or Td without TT *	29 (13, 50)	63 (27, 95)
≥ 1 Tdap or Td or TT	29 (13, 50)	63 (27, 95)
≥ 1 Tdap without Td and TT	29 (13, 50)	63 (27, 95)
≥ 1 Td without Tdap and TT	25 (11, 47)	61 (27, 95)
≥ 1 TT without Tdap and Td	52 (22, 69)	57 (27, 95)
<i>HZ Vaccination versus Unvaccinated</i>		
≥ 1 Zostavax or Shingrix*	37 (13, 69)	61 (27, 95)
Completed Shingrix (2 doses) without Zostavax <sup>a</sup>	10 (5, 14)	23 (22, 23)
≥ 1 Zostavax with 2 doses Shingrix	73 (55, 84)	63 (27, 95)
≥ 1 Shingrix without Zostavax <sup>a</sup>	7 (3, 13)	23 (21, 23)
≥ 1 Zostavax without Shingrix	48 (24, 72)	61 (27, 95)
<i>Pneumococcal Vaccination versus Unvaccinated</i>		
≥ 1 PCV-13 or PPSV-23*	43 (25, 67)	37 (17, 66)
≥ 1 PCV-13 without PPSV-23 <sup>b</sup>	27 (12, 43)	53 (20, 59)
≥ 1 PPSV-23 without PCV-13	46 (27, 79)	39 (19, 74)

The median, and first and third quartiles for follow-up duration (in months) prior to incident AD, death, or censoring for the post-PSM groups in each analysis are provided above. For the vaccinated groups, time begins when the first target vaccine is given. Censoring is defined as the date of the last record in the system. For the vaccinated cohorts, The look-back period was defined as 2009-2011 and the follow-up period as 2011-2019, with the exceptions noted below. Each analysis performed includes a unique unvaccinated cohort. The unvaccinated cohort refers to patients who are not vaccinated with the specified vaccine for that analysis; patients may have still received other vaccinations that were not the exposure variable. For example, for the Zostavax or Shingrix vaccine analysis, the unvaccinated group would be those who received neither Zostavax nor Shingrix; however, this group could have received a Tdap/Td/TT or pneumococcal vaccine. \*Denotes a main analysis. <sup>a</sup>The analysis was performed using a look-back period of 2009-2017 and the follow up period of 2017-2019. <sup>b</sup>The analysis was performed using a look-back period of 2009-2014 and the follow-up period of 2014-2019. AD, Alzheimer's disease; HZ, Herpes zoster; ICD, International Classification of Diseases; PCV-13, pneumococcal conjugate vaccine 13; PPSV-23, Pneumococcal polysaccharide vaccine 23; Tdap, Tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis; Td, Tetanus toxoid and reduced diphtheria toxoid; TT, Tetanus toxoid.

## **Description of Secondary Analysis: Time-to-Event Analysis Using Competing-Risk Regression**

For the secondary analysis, we used competing-risk regression models to investigate the effects of Tdap/Td, HZ, or pneumococcal vaccinations, as well as age, on the cumulative incidence function (CIF) of AD using an unmatched cohort (Supplementary Figure 1A-C). An unmatched cohort was utilized because the exposure variables (i.e., Tdap/Td vaccination, etc.) were measured in the look-back period instead of the follow-up period, stopping us from using PSM.

The secondary analysis used the same look-back and follow-up periods as the primary analysis (September 1, 2009 to August 31, 2011 for the look-back period, and September 1, 2011 to August 31, 2019 for the follow-up period). We applied the following measurements and eligibility criteria using the look-back period: 1) exclude patients with zero *ICD* records or with any *ICD* codes indicative of pre-existing dementia, mild cognitive impairment, or encephalopathy, and 2) determine vaccination status and measure covariates. Eligibility criteria applied using data from the follow-up period were: 1) exclude patients with less than two records containing *ICD* codes during follow-up, 2) exclude those younger than 65 years at the start of follow-up, and 3) determine the number of months from beginning of the follow-up period to an outcome event or the end of the study period. Because Optum's CDM provides mortality data, an outcome event is considered AD onset, death, or censoring. We used proportional hazard models, specifically the subdistribution hazard, to account for the competing risk of death during the follow-up period [1]. In addition, patients who received a vaccine in the follow-up period but not during the look-back period were excluded from the study cohort (i.e., a per-protocol analysis).

We used the covariates listed in Supplementary Table 1, with the exception of geographic information, number of routine 'well-visits,' and health care visits during look-back, as these were considered not directly associated with risk of AD. In order to assess for collinearity, we utilized a pairwise correlation matrix (Supplementary Figure 2). The matrix demonstrated that there are high levels of collinearity among three subsets of covariates within our cohort, specifically: 1) hyperlipidemia and statins, 2) type 2 diabetes, metformin, and sulfonylurea, and 3) anxiety and depression. For each of these three subsets, we created a composite variable. If any of the covariates that make up the composite variable were coded as "yes," the composite

variable was coded as “yes.” The collinearity analysis and composite variable creation were completed prior to the construction of the competing risk regression model.

The AD CIF curves by Tdap/Td, HZ, and pneumococcal vaccines during an 8-year follow-up period are shown in Supplementary Figure 1A-C. For each covariate, we reported the coefficient, subdistribution hazard ratio (sHR), and the 95% CI (Supplementary Table 4A-C). The sHR for the Tdap/Td vaccination was 0.72 (95% CI: 0.629,0.838), for HZ vaccination was 0.605 (95% CI: 0.553, 0.662), and for pneumococcal vaccination was 0.898 (95% CI: 0.803, 1.004).

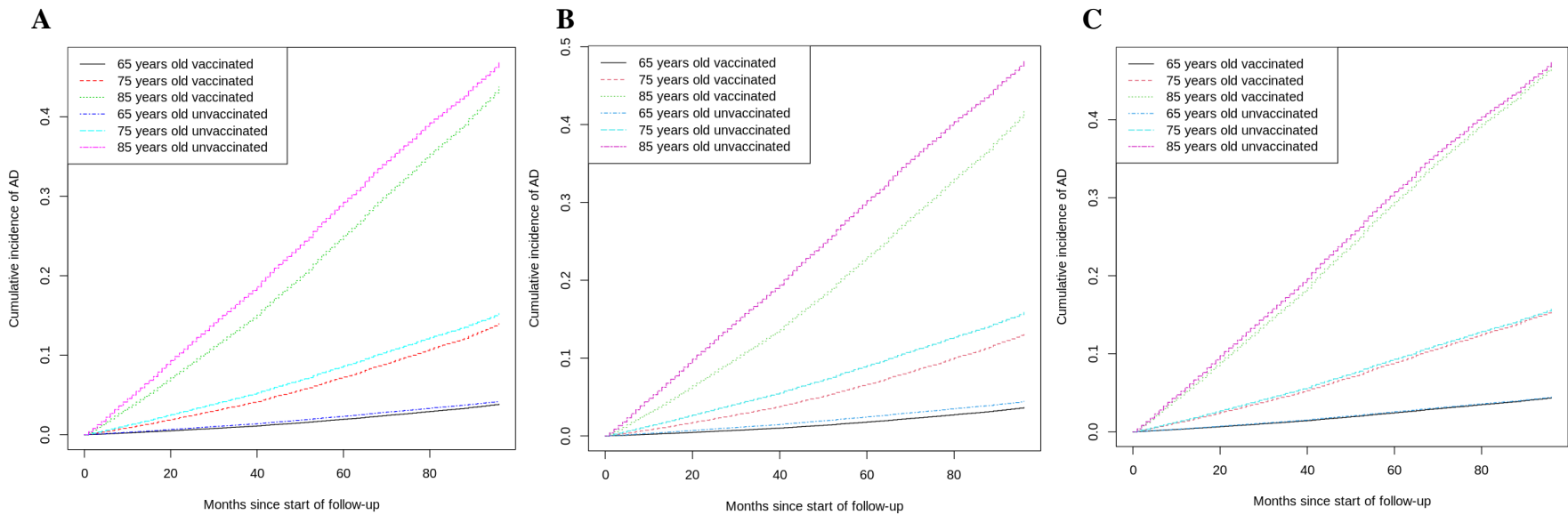
As an estimate of the goodness of fit for the proportional subdistribution hazard model, we performed pseudo-likelihood ratio tests [2]:

- Tdap vaccination model: 98,194 on 48 degrees of freedom, p-value <0.0001
- HZ vaccination model: 27,300 on 48 degrees of freedom, p-value <0.0001
- Pneumococcal vaccination model: 89,251 on 48 degrees of freedom, p-value <0.0001

The results indicate that we can firmly reject the null hypothesis that the covariate estimates are not different from zero, meaning that all three models performed significantly better than the corresponding null models.

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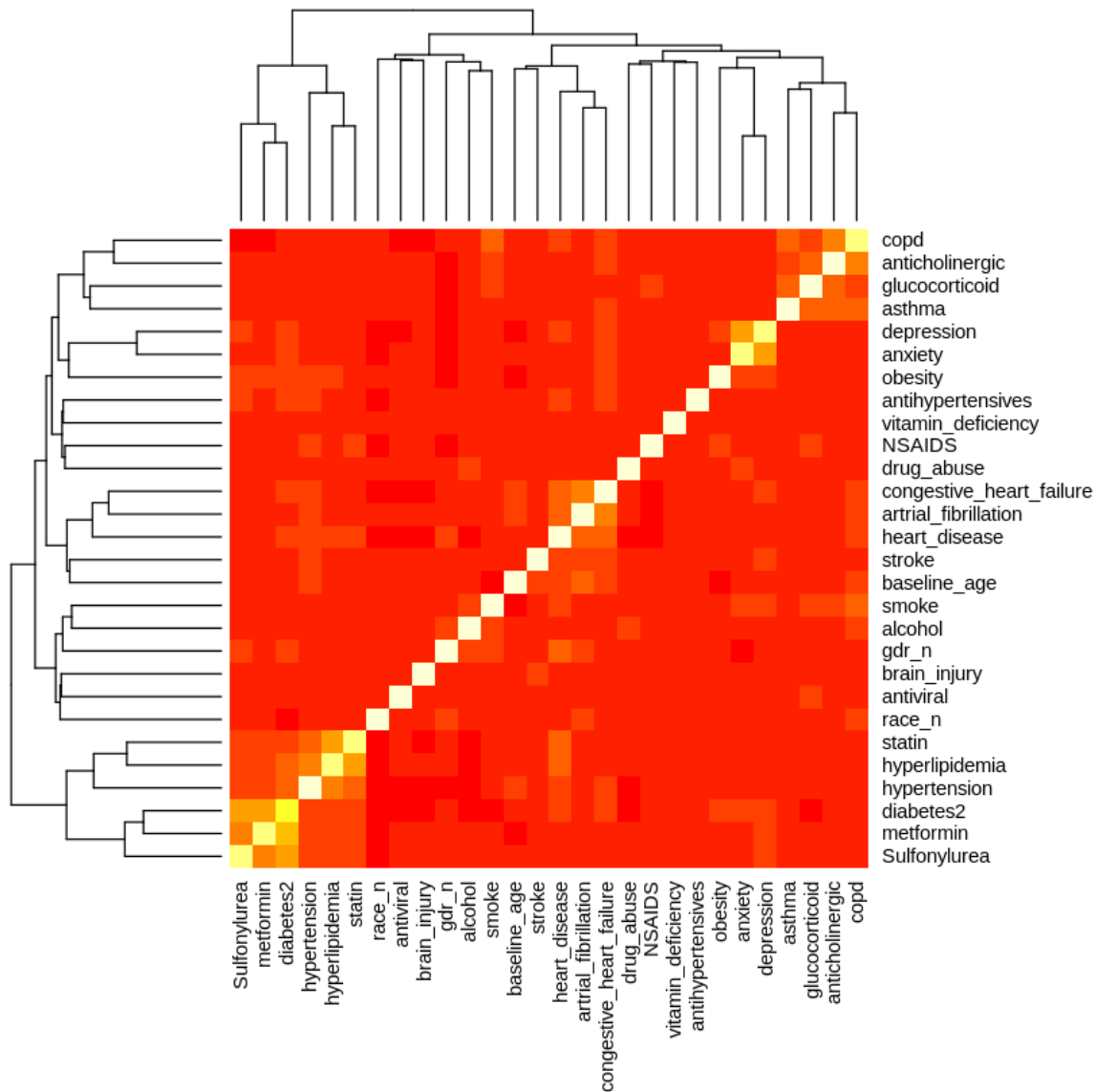
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### Supplementary Figure 1A-C. Estimated CIF Curve of AD by Age and Vaccination Status

Results of a risk regression model on a) Tdap/Td, b) HZ, and c) pneumococcal vaccinations, stratified by three different ages (65, 75, 85) as measured at the start of the follow-up period, on the cumulative incidence function (CIF) of AD. HZ, Herpes zoster; Tdap, Tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis; Td, Tetanus toxoid and reduced diphtheria toxoid.

Figure adapted from Bukhbinder et al. (2022). Reprinted from *Journal of Alzheimer's Disease*, vol. 88, no. 3, Bukhbinder AS, Ling Y, Hasan O, Jiang X, Kim Y, Phelps KN, Schmandt RE, Amran A, Coburn R, Ramesh S, Xiao Q, Schulz PE, Risk of Alzheimer's disease following influenza vaccination: a claims-based cohort study using propensity score matching, pp. 1061-1074, 2022, with permission from IOS Press. The publication is available at IOS Press through <http://dx.doi.org/10.3233/JAD-220361>.



**Supplementary Figure 2. Pairwise Correlation of Covariates in the Unmatched Cohort Prior to Use in the Competing-Risk Regression Model for the Secondary Analysis**

In order to assess for collinearity in the unmatched cohort prior to use in the competing-risk regression model, a heatmap of the pairwise correlations between covariates was created (see Secondary Analysis description on page 12 of the Supplement). Whiter colors indicate greater correlation; redder colors indicate weaker correlation. Brain\_injury, traumatic brain injury; COPD, Chronic Obstructive Pulmonary Disease; diabetes2, Type II Diabetes Mellitus; gdr\_n, gender; heart\_disease, ischemic heart disease; NSAIDS, Nonsteroidal Anti-Inflammatory Drugs; vitamin\_deficiency, vitamin B12 deficiency.

Figure adapted from Bukhbinder et al. (2022). Reprinted from *Journal of Alzheimer's Disease*, vol. 88, no. 3, Bukhbinder AS, Ling Y, Hasan O, Jiang X, Kim Y, Phelps KN, Schmandt RE, Amran A, Coburn R, Ramesh S, Xiao Q, Schulz PE, Risk of Alzheimer's disease following influenza vaccination: a claims-based cohort study using propensity score matching, pp. 1061-1074, 2022, with permission from IOS Press. The publication is available at IOS Press through <http://dx.doi.org/10.3233/JAD-220361>.

**Supplementary Table 4.** Results of the Proportional Subdistribution Hazards Regression Model by Vaccination for the Secondary Analysis

**A) Tdap/Td Vaccination**

		<b>Coefficient</b>	<b>sHR</b>	<b>95% CI</b>
<b>Tdap/Td vaccination during look-back</b>		-0.320	0.726	(0.629, 0.838)
	<i>(Tdap/Td vaccination during look-back)*t</i>	<i>0.004</i>	<i>1.004</i>	<i>(1.002, 1.007)</i>
<b>Age</b>		0.134	1.144	(1.137, 1.150)
<b>Sex<sup>a</sup></b>	Male	-0.157	0.855	(0.838, 0.872)
<b>Race<sup>b</sup></b>	Black	0.314	1.368	(1.325, 1.413)
	Hispanic	0.121	1.128	(1.092, 1.166)
	White	0.080	1.083	(1.051, 1.116)
<b>Asthma</b>		-0.160	0.852	(0.823, 0.883)
<b>Atrial fibrillation or flutter</b>		0.185	1.203	(1.168, 1.239)
	<i>(Atrial fibrillation or flutter)*t</i>	<i>-0.005</i>	<i>0.995</i>	<i>(0.994, 0.997)</i>
<b>B12 deficiency</b>		0.245	1.278	(1.227, 1.332)
	<i>(B12 deficiency)*t</i>	<i>-0.003</i>	<i>0.997</i>	<i>(0.996, 0.998)</i>
<b>Congestive heart failure</b>		0.270	1.311	(1.268, 1.354)
	<i>(Congestive heart failure)*t</i>	<i>-0.008</i>	<i>0.992</i>	<i>(0.989, 0.994)</i>
<b>COPD</b>		0.171	1.187	(1.154, 1.221)
	<i>COPD*t</i>	<i>-0.005</i>	<i>0.995</i>	<i>(0.994, 0.997)</i>
<b>Hyperlipidemia and/or statins</b>		-0.306	0.737	(0.720,0.753)
	<i>(Hyperlipidemia and/or statins)*t</i>	<i>0.005</i>	<i>1.005</i>	<i>(1.004, 1.006)</i>
<b>Hypertension</b>		0.137	1.147	(1.119, 1.176)
	<i>Hypertension*t</i>	<i>-0.002</i>	<i>0.998</i>	<i>(0.998, 0.999)</i>
<b>Ischemic heart disease</b>		0.131	1.140	(1.114, 1.167)
	<i>(Ischemic heart disease)*t</i>	<i>-0.002</i>	<i>0.998</i>	<i>(0.998, 0.999)</i>
<b>Obesity</b>		-0.356	0.701	(0.672, 0.730)
	<i>Obesity*t</i>	<i>0.005</i>	<i>1.005</i>	<i>(1.004, 1.006)</i>



<b>Traumatic brain injury</b>	0.362	1.436	(1.305, 1.580)
<i>(Traumatic brain injury)*t</i>	-0.002	0.998	(0.996, 1.000)
<b>T2DM, metformin, and/or sulfonylureas</b>	0.168	1.183	(1.157, 1.208)
<i>(T2DM, metformin, and/or sulfonylureas)*t</i>	-0.001	0.999	(0.998,0.999)
<b>Stroke</b>	0.615	1.850	(1.767, 1.913)
<i>Stroke*t</i>	-0.006	0.994	(0.992, 0.995)
<b>Alcohol use disorder</b>	0.438	1.549	(1.429, 1.689)
<i>(Alcohol use disorder)*t</i>	-0.003	0.997	(0.995, 0.998)
<b>Depression and/or anxiety disorder</b>	0.439	1.550	(1.517, 1.593)
<i>(Depression and/or anxiety disorder)*t</i>	-0.002	0.998	(0.997, 0.998)
<b>Substance use disorder</b>	0.225	1.252	(1.185, 1.375)
<i>(Substance use disorder)*t</i>	-0.001	0.999	(0.999, 1.002)
<b>Tobacco use</b>	-0.002	0.998	(0.954, 1.019)
<i>(Tobacco use)*t</i>	0.001	1.001	(1.000,1.001)
<b>Anticholinergics</b>	0.156	1.169	(1.102, 1.204)
<i>(Anticholinergics)*t</i>	-0.004	0.996	(0.995,0.997)
<b>Antihypertensives</b>	0.171	1.186	(1.128, 1.238)
<i>(Antihypertensives)*t</i>	-0.003	0.997	(0.996,0.998)
<b>Antivirals</b>	-0.045	0.956	(0.914, 1.000)
<b>Glucocorticoids</b>	-0.055	0.946	(0.916, 0.978)
<i>(Glucocorticoids)*t</i>	0.001	1.001	(1.000, 1.001)
<b>NSAIDS</b>	0.076	1.079	(1.051,1.109)
<i>(NSAIDS)*t</i>	0.001	1.001	(1.000, 1.001)

## B) Herpes Zoster Vaccination

	<b>Coefficient</b>	<b>sHR</b>	<b>95% CI</b>
<b>Herpes Zoster vaccination during look-back</b>	-0.503	0.605	(0.553, 0.662)
<i>(Herpes Zoster vaccination during look-back)*t</i>	0.005	1.005	(1.004, 1.007)

<b>Age</b>		0.134	1.143	(1.137, 1.149)
<b>Sex<sup>a</sup></b>	Male	-0.163	0.849	(0.834, 0.864)
<b>Race<sup>b</sup></b>	Black	0.278	1.321	(1.279, 1.365)
	Hispanic	0.101	1.107	(1.070, 1.444)
	White	0.055	1.057	(1.025, 1.089)
<b>Asthma</b>		-0.159	0.853	(0.822, 0.884)
<b>Atrial fibrillation or flutter</b>		0.174	1.107	(1.252, 1.231)
	<i>(Atrial fibrillation or flutter)*t</i>	-0.004	0.995	(0.994, 0.997)
<b>B12 deficiency</b>		0.247	1.281	(1.252, 1.336)
	<i>(B12 deficiency)*t</i>	-0.003	0.997	(0.996, 0.998)
<b>Congestive heart failure</b>		0.268	1.308	(1.252, 1.367)
	<i>(Congestive heart failure)*t</i>	-0.009	0.992	(0.989, 0.994)
<b>COPD</b>		0.164	1.179	(1.034, 1.264)
	<i>COPD*t</i>	-0.005	0.995	(0.995, 0.996)
<b>Hyperlipidemia and/or statins</b>		-0.284	0.752	(0.735, 0.771)
	<i>(Hyperlipidemia and/or statins)*t</i>	0.005	1.005	(1.004, 1.006)
<b>Hypertension</b>		0.139	1.149	(1.120, 1.178)
	<i>Hypertension*t</i>	-0.002	0.998	(0.998, 0.999)
<b>Ischemic heart disease</b>		0.120	1.128	(1.101, 1.155)
	<i>(Ischemic heart disease)*t</i>	-0.001	0.999	(0.998, 0.999)
<b>Obesity</b>		-0.351	0.704	(0.675, 0.735)
	<i>Obesity*t</i>	0.005	1.005	(1.004, 1.006)
<b>Traumatic brain injury</b>		0.379	1.462	(1.326, 1.611)
	<i>(Traumatic brain injury)*t</i>	-0.002	0.998	(0.996, 1.000)
<b>T2DM, metformin, and/or sulfonylureas</b>		0.167	1.182	(1.157, 1.208)
	<i>(T2DM, metformin, and/or sulfonylureas)*t</i>	-0.001	0.999	(0.998, 0.999)
<b>Stroke</b>		0.609	1.839	(1.767, 1.913)

<i>Stroke</i> * <i>t</i>	-0.006	0.994	(0.992, 0.995)
<b>Alcohol use disorder</b>	0.441	1.554	(1.429, 1.689)
<i>(Alcohol use disorder)</i> * <i>t</i>	-0.003	0.997	(0.995, 0.998)
<b>Depression and/or anxiety disorder</b>	0.441	1.555	(1.517, 1.593)
<i>(Depression and/or anxiety disorder)</i> * <i>t</i>	-0.007	0.997	(0.997, 0.998)
<b>Substance use disorder</b>	0.225	1.252	(1.185, 1.375)
<i>(Substance use disorder)</i> * <i>t</i>	-0.000	1.000	(0.999, 1.002)
<b>Tobacco use</b>	-0.014	0.986	(0.954, 1.019)
<i>(Tobacco use)</i> * <i>t</i>	0.001	1.001	(1.000,1.001)
<b>Anticholinergics</b>	0.174	1.190	(1.102, 1.204)
<i>(Anticholinergics)</i> * <i>t</i>	-0.004	0.996	(0.995,0.997)
<b>Antihypertensives</b>	0.211	1.235	(1.128, 1.238)
<i>(Antihypertensives)</i> * <i>t</i>	-0.003	0.997	(0.996,0.998)
<b>Antivirals</b>	-0.178	0.837	(0.926, 1.016)
<b>Glucocorticoids</b>	-0.055	0.946	(0.915, 0.979)
<i>(Glucocorticoids)</i> * <i>t</i>	0.001	1.001	(1.000, 1.001)
<b>NSAIDS</b>	0.099	1.104	(1.074,1.135)
<i>(NSAIDS)</i> * <i>t</i>	0.000	1.000	(1.000, 1.001)

### C) Pneumococcal Vaccination

		<b>Coefficient</b>	<b>sHR</b>	<b>95% CI</b>
<b>Pneumococcal vaccination during look-back</b>		-0.107	0.898	(0.803, 1.004)
<i>(Pneumococcal vaccination during look-back)</i> * <i>t</i>		0.002	1.002	(1.000, 1.004)
<b>Age</b>		0.132	1.142	(1.140, 1.143)
<b>Sex<sup>a</sup></b>	Male	-0.166	0.847	(0.838, 0.856)
<b>Race<sup>b</sup></b>	Black	0.350	1.420	(1.374, 1.467)
	Hispanic	0.137	1.147	(1.110, 1.185)
	White	0.106	1.112	(1.080, 1.146)

<b>Asthma</b>	-0.154	0.858	(0.828, 0.889)
<b>Atrial fibrillation or flutter</b>	0.176	1.192	(1.159, 1.226)
<i>(Atrial fibrillation or flutter)*t</i>	-0.005	0.995	(0.995, 0.996)
<b>B12 deficiency</b>	0.248	1.281	(1.229, 1.336)
<i>(B12 deficiency)*t</i>	-0.003	0.997	(0.996, 0.998)
<b>Congestive heart failure</b>	0.238	1.269	(1.231, 1.309)
<i>(Congestive heart failure)*t</i>	-0.008	0.992	(0.991, 0.992)
<b>COPD</b>	0.152	1.164	(1.132, 1.197)
<i>COPD*t</i>	-0.005	0.995	(0.995, 0.996)
<b>Hyperlipidemia and/or statins</b>	-0.270	0.764	(0.747, 0.781)
<i>(Hyperlipidemia and/or statins)*t</i>	0.005	1.005	(1.004, 1.006)
<b>Hypertension</b>	0.140	1.151	(1.122, 1.179)
<i>Hypertension*t</i>	-0.002	0.998	(0.998, 0.999)
<b>Ischemic heart disease</b>	0.125	1.133	(1.108, 1.160)
<i>(Ischemic heart disease)*t</i>	-0.001	0.999	(0.998, 0.999)
<b>Obesity</b>	-0.366	0.693	(0.666, 0.722)
<i>Obesity*t</i>	0.005	1.005	(1.004, 1.006)
<b>Traumatic brain injury</b>	0.356	1.427	(1.297, 1.572)
<i>(Traumatic brain injury)*t</i>	-0.002	0.998	(0.996, 1.000)
<b>T2DM, metformin, and/or sulfonylureas</b>	0.163	1.177	(1.152, 1.202)
<i>(T2DM, metformin, and/or sulfonylureas)*t</i>	-0.001	0.999	(0.998, 0.999)
<b>Stroke</b>	0.593	1.809	(1.745, 1.875)
<i>Stroke*t</i>	-0.006	0.994	(0.993, 0.995)
<b>Alcohol use disorder</b>	0.416	1.516	(1.394, 1.648)
<i>(Alcohol use disorder)*t</i>	-0.003	0.997	(0.995, 0.998)
<b>Depression and/or anxiety disorder</b>	0.428	1.535	(1.498, 1.572)
<i>(Depression and/or anxiety disorder)*t</i>	-0.007	0.997	(0.997, 0.998)

<b>Substance use disorder</b>	0.174	1.190	(1.092, 1.297)
<i>(Substance use disorder)*t</i>	-0.001	0.999	(0.998, 1.001)
<b>Tobacco use</b>	0.005	1.005	(0.973, 1.739)
<i>(Tobacco use)*t</i>	0.000	1.000	(1.000,1.001)
<b>Anticholinergics</b>	0.170	1.185	(1.139, 1.233)
<i>(Anticholinergics)*t</i>	-0.004	0.996	(0.995,0.997)
<b>Antihypertensives</b>	0.162	1.175	(1.122, 1.232)
<i>(Antihypertensives)*t</i>	-0.003	0.997	(0.996,0.998)
<b>Antivirals</b>	-0.178	0.837	(0.926, 1.016)
<b>Glucocorticoids</b>	-0.033	0.967	(0.936, 1.000)
<i>(Glucocorticoids)*t</i>	0.001	1.000	(0.999, 1.001)
<b>NSAIDS</b>	0.091	1.095	(1.066,1.125)
<i>(NSAIDS)*t</i>	0.001	0.999	(1.000, 1.001)

Proportional subdistribution competing-risk hazards regression model results for Tdap/Td, herpes zoster, and pneumococcal vaccinations. Main effect terms are bolded; covariate-time interaction terms, when present, are indented and italicized. <sup>a</sup> Sex = female was used as the referent level. <sup>b</sup> Race = Asian was used as the referent level. CI, Confidence Interval; COPD, Chronic Obstructive Pulmonary Disease; HZ, Herpes Zoster; NSAIDs, Nonsteroidal Anti-Inflammatory Drugs; sHR, Subdistribution Hazard Ratio; t, Time; Tdap, Tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis; Td, Tetanus toxoid and reduced diphtheria toxoid; T2DM, Type II Diabetes Mellitus.

Table adapted from Bukhbinder et al. (2022). Reprinted from *Journal of Alzheimer's Disease*, vol. 88, no. 3, Bukhbinder AS, Ling Y, Hasan O, Jiang X, Kim Y, Phelps KN, Schmandt RE, Amran A, Coburn R, Ramesh S, Xiao Q, Schulz PE, Risk of Alzheimer's disease following influenza vaccination: a claims-based cohort study using propensity score matching, pp. 1061-1074, 2022, with permission from IOS Press. The publication is available at IOS Press through <http://dx.doi.org/10.3233/JAD-220361>.