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Pneumococcal Vaccination Lowers the Risk of Alzheimer's Disease: A Study Utilizing Data from the IBM® MarketScan® Database

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Introduction

- Pneumococcal disease is an infectious disease caused by the Streptococcus pneumonia.
- 2 types of pneumococcal vaccines:
  - pneumococcal conjugate vaccines (PCV13, PCV15, and PCV20)
  - pneumococcal polysaccharide vaccine (PPSV23)
- CDC recommends pneumococcal vaccination for all adults 65 years or older.

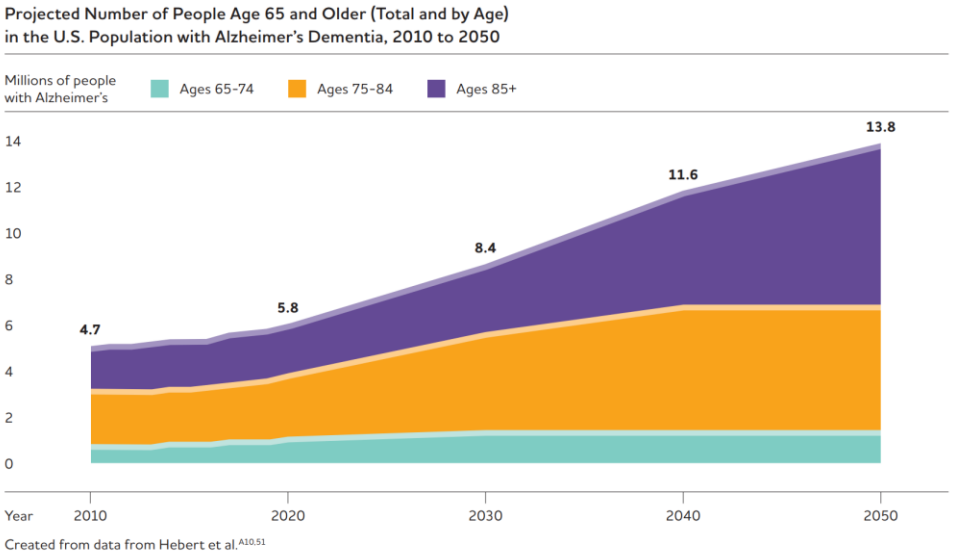
Adults ≥65 years old
Complete pneumococcal vaccine schedules

Prior vaccines	Option A	Option B
None*	PCV20	PCV15 → ≥1 year† → PPSV23
PPSV23 only at any age	≥1 year → PCV20	≥1 year → PCV15
PCV13 only at any age	≥1 year → PCV20	≥1 year† → PPSV23
PCV13 at any age & **PPSV23** at <65 yrs	≥5 years → PCV20	≥5 years§ → PPSV23

Source: https://www.cdc.gov/vaccines/vpd/pneumo/hcp/who-when-to-vaccinate.html

Introduction

- Alzheimer's disease (AD) is a chronic neurodegenerative disease with multiple pathogenesis pathways and is currently the 7th leading cause of death in the United States.

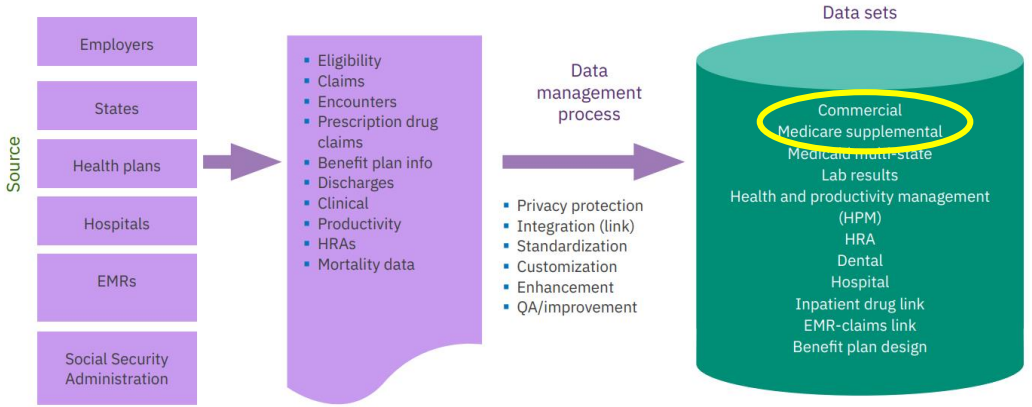


Source: https://www.alz.org/media/documents/alzheimers-facts-and-figures-2019-r.pdf

Introduction

- The IBM® MarketScan® Databases are the largest collections of de-identified US patient data:
  - > 32 billion service records
  - > 245 million covered individuals
  - > 260 contributing employers and 40 contributing health plans
- Data comprise service-level claims for inpatient and outpatient services and outpatient prescription drugs

Figure 3. MarketScan Research Databases: Integrated at the patient level



Source: https://www.ibm.com/downloads/cas/ONKLE57Y

Method

Data Source: IBM® MarketScan® Commercial and Medicaid Supplemental Database

Study period:

- Follow-up Period: Sep. 1, 2016 – Aug. 31, 2019.
- Look-back Period: Sep. 1, 2013 – Aug. 31, 2016.

Inclusion Criteria:

- Continuous insurance coverage from 2013 to 2019;
- Age ≥ 65 years and older.

Exclusion Criteria:

- *Prior diagnosis of mild cognitive impairment, encephalopathy, or related dementia during the look-back period;
- *Prescription for AD medications during the look-back period;
- Influenza vaccine received during the entire follow-up and look-back periods;
- Pneumococcal vaccines received after the AD's diagnosis date.

Method

Exclusion Criteria: MCI, encephalopathy, or any dementia	ICD-9 codes: 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 ICD-10 codes: 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
AD medications	Donepezil, Galantamine, Rivastigmine, Memantine
Outcome: AD and Related Dementia	ICD-9 codes: 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 ICD-10 codes: 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
Covariates: Physical and Psychiatric Comorbidity	asthma, atrial fibrillation, B12 deficiency, congestive heart failure, chronic obstructive pulmonary disease, hyperlipidemia, hypertension, ischemic heart disease, obesity, traumatic brain injury, type II diabetes, stroke, alcohol use disorder, anxiety disorder, depression, substance use disorder, and tobacco use

Method

Outcome*: Diagnoses of AD (≥ 2 medical records, either the AD diagnosis or a claim for AD medication prescription)

Cohort: Non-pneumococcal-vaccinated and Pneumococcal-vaccinated cohort (one does of PCV13 followed by one does of PPSV23 or one dose of PCV20)

Covariates:

- Age (ages 65-74, ages 75-84, and ages 85+)
- Sex
- Physical and Psychiatric Comorbidity* (e.g., asthma, hyperlipidemia, hypertension, depression)

Statistical Analysis:

- Propensity-score matching at a ratio of 1:1, using greedy nearest-neighbor algorithm with a caliper of 0.2
- logistic regression models were utilized to perform the odd ratios (ORs) of developing AD between Pneumococcal vaccination cohorts and non- Pneumococcal vaccination cohort.

Result

14,392 individuals in each of the pneumococcal-vaccinated cohort and non-pneumococcal-vaccinated cohort among the PSM-matched study population.

There are no significant differences in sex, age, or comorbidities between the matched cohorts (p>0.05)

Characteristics	Before PSM			After PSM		
	Pneumococcal Vax (-)	Pneumococcal Vax (+)	P-Value	Pneumococcal Vax (-)	Pneumococcal Vax (+)	P-Value
	N(%)	N(%)		N(%)	N(%)	
Sex			0.21			0.78
Male	63,399 (44.4%)	6,465 (44.9%)		6,489 (45.1%)	6,465 (44.9%)	
Female	79,475 (55.6%)	7,927 (55.1%)		7,903 (54.9%)	7,927 (55.1%)	
Age	Mean=76.2 (SD=6.44)	Mean=74.7 (SD=5.67)	<.0001	Mean=74.7 (SD=5.67)	Mean=74.7 (SD=5.67)	0.93
Comorbidities						
Asthma	14,018 (9.8%)	1,650 (11.5%)	<.0001	1,593 (11.1%)	1,650 (11.5%)	0.29
Atrial fibrillation or flutter	19,528 (13.7%)	1,763 (12.3%)	<.0001	1,709 (11.9%)	1,763 (12.3%)	0.33
B12 deficiency	6,987 (4.9%)	748 (5.2%)	0.11	704 (4.9%)	748 (5.2%)	0.24
Congestive heart failure	13,142 (9.2%)	1,116 (7.8%)	<.0001	1,084 (7.5%)	1,116 (7.8%)	0.48
COPD	19,402 (13.6%)	1,963 (13.6%)	0.84	1,899 (13.2%)	1,963 (13.6%)	0.27
Hyperlipidemia	103,347 (72.3%)	11,121 (77.3%)	<.0001	11,115 (77.2%)	11,121 (77.3%)	0.93
Hypertension	106,913 (74.8%)	10,800 (75.0%)	0.58	10,802 (75.1%)	10,800 (75.0%)	0.98
Ischemic heart disease	40,683 (28.5%)	3,891 (27.0%)	0.0003	3,855 (26.8%)	3,891 (27.0%)	0.63
Obesity	18,986 (13.3%)	2,182 (15.2%)	<.0001	2,174 (15.1%)	2,182 (15.2%)	0.90
Traumatic brain injury	9,195 (6.4%)	755 (5.3%)	<.0001	745 (5.2%)	755 (5.3%)	0.79
Type II diabetes	38,224 (26.8%)	3,779 (26.3%)	0.12	3,790 (26.3%)	3,779 (26.3%)	0.88
Stroke	22,682 (15.9%)	2,168 (15.1%)	0.01	2,131 (14.8%)	2,168 (15.1%)	0.54
Alcohol use disorder	1,465 (1.0%)	162 (1.1%)	0.26	131 (0.9%)	162 (1.1%)	0.07
Anxiety disorder	17,037 (11.9%)	1,792 (12.5%)	0.06	1,771 (12.3%)	1,792 (12.5%)	0.71
Depression	14,072 (9.9%)	1,389 (9.7%)	0.45	1,353 (9.4%)	1,389 (9.7%)	0.47
Substance use disorder	916 (0.6%)	72 (0.5%)	0.04	62 (0.4%)	72 (0.5%)	0.39
Tobacco use	10,009 (7.0%)	1,157 (8.0%)	<.0001	1,113 (7.7%)	1,157 (8.0%)	0.34

Result

Pneumococcal vaccination was associated with a significantly lower risk of Alzheimer's disease (OR=0.37, 95% CI: 0.33-0.42, p<0.0001).

After adjusting for covariates, the association between pneumococcal vaccination and reduced risk of AD remained significant (OR=0.37, 95% CI: 0.33-0.42, p<0.0001).

Variables	Effect	Odds ratio	95% CI		P-Value
Crude analysis					
Pneumococcal vaccination	Pneumococcal (+) vs Pneumococcal (-)	0.37	0.33	0.42	<.0001
Adjusted analysis					
Pneumococcal vaccination	Pneumococcal (+) vs Pneumococcal (-)	0.37	0.33	0.42	<.0001
Sex	Female vs Male	1.19	0.73	1.94	0.49
Age	75-85 vs 65-75	1.69	0.74	3.82	0.21
	85+ vs 65-75	1.87	0.52	6.75	0.34

Discussion

Conclusion: Pneumococcal vaccination was significant associated with a 63% reduced risk of AD in older adults.

Novelty: Novel approach utilizing big data to test the hypothesis. Overcomes limitations of previous smaller retrospective studies with inconclusive results.

The result was congruent with smaller dataset studies. Slight differences in risk reduction due to observation period, sample size, and comorbidities.

Limitation:

Lack of demographic variables in the IBM® MarketScan® Database.
Social determinants of health not accounted for, potentially impacting the study's findings.